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Meeting abstracts

50th Annual Meeting of the Society for Research into Hydrocephalus and Spina Bifida

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INTRODUCTION

S1

50th Annual Meeting of the Society for Research into Hydrocephalus and Spina Bifida

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S1

The 50th Annual Scientific Meeting of the Society for Research into Hydrocephalus and Spina Bifida took place in the historic surroundings of Queens' College in Cambridge, England. Delegates were warmly welcomed by Professor John Pickard and his organising team from the Department of Academic Neurosurgery, and we are especially indebted to Dr. Hugh Richards for his tireless work to make this conference a success. A feature of the 50th anniversary meeting was a presentation from archivists Ewen Mackinnon and Leonie Holgate, featuring documents and photographs illustrating the society's activities over the past 50 years.

We were also happy to welcome a large delegation from Association for Spina Bifida and Hydrocephalus, who helped with the administration of the conference as well as making a contribution to proceedings. Their chief executive, Andrew Russell, gave a talk outlining his tireless efforts in the cause of flour fortification with folic acid.

Cambridge is an ancient and beautiful city and delegates enjoyed taking in the wonderful architecture, both on foot and by punt. A particular pleasure after a tiring day was to be able to relax in the historic surroundings of King's College Chapel and listen to an organ recital by Stephen Cleobury.

The chairman of our host committee, Professor John Pickard, delivered a presentation entitled "Idiopathic Intracranial Hypertension". His talk ranged from the history and traditions of this difficult condition, to cutting edge science. Overall, it was a valuable and erudite exposition on the subject.

Miss Carole Sobkowiak, in her presidential address, drew on a long and distinguished career helping children and families deal with physical disability. She stressed the importance of management from early infancy, and emphasised the relevance of posture and vision.

The scientific sessions varied from presentations on experimental hydrocephalus to considerations of social well being in our client group. The abstracts are published below. The Society emphasises that it is our policy to publish the abstracts without

any editing. Readers who wish to comment on the content of the abstracts should contact the authors, whose email addresses are included with each published abstract.

Finally, we were cordially invited by Professor Alfred Aschoff to the 51st Annual Conference to take place in Heidelberg, Germany, on June 27–30th 2007.

ORAL PRESENTATION

S2

Controversies about the adjustment of gravitational valves in respect to a new device

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Background: The essential drawback of available adjustable devices for the treatment of hydrocephalus is the fact that the adjustment is valid for both positions of the patient. If the opening pressure is increased to decrease the risk of over drainage in the upright position of the patient the same adjustment leads to a very high opening pressure while the patient is lying and consequently to an under drainage in the horizontal position. On the other hand the lowering of the opening pressure automatically increases the risk of subdural effusion as soon as the patient is in upright position.

Materials and methods: A new device has been developed to introduce the possibility of a valve adjustment, which is effective only in the upright position of the patient. Hereby it is possible to ensure a very low opening pressure of the device in the horizontal position and an adjustment of the high-pressure chamber for the upright position depending on the needs of the individual patient. The adjustment of the valve works similar to the proGAV, which introduces a mechanical brake to avoid unintended readjustments of the device. To establish a posture depending function of the valve the gravity of a titanium disc acting on a sapphire ball defines the opening pressure of the upright position. The weight of this titanium disc is counterbalanced by an adjustable spring-force. At the lowest adjustment the whole weight of the titanium disc acts against the sapphire ball, at the highest adjustment the whole weight is counter-

balanced and the gravity of the titanium disc has no impact on the opening pressure of the valve.

Results: The new device fulfils the physical requirements for a shunt to differentiate between the horizontal and vertical position of the patient. The adjustment of the valve pressure independent of the posture of the patient is important especially for patients with untypical intra-abdominal pressures, for female patients during pregnancy or patients with unclear clinical outcome.

Conclusion: The new device offers new possibilities especially for patients with NPH and children.

S3

A new technology for adjustability and MR-resistance of shunt-valves – experience after implantation of 54 proGAVs

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Background: The new proGAV represents the combination of a new adjustable differential-pressure unit including a “brake” in series with a gravitational device. By its construction principle the proGAV should be capable to avoid the main disadvantages of other so-called “programmable” valves: The burden of the necessity for repeated X-ray-controls, the sensitivity to irregular adjustments in MR and the ongoing danger to over drain of adjustable differential-pressure-valves.

Materials and methods: Since February 2004 to September 2005 we conducted a series of 54 patients (with one exception adults) suffering from hydrocephalus of different etiologies implanting a proGAV-shunt. As first step we were interested in the security of the new tools to determine the opening pressures avoiding X-rays, in the capability to adjust the valve epicutaneously safely and in the ability to avoid irregular maladjustments. We focused then on reasons to change the opening pressure or complications and the clinical results including the possibilities for improvement by readjustments.

Results: The outcome with 12 excellent and 15 good results among the 34 patients without the necessity of readjustments give evidence for the reliability of the proGAV to avoid most of the disadvantages of other adjustable devices. In 16 cases we saw an indication to lower the opening pressure because we suspected functional under drainage; 12 patients improved more clinically than radiologically. Out of 4 patients with over drainage 1 case of slit-ventricles revealed significant improvement and 3 hygromas resolved after increasing the opening pressure. The outcome of our series proves the ability of the new construction to avoid surgical exchange of the valve in at least 10 cases, but on the other hand you should refrain from the tendency to use adjustability only because the possibility is there. No spontaneous readjustments have been seen up to now.

Conclusion: The new theoretical concept and the first clinical and radiological results give evidence of the proGAV to be superior to other adjustable devices at least in adults. The series is still small and the follow-up relatively short, thus the comparison of our cohort to series with other adjustable valves remains preliminarily up to now.

S4

In-vitro tests of 123 adjustable valves (10 designs)

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Background: Adjustable differential pressure valves (AV) have been inaugurated by Bush & Matson in the early fifties and Kuffer & Strub in 1969. More recently we overview 5 historical models and 13 concepts resp. prototypes; 12 different designs are on the market, using 6 basic constructions. In 1987 Loayza published the first clinical Sophy-report, we the first Medos-P-experiences in 1990. Especially in Europe the AVs are used in ca. 40% of all shunts, especially in children and NPH. In 1989 bench-tests were inaugurated by Richard and our group, followed by Trost, Schöner, Czsonyka, Eklund and others. The problematic electromagnetic safety of AVs – rarely thematized and underestimated in the early papers – found an increasing interest.

Materials and methods: We investigated in laboratory 79 adjustable Medos, 6 Medos Micro-Valves, 16 Sophy SU8/3, each 1 Sophy Mini SU8/3, 3 Sophysa Polaris, 6 Miethke ProGAV and 2 historical Kuffer-valves. 34 were new, 89 explanted, of them 14 defective (not testable). The most new specimen had long-term-tests (n = 17) up to 500 days and multiple subtests for resistance, pressure-flow, safety (external pressure, reflux, etc). Explanted probes passed selected tests only, but had an inspection with magnifier or microscope. Special subtests were dedicated the adjustability, decentration tolerance (5 directions) and stability in magnetic fields. 16 valves were positioned in a 3-T-MRI over 0.25, 1, 6 and 12 h and tested for adjustability.

Results: Except of the early Sophy-specimen the accuracy of new AV-valves was sufficient. However, many valves showed deviations due to debris/protein, preferably precipitated on the rotors. After successful cleaning failures often were reversible. The pressure-flow-graphs of AV showed similar properties of ball-in-cone-valves with fixed adjustment: With 30 cmH₂O in low pressure settings the excessive flow reaches 1500–2000 ml/h, but in the highest adjustments it is still 600–700 ml/h. Over drainage is never excluded. – After 3-T-MRI 6/12 Medos-P showed failures in adjustability, preferably in high settings; 4 Sophysa remained adjustable.

Conclusion: In Medos and older Sophysas the fine-tuning of opening pressure and other advantages are counterbalanced by risks of over drainage even in the highest settings and unintended disadjustments. Medos-P can be irreversibly chanced in 3-T-MRI. The third generation (Miethke ProGAV, Sophysa Polaris) avoids these problems.

S5

A survey of people with ventriculoatrial shunts in the community

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S5

Background: Though most shunts originally used in UK were ventriculoatrial (VA), they are now rarely used and the ventriculo-peritoneal (VP) route is preferred. Stated reasons include that VA shunts require more revisions, that they are more prone to infection, and that such infections are likely to lead to septicaemia and nephritis. Adult shunted patients are often discharged from follow-up and do not see a neurosurgeon thereafter, and those seen because of problems might present a skewed picture of the whole. We therefore decided to survey people with VA shunts in the community to determine whether they still had their VA shunt and whether they had had problems with it.

Materials and methods: A request for assistance was published in LINK, ASBAH's quarterly journal. This was followed by the mailing of a questionnaire to all those on ASBAH's database recorded as having a VA shunt. The questionnaire asked only 5 questions, to maximise response rate: 1) Do you have a VA shunt? 2) If so, for how long have you had it? 3) Have you had a VA shunt? 4) If so, how long did it last? 5) Have you ever had problems with your VA shunt such as blockage or infection? (if "yes" please say what they were). The responses were then collated.

Results: Of 405 VA-shunted people on the database, 11 had been incorrectly entered and 5 had died. 157 responded. Six were excluded (one had a Torkildsen shunt and in 5 the data were not analysable). One hundred and eleven people still had their VA shunt, and 38 no longer had it; 37 of these had been converted to VP (4 retaining their VA shunt). One no longer had a shunt. In those who still had one, it had been in place for a mean of 30.8 yrs (0.3–44 yrs), while in those who no longer had one, it had been in place for a mean of 12.3 yrs (0.12–43 yrs) before removal. Fifty-six people (38%) reported no problems with their VA shunt. Of the remainder, obstruction occurred in 48% of those still with a VA shunt, and in 79% of those who no longer did, these involving the VA shunt. Infection was reported in 12.75%, with one certain and one doubtful case of nephritis. Two reported thrombus formation but there were no reports of pulmonary hypertension in this series. There were 3 cases of catheter migration, one to the lung and two to the heart. Thirteen had converted from VP to VA, 2 for infection, 4 for obstruction, 3 because of elective abdominal surgery and one because of CSF malabsorption.

Conclusion: VA shunts appear to perform better and for longer than current opinion suggests.

S6

Trends in neuroendoscopic practice into the 21st century: a 12 yr review of a single unit's activity

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S6

Background: Neuroendoscopy was first introduced in the early 20th century, but with little success due to limitations of

the equipment available. Technical advances and the vision of a few pioneers led to the redevelopment of the field in the 1970s. By the end of the 20th century it had become an established part of general neurosurgical practice and the preferred treatment option for obstructive hydrocephalus. The neurosurgical unit in Nottingham was among the first in the UK to establish a large routine neuroendoscopic practice and was instrumental in extending its applications beyond pure ventriculostomy. Here we report on our trends in neuroendoscopic activity before and after the millennium, over a 12 yr period.

Materials and methods: A prospective operative record of all neuroendoscopic procedures kept in our department was used to provide the data for this audit along with further clinical and radiological information held on the patients electronic hospital file.

Results: In the 6 yr period before 2000, 284 neuroendoscopic procedures were carried out in 216 patients. In comparison from 2000 to the end of 2005, 187 procedures were performed in 182 patients. The age range was similar for each period (1 week to 70 and 80 years, respectively) but the average age was higher in the later group. NTV (neuroendoscopic third ventriculostomy) alone was by far the most common procedure performed (54% and 48%) and was successful in relieving hydrocephalus in 77% of all cases in which NTV was a component up to 2000 and in 66% of cases since this time. Endoscopic biopsies and marsupialisation continued to be performed equally frequently across the 12-year period and with consistent success rates. However, there were fewer procedures carried out for hydrocephalus due to IVH (intraventricular haemorrhage) (18 compared with 55) and shunt dysfunction (10 compared with 83) in recent years. The number of complications since 2000 has fallen, especially in terms of neurological damage, whilst the infection rate has remained at 3%.

Conclusion: Neuroendoscopy remains a routine and well-established part of neurosurgical practice in Nottingham, providing safe and effective treatment for a number of conditions. However, both the number of procedures and the number of patients treated have dropped in recent years and in particular there has been a drop in treatment for IVH and shunt dysfunction. This reflects both an evolving hydrocephalic population and a refinement of the indications for neuroendoscopy.

S7

In-vivo assessment of shunts inserted for the treatment of hydrocephalus

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S7

Background: Over a three-year period (2002–2004), we have performed 312 constant rate normal saline infusion studies in 197 patients with CSF shunts inserted to treat varying types of hydrocephalus. The data has been analysed retrospectively with two main objectives: 1. To investigate which parameters describing CSF dynamics correlate with the clinical finding of shunt malfunction (under drainage or over drainage). 2. To estimate accuracy of this method.

Materials and methods: A constant rate infusion of normal saline was performed into the shunt prechamber or previously

implanted Ommaya reservoir. The CSF pressure and arterial pressure (from Finapres finger cuff) were monitored continuously during 10 minutes of baseline recording and during the infusion in 99 tests. CSF compensatory parameters, steady state pressure levels, cerebrovascular pressure reactivity and vaso-genic waveforms of CSF pressure were calculated.

Results: In 161 of the 312 infusion tests results indicated under draining shunts. Patients with under draining shunts had higher baseline and plateau CSF pressures, higher resistance to CSF outflow and higher levels of baseline respiratory and pulse amplitude waveforms. A significantly greater increase in intensity of vasogenic waves during the test was seen in cases where shunts were under draining. In 21 patients who underwent operative revision of the shunt, reports of intraoperative shunt assessment were available in patients' notes. Shunt malfunction was confirmed at surgery in 19 cases. None of the patients in whom shunt was assessed as patent were admitted to hospital with symptoms of acute intracranial hypertension within subsequent 2 weeks. There was no increase in complications related to the performance of the constant rate infusion of normal saline.

Conclusion: Shunt testing in-vivo to detect malfunction and under drainage by a constant rate infusion of normal saline is easy, safe, clinically useful and has satisfactory positive prediction power (estimated 90%).

S8

The accuracy of ventricular catheter placement: does it influence shunt revision rates?

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S8

Background: Ventricular catheter blockage is the commonest indication for shunt revision. Placement of a ventricular catheter in a region free of choroid plexus prolongs catheter survival. Positioning the tip of the ventricular catheter in the ipsilateral frontal horn anterior to the foramen of Munro is commonly considered the optimum position and is the standard position for catheter placement in our unit. Yet ventricular catheter placement is performed blindly and often misses the optimum position. In this study we aim to see how accurate we are in the placement of ventricular catheters and see whether the good positioning can reduce the rate of shunt revision.

Materials and methods: All ventricular catheters (i.e. VP shunts, external ventricular drains and Ommaya reservoir) inserted over a six-month period were studied prospectively. Adequacy of ventricular catheter placement was assessed on post-operative CT images. Information was recorded on the seniority of the surgeon, positioning of occipital burr holes and pre-operative ventricular size and time of day. Patients were followed up over 3 1/2 years using data from the UK Shunt Registry to determine rates of shunt revision with adequately placed and inadequately placed catheters in both frontal and occipital locations.

Results: 187 catheters were placed in 184 patients. Post-operative imaging was available on 139 patients. Frontal catheters were adequately placed in 67% of cases; occipital catheters were adequate in 52%. Frontal catheters were

frequently too long, whereas occipital catheters commonly crossed the midline. 43% of the burr holes were incorrectly positioned; this may improve with experience. When the burr hole was too lateral, the catheter position was inadequate in 90% cases. The revision rate for inadequately placed occipital catheters was far higher than adequately placed catheters (54% vs 15% at 140 weeks), yet there was no difference for the frontal catheters (50% vs. 44% at 140 weeks).

Conclusion: Occipital catheters are more difficult to place adequately than frontal catheters. The accuracy of placement of frontal catheters could improve if the depth of insertion could be better controlled. Occipital catheter placement is poor largely due to problems in placing the burr hole. The position of occipital catheters is more critical to shunt survival than frontal catheters.

