INTRODUCTION

S1 53rd Annual Meeting of the Society for Research into Hydrocephalus and Spina Bifida
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The 53rd Annual Meeting of the Society for Research into Hydrocephalus and Spina Bifida was held at Queen’s University in Belfast, Northern Ireland at the invitation of the local organizing committee; Stephen Brown, Nan Hill, John McCann, Alan Bailie, David Marshall, Tabib Dabir, Fiona Stewart and Nan Hill. Proceedings began as usual on Wednesday afternoon with the Annual General Meeting of Members. This was followed by a reception for all delegates and guests where we were welcomed to Belfast by the Lord Mayor, Councillor Naomi Long.

The scientific programme was opened by a welcome from Dr. Michael McBride, Chief Medical Officer for Northern Ireland, and included sessions on ‘Spina Bifida: Incidence, Survival and Cognitive Outcome’, ‘Hydrocephalus’, ‘Animal Studies’, ‘Hydrocephalus Shunts’, ‘Long Term Management of Spina Bifida Patients’, ‘Urology and Bowel Management’ and ‘Spina Bifida’. We also had two Invited Lectures, firstly from Neil Buxton (Liverpool, UK), on ‘Pain Management in Spina Bifida: a Neurosurgical Perspective’ and from Professor Sivert Lindstrom, (Linköping, Sweden) on ‘The Bladder Cooling Test in Spina Bifida’. Retiring President, Professor Ray Fitzgerald (Dublin, Ireland) gave his valedictory lecture entitled ‘Here and There with Hydrocephalus’, describing changes in treatment he has witnessed through his long and distinguished career. Friday morning’s programme included a parallel break-out session on ‘Long-term Management of Children with Spina Bifida’, aimed at Nurses and Health Care Professionals.

The social programme continued on Thursday afternoon with a visit to the Thompson Graving Dock. This dry dock is where RMS Titanic underwent a final hull inspection in February and March 1912 before final sea trials and sailing to Southampton before sailing on her maiden voyage on Wednesday 10th April. She hit an iceberg on the night of Sunday 14th April and sank with the loss of over 1,500 lives. The afternoon continued with a visit to Stormont, the home of the Northern Ireland Assembly at the invitation of Michael McGimpsey, Minister of Health. We were able to visit both assembly chambers and were then entertained in the Great Hall by Belfast’s Open Arts Community Choir, a nationally acclaimed choir featuring people with disabilities and those without, and traditional Irish music from The O’Malley Experience. The final event of the social programme was a gala dinner in the magnificent Great Hall of Queen’s University.

ORAL PRESENTATIONS

S2 Neural tube defects in 21st century: is Northern Ireland changing?
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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S2

Background: Neural tube defects (NTD), which include spina bifida, anencephaly, and encephalocele, are an important group of severe birth defects whose prevalence has fallen significantly in past few decades in many countries. Northern Ireland (NI) is known to have the highest prevalence of neural tube defects (NTD) in Europe. The prevalence rate of 60 and 40 per 10,000 births was reported in 1970’s and 1980’s, respectively. However no NI data has been published since then to assess the trend of decline in NTD prevalence as noted in other previously high prevalent regions of UK and Ireland. The aims of the study were (1) To describe the current epidemiology of NTD in Northern Ireland (2) To assess the impact of prenatal diagnosis on the birth prevalence of spina bifida and anencephaly (3) To compare the current prevalence, antenatal diagnosis and termination trend with previously published reports from the province (3) To compare the current NI data with rest of UK and Europe for the same period.

Materials and methods: Total births, all births and terminations of pregnancy affected with NTD in the province were ascertained for the study period 2000-2004. The relevant information regarding maternal age, family history, maternal folate intake, antenatal versus postnatal diagnosis and genetic investigations was obtained, crosschecked and analysed. The data was compared with the published figures for the same period.
The human nervous system develops from a cleft spine. Spina bifida, which literally means "spina" meaning "spine" and "bifida" meaning "split", occurs when there is a failure of fusion in the caudal region of the neural tube. This results in failure of the neural tube to form the brain and spinal cord of the embryo. As development progresses, the top of the tube becomes the brain and remainder becomes the spinal cord. This process usually completes by 28th day of pregnancy. But, if problem occurs during this process, the tube fails to become the spinal cord. This can be seen as the most common risk factors for Spina Bifida.