S9

Cerebrospinal fluid transport across the cribriform plate into extracranial lymphatics in rats: development and quantification

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S9

Background: The notion that cerebrospinal fluid (CSF) absorption occurs mainly through the arachnoid granulations and villi is being challenged by studies that support a major role for the lymphatic circulation in CSF transport. An important pathway by which CSF is removed from the cranium is movement through the cribriform plate in association with the olfactory nerves. CSF is then absorbed directly into lymphatics located in the submucosa of the olfactory epithelium. In this report, (A) we determined the time during development at which the CSF compartment and extracranial lymphatic vessels connect anatomically in neonatal rats and (B) we investigated an indirect method to quantify this transport in adult rats.

Materials and methods: In a total of 115 Fisher 344 rats, CSF-lymphatic connections were investigated using the silastic material Microfil or a soluble Evan's blue-protein complex injected into the subarachnoid space. We examined animals at E21 (birth at 21 days), and postnatal days P1-P9, P12, P13, P15, P22 and adults. To quantify this transport in adult animals, ¹²⁵I-human serum albumin (HSA) was injected into the lateral ventricles of ~200 gm animals using a stereotactic device. After 10 (n = 7), 20 (n = 7), 40 (n = 4) and 60 minutes (n = 8), the animals were sacrificed. Angled coronal tissue sections were cut from the head region anterior to the cribriform plate to sample the olfactory turbinates and various other tissues were excised.

Results: Associations between the CSF compartment and extracranial lymphatic vessels were not obvious until about a week after birth, a period during which CSF secretion is markedly up-regulated in this species. After injection of tracer into the subarachnoid compartment, the highest concentrations of ¹²⁵I-HSA were observed in the middle olfactory turbinates with peak concentrations achieved 20 minutes after injection. At this point, the recoveries of injected ¹²⁵I-HSA (percent injected/

gm tissue) were (mean \pm SE) 29.1 \pm 7.2% middle turbinates, 3.8 \pm 1.2% blood, 0.1 \pm 0.04% skeletal muscle, 0.6 \pm 0.2% spleen, 1.4 \pm 0.5% liver, 1.0 \pm 0.3% kidney and 0.2 \pm 0.1% tail.

Conclusion: These data suggest that the ability of extracranial lymphatic vessels to absorb CSF develops around the time that significant volumes of CSF are being produced by the choroid plexus. The rapid movement of the CSF tracer into the olfactory turbinates supports further a role for lymphatics in CSF absorption and provides the basis of a method to investigate the potential for impaired absorption in various CSF disorders.

S10

The CSF of normal H-Tx rats promotes neuronal differentiation from neurospheres but CSF of hydrocephalic H-Tx rats does not

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S10

Background: There is evidence that in both animal models and humans, hydrocephalus affects neuronal migration and maturation. In HTx rats evidence points to a critical role of CSF in maintaining the normal proliferation of the stem cells in the developing cortex. Furthermore, such an activity is affected by CSF of HTx rats with early-onset hydrocephalus. The source and nature of these signals is not known. However, the presence in the CSF of hydrocephalic HTx rats and *hyh* mice of abnormal forms of the proteins secreted by the subcommissural organ points to them as good candidates for conveying signals to the developing brain cortex. The present study was designed to investigate the effect of CSF on neurospheres obtained from neural stem cells of normal H-Tx rats.

Materials and methods: Neurospheres were obtained by dissecting the lateral walls of lateral ventricles of normal PN7 H-Tx rats. The tissue was mechanically dissociated to obtain a single-cell suspension. The cells were plated at 20 viable cells/ μ l in serum-free medium supplemented with N2 and EGF (20 ng/ml). CSF samples were collected from normal and hydrocephalic H-Tx rats and from hydrocephalic and non-hydrocephalic human patients. After 4 days *in vitro*, neurospheres were treated with CSF (1:10) and further cultured for 1–2 days. Neurospheres were analysed by immunocytochemistry, transmission and scanning electron microscopy and immunoblotting.

Results: After 3–4 days *in vitro*, clonally-derived neurospheres were seen. Neurospheres were formed by undifferentiated cells and a small number of immature neurons, astrocytes and ependymal cells. The cells were joined together by adherent junctions. After addition of normal and hydrocephalic CSF, neurospheres disassembled and cells started to migrate and grow. Neurons and astrocytes became more differentiated and readily distinguishable. Normal CSF displayed a twofold higher neurite extension promoting activity than hydrocephalic CSF. Western blots of both types of CSF, using a set of antibodies including those against the subcommissural organ secretory proteins, revealed qualitative and quantitative differences. Preliminary findings indicate that CSF of human hydrocephalic patients has an effect similar to that of hydrocephalic H-Tx rats. Studies are in progress to identify the CSF-polypeptides responsible for (i) disassembling of neurospheres and (ii) stimulating and/or interfering with neuronal differentiation.

Conclusion: (i) The CSF of normal H-Tx rats promotes neuronal and glial differentiation from neurospheres; (ii) The CSF from hydrocephalic H-Tx rats interferes with neuronal differentiation.

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S11

Mechanism of CSF outflow through human arachnoid granulations using *in-vitro* and *ex-vivo* perfusion models

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S11

Background: In communicating hydrocephalus and also idiopathic intracranial hypertension, disturbed CSF dynamics may result from an increased resistance to CSF outflow at the arachnoid granulations (AGs). To better understand the mechanism of CSF egress, we modeled the outflow of CSF through human AGs using both cell culture (*in-vitro*) and whole tissue (*ex-vivo*) perfusion models.

Materials and methods: Human AG tissue was harvested within 24 hours post-mortem and used to isolate AG cells for growth on filter inserts or fit into an Ussing perfusion chamber. Cell phenotype was identified in culture with immunocytochemical staining. Cells and/or tissue were perfused at a physiologic pressure drop. Cells/tissue were perfused with fluorescent microparticles and then fixed under experimental pressure. Fixed tissue was processed for TEM or cryo-sectioned and stained for visualization.

Results: *In-vitro* permeability results showed flow through the AG cells was uni-directional in the physiologic direction from the basal to apical (B \rightarrow A) cell membrane. The average cellular hydraulic conductivity ($L_{p_{ave}}$) for AG cells perfused B \rightarrow A was 4.49 \pm 0.53 μ l/min/mmHg/cm² (n = 17) with average perfusion pressure (ΔP_{ave}) across the cell layer of 3.15 mmHg which was statistically higher (p < 0.001) than $L_{p_{ave}}$ for cells perfused A \rightarrow B (non-physiologic direction), 0.28 \pm 0.16 μ l/min/mmHg/cm² (n = 6) with ΔP_{ave} of 3.33 mmHg.

Cells perfused physiologically (*in-vitro* model), showed extra-cellular cisternal spaces between overlapping AG cells suggesting a pathway for para-cellular fluid transport. Several vacuoles within the cytoplasm were shown and suggest a trans-cellular pathway for fluid flow.

Ex-vivo perfusion experiments performed at 5 mmHg pressure in the physiological direction (B \rightarrow A) resulted in $L_{p_{ave}}$ of 1.05 \pm 0.15 μ l/min/mmHg/cm² (n = 20). The $L_{p_{ave}}$ of tissue perfused in the A \rightarrow B direction was 0.11 \pm 0.03 μ l/min/mmHg/cm² (n = 3).

Conclusion: AG perfusion results in both *in-vitro* and *ex-vivo* models showed that flow was uni-directional and physiologic. Electron microscopy showed large intracellular vacuoles and extra-cellular cisternal spaces. These structures may represent two distinct mechanisms by which AG cells move fluid: 1: Trans-cellular transport via intra-cellular vacuoles, 2: Para-cellular transport via extra-cellular cisterns.

S12**The cranium as an oscillator: analysis of phase relationships in intracranial blood and CSF pulsations using flow sensitive MRI**

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S12

Background: Over the past two decades, flow sensitive MRI has been used to demonstrate phase relationships between waveforms of blood and CSF pulsations in the cranium and marked changes in phase of CSF pulsatility have been described in hydrocephalus. However, there is no systematic explanation for the normal phase relationships between blood and CSF pulsations, and we have no theoretical framework for understanding these phase relationships in normal subjects and no theoretical framework for understanding why they change in hydrocephalus. We have undertaken a systematic study of the phase relationships of intracranial blood and CSF flow in normal individuals using flow sensitive MRI, and interpret the results using a model of the cranium as a forced oscillator.

Materials and methods: Fifteen healthy volunteers were studied on a 1.5T Philips Edge scanner. Arterial flow into the cranium was used as the reference waveform. Phase contrast images were collected using an encoding velocity of 5 cm/s for the CSF images and 60 cm/s for the vascular study. After Fourier transformation of the flow waveform from each CSF region, the phase was determined from the phase of the fundamental harmonic frequency of the flow waveform.

Results: A clear phase lag of velocity was demonstrated in the cerebral aqueduct (-55.3 ± 15.8 degrees) as well as in the prepontine cistern (-23.9 ± 7.6 degrees) relative to the phase in the carotids. In comparison, the flow phase at the craniocervical junction was zero (4.4 ± 10.8 degrees), i.e. a pulse waveform that is synchronous with the arterial input waveform. Sagittal images showed a progressively decreasing phase lag moving from the prepontine region down to the midbrain and spine levels.

Conclusion: Based on the oscillator model, a CSF phase lag occurs due to low elastance (high compliance) with respect to the inertia of the pulse, such as would occur in the ventricular system. A CSF phase lead would occur in a region with low inertia with respect to elastance, which would occur in a cyst and has been described as the "rebound sign". Zero phase at the foramen magnum represents high impedance resonance, and may play a role in the intracranial windkessel mechanism. In this theoretical model, changes in compliance in the subarachnoid spaces would alter pulsatile intracranial dynamics, particularly the windkessel mechanism, and would account for several

important dynamic features characteristic of clinical and experimental hydrocephalus.

S13**Human arachnoid granulation probability of occurrence and surface area quantification**

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S13

Background: We developed a method to measure the en-face surface area of human arachnoid granulations (AGs) on a standardized superior view of the brain. This technique permits the topographical mapping of AG distribution on the surface of the brain. Surface area measurements are correlated with donor age, sex, and race.

Materials and methods: Formalin fixed brains were imaged with a 35 mm Nikon camera set at a fixed distance. Images were segmented and AGs identified in Adobe Photoshop by two independent investigators. Twenty-five fiducial points were identified in a standard method for each cerebral hemisphere, and an average hemisphere template was calculated. Each segmented image was transformed to the standard template; an average hemisphere template was calculated. The transformed images were used to calculate a probability-of-occurrence map that depicts the spatial distribution of AGs. A linear regression was used to assess reproducibility.

Results: Images have been analyzed from 56 brains. Regression analysis confirms reproducibility of AG identification between independent researchers ($r^2 = 0.98$). Topographic probability distribution is primarily along the longitudinal fissure.

Analysis of these brains has revealed an average AG surface area of 75.1 mm² for age group 38–53 years old, 67.5 mm² for 54–68, and 82.3 mm² for >68. The proportional analysis of AG surface area to total brain surface area indicates a positive relationship with age which was not statistically significant. Total brain surface area broken down by age shows a trend which declines with age.

Analysis also revealed an average AG surface area of 58.9 mm² for females and 103.5 mm² males, a difference which was statistically significant. Proportion of positive AG surface area broken down by age and sex indicates that females have a smaller proportion surface area in most age groups. A statistically significant difference in race was also found, with whites having a smaller proportion of positive area compared to African Americans.

Conclusion: The probability-of-occurrence maps, based on the image analysis methods, show that AGs are localized in a characteristic distribution with regions of high and low probability. These measurements provide age-related surface area quantification data as absolute values and proportional area with respect to total brain area. Statistically significant differences in AG surface were found between sex and race. Additional brain specimens will provide greater statistical power

for determination of the effects of independent variables such as age, sex, race, height, weight, and BMI on the topographic distribution and quantity of human AGs.

S14

Pressure phase relationships between carotid arterial pressure and intracranial pressure: the 'violin' analogy of intracranial pulsations

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Background: Many investigators have shown marked abnormalities of CSF and parenchymal pulse pressure in hydrocephalus, and Greitz, Bateman, and Egnor have proposed that abnormalities of pulsatility are at the root of the pathophysiology of hydrocephalus. Our work is aimed at a more rigorous understanding of pulsatility in the cranium. We have studied the phase relations between the carotid arterial pressure pulse and the intracranial pressure (ICP) pulse in dogs as a function of mean intracranial pressure.

Materials and methods: Carotid arterial pressure and intracranial pressure in 12 dogs were measured with progressive withdrawal and infusion of CSF to change intracranial pressure and compliance. The waveforms were recorded and synchronized in time. Phase between the carotid and ICP pulse was determined using the phase difference between the fundamental harmonics of the Fast Fourier Transform.

Results: The normal ICP pulse led the carotid arterial pulse by an about 50 degrees. With lowering of ICP, there was an increase in the lead of the ICP pulse with respect to the carotid pulse to about 100 degrees. Increasing ICP caused a progressive phase lag of ICP pulse with respect to carotid pulse, up to a maximum lag between arterial and intracranial pulse of approximately 30 degrees.

Conclusion: These data clearly show that there are conditions in which the ICP pulse precedes the carotid pulse. With raising and lowering of the mean ICP, the phase versus mean ICP curve is sigmoid-shaped, with the normal ICP phase is the inflection point of the sigmoid curve. The observation that the ICP pulse of the dog normally precedes the carotid arterial pulse is counterintuitive. It forces us to rethink our current understanding of the way in which the ICP pulse is generated. We propose that the ICP pulse is a standing wave, not a transmitted wave. Standing waves can be generated in chambers with elasticity, such as in the body of a violin. The vibrations from the

violin strings excite the vibrations in the body of a violin, but the vibrations in the body of the violin can lead or lag the string vibrations. The concept that the ICP wave is a standing wave is important, because it suggests that the cranium can suppress (or accentuate) certain frequencies of arterial pulse entering it. This may shed new light on cerebral blood flow, the cerebral windkessel mechanism, and on the pathogenesis of hydrocephalus.

S15

Long-lasting hydrocephalus in *hyh* mutant mice: gain and loss of a brain surviving hydrocephalus

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Background: A population (30%) of hydrocephalic *hyh* mutant mice develop a slowly progressive hydrocephalus and survive for periods ranging between 2 months and 2 years. Certain characteristics of these mice, such as time of onset of hydrocephalus, type of abnormality of CSF dynamics, clinical evolution and survival/death rate, resemble several types of human congenital hydrocephalus. They represent an exceptional animal model to investigate neuropathological and physiopathological aspects of a brain "adapting" to a virtually life-lasting hydrocephalus

Materials and methods: (i) The clinical evolution of more than 3,000 *hyh* mice, (ii) certain cellular and molecular aspects involved in the pathogenesis of hydrocephalus of several hundreds of embryos and postnatal *hyh* specimens and, (iii) the neuropathology of more than one hundred hydrocephalic mice with arrested hydrocephalus have been investigated with a large series of techniques.

Results: The events occurring in the brain of aging hydrocephalic mice may be regarded as loss and gain. *Loss:* Neuroepithelium/ependyma denudation is a severe loss, since it leads to (i) Sylvius aqueduct obliteration and severe hydrocephalus; (ii) abnormal development of certain populations of cerebral neurons resulting in a permanent neurological impairment. Abnormalities in the subcommissural organ contribute to the development of hydrocephalus and to changes in the protein composition of CSF. Severe alterations of hypothalamus lead to neuroendocrine deficiencies. *Gain:* (i) A subpopulation of astrocytes responds to denudation by repairing the denuded areas forming an ependymal-like new barrier. (ii) Once severe hydrocephalus has been turned on, two ependymal populations located in the aqueduct and third ventricle start to proliferate allowing the large expansion of these cavities. This ependymogenesis continues for several weeks after birth. (iii) All mice surviving hydrocephalus developed spontaneous ventriculostomies.

Conclusion: (i) Essential events of the hydrocephalic phenomenon occur at a rather well defined temporal and spatial pattern

in which a program of sequential events may be envisaged. (ii) None of the pathological events should be regarded as the result of mechanical phenomena. Rather, abnormalities occurring at molecular and cellular levels and leading to ependymal denudation and abnormal neurogenesis, precede the onset of hydrocephalus. (iii) Postnatal ependymogenesis and spontaneous ventriculostomies are essential for the hydrocephalic mice to live a long life.

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S16

Molecular mechanisms underlying neuroepithelial/ependymal denudation in the hydrocephalic *hyh* mutant: spatial and temporal expression of alpha-SNAP and N-cadherin

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Background: The *hyh* mutant mouse develops fetal-onset neuroepithelial/ependymal denudation that precedes cerebral aqueduct obliteration and hydrocephalus [1, 2]. A hypomorphic point mutation (M105I) in alpha-SNAP protein has been identified as responsible of the *hyh* phenotype [3]. Alpha-SNAP is widely distributed in all mammalian tissues and cell types [4]. It is a key component of the SNARE machinery for membrane fusion and participates at different levels of vesicular traffic of proteins, including transport to plasma membrane [5]. But, why does a mutation in such an ubiquitous protein lead to selective developmental disorders of the central nervous system? How is alpha-SNAP mutation involved in neuroepithelial/ependymal denudation? Considering that (i) the pattern of ependymal denudation matches that of ependymal differentiation [1], and (ii) the ependyma of circumventricular organs, endowed with a special set of junctions, never detach; it is proposed that alpha-SNAP mutation could result in a failure in the adhesion/junction proteins physiology during brain development leading to neuroepithelial/ependymal denudation. The aim of the present investigation was two fold: (a) to study the temporal and spatial expression of alpha-SNAP, NSF, and some proteins involved in intercellular junctions, and (b) to evaluate the importance of these proteins on ependymal physiology and stability.

Materials and methods: (i) Brain samples of non-hydrocephalic (wild type) and hydrocephalic (mutant) mice from the *hyh* strain (B6C3Fe-*a/a-hyh*) were studied by immunocytochemistry (IMC) and transmission electron microscopy (TEM) at various developmental stages. Protein homogenates from telencephalon, mesencephalon/brain stem and cerebellum were analyzed by Western blot. The expression levels of mRNA encoding for alpha-SNAP and NSF were analyzed by semi-quantitative PCR. (ii) Ependymal explants obtained from adult bovine Sylvius aqueduct were cultured for 24 hours and used to evaluate the role of adherens junctions and N-cadherin in ependymal stability. Basically, after validation of this *ex-vivo* model, N-cadherin functional blocking assays in IDIV explants using specific antibodies and competitive peptides were performed. The effect of N-cadherin blockage was evaluated by light microscopy (quantitative analysis), IMC, and TEM.

Results: (1) alpha-SNAP and NSF are preferentially expressed in the CNS and at early developmental stages; (2) alpha-SNAP is preferentially expressed at ventricular lining; (3) in mutant animals, the decrease of alpha-SNAP protein varies at different stages and at different brain regions; (4) *hyh* mutant mice present an increase in NSF protein, probably due to its overexpression; (5) ependymal cells express N-cadherin but not E-cadherin; (6) different ependymal subpopulations showed a differential expression of alpha-SNAP and N-cadherin; (5) functional blocking of N-cadherin led to (i) changes in N-cadherin immunocytochemical pattern, (ii) ultrastructural modifications of adherens junctions, (iii) increase of the intercellular space, and (iv) detachment of the ependyma leading to large denuded areas of the explants.

Conclusion: The selective expression of alpha-SNAP in the brain, and its differential expression at distinct brain regions and cell types may contribute to the understanding of the molecular mechanisms underlying *hyh* phenotype. N-cadherin-dependent adherens junctions play a key role in ependymal stability. An alteration in the physiology (traffic?) of N-cadherin appears to be the one of the mechanisms operating in the ependymal denudation of *hyh* mice.

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S17

Inhibitory effects of minocycline on gliosis in the hydrocephalic H-Tx rat

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Background: Persistent gliosis, if present in the hydrocephalic brain, has the potential to alter the biomechanical properties of the brain, impair cerebral perfusion, impede neuronal regeneration and affect plasticity. The purpose of this study was to determine the ability of minocycline, a specific inhibitor of glial reactivity, to reduce glial scar formation in the H-Tx rat model of congenital hydrocephalus.

Materials and methods: Minocycline (45 mg/kg/day i.p. in 5% sucrose) was administered to 6 hydrocephalic and 5 non-hydrocephalic animals, from postnatal days 15 through 21. These treated animals were compared to age-matched 21 day untreated control and hydrocephalic littermates (n = 5 each). Cortical tissue was paraffin embedded and selected regions subjected to immunohistochemistry using Ionized calcium binding adaptor molecule 1 (IBA1) to label microglia and Glial Fibrillary Acidic Protein (GFAP) to label astrocytes. Tissue sections were then analyzed using light microscopy and non-biased stereology to quantify the density of these specific glial cells.

Results: Minocycline was effective in reducing the relative amount of both microglia and astrocytes present in the treated hydrocephalic animals compared to untreated animals. Hydrocephalic animals receiving minocycline exhibited a significant ($p < 0.05$) reduction in astrocyte density by 2.93 fold and a significant ($p < 0.05$) reduction of microglial density of 3.41 fold. Although minocycline treatment reduced the overall concentration of these glial cells compared to the untreated hydrocephalic animals, the treated hydrocephalic animals still possessed a significantly higher ($p < 0.05$) density of astrocytes (1.76 fold) and microglia (1.51 fold) than the untreated control animals. Minocycline also increased cortical thickness in the treated hydrocephalic group. The anterior portion of the occipital cortex in the treated hydrocephalic animals possessed a significantly ($p < 0.05$) thicker cortex compared to the untreated hydrocephalic animals when measured at the dorsal (1.97 fold), lateral (2.10 fold) and temporal (2.88 fold) regions of the cerebral hemisphere.

Conclusion: Overall, our data suggest that relatively short-term minocycline treatment is effective in reducing the astrogliosis and microgliosis that accompanies ventriculomegaly while also increasing cortical thickness. The administration of this drug may therefore provide an added benefit when used as a supplement to ventricular shunting for the long-term control of gliosis.

S18

Selective ependymal denudation and expansion of lateral ventricles of H-Tx rats appear as interrelated phenomena

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Background: The mutant H-Tx rat starts to develop hydrocephalus around E18. In these rats, lateral ventricles are the only brain cavities becoming expanded. Although this dilatation has been ascribed to the stenosis of Sylvius aqueduct, the actual mechanism of such a selective ventricular dilatation remains to

be elucidated. In other mutant rodents denudation of the ependyma has been shown to play a role in the development of hydrocephalus. With this in mind, the possibility that ependymal denudation also occurs in H-Tx rats has been investigated.

Materials and methods: The brains of normal and hydrocephalic E20, PN1, PN3, PN5, PN7 and PN10 H-Tx rats were processed for (i) scanning electron microscopy, (ii) immunocytochemistry, using a set of antibodies for the analysis of secretory (subcommissural organ) and ciliated ependyma.

Results: Lateral ventricles were the only brain cavities undergoing ependymal denudation. Such a process was already detected at E20, indicating that it may start at earlier stages of development. Studies are in progress to establish time of onset of ependymal denudation. In the lateral ventricles, only the dorsal ependyma detached. The denudation process started with the detachment of a few ependymal cells forming a small denuded area that could be regarded as a denudation centre. From this point, denudation expanded radially to form large circular denuded areas. At PN1, the dorsal wall of lateral ventricles displayed several denuded circles of different diameters. Surprisingly, the number, size and location of the circular denuded areas were similar in both lateral ventricles, suggesting that the ependymal denudation follows a pattern. Macrophages were abundant on either side of the denudation front. The total denuded surface increased with age by the confluence of the circles of denudation, so that at PN10 most of the dorsal ependyma was missing. In recently denuded areas all elements of nervous tissue became exposed and readily visualized under the scanning electron microscope. After a few days, the denuded areas appeared covered by astrocytes.

Conclusion: (i) In the H-TX rat, ependymal denudation of lateral ventricles follows a temporal-spatial pattern; (ii) denudation starts during foetal life, when hydrocephalus is not severe; (iii) ependymal denudation and hydrocephalus may be related at the etiopathological level, rather than the former being consequence of the latter; (iv) the early and selective denudation of lateral ventricles may explain the selective expansion of these ventricles.

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S19

A model of communicating hydrocephalus based on the spatial and spectral redistribution of intracranial pulsations

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Background: Hydrocephalus has traditionally been understood as a disorder of the absorption of CSF. Recent work by Johnston, Cserr and others has challenged the traditional understanding of CSF absorption, and flow MRI studies of Greitz, Bateman, and others suggest that pulsatility plays a central role in the pathogenesis of hydrocephalus. Based on our recent experimental insight into the dynamics of intracranial pulsatility in dogs, and a new model of intracranial dynamics, we discuss a model of the pathophysiology of hydrocephalus in which ventriculomegaly is driven by the redistribution of pulsations in the brain.

Materials and methods: We model the cranium as a frequency-sensitive notch filter that suppresses the arterial pulse in the brain. This redistributes the kinetic energy of pulsatility at the heart rate (i.e. cardiac frequency) to smooth, pulseless arterial flow (i.e. zero frequency), which is the cerebral blood flow. This represents the normal spectral distribution of the transfer function between the arterial pulse and the ICP pulse, and is a manifestation of the normal cerebral windkessel mechanism.

Results: Disturbance of the normal compliance and resistance in the subarachnoid space, such as occurs in communicating hydrocephalus, alters the normal distribution of pulsatility in the cranium. This redistribution can have two distinct manifestations: 1) spatial redistributions in which pulsations are redirected from one part of the cranial cavity to another, such as increased ventricular pulsation at the expense of subarachnoid pulsation, and 2) spectral redistributions in which pulsations are redistributed between flow components at the cardiac frequency and alternate frequency components, such as the enhanced cardiac-related pulsatile flow at the expense of zero-frequency smooth flow. The loss of cerebral blood flow and augmentation of pulsatility is the main manifestation of an impaired windkessel mechanism, and leads to venous stasis, venous hypertension, and reduction in cerebral blood flow.

Conclusion: We propose that the salient features of clinical and experimental hydrocephalus can be explained as consequences of impairment of the cerebral windkessel mechanism, the mechanism by which the cerebral vasculature renders vascular perfusion of the microvasculature nearly smooth. Asymmetrical obstruction of the CSF pathways causes spatial and spectral redistribution of vascular and CSF pulsations in the cranium. In this model, communicating hydrocephalus is fundamentally an impairment of cerebral blood flow and of the cerebral windkessel mechanism. Ventriculomegaly and CSF malabsorption are the consequences of this impairment. Based on this model, we can suggest significant new and non-intuitive approaches to the treatment of hydrocephalus.

S20

Hydrocephalus-induced ischemia relating to VEGF-R2 and blood vessel density in hippocampus

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Background: Chronic hydrocephalus (CH) is characterized by increased cerebrospinal fluid volume with or without increased intracranial pressure (ICP), and often associated with impaired cognition thought to be related to decreased cerebral blood flow and oxygen delivery. In hydrocephalus, increased ICP and vascular compression as the result of enlarged ventricles may be directly responsible. VEGF plays a critical role in angiogenesis, neuronal protection as it relates to ischemic/hypoxic events. Previously, using an experimental model of hydrocephalus, we have shown decreased cerebral blood flow, oxygen delivery and increased capillary density.

Materials and methods: In a model of chronic obstructive hydrocephalus developed in our laboratory, we investigated the relationship between the duration and severity of CH and the density of VEGF+ neurons, glial, endothelial cells and blood vessels (BV) in ventral hippocampus: CA1, CA2-3, dentate gyrus (DG, granule cell layer) and hilar region. CH animals were divided into Short Term (ST, n = 5) and Long Term (LT, n = 5) and compared with Surgical Controls (SC, n = 5). The density of blood vessels and cellular VEGF-R2+ was estimated using stereological cell counting methods. Values were expressed as %VEGF-R2+ cells to the total number of cells in each region.

Results: Overall, there was approximately six to eight fold increase in %VEGF-R2+ neurons, and approximately six-fold increase in %VEGFR-R2 glial and endothelial cells in the hippocampus of CH compared to SC. Specifically, %VEGFR-R2+ neurons were significantly greater in CH (50–75%) than SC (10–25%). Similarly, %VEGF-R2+glia were significantly higher in CH (57–62%), then SC (5–10%). BV density was found to be double in CH than SC. Overall, we did not find regional differences in VEGFR-2 cellular and BV density. %VEGFR-2+ cells was significantly correlated to BV density (p 0.05). Finally, VEGFR-2 and BV density was significantly correlated to changes in CSF ventricular volume, and not ICP.

Conclusion: CH resulted in increased VEGFR-2 and BV density in hippocampus. Increased % VEGF-R2 of neurons and glia in CH indicates a stimulated VEGF response that may be related to mechanical injury and hypoxia seen with CH. Similar density distribution suggests similar neuroprotective mechanisms and/or vulnerability to CH-induced ischemia. However, VEGF also having adverse effects such as increasing vessel permeability may exacerbate the development of CH. Modulation of VEGF receptors may be important in our understanding of hypoxic conditions and its role in the pathophysiology of hydrocephalus.

S21

Pathophysiology of communicating hydrocephalus in two novel animal models

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Background: Communicating hydrocephalus (CH) occurs frequently but clinically-relevant animal models amenable to diagnostic imaging and cerebrospinal fluid shunting do not exist. This deficiency has inhibited our understanding of the pathophysiology of CH, which may be quite different from obstructive hydrocephalus. The purpose of this study was to perfect two novel models of CH and to characterize the histopathology that occurs in each.

Materials and methods: Two methods were employed using 25% kaolin or saline injected into the sub-arachnoid space (SAS). For injections into the basal cisterns (n = 7), after anterior exposure of the C1-clivus interval, a blunt 30–36 gauge needle was advanced into the SAS and 20–50 µl of kaolin was injected. For the cortical approach (n = 9), a craniotomy was created over both cerebral hemispheres, and a curved, blunt tip 25G needle was advanced gently into the SAS. After separating the partitions in the SAS, a total of 50–60 µl of kaolin was injected. Animals were sacrificed after chronic ventriculomegaly had developed, and the brains analyzed for cytoarchitectural changes, astrocytosis, microgliosis, neuron death, and axonal degeneration.

Results: All rats with kaolin injections appeared relatively normal, but preliminary motor learning testing showed transient neurological deficits. In rats with ventral brainstem injections, kaolin was observed grossly in the basal cisterns, but not into the cerebello-pontine angle, indicating that communicating – not obstructive – hydrocephalus had been induced. MRI studies with gadolinium injections into the lateral ventricle confirmed these findings. MRI also revealed that ventriculomegaly progressed steadily in 86% of these animals and in 2–14 days post-kaolin the mean Evan's ratio (0.43) increased significantly. In rats with cortical injections, kaolin covered approximately 80% of the hemispheres, and 89% developed mild protracted (4 months) ventriculomegaly (mean Evan's ratio 0.39) not significantly different from controls. In the periventricular white matter, the number of reactive astrocytes and microglia increased only after basal cistern injections. No degeneration of neuron cell bodies was noted in either injection group, but axonal degeneration was present in the periventricular white matter after basal cistern obstruction. These cytological changes correlated with the severity of ventriculomegaly.

Conclusion: These preliminary results suggest that CH can be induced with blockage of the cortical SAS and basal cisterns, that ventriculomegaly is much more protracted in the former model, and the time course of hydrocephalus correlates with the extent of cytological damage. Ongoing studies will help reveal why the time course of ventriculomegaly is so different in these two models.

S22

Outcome for fetuses with a diagnosis of myelomeningocele, Hydrocephalus and Brain Anomalies

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Background: Since the early 1980's foetal malformations can be diagnosed by increasingly sophisticated ultrasound (US)

examinations. Long term developmental follow up has not been reported.