**Conclusion:** This study shows that NI does not have the highest prevalence of NTD as noted in the past and the prevalence rate is in keeping with the trend noted in other UK and Irish centres during the same period. Over four fifths cases were diagnosed antenatally and the antenatal diagnosis has made significant impact on the birth prevalence of neural tube defects.

**S3 To study the epidemiology of spina bifida at our centre in India**

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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S3

**Background:** The human nervous system develops from a small, specialized plate of cells along the back of an embryo. Early in development, the edges of this plate begin to curl towards each other, creating the neural tube - a narrow sheath that closes to form the brain and spinal cord of the embryo. As development progresses, the top of the tube becomes the brain and remainder becomes the spinal cord. This process usually completes by 28th day of pregnancy. But, if problem occurs during this process, the result can be brain disorders called neural tube defects, including spina bifida. Spina bifida, which literally means "cleft spine", is characterized by the complete development of the brain, spinal cord and/or meninges (the protective covering around the brain and spinal cord).

**Etiology:** The exact cause is unknown: genetic and environmental factors, malnutrition, exposure to harmful substances, inheritance (10% greater chance in 2nd child with spina bifida), folate acid deficiency. Epidemiological Factors considered in the study; sex of the patient, sex incidence in newborns, birth order of the patients, risk factors, and socioeconomic status.

**Materials and methods:** The study has been carried out in the paediatric surgery department at our centre. We evaluated the 60 patients with Spina Bifida at our centre with the comprehensive evaluation format, history taking format, follow up chart.

**Results:** The following results have been obtained:
- Incidence is more common in males.
- Incidence at birth is more in males.
- Inadequate intake of folic acid and low socioeconomic status are seen in almost all of the patients.
- Maximum patients are of 1st birth order.

**Conclusion:** Spina Bifida is one of the most common, serious malformations of human structures after congenital heart defects. It is the defect of primary neurulation that results from failure of fusion in the caudal region of the neural tube. In this study, 60 cases of Spina Bifida have been recorded and it has been found that:
- Incidence at birth and in children with spina bifida is more in males.
- Inadequate intake of Folic acid and low socioeconomic status have been seen as the most common risk factors for Spina Bifida.
- Maternal Fever during first trimester increases the risk of Spina Bifida to two to three folds.
- 1st and 2nd child are most commonly affected.

**S4 Expectation of life and unexpected death in open spina bifida: 40 year complete, non-selective longitudinal cohort study**

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**Background:** There are few data on long term survival in open spina bifida. Predictions based on hospital studies with relatively short follow up may be over optimistic and omit unexpected deaths occurring in the community. We investigated survival, causes of death, and lifestyle in a complete cohort of open spina bifida at the mean age of 40 years.

**Materials and methods:** Participants comprised a well documented cohort of 117 consecutive cases of open spina bifida whose backs were closed non-selectively within 48 hours of birth between 1963 and 1971 at Addenbrooke’s Hospital, Cambridge, UK. In 2007, all survivors were surveyed by postal questionnaire backed up by telephone interview with patient or carer. Details of deaths were obtained from the Office for National Statistics, medical records and autopsy reports.

**Results:** One in three (40/117) died before the age of 5 years. A further 26% (31/117) died over the next 35 years, over 10 times the national average. Half the deaths (16/31) after the age of 5 were sudden and unexpected. All occurred in the community and were followed by a coroner’s autopsy. The most frequent causes of these unexpected deaths were epilepsy, pulmonary embolus, acute hydrocephalus and acute renal sepsis. In terms of neurological deficit only 17% (7/42) of those born with a high sensory level above T11 survived compared with 61% (23/38) of those with a low sensory level below L3 (p = 0.001). The mean age of the 46 (39%) survivors was 40 years (range 37 to 43). Fourteen (30%) could walk >50 metres, 37 (80%) had an IQ ≥80, 38 (83%) had a cerebrospinal fluid shunt and 9 (20%) were continent of urine and faeces without pads or appliances. Fifteen (33%) worked in open employment, 21 (46%) drove a car and 14 (30%) lived independently. However 16 (35%) needed daily care.