Materials and methods: We will report the outcome for all 241 patients referred over the past 25 years by tertiary level Obstetricians to our Neurodevelopmental team to either explain the options for treatment of their affected foetus or to provide prognosis for their determination to terminate the pregnancy or carry to term. They include all patients in the cohort and include the following diagnoses: Major brain malformations –22, Hydrocephalus –45, Syndromes –3 and Myelomeningocele (MM) –171. All but one case with MM were delivered by caesarean section birth before the rupture of amniotic membranes. Analysis was by χ^2 or Fishers Exact.

Results: We averaged 7 to 8 consults per year with a range of 1 to 18. The fetal ages ranged from 17 to 36 weeks. Foetuses with MM 24 weeks gestational age (EGA) or older were terminated less frequently 4 of 74 (4%) than those of less than 24 weeks EGA, 8 of 41 (19.5%), $P = 0.015$. Termination rates for the same EGA groups with hydrocephalus were 0% and 17%, an insignificant difference. Of the foetuses with MM given a “unfavorable” prognosis – high rate of mental retardation and “severe” disability, 21% were terminated and 17% of those assessed as having sufficient intellectual ability to become self sufficient, $P = 0.5$. For all foetuses with MM the outcomes were: terminations 20%; still born 3%; severe Chiari II symptoms 2%; postnatal motor level 2 levels higher than predicted from in utero estimates 5%, 1 level 10%, equal 32%, and lower by 1 level 14%, 2 levels 9% and 3 levels 5% and ? = 25%. Sensory levels were assessed postnally compared to the patients' motor level at the same time as follows; sensory level was higher by 3 levels = 2%, 2 levels = 17%, 1 level = 42 % and equal only in 39% with none lower than the motor level. Functional level achieved by those old enough to evaluate were as follows, Preschool and Kindergarten L3 and above 36% with L4 and below = 13%; grade school = 28% and 52%, normal = 20% and 22%, mentally deficient 16% and 13% respectively, $P = 0.12$. The L3 and above group had 16% moderate and severely mentally retarded (MR) and the L4 and below had mild and moderate MR = 13%. For those foetuses with MM who survived to be older than 8 years of age, 11 of 15 (73%) with a favourable prognosis were developing normally and 13 of 22 with an unfavourable prognosis, $P = 0.7$. The small numbers in the hydrocephalus and brain anomalies groups prevent statistical analysis.

Conclusion: Some parents in the USA carry the pregnancy to term despite severe fetal diagnoses. We lack data about long term outcome of anomalies with poor prognoses.

S23

The assessment of management morbidity in children with myelomeningocele

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Background: Throughout childhood, numerous operative procedures and therapeutic interventions are required to optimise the functional abilities of children with myelomeningo-coele. A previous study determined that families sought normal ambulation, continence and cerebral function from intrauterine interventions. Similar goals guide recommendations for treatment and parental consent for post-natal management. The purpose of this paper is to describe the surgical interventions performed, to optimize functional ability, on a cohort of patients with myelomeningo-coele during the first 18 years of life.

Materials and methods: Patients with myelomeningo-coele born between 1965 and 1990 and managed through the Spinal Cord Clinic at British Columbia Children's Hospital, Vancouver were reviewed to determine the number and sequence of operative procedures performed during the first 18 years of life. Operative interventions were categorized on the basis of the intent of the procedure to maintain function as follows: 1) Cerebral function (shunt procedures, craniocervical decompression etc), 2) Mobility (spinal neural and orthopaedic procedures), 3) Urinary and faecal continence (urological and general surgical procedures), 4) Other procedures.

Results: (Preliminary): The cohort totals 207 patients of which 57 patients have been reviewed. Five hundred and eighty-six operations were performed on these 57 patients with a mean of 10.3 operations per person. There were 224 procedures to maintain and optimize cerebral function, 183 operations to optimize mobility, 106 procedures to address urinary and faecal continence. Seventy-three other operations were also performed. Forty-nine patients (86%) required shunting for hydrocephalus and to maintain cerebral function, they required an additional 175 procedures; averaging 3.6 procedures per patient. In support of independent mobility, following closure of myelomeningo-coele, an average 2.2 spinal neural & orthopaedic operations were required per patient. Thirty-one patients required an average of 2.8 urological operations and 8 patients required a mean of 2.4 procedures to achieve urinary and faecal continence. The operations to optimise cerebral function and ambulation tend to happen at the first year of life with at least 50% occurring in this period. Then it tends to intersperse quite regularly throughout the years. The other procedures usually occur after the first few years and increasing in frequency later on.

Conclusion: The multidisciplinary management of patients with myelomeningo-coele has resulted in significant improvement in mortality and functional morbidity achieved through multiple operative interventions. This observational study has enumerated the frequency of surgical procedures performed to maintain or further functional abilities in these children. While further analyses are necessary to determine the efficacy of these procedures, this basic data is useful for counselling families on the impact of management directed to achieve optimal functional ability.

S24

Different natural rubber latex sensitisation and allergy in patients with spina bifida, urogenital disorders and oesophageal atresia compared with a normal paediatric population and atopic children
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Table 1 (abstract S24)

Group	I	II	III	IV	V
Number of patients	54	44	183	53	47
% NRL-sensitized	4	14	48	17	17
% NRL-allergic	0	0	18	8	0

Cerebrospinal Fluid Research 2006, 3(Suppl 1):S24

Background: Natural rubber latex (NRL) contains proteins, which after repeated contacts with latex products and an allergic predisposition (atopy) can lead to a sensitization (specific IgE against NRL proteins) or allergy (type I allergy with symptoms from urticaria to allergic shock). From previous investigations spina bifida patients are known to be a high risk group for latex allergy and sensitization due to numerous operations beginning soon after birth. In the study presented we compared spina bifida patients with patients who also underwent operations repeatedly beginning soon after birth (urologic malformations) or with one surgery in the neonatal period and numerous anaesthesias due to repeated treatment with a bougie (oesophageal atresia).

Materials and methods: We investigated the prevalence of NRL-specific IgE (>0.35 kU/l, ImmunoCAP system) in a normal pediatric population (neither atopy nor surgeries) [group I], atopic children [group II], spina bifida patients [group III], children with urogenital malformations [group IV] and oesophago-tracheal malformations [group V].

Results: Apart from atopy the number of operations could be identified as risk factor for developing NRL-sensitization and allergy (group III, IV). The prevalence of latex allergy seems to be lower after repeated anaesthesia (group V) than after repeated surgery. See Table 1.

Conclusion: Besides the known high-risk group of spina bifida patients also other patients with congenital malformations and early surgery present with a remarkable risk for latex sensitization. For patients with malformations where repeated surgery can be expected, prophylactic measures similar to those for spina bifida patients should be established.

S25

Histological characterisation of segmental neuromuscular dysfunction in fetuses with spina bifida aperta

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Background: In spina bifida aperta (SBA), fetal leg movements caudal to the meningomyelocele (MMC) are quantitatively

impaired and disappear shortly after birth. The time of initiation and the histological “substrate” for this motor dysfunction is still unclear. If motor dysfunction is primary related to the fusion defect, neuromuscular histological impairment would appear independent of gestational age or delivery. In contrast, if motor dysfunction were related to secondary damage, one would expect histological spinal detriment caudal to the MMC (such as apoptotic lower motor neurones (LMNs), infection and bleedings), especially at elder gestational ages. In the present study, we investigated segmental neuromuscular histology in SBA fetuses of various gestational ages.

Patients/methods: After informed consent by the parents, histological material of 8 SBA fetuses (median GA, 30 wks; range 16–40) was investigated. The MMC was at cervical (n = 1), thoracic (n = 5) or lumbar (n = 2) level. Pregnancies ended after abortion (n = 3, GA <24 wks), abruptio placentae (n = 1), or delivery-related ventricular puncture (n = 4; in SBA fetuses with additional pathology: encephalocele, atrium septum defect, lung hypoplasia, palatoschisis and massive hydrocephalus). Histology was investigated in spinal segments (n = 8) and myotomes (n = 6) cranial, at and caudal to the level of the MMC. Histological and immunohistochemical staining was performed by HE and caspase-3. Prior to delivery, fetal ultrasound recordings were performed in 6 fetuses.

Results: In all (8/8) fetuses, spinal histological analysis indicated presence of LMNs and neural tracts cranial and caudal to the MMC. Caudal to the MMC, LMN quantity was reduced (compared to cranial to the MMC) without signs of ongoing apoptosis (caspase-3 negative in 8/8 fetuses). Spinal vascularisation caudal to the MMC appeared superfluously aberrant in 6/8 fetuses, compatible with abnormal mesenchymal migration. Fresh spinal haemorrhages appeared in all (8/8) fetuses. In all (6/6) fetuses, muscle histology was normal cranial to the MMC and abnormal caudal to the MMC (dystrophic and compensatory hypertrophic muscle fibres). All histological abnormalities were unrelated to gestational age and to prenatal presence of leg movements (observed in 5/6 fetuses).

Conclusion: In fetal SBA, segmental histological analysis caudal to the MMC shows presence of developmental abnormalities (i.e. quantitatively reduced LMNs, dystrophic/hypertrophic muscle fibres and aberrant vascularisation) throughout gestation. Superimposed on this, secondary spinal haemorrhages are observed, which appear to be delivery-related. In neonatal SBA, we suggest that these spinal haemorrhages may contribute to the final disappearance of leg movements.

S26

The role of bladder neck repairs in the management of urinary incontinence in spina bifida patients

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S26

Background: To analyse the role of bladder neck repairs (BNRs) in the management of urinary incontinence in spina bifida patients and to compare the results of the various techniques done by us.

Materials and methods: 10 patients of spina bifida with urinary incontinence who underwent bladder neck tightening

procedures as a part of their incontinence management were included in this retrospective analysis. These included 4 -Young Dee Leadbetter (YDL), 3-Slings, 2 Submucosal injections (SM), 1 Kropps procedure. The mean postoperative follow-up period was 3 years.

Results of these procedures were assessed with respect to technical difficulty, complications, predictability, ease of post-op catheterizations, postoperative improvement in leak-point pressures and their synergy with other adjuvant surgical procedures such as augmentations and stomas.

Results: Of the 4 YDL repairs 2 failed completely and did not improve the resistance at all. In 1 case the increase in resistance was very high and in one it was optimal. In all the 3 sling cases there was very good response in the short term (up to 1–2 years post-operatively) but later they were back to their original leak point pressures. There was also a complication of sling erosion in one case. The 2 SM injections were technically difficult and even on the table we could not appreciate any significant decrease in the size of bladder neck opening. The Kropps procedure was considered a failure because it resulted in a non-catheterisable bladder.

Conclusion: Most BNRs are not very useful procedures in the management of Urinary incontinence in SB. They should certainly not be done in isolation. The technical aspects, results and pro and cons of each type of procedure are discussed.

S27

Lumbo-peritoneal shunting for idiopathic intracranial hypertension: what is the optimum catheter length and placement to avoid low-pressure headaches?

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S27

Background: Lumbo-peritoneal shunting is a standard treatment for Idiopathic (“Benign”) Intracranial Hypertension. Despite the routine nature of the procedure, complications are common, particularly the problem of over-drainage leading to low-pressure symptoms. We have audited the senior author’s results over the last ten years to identify the extent of the problem, and designed a simple bench-testing of catheters of different lengths, draining at different pressure heads and with different vertical drops, in an attempt to ascertain the optimum catheter placement and length that might reduce the occurrence of low pressure headaches.

Materials and methods: There were two arms to the project. The first was a retrospective case-notes clinical audit of complications from lumbo-peritoneal shunts inserted by the senior author over the last 10 years. The second was the design, construction and application of a simple bench experiment to ascertain the flow rates through catheters of three different lengths (60, 83 and 100 cms), at three different pressure heads (15, 25, and 35 cms H₂O – to simulate 3 different placements in the lumbar theca), and three different vertical drops (10, 20 and 30 cms – to simulate the possible effect of siphoning).

Results: Complication rates from LP shunts are high, but rarely serious. One of the most common is over-drainage. The

incidence of idiopathic intracranial hypertension is rising, perhaps related to a significant rise in the incidence of obesity. The flow rate through the catheters is dependent on many variables including catheter length, the pressure head at the proximal end, and the vertical drop of the distal end. Our results indicate that the most significant factor of these three is catheter length, but the pressure head and vertical drop can still affect flow rates by over 50%.

Conclusion: The incidence of IIH is rising, and the need for LP shunting will increase. Catheter length and placement are important in reducing the risk of low pressure symptoms, but further research and development is required to design innovative ways of over-coming problems related to LP shunting, particularly the problems with over-shunting.

S28

Cardiac mediated cerebral blood flow changes in chronic hydrocephalus

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S28

Background: Increased intracranial pressure (ICP), vascular compression as the result of enlarged cerebrospinal fluid (CSF) spaces, or impaired metabolic activity may be responsible for decreased cerebral blood flow (CBF) seen in hydrocephalus. Little attention has been given to the relationship between cardiac function and systemic blood flow in chronic hydrocephalus (CH).

Materials and methods: Using an experimental model of chronic obstructive hydrocephalus developed in our laboratory, we investigated the relationship between hydrocephalus duration and severity and cardiac output (CO), cerebral blood flow (CBF), myocardial tissue perfusion (MTP), and peripheral blood flow (PBF). Blood flow measures were obtained via microsphere injection method under controlled hemodynamic conditions in experimental CH (n = 23) and surgical control (n = 8) canines at baseline and 2, 4, 8, 12, and 16 weeks. CO measures were made using the Swan-Ganz thermodilution method. Intracranial compliance (ICC) via CSF bolus removal and infusion, and oxygen delivery in CSF and prefrontal cortex (PFC) were also investigated.

Results: We observed an initial surgical effect relating to 30% CO reduction and ~50% decrease in CBF, MTP, and PBF in both groups 2 weeks post-operatively that recovered in control animals but continued to decline further in CH animals at 16 weeks. CBF, which was positively correlated with CO (p = 0.028), showed no significant relationship with either CSF volume or pressure. Decreased CBF correlated with oxygen deprivation in PFC (p = 0.006). CO was inversely related with ventriculomegaly (p = 0.019), but did not correlate with ICP. Decreased CO corresponded to increased ICC as measured via CSF infusion (p = 0.04).

Conclusion: Our results suggest that CH may have more of an influence on CO and CBF in the chronic stage than in the early condition, which was dominated by surgical effect. The cause of this late deterioration of cardiac function in hydrocephalus is uncertain, but may reflect cardiac regulation secondary to physiological response or brain injury. The relationship between cardiac function and cerebral blood flow should be considered in the pathophysiology and clinical treatment of chronic hydrocephalus.

S29

Expression of the beta-amyloid transporter, LRP-1, in aging choroid plexus: implications for the CSF-brain system in NPH and Alzheimer's disease

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Background: The CSF system, including the choroid plexus, is an important route for removing the A-Beta peptides that, in high concentrations, injure neurons. Central retention of A-Beta peptides occurs when the blood-CSF and blood-brain barriers suffer deficits in aging and disease. LRP-1, a transporter, which actively removes A-Beta from extracellular fluid, undergoes expression changes in senescence, which is a risk factor for NPH and AD. We hypothesize that LRP-1 activity in the 'barriers' is essential for the well-being of the brain's interstitial and cerebrospinal fluids. This study has assessed the expression of LRP-1 in the choroid plexus and cerebral capillaries of aging rats in order to elucidate the state of this A-Beta clearance transporter in senescence. Faulty A-Beta disposal from the CNS may predispose to NPH and the reduced CSF turnover rate in AD.

Materials and methods: Lateral ventricle choroid plexus and cortical capillaries, for comparison, were assessed for LRP-1 expression by immunohistochemistry (IHC) and RT-PCR. Tissue specimens were taken from Brown-Norway/Fischer (B-N/F) rats at various ages from 3 to >30 mo. It was of interest to compare the time course of LRP-1 expression in the blood-CSF vs. the blood-brain barrier to obtain information about the relative abilities of these major transport interfaces to clear A-Beta from the CNS in young vs. senescent adults.