**Conclusion:** This study indicates ‘survival of the fittest’ since most of those dying were severely affected. Doctors and care planners need to be aware that contrary to previous suggestions, there is a continuing high mortality throughout adult life, and many of the deaths are unexpected.
S5

Pregnancy and labour in women with spina bifida
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Background: In general fertility is not reduced in women with spina bifida and hormonal contraception is more difficult to perform due to an increased risk of thrombosis in paraplegia. Thus pregnancies of women with spina bifida are possible. There is a lack of larger cohorts in the literature to manage pregnancy and birth evidence based.

Patients: We present five pregnancies in four women out of 180 patients of our spina bifida outpatient clinic.

Results: Only one of five pregnancies was terminated preterm, none of the five fetuses had a neural tube defect, only in 3 pregnancies appropriate folate prophylaxis had been given and no father had a neural tube defect. The two mothers with a shunted hydrocephalus had no complications of their shunting devices during pregnancy and labour. Urinary tract infection was a major problem only in one woman, who also had a single kidney and severe urinary tract infections before pregnancy. Intermittent catheterisation was performed by three women during their pregnancies without complications. None of the women needed antihypertensive drugs during pregnancy.

All full term newborns were born by Caesarean section and had no peripartual problems. Care for the infants after birth was given by the father (in two children) or by help of the grandparents.

Conclusion: Before planning to get pregnant a genetic counseling should inform about the recurrence risk for neural tube defects (about four percent). A folate prophylaxis is not taken regularly even in this high risk group. The rate of abortions in pregnancies of mothers with spina bifida is not well documented in the literature due to a lack of larger cohorts. In our cohort the low rate of urological and shunt-related complications is remarkable. During pregnancy and labour a very individual care of the pregnant women has to be established due to the complexity of problems (different mobility, the presence of a CSF shunting valve, urological situation with neurogenic bladder and different methods for bladder emptying). Pregnancy and labour as well as postnatal care of the infant are new tasks for spina bifida outpatient clinics. New co-operations with obstetrical departments have to be established, to solve the demanding medical and social problems together.

S6

Living with spina bifida: neurological and neuropsychological functioning in adults with severely impaired psychosocial adaptation
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Background: Spina Bifida (SB) is a birth defect caused by incomplete neural tube development, affecting physical, cogni-

tive, and adaptive function. Findings from our previous study indicated that the visual-spatial and executive functions were especially important for psychosocial adaptation in young males. The aim of this study was to describe and examine a group of patients with severely impaired psychosocial adaptation, and to find out if there were gender specific differences with regard to clinical history, neurological and neuropsychological functioning.

Materials and methods: 12 adults (6 males, 6 females; age range 24 to 41) with SB were recruited from TRS National Resource Centre for Rare Disorders. Inclusion criteria were (1) interruptions in the course of education, (2) unemployment, and (3) absence of social relations. The subjects underwent a clinical history, a neurological investigation, and a neuropsychological assessment consisting of Wechsler Abbreviated Scale of Intelligence (WASI), Grooved Pegboard, Stroop Test from the Delis-Kaplan Executive Functioning System (D-KEFS), letter-number sequencing from Wechsler Adult Intelligence Scale III (WAIS-III), and the Trail making Test. Additionally, the Behaviour Rating Inventory of Executive Function (BRIEF-A), and the Symptom Checklist 90-R (SCL-90) were used.

Results: Most of the patients were severely disabled by paralysis in the lower limbs, multiple shunt revisions, Arnold Chiari malformation, tethered cord, orthopedic surgeries, and reduced sexual function. The neuropsychological results showed deficits in the executive functions, especially working memory, mental flexibility, initiative, and organizing. Visual-spatial function and visual motor coordination were also affected. The neuropsychological findings showed similar results for both males and females. SCL-90 revealed some symptoms of psychopathology. These were more pronounced for the females. The males were less capable to structure daily living.

Conclusion: All the patients had major neurological and neuropsychological deficits. The neuropsychological findings disclosed that the executive and visual-spatial functions were most impaired for both males and females. Interestingly, even though the males reported less psychopathological symptoms, they had more problems with structuring daily living. We emphasize that findings from both neuropsychological and psychological assessment are incorporated in the follow up of SB patients in order to improve psychosocial adaptation.

S7

Cognitive and psychological sequelae of hydrocephalus and spina bifida: correlating subjective data and objective neuropsychological data to establish insight and inform clinical intervention and guidelines
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Background: Despite significant advances in treating and improving the prognosis of individuals with hydrocephalus and
spina bifida, many of these individuals continue to experience specific cognitive difficulties in the areas of memory, language, attention and executive function and these can often have a significant negative impact on everyday functioning [1–3].

Materials and methods: A comprehensive questionnaire was designed, based on known cognitive and emotional sequelae, to assess patient and caregiver perceptions of the specific difficulties experienced by people with hydrocephalus and spina bifida and the extent to which these are being addressed. In order to establish levels of insight, this questionnaire was correlated with detailed neuropsychological data to triangulate actual cognitive performance with subjective self-assessment obtained from patients and the objective view of caregivers.

Results: Questionnaire data will be presented that will highlight specific areas of discrepancy and concordance between patients and their caregivers (n = 60) and will be discussed in relation to actual performance on a range of cognitive tasks and the subsequent implications for strategic advice and intervention.

Conclusion: The data is being used to tailor specific cognitive strategies based on enhanced self-awareness, as part of small group and individual cognitive training interventions, within a multidisciplinary setting. It is hoped that the dissemination of the materials and methods designed for this study will inform best practice guidelines for these individuals and their caregivers and provide measurable outcomes for cognitive performance discrepancy meta-awareness, strategy implementation and evaluation.

References

S8
Visual field examination for children with shunted hydrocephalus
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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S8

Background: In conjunction with hydrocephalus many ophthalmological abnormalities are described. Results of visual field diagnosis remain a matter of further discussion. The aim of this study was to investigate visual field deficits of children with shunted hydrocephalus.

Materials and methods: From Dec. 2007 until Dec. 2008 all children over 6 years of age treated with hydrocephalus in our institute were included. The children received an ophthalmological investigation concerning strabismus and binocular function, ophthalmoscopy, visual acuity and refraction. The special focus was visual field diagnosis, which we made with all children having cognitive conditions. The investigation was made by using the ‘Goldmann’–perimeter (static perimetry). Children with and without visual field defects were compared concerning age at the time of ophthalmological examination, genesis of hydrocephalus and FOH of current CT or MRI scans.

Results: Fifty-six children were investigated. There were 24 females and 32 males. The mean age was 14.7 years. The following orthoptic pathologies were diagnosed: 29 children had strabismus, 17 exotropia, 12 esotropia, 4 children hypertropia, 2 hypertropia and 3 children heterophoria. Nystagmus was found in 10 children. The ocular fundus investigation showed 13 children with optic nerve atrophy.

A visual field diagnosis was possible with 42 of the 56 patients. The investigation was incomplete in 14 patients with cognitive deficits or inadequate compliance. 24 of 42 children showed a concentric visual field constriction between 10° and 50° out of the centre. Children with visual field deficits were older than those with normal visual field (p = 0.1). Nine of 10 children with postmeningitic hydrocephalus had a visual field defect (p = 0.035). Children with visual field defects had a significant higher FOH (p = 0.017).

Conclusion: Our results suggest that children with shunted hydrocephalus have a superior risk of having ophthalmological abnormalities. Visual field deficit is often a problem of these patients. Visual field diagnostic can complete the ophthalmological monitoring in patients with hydrocephalus especially in patients with large ventricles. Children with postmeningitic hydrocephalus should be monitored more frequently and intensively.

S9
Efficacy of conventional valves compared to programmable valves in managing children & adolescents with hydrocephalus: a 450 valve retrospective study
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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S9

Background: During the past 10 years, programmable cerebrospinal fluid (CSF) shunts (PVS) have increasingly replaced conventional non-programmable shunts (NPVS). However, previous studies are inconclusive to the comparative effectiveness of the valve systems for the treatment of patients with hydrocephalus.