Results: LRP-1 by IHC assessment was expressed extensively in the choroid plexus epithelium of healthy young adults; expression of this A-Beta transporter was sustained even in the oldest animals. This was confirmed by RT-PCR, which showed mRNA for LRP-1 in the choroidal epithelium at all ages, with enhancement of the transcript in the oldest B-N/F animals. In contrast, LRP-1 expression in cerebral microvessels declined throughout aging, and was virtually not present at 12 mo. The IHC findings for LRP-1 in brain capillaries at various ages were in agreement with the corresponding PCR data.

Conclusion: Our findings demonstrate that the LRP-1 'barrier transporter system' that removes the potentially harmful A-Beta from the CNS undergoes a different time course in expression (choroid plexus vs. cortical capillaries) as adulthood progresses into senescent debilitation. In early adult life, the BBB may have the prominent role in protecting the brain from excessive

A-Beta buildup. However, with advanced aging, the neurons may become progressively more dependent upon the choroid plexus-CSF system for maintaining A-Beta homeostasis in the extracellular fluid of the CNS. Stabilizing (or even augmenting) the capacity of the LRP-1 transporters in the 'barriers' may be significant in slowing down the onset of NPH and/or the more severe stages of CSF-brain disruption in AD. Supported by the Rae Richter, Saunders and Brown Neurosurgery Foundations.

S30

Using cognitive profiling to aid diagnosis and monitor or predict recovery in idiopathic normal pressure hydrocephalus

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Background: Recent work has highlighted the value of neuropsychological profiling in the differential diagnosis of normal pressure hydrocephalus (NPH) from Alzheimer's disease and other dementias (Iddon et al., 1999; Devito et al., 2005). Iddon et al (1999) also showed that there may be improvement in cognitive function 6 months after shunt treatment. Studies have yet to establish the extent to which cognitive functioning changes in response to treatment over longer periods of time and whether recovery can be predicted.

Materials and methods: One hundred patients with a diagnosis of NPH were assessed using a short but carefully designed neuropsychological battery that measured key components of memory and executive function. All patients were also assessed by a nurse practitioner for relevant physical function including continence and mobility. Patients also completed a self-rating depression scale.

Results: We show that in a population of 100 patients diagnosed with NPH, there is a group with a characteristic neuropsychological profile of relatively intact global functioning and impaired fronto-striatal function. We also show that in a longitudinal study of 25 patients who have had shunts inserted, there is clear improvement in memory function for a significant proportion of patients but little improvement in executive functioning. In some cases improvement is very rapid, whilst in others it may take 18 months or more, and in patients with mixed pathology long-term outcome is not always positive. Finally we report three case studies: one with dramatic and immediate improvement; one with significant but considerably slower improvement and one where there is no improvement at all.

Conclusion: A characteristic profile of cognitive impairments can be observed in NPH, using a short and easily administered neuropsychological battery. In a large proportion of cases, shunt treatment leads to notable improvement in cognitive function though this may sometimes take over a year. Pre-shunt scores on the cognitive tasks and other measures of physical function may aid the prediction of timing and extent of recovery.

S31

A comparative study of quality of life among adults with spina bifida

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Background: The goal of treatment of persons with spina bifida (SB) is to add quality to their living. Few studies have examined QoL of adult persons with SB. In this study, we explored the similarities and differences in QoL of community-residing adults living in Norway and Oregon.

Method: The Norwegian sample consisted of 57 adults registered with the Norwegian Association of SB and Hydrocephalus. Adults included 38 females and 19 males, mean age 31.8 years (17 – 54 years). The Oregon sample included 34 adults attending the Child Development Rehabilitation Center, at Oregon Health Science University. Adults included 15 females and 19 males, mean age of 29.5 (17 – 49 years.) By postal survey, information was obtained assessing subjective QoL (WHOQOL – BREF, psychological distress (Hopkins Symptom Checklist), disability cognitions (Harowitz Impact of Events Scale) coping efforts (Lazarus Revised Ways of Coping Checklist), and cognitive difficulties (1- item and Broadbent Cognitive Failures Questionnaire).

Results: No significant differences were found between the samples concerning QoL, psychological distress, intrusive thoughts, coping, and cognitive problems. In the Norwegian sample, 41% suffered from depression, 19% anxiety, 38% intrusive thinking, and 43 % avoidance thinking. Further, 59% were shunted, 61% had cognitive problems affecting daily activities and 31% experienced cognitive decline during the past six months. In the Oregon sample, 47% suffered from depression, 23.5% from anxiety, 48% intrusive thinking and 69% avoidance thinking. Further, 71% were shunted, 65% reported cognitive problems affecting everyday activities, with 33% reporting declining cognitive status. The Oregon sample used more avoidance thinking ($x^2 = 5.27$; $df = 2$; $p = 0.07$). Two multiple regressions equations were explored to assess the predictive strength of generic QoL, psychological distress, disability cognitions, coping efforts, cognitive difficulties and country (independent variables) on 1- item overall QoL (dependent variable) in a pooled model. Results displayed a significant model ($F 3.38$; $p = 0.004$) explaining 28% of the variance in overall QoL. Generic QoL was the strongest predictor, followed by psychological distress. In investigating the same independent variables with overall health satisfaction (dependent variable), results confirmed a significant model ($F 4.29$, $p = 0.001$) explaining 33% of the variance in health satisfaction. Again, generic QoL was found to be the strongest predictor of health satisfaction. Country was not a significant predictor in these models.

Conclusion: Findings confirm cross-cultural similarities in subjective factors impacting QoL in community-residing adults. Work was supported by grants from the Elizabeth Foundation in Oregon and Diakonova University College in Oslo.

S32**Cognitive and psychological sequelae of hydrocephalus and spina bifida: turning interesting theoretical research into useful clinical intervention and guidelines**JL Iddon^{1,2}, C Loveday^{1,2,3}, JD Pickard² and DJR Morgan¹¹Department of Medicine & Therapeutics, Level 4, Chelsea and Westminster Hospital, 369 Fulham Road, London, SW10 9NH, UK²Department of Academic Neurosurgery (Box 167), Addenbrooke's Hospital, Cambridge, CB2 2QQ, UK³Department of Cognitive Neuroscience, University of Westminster, Watford Road, Harrow, HA1 3TP, UK
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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S32

Background: Ventricular shunts have significantly improved the prognosis of people with hydrocephalus and spina bifida; nevertheless, there are lifelong effects, which in many cases is associated with a cognitive profile of short term memory, attention and executive function difficulties (Iddon et al, 1996, 2001, 2003, 2004). There can also be psychological sequelae including depression and low self-esteem. The aim of this study is to develop clinical practice guidelines to inform intervention strategies to help patients and their carer to manage these difficulties.

Materials and methods: A three-stage project is being developed.

Stage 1: A survey will be carried out to ascertain the needs of the client group, including gaps in local service provision and the impact of cognitive and psychological difficulties on everyday lives.

Stage 2: Using data previously collected as well as new data, a detailed review will take place of specific cognitive difficulties and how these relate to everyday functions.

Stage 3: A cognitive training programme will be developed as a guideline for practical clinical intervention.

Results: Data will be presented, showing the unmet need of people with hydrocephalus and spina bifida (N = 150, range of IQ's). Preliminary results of the new project will be presented and discussed.

Conclusion: It is not possible to provide a complete psychological support for individuals with hydrocephalus attending one London hospital clinic for their annual multi-disciplinary review. However, this project aims to bridge the theoretical/clinical gap we have previously identified in order to inform and guide their local services of the unmet needs of these clients, and to recommend appropriate interventions. This we anticipate will improve patients' quality of life.

S33**The UK campaign on folic acid and flour fortification**

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S33

Background: Following the UK Medical Research Council's (MRC) international study of folic acid and neural tube defects (NTD) reported in 1991, the mandatory fortification of flour as

a population measure to reduce NTD pregnancies has been adopted by several nations. However, no European Union state has yet introduced fortification. A key policy outcome, arising from important research, is therefore still to be achieved. Factors, which militate against fortification, include exaggeration of risk, cultural opposition to "mass medication", political and administrative inertia, and the perception that NTDs are no longer an important health issue. ASBAH has been campaigning for over 10 years in the UK, and a policy movement towards mandatory fortification may now be apparent.

Materials and methods: The campaign's story is outlined, from the MRC's groundbreaking results, through the recommendation in favour of flour fortification by the Committee on Medical Aspects of Nutrition (COMA), and the UK-wide health education campaign on folic acid, to the refusal of the Food Standards Agency (FSA) to recommend fortification in 2003, and a possible change of heart in 2006.

The cases for and against fortification are summarised, including the significant fall in NTD pregnancies in nations that have fortified, and the allegation that folic acid might 'mask' anaemia symptoms in older people with vitamin B12 deficiency. Meanwhile, over 1,200 NTD pregnancies are continuing to occur annually in the UK.

ASBAH's activities have included lobbying politicians, enlisting the support of experts and organisations, seeking media publicity, and liaising with key government agencies.

Results: The question of folic acid flour fortification is currently back with the Food Standards Agency for decision, and ASBAH's hope is that a positive decision by government will result.

Conclusion: Close links between experts, researchers and the voluntary sector can result in powerful lobbying efforts to put research progress into effect in public health policy. However, opposition from special interest groups, poorly-informed media, and the inertia of politicians, should not be underestimated.

S34**Long-term outcome in childhood hydrocephalus: a comparison of child and parental perceptions of health outcome**

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S34

Background: Assessment of outcome and quality of life in children with hydrocephalus should attempt to obtain the perspective of the children themselves, when possible. Although we have developed the Hydrocephalus Outcome Questionnaire (HOQ) for parents, the aim of this study was to assess the scientific properties of a child-completed version of the HOQ (cHOQ) and compare child and parent responses in a select group of older, higher-functioning children with hydrocephalus.

Materials and methods: All children with previously treated hydrocephalus and between 10 and 18 years old attending the neurosurgery out-patient clinic at Hospital for Sick Children (Sick Kids), Toronto were asked to participate, if their parents felt they were cognitively capable of completing the cHOQ. The parents then completed the HOQ and the Health Utilities Index,

while the child completed the cHOQ. The children were also asked to complete the cHOQ again, approximately 2 weeks later. Reliability coefficients were calculated and comparisons were made between parent HOQ and child cHOQ responses.

Results: A total of 154 children participated (mean age 14.3 years, SD 2.4). Their mean cHOQ Overall Health score was 0.79 (on a scale of 0 = worst outcome to 1.0 = best outcome), SD 0.14. For the cHOQ Overall Health score, the internal consistency reliability was 0.92 and the test-retest reliability was 0.87 (95% CI 0.79–0.92). Mother-child agreement and father-child agreement were 0.67 and 0.74, respectively. Agreement was higher for assessments of physical health, but lower for assessments of cognitive health and social-emotional health. When there was disagreement, it seemed that children tended to rate their health better than their parents did.

Conclusion: In a select group of older children with hydrocephalus, the cHOQ appears to be a scientifically reliable means of assessing long-term outcome and quality of life. Agreement with parental responses was reasonably good for physical health, but poorer for cognitive and social-emotional health, with parents generally providing a relative underestimate of quality of life. The differences in child and parent perception of health need to be appreciated when conducting outcome studies in this population.

S35

Goal setting in CIC training for children with spina bifida

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S35

Background: Children with Spina Bifida are late in developing independence in activities of daily living specially toileting. Almost all of them use Clean Intermittent Catheterisation (CIC) which demands competence in fine motor-, perceptual- and cognitive skills. The children need time and structured practice to be independent in this area. This involves the whole family why models of family centred practice and goal setting become important in planning the intervention. In a study that was presented at the SRHSB Conference in Barcelona, 2005 Allbrink Oscarson showed that the children seldom take part in the goal setting process for therapy. The goals are set by parents, caregivers and teachers and only in few cases are the children able to participate, often because the discussions are far too abstract for their cognitive ability. But children know about their occupational performance and they can participate in setting goals and objectives. Missiuna & Pollock (2000) developed an instrument, the Perceived Efficacy and Goal Setting instrument (PEGS), which can be used for goal setting in children age 5–9 years in activities of daily living. By using pictures, verbal instructions and comparing their capacity to that of their peers, it is possible to involve children with cognitive problems in planning intervention and treatment. This is important because motivation facilitates learning.

Methods: Inspired by the PEGS we are developing cards with additional pictures showing the CIC, called the Clean Intermittent Occupational Performance Assessment (CICOPA), in order to involve children in planning interventions for

independent CIC through urotherapy and occupational therapy. The instrument is based on an extensive analysis of the CIC procedure resulting in 45 pair of cards describing the process of CIC and additional activities, as mobility and dressing, connected to toileting.

Results: The first validation process of the instrument is done by five children performing the assessment and discussing the content and importance of the cards. The CICOPA cards and protocol will be presented at the SRHSB Conference plus preliminary results from the validity test.

Conclusion: Our preliminary conclusion is that this instrument may be useful in order to involve children with Spina Bifida and cognitive disabilities in the goal-setting process, to motivate and facilitate the early learning of Clean Intermittent Catheterisation, for independence in toileting.

S36

The meaning of quality of life in adolescents with spina bifida and their parents

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Background: Children and adolescents with complex neurological conditions require a holistic approach to care in order to achieve to two major distinct outcomes, condition management and quality of life (QOL). However, the meaning of QOL for adolescents with spina bifida (SB) and their families has not been well delineated. This preliminary analysis, a part of a larger study of adaptation and secondary conditions in SB, addresses quality of life from the perspective of the adolescent living with SB and his/her parent.

Materials and methods: A correlational descriptive study of 100 adolescents with SB 12–21 years of age and their parents was conducted using telephone interviews. All adolescents reported on SB Health Related Quality of Life Tool (HRQOL) and they and their parents reported on three single items of overall QOL (adolescent QOL, parent QOL, and family QOL). The HRQOL tool uses a 1–5 scale and has good reliability ($\alpha = .85$). The single items use a 0–100 scale. Open ended questions were used to gather data on what QOL means and what goes into making a good QOL.

Results: All quantitative measures of HRQOL and QOL were positive and generally fairly high. The mean values were: HRQOL M = 4.2 (SD = 0.48), adolescent report of their QOL M = 85.54 (SD = 22.39), their parent's QOL M = 87.67 (SD = 19.96) and their family's QOL M = 86.55 (SD = 20.84) and parent report of their adolescents QOL M = 77.91 (SD = 17.49), their own QOL M = 82.07 (SD = 16.77) and family QOL M = 82.32 (SD = 17.46). However, the relationship of HRQOL and adolescent overall QOL were general modest (adolescent

$r = 0.26$, $p = 0.01$; parent $r = .32$, $p = 0.01$). The qualitative data indicated that although adolescents occasionally mentioned health or independence (and rarely SB specifically) most cited happiness, friends, family, education or fiscal factors as determinants of QOL. Parents, although more likely to mention health, independence and SB specifically, also focused on the larger picture of individual happiness, family togetherness, school and job.

Conclusion: In addition to optimal clinical management of SB, health care providers need to assess the meaning of QOL for adolescents and their families and seek interventions at the individual and policy level that address these perceptions.

S37

Further development of the adolescent self management and independence scale: AMIS II

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Background: Measuring outcomes of care remains a challenge in providing care to families who have a child with spina bifida (SB). One goal frequently cited by family and clinicians is the development of self-management and independence skills in adolescents. The purpose of this paper is to report data on the expanded version of a newly developed tool designed to capture these components.

Materials and methods: Data for this analysis comes from a multi-site descriptive study focused on adaptation and secondary conditions in adolescents ages 12–21 with spina bifida (SB). Separate Interviews of adolescents and a parent were conducted by telephone using computer assisted direct entry. The 17 item Adolescent Self-Management and Independence Scale (AMIS II), expanded from the 10 item first version, was used to measure the amount of assistance the adolescents needed in the tasks. The AMIS II was rated using a 7-point response category (1 total assistance to 7 no assistance) by data collectors who were health care professionals.

Results: Factor analysis revealed three subscales explaining 58% of the variance in the parent's AMIS scores. The factor analysis of adolescent data generally supported the subscales. Two of the factors were identified in the analysis of the original 10-item instrument. Generally assistance scores reflect need for overall moderate to large amount of assistance ($M = 3.5$, $SD = .5$). Adolescents needed the least assistance on general independence subscale (includes safety, access, problem solving, advocacy and communication items $M = 4.9$, $SD = 1.6$) and minimal assistance in self management activities (knowledge of medication, able to explain condition to others, knowledge and prevention of complications and overall independence in managing condition $M = 4.11$, $SD = 0.6$). Finally adolescents needed maximal assistance with specific independence activities

(managing money, obtaining supplies for self-care, planning a meal, managing household task, making health care appointments, and managing insurance ($M = 2.4$, $SD = 38$). Reliability of the subscales ($\alpha = .70$ to $.83$) and the total scale for both parent and teen remain high ($\alpha = 0.87$ – 0.89).

Conclusion: This analysis provides preliminary support for the reliability and validity of the 17-item AMIS. Although this instrument requires rating by a health care provider, it can be administered fairly quickly. Further it provides data that allows the individual's families and providers to measure the development of critical skills for transition to young adulthood.

S38

Shunt infections in children: aetiology, treatment, cerebrospinal fluid concentration of intravenous antibiotics and therapeutic outcome in a 13-year material

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Background: Despite improved operative technique and prophylactic antibiotics shunt infections still are a major problem in hydrocephalic children with risk for sequels and even mortality. The aim of the study was to analyse the incidence, aetiology, and therapeutic outcome of shunt-infections in paediatric hydrocephalus.

Materials and methods: All children (0–15 years) with hydrocephalus operated from January 1992 and December 2004 were retrospectively reviewed to identify shunt infections. Patients with shunt infections were further analysed focusing on aetiology, clinical presentation, glucose ratio, treatment, and outcome. In eight children the treatment was started with intravenous antibiotics alone and in these cerebrospinal fluid (CSF) antibiotic concentrations were monitored.

Results: During this period 472 shunt operations were performed on 237 children. 37 infections with positive culture from cerebrospinal fluid (33 cases) or from the valve (4 cases) were found. The infections occurred predominantly in children less than 1 year of age (57%). In 80 % of the cases skin bacteria, such as coagulase-negative staphylococci (18 cases), *Staphylococcus aureus* (7 cases) and *Propionibacterium* (5 cases) were found. Children less than 12 months of age were more commonly affected by systemic symptoms such as fever and redness over the shunt system than older children. Infections caused by *S. aureus* presented with fever and low glucose ratio in all the investigated cases. *Propionibacterium* infections were detected in 5 children, all presented with signs of distal obstruction. Only one of these had a pathologic glucose concentration. Infections secondary to blood stream infection occurred in 7 (19%) children of all ages with systemic symptoms and high fever. Children with adequate systemic and intra-ventricular antibiotics recovered within 5 days. In children with intravenous antibiotics alone, cultures were still positive after 4–37 days and CSF antibiotic concentrations were low. Addition of intra-ventricular antibiotics resulted in recovery within a few days.

Conclusion: More than half of the infections were found in children less 12 months of age. Most frequently found bacteria were coagulase-negative staphylococci. Neonates and infants

had more systemic symptoms than older children. Systemic antibiotics combined with intra-ventricular resulted in fast recovery and eradication of bacteria.

S39

48 shunt catheters impregnated with antibiotics a critical comment on the status of evaluation

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Background: The published quote of infections in 108 papers concerning 24.436 shunt-treatments between 1959 and 1993 counts, with a decreasing trend, 8.7%. In three meta-analyses (Haines, Langley, Aschoff 94) a systemic antibiotic prophylaxis, that is standard since 20 years, showed some effect, however, due to low local tissue concentrations and insufficient penetration of the bacterial slime barrier in current studies the improvement of infection rates stagnate at around 8% and rise up to 21.7% at children (Vinchon 03). An encouraging step was the development of silicones with antibiotic impregnations (Bayston 89, Kockro 00) in the late eighties. Catheters with 1% Rifampin and Clindamycin are commercially available since years (Codman BactiSeal®). Up to 2005 30.000 sets were sold.

Materials and methods: In this study we did a retrospective evaluation of the infection rate of BactiSeal shunt-catheters at 48 patients (4 of them <18 years), who were estimated by the surgeons getting infections with a higher risk, e.g. after systemic inflammations or external CSF drainage.

Results: Five of 48 (higher-risk)-patients developed a shunt infection in the first year (10.4%).

Discussion: Surprisingly, in the literature we found two prospective randomised studies with 82 patients concerning the use of BactiSeal catheters, only (4.9% infections). In addition we registered one sequential and two retrospective series, all without randomisation; 268 patients showed a mean quote of 2.6% (no-high risk patients). Inclusively of our own data we summarized 398 BactiSeal-cases with an infection rate of 4.0% (range 1.4–10.4%) that appeared, compared to control groups without antibiotic impregnation, as effective. But generally the statistic power of published evaluations is very poor; they represent 0.27% of 30.000 sold units, only (status 2005).

Conclusion: The infection quote of BactiSeal-shunts in patients with higher risks is about 7.5% (Will 02) resp. 10.4% (own results). The cumulative quote of impregnated catheters counts 4.0%, that may appear as improved compared to standard experience with infection rates about 8%.

Nevertheless, randomised prospective studies are necessary to prove the effect of antibiotic impregnated catheters especially in patients with a higher risk of infection.

S40

Rifampicin-loaded silicone: a new approach to tuning release rate with self assembled monolayers and cast molding

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Background: Treatment of CSF shunts with antimicrobial agents has shown great potential for preventing shunt infections. Providing a longer period of sustained antibiotic release is an important challenge to the development of clinical shunts for long-term implantation. This study aimed to evaluate the long-term *in vitro* drug release performance of cast-molded catheters with self-assembled silane monolayer coatings to provide a tuneable release rate.

Materials and methods: A cast molding approach was used to load rifampicin into the silicone precursor prior to curing. Self-assembled perfluorodecyltrichlorosilane (FAS) and octadecyltrichlorosilane (OTS) monolayers and FAS multilayers were deposited on the drug-loaded silicone surface by chemical vapor deposition and molecular vapor deposition, respectively. The morphology of adhered bacteria was observed by scanning electron microscopy and atomic force microscopy. The antibiotic release rate was determined by UV spectrometry. The efficacy of the rifampicin was determined by measurement of *S. epidermidis* adhesion on treated and untreated silicone surfaces using a colony counting method.

Results: The cast molding approach avoided the microstructural changes and minimized the initial "burst effect" compared with the diffusion-controlled technique. Compacted multilayered structures and sparsely-dispersed, single-layered structures of *S. epidermidis* colonization were observed on untreated silicone surfaces and rifampicin-loaded silicone surfaces, respectively. Deformation of the *Staphylococcus epidermidis* cells was observed. Sustained *in vitro* release from rifampicin-loaded silicone for at least 110 days at a level of approximately 2–4 µg/cm²-day was achieved. The rifampicin-loaded silicone decreased bacterial adherence by 99.8% on fresh 8.3% rifampicin-loaded silicone and by 94.8% on rifampicin-loaded eluted silicone. Additionally, FAS multilayers were effective in moderating the burst effect and achieving a longer-term delivery compared with FAS and OTS monolayers.

Conclusion: Incorporation of antibiotics into shunt catheters has been accomplished by others. However, the surfactant used in Cook Spectrum catheters to bind minocycline is toxic to nervous tissue, and drug release from Bactiseal™ catheters is reported to be only 28 days. Combining molecular vapor deposition of FAS or OTS with cast molding impregnation of rifampicin into silicone, we have prolonged drug release well beyond this time. Moreover, it was demonstrated that the FAS coatings are effective in controlling and tuning the drug release rate. Cast molding can be adapted to a host of pharmacologically active ingredients or combinations as desired and be applied to a variety of shunt-based drug release treatments. This novel coating approach can also create different designs for surface coatings to customize and tailor the delivery rates for specific patients.

S41

Polymer and protein surface coatings on silicone: effect on *Staphylococcus epidermidis* adhesion and colonization

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Background: Surface modifications of silicone have been attempted to reduce the incidence of shunt infections. However, the influence of surface hydrophobicity, roughness, and functional groups on bacterial adhesion has not been fully elucidated, and reports of protein effects are conflicting. Therefore, we have tested silicone coated with different biopolymers, silanes, and proteins to determine how these modifications influence *Staphylococcus epidermidis* adhesion and colonization.

Materials and methods: Silicone was coated with heparin, hyaluronan, octadecyltrichlorosilane (OTS), and perfluorodecyltrichlorosilane (FAS). Proteins, including bovine serum albumin (BSA), human serum albumin (HSA), γ -globulin, and fibrinogen were immobilized on the surface of silane-modified silicone. Comparisons were also made with physically adsorbed protein on silicone. The quality and stability of these coatings were examined by contact angle measurement, X-ray photoelectron spectroscopy, and atomic force microscopy. A colony-counting adhesion assay and scanning electron microscopy (SEM) were used to quantify bacterial adhesion and colonization.

Results: The contact angles of FAS, OTS, heparin, and hyaluronan coating on silicone were 112.2°, 102.3°, 55.3°, and 55.3°, respectively, and these coatings were stable for 30 days. After a 4 hr incubation with *S. epidermidis*, the pattern of least to greatest colony counts was: FAS – OTS – hyaluronan – silicone – heparin. After a 12 hr incubation, the size and number of colonies increased significantly, hyaluronan/OTS/silicone and heparin/OTS/silicone showed the least and greatest degree of bacterial adhesion, respectively. Immobilized protein on modified silicone surfaces was stable in saline for 30 days, while physically adsorbed protein showed instability within hours. The amount of nitrogen on all types of immobilized proteins was similar, but less on physically adsorbed protein. All protein immobilized on OTS/silicone surfaces significantly reduced bacterial adhesion by around 75% compared to untreated silicone, while physically adsorbed BSA on silicone reduced adhesion by only 30%.

Conclusion: While surface hydrophobicity and roughness did not appear to be determining factors on overall bacterial adhesion, the nature of surface functional group had a significant influence on the initial adhesion and subsequent colonization processes. FAS-coated silicone surfaces displayed the greatest inhibition of bacterial adhesion and colony formation. Protein covalently immobilized on OTS/silicone reduced bacterial adhesion and colonization, with BSA having a greater effect than physically adsorbed BSA. However, different types of protein inhibited bacterial adhesion to a similar extent, possibly due to a comparable surface concentration of -NH₂ groups. These findings are helpful for devising novel strategies to reduce shunt infections.

POSTER PRESENTATION

S42

Predictors of employment in people with open spina bifida at the mean age of 35 years

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Background: Many people with spina bifida work in open employment, some despite severe disability.

Objective: To identify predictors of employment in open spina bifida in mature adulthood.

Methods: The Cambridge Cohort comprises 117 consecutive cases of open spina bifida whose backs were closed non-selectively at birth between 1963 and 1971. They have been regularly reviewed with no loss to follow up. In 2002 the survivors were surveyed by postal questionnaire and telephone interview.

Results: Fifty-four (46%) of the cohort survived to the mean age of 35 (range 31 to 38 years). Of these 13 (25%) worked in open, competitive employment. A further four worked in sheltered employment. All the 13 in open employment were of normal intelligence (IQ>80). Only 10 of them needed a CSF shunt, and in 6 of them the shunt had never needed revision. None of them had a severe visual defect or suffered from epilepsy. Only 5 used a wheelchair and 12 drove a car. Six were fully continent without catheter or appliances and none needed daily care. Those in open employment were more likely than the remainder to have an IQ>80 (13/13 versus 26/41, $p < 0.05$), no CSF shunt or no revisions of shunt (9/13 versus 15/41, $p < 0.05$), not to need a wheelchair (8/13 versus 8/41, $p < 0.05$), to drive a car (12/13 versus 8/41, $p < 0.0001$), and not to need daily care (13/13 versus 21/41, $p < 0.01$).

Conclusion: Although those working in open employment tended to be less severely affected, two of them were severely disabled showing this is not necessarily a bar to employment. However their motivation was striking. It seems likely that employment prospects were adversely influenced by episodes of symptomatic shunt malfunction, which in some patients markedly reduced both drive and energy.

S43

Laparoscopic abdominal shunt revisions in children

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Background: Abdominal complications of ventriculo-peritoneal shunt systems are too short catheters, disconnections of the distal catheter, the development of intraperitoneal pseudocysts or peritoneal absorptive failure. There are many well-known problems related to abdominal shunt surgery, such as difficulties in reaching the abdominal cavity because of pseudocysts or enteric adhesions. In some cases it might be difficult and time-consuming to locate and remove lost catheters by open surgery. Especially in adipose patients the repositioning of the distal shunt can be difficult.

Materials and methods: In the time between 1996 and 2005 we used the laparoscopic abdominal revision with 74 children with Hydrocephalus aged from 5 to 16 years, in the last 5 years with a single-trocar-technique. The approach is a small umbilical incision and the 5 mm optical system (optic) with integrated 3.5 mm working channel allows access to the abdominal cavity,

adhesions and the free peripheral catheter without additional incisions. The catheter can be disconnected at the lower valve connector (using a small incision behind the ear) and connected to the new (longer) drainage system. This one will be pulled into the abdominal cavity of the old catheter. Peripheral catheters which do not reach into the free abdominal cavity any more can be implanted again safely with an adapted puncturing technique.

Results: The Operation times lasted from 17 to 42 minutes. The cosmetic results were good. It was not possible to implant the peripheral shunt system into the abdominal cavity using the laparoscopic approach in 5 cases because of laparoscopically visible pseudocysts and chronic inflammation of the peritoneum, making it likely that absorptive failure would occur. In these cases we performed a ventriculo-atrial shunt implantation.

Conclusion: We recommended the laparoscopic procedure in all cases of abdominal shunt blockage. The 5 mm laparoscopic optical device is sufficient in most cases to give a good view inside abdomen and to control the insertion and catheter replacement. The operation is easy to perform and less invasive than a conventional laparotomy. We have short operation times and good cosmetic results especially in adipose patients. The hospitalisation time is reduced. If necessary additional operative steps in the abdominal cavity are possible without any problems.

S44

Front decompression of sacrum nerve for treatment of congenital spina bifida with meningocele and neural herniation

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Background: From 1999 to 2004, our hospital treated 4 patients with nerve herniation caused by congenital cystic spina bifida using a new operation method. Case 1, a 5-month girl; case 2, a 3-month-old male infant; case 3, a 10 years old girl and case 4, a 14 years old boy. All 4 patients had fecal and urinary incontinence, all four had talipes calcaneus and impediment of lower limbs; 2 cases have sexual function hypoesthesia; 2 cases have skin ulcer; 1 case has chronic osteomyelitis; 1 case has complicated uraemia; 1 case had a bladder fistulization of abdominal wall and 1 case has hydrocephalus.

Materials and methods: 1) Patients lie on one side;
2) Epidural anesthesia or general anesthesia;
3) A longitudinal incision of about 8 cm is made along the sacrum and lower lumbar;
4) Cut the tissue under the dural cyst to expose the dural cyst and vertebrae
5) Dissect the sacral nerve and lumbar nerve, loosen the conglutination and release the pressure;
6) Cut open the dural cyst and drain some cerebrospinal fluid;
7) Release the tethered sacrum nerve and sacrum vertebrae, move up the dural cyst, and surrounding nerves about 3–5 cm;
8) Repair the meninges containing no nerves, put back the meningeal cyst and cover under the hypodermis.
9) Clean the incision with physiological saline and place a drainage tube;
10) Incision is closed with interrupted suture.

Results: Assessment aspects: 1). meningocele and neural herniation; 2). Bladder function; 3). Bowel function, 4). Sexual function; 5). Function of lower limbs and talipes calcaneus; 6). Hydrocephalus; 7). Skin ulcer;

Assessment criteria: 1) Excellent: all aspects restored; 2) Good: 4–6 aspects restored; 3) Fair: 1–3 aspects restored; 4) Poor: no respect restored and 5) Failure: 1–7 aspects become worse.

Assessment result: Excellent 4 cases, Good 0 cases, Fair 0 cases, Poor 0 cases and Failure 0 cases. One case with osteomyelitis complication is cured by combination of Chinese traditional and Western medicine; one case with uraemia complication is cured.