Materials and methods: The authors collected computerized data for all patients subjected to a CSF shunt insertion or revision except those with brain tumours from the Patient Data Management System and the Computer Information System of the Seattle Children’s Hospital from 1 January 2000 through 31 December 2008. Data collected included the patient’s diagnosis, birth date, details of the operation insertion and components of
survival compared to the NPVS. As there is a using preoperative WBC and RBC counts in the CSF to compare

**Background:** Hydrocephalus is associated with increased pulsations in the cerebral aqueduct, as demonstrated by cine MRI, as well as increased pulse pressure, as demonstrated by invasive intracranial pressure monitoring. What has yet to be elucidated is the relationship between increased pulsations and the pathophysiology of hydrocephalus. Are increased pulsations an important component of the pathophysiology, or simply an artefact of decreased intracranial compliance? We have shown that under normal circumstances, the transmission of arterial pulsations into the cranium is minimized (the so-called Wind-kessel effect). In this paper, we sought to demonstrate this effect directly by measuring capillary pulsations with two-photon laser scanning confocal microscopy.

**Materials and methods:** Sprague-Dawley rats (4) were anesthetized and a cranial window was created. The dura was left intact and the craniotomy sealed with a coverslip to maintain intracranial physiology. Imaging was performed with a custom-built microscope (Olympus FV300 confocal microscope with a 1.5 W Ti: Sapphire laser, externally mounted Hamamatsu PMTs and an NA 0.9, 60× water immersion objective). A fluorescent dye (70 KDa Dextran fluorescein) was injected into the tail vein. Fluorescent vessels with diameters from 5-15 μm and depths of 50-300 μm below the pial surface were chosen. Flow was measured by repeatedly scanning a vessel and observing the dark unlabeled red blood cells flowing through the bright labelled plasma background. Flow pulsatility was defined by the pulsatility index, i.e. peak to peak flow (over each cardiac cycle) divided by mean velocity.

**Results:** Reliable flow waveforms were detected in approximately 100 vessels with a mean diameter of 10.96 ± 2.54 μm, and at a mean depth of 175.62 ± 56.58 μm from the pial surface. Mean flow velocity was 0.75 ± 0.55 mm/sec and mean pulsatility index was 21.2 ± 13.2%. Data from ongoing experiments in hydrocephalic animals will also be presented.

**Conclusion:** We have demonstrated the feasibility of measuring intracranial capillary pulsatility within the neocortex of healthy rats. These preliminary measurements show that pulsations are transmitted from the macrovascular arterial flow into the microvasculature. However, the amplitude of these flow pulsations is small compared to the mean blood flow velocity. As a comparison, pulsatility is commonly measured in humans within the intracranial macrovasculature (e.g. MCA) using transcranial ultrasound Doppler studies and is found to be 80-90% of the mean flow. This technique will enable the study of changes in capillary pulsatility in rat models of hydrocephalus and its relationship to disease pathophysiology.

**S11**

**Brain damage in experimental neonatal hydrocephalus: correlations between diffusion tensor imaging and cytopathology**

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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S11

**Background:** Diffusion tensor imaging (DTI) is an advanced non-invasive magnetic resonance imaging (MRI) technique used clinically to quantify white matter (WM) abnormalities in various pathologic conditions, and thus could be beneficial in detecting progressive brain damage in hydrocephalus. This study was designed to correlate DTI and cytopathology in a rat model of neonatal hydrocephalus.

**Materials and methods:** Obstructive hydrocephalus was induced by intracisternal injection of kaolin on postnatal day 1 (P1); age-matched control animals were either intact or received intracisternal injections of saline. Six animals (3 hydrocephalics and 3 intact controls) were imaged in vivo at 8-9 days of age (P8-9) and then sacrificed by cardiac perfusion of paraformaldehyde. Four animals (2 hydrocephalics and 2 saline controls) were sacrificed at postnatal day 21 (P21) and paraformaldehyde-fixed brains were imaged ex vivo with a Bruker 7 T MRI scanner. DTI was acquired in 6 directions to obtain measurements of the directionality of water diffusion through tissue (Fractional Anisotropy, FA; 0 = isotropic where water can move freely in any direction; 1 = anisotropic where water can move in only one
direction) and the magnitude of diffusivity of water in tissue (Mean Diffusivity, MD). Values were computed bilaterally in the genu of the corpus callosum (gCC), external capsule (EC), internal capsule (IC), and cortical gray matter (Ctx).