Conclusion: It is difficult to treat complicated meningocele and nerve herniation caused by congenital spina bifida. We have treated 4 patients using the new operation method. According to the knowledge and treatment condition of this disease, we think the cure rate for patients with meningocele and nerve herniation is higher than that for patients with meningocele only.

S45

Epidemiologic evidence linking ABO and Rh blood groups in the mother with neural tube defect lesion level in the child

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Background: Few epidemiological studies of neural tube defects (NTD) have reported on the blood type of family members. This study examined the relationship between mother's ABO and Rh blood groups with characteristics of the child affected with spina bifida (proband).

Materials and methods: The reproductive history of 152 mothers with spina bifida offspring was investigated. Mothers were selected retrospectively from a publicly maintained registry of spinal cord disabled individuals. Only mothers who knew their blood type with singleton pregnancies were included. Primiparas (19 mothers) were included. All responses were by self-report. Lesion level was determined by muscle action against gravity and was divided into upper (thoracic) and lower (lumbar and sacral). Statistical tests included χ -square, Fisher's exact and student's t with rejection of the null hypothesis at the 0.05 level.

Results: Maternal ABO blood group was associated with proband's lesion level ($p = 0.018$); 61.8% of blood type A were upper lesions and 58.5% of blood type O were lower lesions. Rh blood group was not associated with lesion level; however, ABO was related to lesion level for Rh+ ($p = 0.002$) but not for Rh- mothers. ABO was related to lesion level for female ($p = 0.040$) but not for male probands. ABO/Rh+ and lesion level was related for mothers without a history of spontaneous abortion ($p = 0.041$), for male ($p = 0.024$) and female ($p = 0.037$) probands and for white mothers ($p = 0.006$); cell frequencies were too small to conduct a similar analysis for ABO/Rh- mothers. Proband birth weight did not differ by gender; however, females of type O mothers weighed less than females of type A mothers ($p = 0.046$). 77.0% of probands had a shunt installed and higher lesion level was related to shunt presence ($p = 0.009$); however, shunt presence, indicating hydrocephalus, was not a significant factor in the blood group analysis.

Conclusion: For these mothers of spinal bifida offspring, maternal ABO and Rh blood groups play an important but unknown role in the development of neural tube defects. Clinical confirmation of these findings in a larger subject population is warranted.

S46

Comparison of prenatal and postnatal MRI findings in the evaluation of intrauterine CNS anomalies

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Background: To assess the diagnostic capability and prognostic value of fetal Magnetic Resonance Imaging (MR) in children suspected antenatally to harbour CNS defects.

Materials and methods: Between 2003 and 2005, 14 foetal MRI scans were performed in mothers suspected on ultrasound scans to have fetuses with congenital CNS defects. Of those, 13 children have been born and assessed with postnatal MR scans. Comparisons between antenatal and postnatal scans were made with particular emphasis on accuracy of diagnosis and consequent prognostic value of the antenatal examinations.

Results: All mothers were scanned using heavily T2-weighted fat-saturated sequences, which allowed rapid acquisitions to avoid movement artefacts. Imaging quality was satisfactory in all 13 patients. Diagnoses made antenatally were: myelomeningocele in 6, diastematomyelia in 1, occipital encephalocele in 1, terminal myelocystocele in 1, meningocele in 2 and isolated hydrocephalus in 2 children. Of the 6 children with antenatal diagnosis of myelomeningocele, 1 proved to have spinal lipoma postnatally. This was one of the early antenatal MR scans. Antenatal diagnosis of hydrocephalus was made in 4 of the 5 confirmed myelomeningocele patients, which was verified postnatally. Antenatal diagnosis of Chiari II malformation was made in all 5 confirmed myelomeningocele patients but in 1 baby this was not verified postnatally. The antenatal diagnoses of occipital encephalocele and isolated hydrocephalus were verified postnatally. Antenatal diagnosis of diastematomyelia was also not verified postnatally.

Conclusion: Fetal MRI scanning is an effective, non-invasive method of assessing in-utero CNS abnormalities. After an initial learning curve, accuracy of diagnosis has improved dramatically. While diagnostic accuracy of antenatal foetal MR scans may not be perfect still to allow counselling for termination of pregnancy, prediction of clinical outcome and counselling for possible necessary treatment can be very effective and has been appreciated by all mothers.

S47

Prenatal diagnosis of LICAM gene mutations in X-linked hydrocephalus

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S47

Background: X-linked hydrocephalus (XLH) (severe type of human LI syndrome) is now known to be due to mutations in the gene for the neural cell adhesion molecule LI. We performed prenatal diagnosis of LICAM gene mutations in 5 families. We evaluated effective methods and discussed contribution for the prenatal diagnosis of XLH.

Materials and methods: We performed a nation-wide LI gene analysis of patients with hydrocephalus and identified LI gene mutations in 36 families. In these families, five obligate carriers were pregnant subsequently and want to perform the LICAM gene analysis of their fetuses. Genomic DNA was extracted from chorionic villus biopsy (CVB) at from 10 to 15 weeks' gestations. Amplification of the exons and the exon-intron boundaries of the LI gene was performed by polymerase chain reaction (PCR). Purified PCR amplification products were directly sequenced using the ABI BigDye™ Terminator Cycle Sequencing Ready Reaction Kit (Applied Biosystems) and analyzed with a capillary DNA sequencer ABI PRISM® 310 Genetic Analyzer.

Results: 1. Two fetuses were male and three were female. LICAM gene in two males did not have mutations. In three females, one did not carry the mutation in LICAM gene and two female fetuses had the same LICAM gene mutation as his mother. 2. Five obligate carriers continued their pregnancy and delivered normal babies.

Conclusion: Prenatal LI gene analyses are useful for the prenatal diagnosis of X linked hydrocephalus.

S48

The cerebral Windkessel and its relevance to hydrocephalus: the notch filter model of cerebral blood flow

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Background: Flow MRI studies have demonstrated that hydrocephalus is associated with significant abnormalities in intracranial pulsatility. A physiologically important aspect of

pulsatility in the cranium is the Windkessel effect, the dissipation of arterial pulsatility rendering capillary blood flow nearly pulseless. We investigate the cerebral Windkessel mechanism using spectral analysis of pressure measurements in dogs.

Materials and methods: Carotid arterial pressure and intracranial pressure (ICP) in 12 dogs were measured during progressive withdrawal and infusion of CSF. Pressure waveforms were recorded and synchronized in time, and analyzed with Fast Fourier Transforms. Using an autoregressive moving average technique, the arterial/intracranial pressure transfer function was derived.

Results: The transfer function provides the frequency dependence of the efficiency of the transfer of arterial pulse waves into the intracranial pulse wave. The transfer function was characterized by a notch (i.e. a transfer for pulsatility from arterial to intracranial pressure) near the cardiac frequency of the animal. With increases in mean ICP, the depth of the notch decreased.

Conclusion: The transfer function measurements show that the cranium suppresses the carotid arterial pulse specifically at the cardiac frequency, allowing transfer of arterial pulsatility into smooth cerebral blood flow. The fact that the effect is diminished with changes in mean ICP implies that this suppression is impaired under altered intracranial conditions. We hypothesize that these results are the first preliminary evidence that the intracranial Windkessel mechanism may operate as a notch filter, a frequency-sensitive filter that suppresses a specific frequency of oscillation. The mechanical properties of the cranium are critical in providing the optimal operation of this suppression. Our spectral analysis suggests that the cerebral Windkessel suppresses the heart rate component of the arterial pulse, and may thus augment cerebral blood flow by transferring pulsatile flow into smooth flow. Elevation of ICP alters the mechanical properties of the brain and thus impairs this mechanism.

There is growing evidence that hydrocephalus is associated with significant abnormalities of intracranial pulsations, and pulsatile abnormalities may play an important role in its pathogenesis. We present evidence that intracranial pulsatility is minimized via suppression of the arterial pulse wave in the brain. Hydrocephalus has been associated with spatial redistribution of pulsations (e.g., increased ventricular pulsations) and we have shown that changes in intracranial pressure may also lead to a "spectral" redistribution of pulsations (increased pulsatility at the expense of smooth cerebral blood flow). This observation may provide further insight into the pathogenesis of hydrocephalus.

S49

Programmable hydrocephalus shunt which cannot be unwillingly re-adjusted even in 3T MRI magnet

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Background: Adjustable hydrocephalus shunts are very popular in management of hydrocephalus. They are supposed to help in minimizing number of revisions. Drawback of almost all constructions is that they may be accidentally readjusted in relatively weak magnetic field (around 30–40 mili Tesla).

Materials and methods: ProGav Miethke shunt contains an adjustable ball- on- spring valve and an integrated over drainage compensating gravitational device (known as ShuntAssistant). Special mechanical 'brake' is supposed to change the valve's performance level even in strong magnetic field. We evaluated the performance and hydrodynamic properties of a sample of three valves at different performance levels and in different orientations (horizontal or vertical).

Results: All the shunts showed good mechanical durability over the period of testing (3 months) and stability of hydrodynamic performance over a 28 day period.

The pressure-flow performance curves, operating, opening and closing pressures fell within the limits specified by the manufacturer, and changed according to the programmed performance levels. Operating pressure increased in vertical position by the value resulting from the performance of Shunt Assistant. The valve has a low hydrodynamic resistance (0.53 mm Hg/(ml/min)). External programming proved to be easy and reliable. Strong magnetic fields (3Tesla MRI scanner) are not able to change the programming of the valve.

Conclusion: From the point of view of its hydrodynamic performance, the ProGAV shunt is reliable, differential pressure, low resistance, and adjustable valve, able to limit posture-related overdrainage. Unlike other adjustable valves, the ProGAV cannot be accidentally re-adjusted by external magnetic field even in 3T MRI magnet.

S50

Best clinical indicators predictive of blocked ventriculoperitoneal/ventriculoatrial shunts in adults

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S50

Background: Complications of cerebral spinal fluid shunts are common, the commonest complication being shunt blockage. The aim of this study is to determine which symptoms are the best clinical indicators predictive of a blocked ventriculoperitoneal or ventriculoatrial shunt in adults.

Materials and methods: Data was collected retrospectively over a 40-month period from patient admissions with suspected shunt blockage. The symptomatology and computerized tomography (CT) findings were compared between patients who had confirmed shunt block and those who had a normally functioning shunt. Odds ratios with 95% confidence intervals were then calculated for the common presenting symptoms. Subjects included in the study were all patients aged 16 and over, referred to the department of neurosurgery with suspected shunt blockage. This comprised of 19 patients and 45 admissions.

Results: There were 12 admissions with confirmed shunt blockage. Common symptoms were headache, vomiting, drowsiness and visual disturbance. Between the admissions with and without shunt block-age, drowsiness had the highest odds ratio of 19.25 (95% confidence interval 2.636 to 140.6, $p < 0.005$). As a combination of symptoms headache with drowsiness had the highest odds ratio of 91.36 (95% confidence intervals of 4.543 to 1837, $p < 0.005$).

Conclusion: Headache with drowsiness is by far the best clinical indicator of a blocked shunt. Other combinations of symptoms are less predictive. All patients with suspected shunt block should undergo a period of observation and a CT scan to assess ventricular size.

S51

Temporary subcutaneous peritoneal shunts for the treatment of cerebrospinal fluid fistulas following operations on the spine for congenital anomalies

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S51

Background: To treat cerebrospinal fluid (CSF) fistulas which occur following operations of the spine for congenital anomalies with a temporary subcutaneous peritoneal shunt.

Materials and methods: Sixteen patients who acquired cerebrospinal (CSF) fistula following spinal congenital repair procedures (9 lipomeningoceles, 3 tethered cords post myelomeningocele repair, 2 myelocystoceles, 1 arachnoid cyst, and 1 postoperative scoliosis surgery) underwent placement of a subcutaneous-peritoneal shunt (Range: 7–510 postoperative days).

Results: The CSF fistulas were resolved in all. Two patients required revisions of the shunt prior to resolving the fistula and subsequent shunt removal. Three patients acquired a lumbar wound/shunt infection, which necessitated shunt removal. Subsequent to removal, the infection resolved and there was no recurrence of the CSF leak. All patients but two had their shunts completely removed within one year of placement (Range: 2–21 months, Mean: 8.7 ± 5.0 months SD). Two patients did not have their shunts removed due to parental decision for no further surgery.

Conclusion: We conclude that spinal postoperative subcutaneous CSF fistulas may be successfully treated with temporary subcutaneous peritoneal shunts. This reduces hospital stay and more extensive or multiple surgical interventions.

S52

A serendipitous diagnosis of familial adenomatous polyposis. What next?

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Background: A seven-year-old boy with shunted hydrocephalus and spina bifida attended eye screening following strabismus surgery. A serendipitous finding of congenital hypertrophy of the retinal-pigmented epithelium (CHRPE) on fundoscopy, led to a diagnosis of probable familial adenomatous

polyposis (FAP). Neither parent had any evidence of CHRPE when screened, consistent with a new mutation in the patient. Genetic assessment was undertaken. Bowel screening was deferred till the second decade of life.

One year previously he had undergone a sigmoid colectomy for a high-pressure bladder and recurrent urinary tract infections. Concurrently, a button caecostomy was sited for ACE washouts for faecal soiling.

Materials and methods: Case Report and Literature Review

Results: Evolution of clinical history: Bladder catheterisation was satisfactory but intractable problems with bowel management fortuitously led to further evaluation at age eight years. Inflammatory markers were found to be raised. Upper and lower gastrointestinal endoscopy were undertaken even though bowel mucosal involvement from FAP would not be expected at this age. Numerous (>100) sessile polyps were found throughout the colon. Colectomy was undertaken to prevent inevitable long-term malignant transformation in the large intestine.

Conclusion: The Dilemma: This boy, now 9 years of age, requires lifelong surveillance for malignant change in the rectal stump and proximal gastrointestinal tract.

The dilemma is to foresee the eventual outcome of his cystoplasty. Augmentation is postulated to increase the risk of malignant change in the bladder. FAP produces a field change in the bowel mucosa predisposing to malignant change and there have been case reports of transitional cell carcinoma of the bladder in FAP. Should the colonic augmentation be removed?

S53

Analysis of twenty-four “failures” of Bactiseal™ antimicrobial shunts reported to FDA

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Background: Shunt infection rates vary considerably depending on patient's age, comorbidities, available follow up facilities and definition of shunt infection, but the rates are generally considered to be unacceptable. Prophylactic antibiotics cannot be shown to make a significant impact, and an antimicrobial shunt has been developed. Approximately 60,000 of the Bactiseal™ shunts (Codman & Shurtleff Inc) have been used worldwide over about 5 yrs. Complications, including infection, are expected to be reported to the Company for notification to FDA. When such a report of infection is received, the clinical data and removed shunt are sent to BRIG UK for investigation. The results of analysis of these reports are presented.

Materials and methods: Infections occurring in Bactiseal shunts were reported on a proforma containing clinical information and sent along with removed shunt components and any supporting material to BRIG, QMC, UK. The shunt components were examined externally and each component (ventricular catheter, valve chamber, peritoneal catheter) aseptically sampled for microscopy and culture. Isolates were tested for MIC to clindamycin and rifampicin (R+C). Clinical data were scrutinized and further information sought from the reporting institution where necessary.

Results: Twenty-four infections were reported (though it is accepted that under-reporting occurred). One was excluded due to lack of data and shunt material. On investigation, 9 were found not to be infected. Of the remaining 14 infections, 2 were due to gram-negative bacilli. In 5 cases, pre-operative CSF infection was present, all due to R+C resistant *Staphylococcus epidermidis*. One case was presumed ventriculitis but showed no growth before or after shunt removal. Two cases had further invasive shunt surgery after the 2-month Bactiseal™ protection period. Two cases were due to R+C – resistant *S epidermidis* contracted at Bactiseal™ shunt insertion and the remaining 2 cases were caused by R+C- susceptible *Staphylococcus aureus* and should have been prevented.

Conclusion: Of the 24 “infections” reported, nine were not infected, only four being contracted during shunt insertion, and these should have been prevented. Audit of shunt infection must include a clear definition as well as “forensic” microbiological assessment to yield accurate data.