Results: At P8-9 ventriculomegaly was severe and by P21 had progressed to where the periventricular white matter and internal capsule were so thin that DTI could only be reliably performed ex vivo. At both times FA values were significantly reduced in the gCC (p < 0.001) but not the EC, IC or Ctx. There was a trend toward higher FA values at P21 than at P8/9 for both hydrocephalic rats and normal controls. In contrast, MD values increased only in the EC. Conspicuous gliosis was prevalent in all structures examined but differed depending on cell type. Younger animals showed a more robust reaction of microglial cells compared to 21-day old hydrocephalics. Astrocytes exhibited the opposite pattern with a more robust reaction in the older animals.

Conclusion: These results demonstrate the feasibility of applying DTI to experimental hydrocephalus in neonatal rats, and reveal impairments in the corpus callosum and external capsule. The reduction in FA with hydrocephalus suggests that structural and perhaps physiological impairments exist in cortical connectivity. Whether the associated gliosis in these structures is causal or a response to axonal and myelin damage requires further study.

S12
Global neuroinflammation patterns in experimental neonatal hydrocephalus
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Background: Hydrocephalus causes reactive astrocytosis and microgliosis throughout the brain but the global response of pro-inflammatory cytokines is not known. Thus we sought to characterize common inflammatory markers in a neonatal model of obstructive hydrocephalus. Our main hypothesis was that neuroinflammation would progress in neonatal hydrocephalus proportional to ventriculomegaly. In addition, the long-standing uncertainty about the possible global inflammatory effects of kaolin could also be addressed.

Materials and methods: Intraventricular (obstructive) hydrocephalus was induced in one-day old Sprague-Dawley rats by intracisternal injections of 25% kaolin (n = 6-7 per tissue sample); aged-matched controls received similar injections of saline (n = 3-6 per tissue sample). MRI was employed to characterize ventriculomegaly, and animals were sacrificed on post-natal day 21. Tissue from the frontal cortex, parietal cortex, hippocampus, midbrain (tectum and tegmentum), and medulla was analyzed. Quantitative real time reverse transcriptase polymerase chain reaction (qRT-PCR) was performed to determine changes in mRNA expression of interleukin 6 (IL-6), tumor necrosis factor alpha (TNF-alpha), glial fibrillary acidic protein (GFAP), and major histocompatibility complex class II (MHC-II). Protein expression was also examined in these animals by Western blotting. Correlative immunocytochemistry was also performed.

Results: All portions of the cerebral ventricles expanded, especially in the lateral ventricles where ventriculomegaly was severe and in the cerebral aqueduct where the posterior recess was separated from the overlying subarachnoid space (which also expanded) by only a thin membrane. Both the frontal and parietal cortices exhibited significant (p < 0.05) increases in IL-6, TNF-alpha, GFAP and MHC-II. Likewise, the midbrain exhibited statistically significant increases in IL-6, TNF-alpha, GFAP and MHC-II. In contrast, the medulla, which was the only region adjacent to kaolin deposits, showed no change in IL-6, TNF-alpha and GFAP, and only a modest non-significant increase in MHC-II.

Conclusion: These results suggest that severe hydrocephalus causes inflammatory changes in the cerebral cortex and midbrain of the developing brain which are probably a direct consequence of ventriculomegaly. Data from the medulla suggest that kaolin itself is not directly involved in a wide-spread inflammatory response. Characterizing the time course and association with ventricular volume will provide baseline data for future studies on pharmacological interventions. In this regard, our previous findings of significant decreases in the number of reactive astrocytes and microglia with minocycline treatment suggest that this agent may also reduce neuroinflammation in hydrocephalus.

S13
CSF circulation and cerebral cortex development
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Over the past decade, studies of a number of CSF conditions, in particular the H-Tx rat and curly tail mouse, have demonstrated a critical role for CSF in the development of the cerebral cortex and, more specifically, in the developmental defect associated with fetal-onset hydrocephalus and neural tube defects. This paper is an attempt to present a CSF hypothesis for CNS and brain development. CNS development proceeds around a fluid-filled neural tube. The source of fluid within the developing central nervous system changes from an active blood-CSF barrier in the mesencephalon transporting specific proteins and water into the growing fluid cavity and maintaining the osmotic potential of the fluid [1–3], to a high volume fluid and protein secreting choroid plexus [4]. The fluid volume output changes coincident with a change in fluid pathway from simply filling a sealed tube to bulk flow, reaching a production of 0.3 ml/min in adult brain, forcing fluid though the ventricles and out into and around the subarachnoid space [5]. Moreover the composition changes driving and supporting development of the brain stem and spinal cord and, later, through CSF output, the cerebral cortex [6]. Evidence from in vitro experiments demonstrates that CSF is sufficient to support the viability, proliferation and differentiation of neural stem/progenitor in age dependent manner [7]. Evidence from the curly tail mouse as well as from brain slice experiments demonstrate that CSF passage through the subarachnoid space is required for correct migration and lamination of the cortex with neurons generated in the ventricular zone. Evidence from the hydrocephalic H-Tx rat shows that CSF composition alone can arrest development through a blockade of cell division. This blockade involves abnormal folate handling and has recently been
shown to be amenable to treatment through maternal folate supplementation, but not folic acid [8].