S54

Cerebrospinal fluid homocysteine and hydrodynamics in chronic hydrocephalus

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Background: Homocysteine seems to have a direct neurotoxic effect and could increase the vulnerability to excitotoxic and oxidative injury. Hydrocephalus, a partially reversible gait and cognitive impairment, is mainly due to an ill-circulating cerebrospinal fluid (CSF). Our hypothesis is that CSF may play a role in the clearance or secretion of Homocysteine. The aim of this study is to gauge homocysteine and other thiols in the CSF of hydrocephalic patients, and to correlate these biological parameters with hydrodynamic patterns.

Methods: 43 patients (24 females, 19 males, mean age: 71,6 years) were included. All patients were suspected of chronic hydrocephalus (gait alteration, urinary incontinence and cognitive decline) and enlargement of the ventricles on brain imaging. To confirm the diagnosis, we performed in clinical routine CSF hydrodynamic tests via lumbar infusion according to Czosnyka's technique. A lumbar needle was inserted. A 2 ml sample of CSF was withdrawn for biochemical analysis. Subsequently, we measured the CSF hydrodynamics: pressure and pulse amplitude of the CSF during baseline and plateau, and calculation of the resistance to CSF outflow. Homocysteine (Hcy), Cysteine (Cys), Cysteinyl-Glycine (Cys-Gly) and Glutathione (G-SH) were measured in CSF by capillary electrophoresis and laser induced fluorescence detection.

Results: In the CSF of the patients, the mean \pm SD values of the various thiols were: Hcy 0.24 ± 0.05 μ mol/L, Cys 3.84 ± 1.26 μ mol/L, Cys-Gly 3.33 ± 0.92 μ mol/L and G-SH 0.5 ± 0.45 μ mol/L. Cys and Cys-Gly were positively correlated ($r = 0.51$, $p < 0.01$).

Baseline CSF pressure and resistance to CSF outflow were not correlated with the thiol levels. However, the baseline pulse amplitude of ICP significantly correlated with Hcy level ($r = 0.36$, $p = 0.02$).

Conclusion: Our preliminary results suggest that in hydrocephalus, hydrodynamics is not related to the level of thiols. Our clearance hypothesis is not supported by our data. However, our results raise the interest of transsulfuration pathway of the thiol metabolism in CSF.

S55

Do antibiotic-impregnated shunt catheters reduce shunt infection? Data from the UK Shunt Registry

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S55

Background: In recent years CSF shunt catheters impregnated with rifampicin and clindamycin have been introduced to the UK market (Bactiseal, Codman). These catheters have been shown to be effective in vitro against cultures of *S. epidermidis*. We have used data collected by the UK Shunt Registry to assess the effectiveness of Bactiseal catheters against shunt infection using a case-control design.

Materials and methods: The UK Shunt Registry contains data on nearly 28,000 CSF shunt related procedures. Our data suggests that primary factors involved in shunt revision (and infection) are patient age, diagnosis and the number of revisions a patient has had.

1099 procedures were identified where Bactiseal catheters were used. Of these 863 had an accurate diagnosis and age entered and we were able to determine the exact number of shunt revisions.

A data base search was performed procedures matched for age, diagnosis and revision status but using conventional catheters. Matches were found for 715 procedures.

Results: Of the 715 procedures where Bactiseal catheters were used, 16 were subsequently revised where shunt infection was the given reason. Of the 715 controls, 31 were subsequently revised for infection. ($p = 0.04$, chi-square).

Conclusion: Unfortunately, we collect no data on causative organisms, and we rely entirely on the surgeon for the diagnosis of infection. However, with the large number of case-controls evaluated, we have attempted to reduce bias to a minimum. Our data suggest that Bactiseal catheters have the potential to significantly reduce shunt infections by up to 50%.

S56

Protein changes in the cerebrospinal fluid of the different types of perinatal human hydrocephalus

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S56

Background: Hydrocephalus is a disorder characterized by brain ventricular dilation and excess of cerebrospinal fluid (CSF), in many cases its etiopathic origin is acquired as: post-hemorrhage, meningitis and tumours. But, there is no attributable cause in 45% of hydrocephalus cases and foetal hydrocephalus due to aqueductal stenosis is one of the two main groups of non acquired or congenital hydrocephalus, however whether narrowing of the aqueduct of Sylvius is cause or consequence of hydrocephalus is discussed by different authors. Anyhow, most investigators describe an alteration in the SCO and certain circumventricular structures in the hydrocephalus, that can even occur before hydrocephalus is present and of course before the aqueduct stenosis. The objective of the present work is to investigate probable changes in the protean composition of the CSF in perinatal hydrocephalus and to analyze, in those liquids, the presence of soluble proteins that are immunoreactive or antibodies against Reissner fibre proteins and human foetal SCO extracts.

Materials and methods: We have used CSF from a total of eight foetal and perinatal hydrocephalic humans: Dandy-Walker malformation, post-hemorrhagic hydrocephalus, mielomeningocele, 38 and 40 gestational weeks (GW) of human foetal hydrocephalus, tetra ventricular hydrocephalus and tri ventricular hydrocephalus. CSF from a normal human newborn was also used. An electrophoresis study (sodium doceyl sulphate-polyacrylamide gel electrophoresis SDS-PAGE, 5–15% gradient) and immunoblot with anti-p15 and AFRU were performed.

Results: The electrophoresis study showed that the total amount of protein in the hydrocephalic CSF was different depending on the kind of hydrocephalus and age. We found a total of four protein bands (90, 250, 550 and 630 kDa) in the hydrocephalic CSF that were not present in normal CSF and four protein bands (17, 30, 120 and 165 kDa) scarcely visible in this liquid. We must emphasize that the 90, 250 and 630 kDa were observed in more than four types of hydrocephalus and not in the normal CSF. Western blot study with AFRU marked the 42, 61, 72 and 100 kDa in all hydrocephalus cases and the control. A 120 kDa band was only observed in 3 types of hydrocephalus. p15 was mainly expressed in the tetra ventricular hydrocephalus.

Conclusion: This finding and the alterations described in the rats, mice and human hydrocephalic foetal circumventricular organs and structures, support the possibility that the secretor material released by the SCO and other circumventricular structures into the CSF is altered in the foetus and infant human hydrocephalus.

POSTER PRESENTATION WITHOUT DISCUSSION

S57

Adjustability of shunt-valves – luxury, progress or necessity?

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S57

Background: Only the development of biocompatible materials and valves with reliable function over a longer period of time enabled a successful shunt-therapy of hydrocephalus in the fifties of last century. After first reports about successful implantations of these differential-pressure-valves critical articles were published dealing mainly with overdrainage-related complications. Therefore different anti-siphon-units and “flow-regulated” valves have been developed, but now mechanical complications related to under-drainage gained increasing attention. As a consequence, the principle of adjustability of valves has been introduced. But up to now the proof of a superiority of “programmable” devices compared to non-adjustable valves is still missing especially in children.

Materials and methods: As the reason for a necessity to inaugurate adjustability of shunt-valves the authors claim, besides the requirement to avoid over-drainage, the still existing impossibility to determine the optimal opening pressure for the individual patient especially in cases of NPH or LOVA-type hydrocephalus. Furthermore the changing physiological parameters in upright position of children with their growth of length after shunting favor the idea of adjustment. Finally the intraperitoneal pressure is still a “black box” and possible changes of important parameters like CSF-production and -absorption are strong arguments for advantages of adjustability. The causes for the missing proof of the superiority of adjustable valves are multifold and will be explained on the basis of our experience after implantation of 230 Dual-Switch-valves and 54 adjustable pro-GAVs.

Results: By analyzing our experience and the literature it became evident that not only different inclusion-criteria but mainly discrepant definitions of the most important complications lead to the impossibility of unequivocal distinctions and dissociations of these entities in different series. Furthermore it is necessary to avoid some existing disadvantages of adjustable valves and it is a matter of controversy whether adjustment should be effective only in the lying and/or in the upright position. A possible solution for this dilemma by a new device will be presented.

Conclusion: As a result of our evaluation we conclude that a reliable non-“programmable” hydrostatic device may be preferable to some adjustable valves on the market. But we are convinced that by avoiding discrepancies of definitions in different series and by improving the construction principle of adjustable shunt-valves the superiority of the latter can be proven also for children in the future.

S58

Intelligent design? Status and perspectives of hydrocephalus valves

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S58

Background: After an explosive development of the first simple valves in the fifties the technology stagnated over 30 years and consisted preferably of cloning. Antisiphon valves

were inaugurated in 1973, gravitational 75, adjustable valves in 84 (open adjustable precursors 50/69!) and negative feed-back regulated Orbis-Sigma 87, but played no role before the nineties. In contrast to sophisticated technologies, theoretical advantages and threefold prices, most studies with adjustable, Orbis- and antisiphon-valves showed similar results as old designs. Especially the prospective studies demonstrated no superiority of new concepts. Is the impression of a minor role of valves correct?

Materials and methods: We tested 750 valves (346 new) in vitro: 89 designs, 25 companies, 123 adjustable, 131 gravitational, 54 antisiphon, 32 feed-back regulated. The explanted specimen had short tests, but careful inspections; the new passed an ISO-conform test battery with max.35 subtests. 234 had long-term-tests, of them 111 over 300–500 days.

Results: 56 years after Nulsen the problems of inaccuracy, drift, instable valve bodies and especially over drainage in upright are not sufficiently solved in most designs. The weak point of all antisiphon-concepts (& Delta/Strata) is the excessive susceptibility to external pressures, of Orbis-Sigma the tiny internal dimensions. Adjustable valves alone over drain. Their magnetic susceptibility is a source of permanent troubles, which increases in the age of omnipresent electric fields and 3-T-MRIs. Safe was Sophysa Polaris and Miethke ProGAV only. With respect to over drainage gravitational valves were superior. However, they need adjustability for adaptation on growth or abdominal counter pressure; one adjustable is patented.

Conclusion: The developmental potential of mechanical designs is not exhausted. The current state-of-the-art may be the crossover of gravitational and adjustable valves with a “brake”.

S59

Adult onset familial normal pressure hydrocephalus? Neuropsychological profile of monozygotic twins

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Background: There are few cases of adult onset familial normal pressure hydrocephalus (NPH) reported in the literature but the rarity of the disease makes coincidence unlikely. Female monozygotic twins presenting with the NPH triad of symptoms were assessed on a neuropsychological test battery. The aims were to determine whether the neuropsychological evidence could support the differential diagnosis of adult onset NPH whilst contributing to a further understanding of the neuropsychological profile of adult NPH.

Materials and methods: Both twins were assessed on neuropsychological tests of pre-morbid IQ, language, attention, speed of processing, frontal executive, visual-perceptual and memory function. Social and medical history was noted by interviews with the twins and a review of the medical records.

Results: Twin 1 showed mild expressive language difficulties and speed of processing impairments especially on more complex tests of executive function. Her good memory results were discrepant from her experiences of daily living. Twin 2

showed impairment on tests of immediate recall and speed of processing shown by difficulties on tests on executive function.

Conclusion: The twins performed worst on tests of executive function, which is consistent with other studies. An impaired speed of processing could be contributing to difficulty with more complex tasks. This could also contribute to their experience of poor memory by either affecting encoding or efficient retrieval of information.

S60

Successful repair of a very large spina bifida back lesion; technical details and comparison with other technical options as described in literature so far

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S60

Background: To highlight the technical details of a successful closure of a very large back lesion in Spina bifida, performed by us recently, and to review the literature on the subject

Materials and outcome: A 6-month old girl with a huge Meningomyelocele (20 cms × 15 cms) with a wide dural defect of almost similar dimensions recently underwent a successful back closure using a large dural graft and Fibrin glue. The entire interesting case history, the exact surgical details, the complications and the eventual successful outcome are depicted and discussed. Our method is compared to other surgical options and techniques described for such large lesions.

Results: The large lesion and wide dural defect could be successfully closed by use of Dural graft and Fibrin glue sealant.

Conclusion: It is possible to successfully close large lesions in a single stage with adequate use of dura graft.

S61

Dopamine β-hydroxylase and p73 expression during aging and ventricular dilation in the cerebrospinal fluid and circumventricular organs of SHR rats

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Background: It has been reported that spontaneously hypertensive rats (SHR) show ventricular dilation variations and changes in CSF proteins. The organum vasculosum of the lamina terminalis (OVLT) and the subfornical organ (SFO) are circumventricular organs located in the third ventricle, which are rich in neuropeptides such as angiotensin II and catecholamines. The SFO has connections with the brain regions involved in the central regulation of blood pressure and cardiovascular

function. p73 is present in developing neurons as a truncated isoform whose levels decrease dramatically during sympathetic neuron apoptosis after nerve growth factor (NGF) withdrawal. Therefore, p73 is necessary for the survival and long-term maintenance of CNS neurons. The purpose of the present work is to study the dopamine beta-hydroxylase (DBH) and p73 expression in the SCO, the OVLT and the SFO and their variations in ventricular dilatation and arterial hypertension.

Materials and methods: Brains and cerebrospinal fluid (CSF) from control Wistar-Kyoto rats (WKY) and spontaneously hydrocephalus rats (SHR) were used. The paraffin section containing the SCO, OVLT and SFO were immunohistochemically processed with anti-DBH and anti-p73. DBH and p73 band were identified in the CSF and circumventricular organ extract by western blot

Results: The SHR of 6 and 12 months of age showed a greater increase in ventricle size than those of normal sized WKY rats. In the electrophoretic study, we detected the presence of five protein bands: 141, 117, 48, 43, 39 kDa in the CSF of the SHR rats, that were scarcely present in the CSF of the WKY rats. We also found that DBH was lower in the SFO of the hypertensive rats than in the WKY rats, and p73 expression was higher in the SFO of the hypertensive rats than in the WKY rats. While p73 was heavily expressed in the SCO and OVLT of the WKY rats this was scarce in the SCO and OVLT of the SHR rats. The SFO extract bands were also marked with anti-DBH and anti-p73 and the intensity of the reaction was higher in SHR than in the WKY rats.

Conclusion: The present results and the fact that the deltaNp73 is necessary for the survival of sympathetic neurons, would indicate that p73 is an essential survival protein in CNS catecholaminergic neurons, therefore there could be a relationship between p73, DBH and these cerebral centres involved in cardiovascular regulation.

S62

Expression of certain cerebrospinal fluid proteins in hydrocephalus and aging. A study on WKY rats

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Cerebrospinal Fluid Research 2006, 3(Suppl 1):S62

Background: Cerebrospinal fluid (CSF) is a functional system closely connected with the brain and the changes in the protein composition of CSF could mean an alteration of the brain as an expression of encephalic disorders. The CSF absolute protein concentration is age-dependent; the CSF mean protein concentrations range from 15–45 mg/dl, but this is quite similar in different species. It has been demonstrated that the CSF protein composition is altered in hydrocephalus and alterations in CSF composition characterize many pathological processes of the central nervous system. In the present work we study the interrelationship between hydrocephalus and aging to explore CSF proteins with anti-p73 and anti-Reissner's fibre (AFRU).

Materials and methods: Cerebrospinal fluid from cistern magna of control WKY rats of 6 and 11–12 months of age, and CSF from induced hydrocephalus (I-WKY) and spontaneously hydrocephalic rats (SH-WKY) of 6 and 11–12 months of age were used. AFRU and p-73 were identified in CSF by western blot analysis. Immunocytochemical study with AFRU and anti-p73 of several circumventricular structures was also performed.

Results: Protein bands were found in the CSF of the WKY rats that were scarcely present or almost undetectable in the CSF of the hydrocephalic rats. AFRU bands were identified in the CSF of three rat groups with variations between them. The protein p73 was found in the CSF of the control WKY and hydrocephalic rats. The subcommissural organ was more intensively marked in the WKY than in the hydrocephalic rats with AFRU. The choroid plexus showed p-73 immunoreactive material and no differences were found when the three rat groups were compared.

Conclusion: These results could mean that aging and hydrocephalus are interconnected in this kind of rat, which produce alterations in the secretions of the circumventricular structures and consequently of certain proteins of the CSF.