Further understanding of the role of CSF in CNS and brain development will help expose many of the missing elements in our understanding of how the CNS develops and how this can go wrong. The future may thus provide treatments to prevent and/or treat conditions of poor development.

References

S14
In hydrocephalus, do protein alterations correlate with gene expression?
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Background: Differences in gene expression between non-hydrocephalic and hydrocephalic rats have previously been studied [1], although no studies have been performed on these isolated genes to determine if there is a corresponding alteration in the proteins they encode. It is important to examine if these alterations equate to equivalent changes in protein levels, as proteins are responsible for carrying out the many different functions of the body. The purpose of this study was to examine proteins and their expression levels, and how they relate to the corresponding genes already identified having altered expression levels in the H-Tx rat model in the presence of hydrocephalus. This will allow us to have a better understanding of the pathophysiology of hydrocephalus, and potentially develop protein therapies which are more palatable than traditional genetic therapies.

Materials and methods: The midbrain section from five day old control non-hydrocephalic and hydrocephalic H-Tx rats previously procured and stored in the -80 freezer were utilized in these experiments. Brains were homogenized and subjected to standard SDS-PAGE electrophoresis, followed by Western blotting techniques. Membranes were probed for proteins (tumor necrosis factor (TNF), paired box homeotic gene-6 (PAX6), cholecystokinin (Cck), nuclear factor 1/x (Nfix), lectin galactose binding soluble 3 (Lga3s), glutathione-S-transferase alpha type Y (Gast1), xanthine dehydrogenase (Xdh), and tissue factor pathway inhibitor 2 (Tfip-2)). Protein levels were analyzed utilizing Bio Image Systems software program.

Results: Preliminary data suggest that protein levels do not directly correlate with genetic expression. Testing with two of the aforementioned antibodies indicate that the opposite is true. With TNF, genetic expression was increased 1.59 times, while protein expression was down regulated 1.99 times when comparing the control animals to the hydrocephalic animals (p < 0.05). With PAX6 the same trend was found, genetic expression was down regulated by 1.51 times, while protein levels in the midbrain increased 2.2 times (p < 0.05).

Conclusion: Overall, our data suggest that there is an inverse relation between gene expression and protein levels. Further studies will solidify the relationship of the aforementioned genes to their proteins. Dependant on these data, proper therapies may be able to be devised to reduce the prevalence of hydrocephalus.

Reference

S15
Microglial downregulation in a double transgenic mouse model associated with early-onset Alzheimer’s disease (AD) after intraventricular implantation of alginate encapsulated Glukagon-like-peptide-1 (GLP-1) producing human mesenchymal stem-cells
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Background: GLP-1 peptide is an endogenous insulinotropic peptide. GLP-1 receptors are expressed throughout the brains of rodents and humans. Intracerebroventricular GLP-1 administration reduced the levels of amyloid-beta peptide (Aβ) in diabetic mice and protected cultured hippocampal neurons against Aβ and iron induced stress suggesting that GLP-1 can modify amyloid precursor protein (APP) processing and protect against oxidative
injury [1]. In the double transgenic mice model associated with early-onset AD, the effect of GLP-1 secreting human mesenchymal stem cells (hMSC) on Aβ40/42 load, Aβ associated gliosis and microglial response were investigated in the present study.

**Materials and methods:** Alginate microcapsules (CellBeads®) containing “native” (CB085) or GLP-1 transfected hMSCs (CB087) were stereotactically implanted into the right ventricle of double transgenic mice mutant expressing APP and presenilin-1 protein (APPSwe, PSEN1ΔE9; JACKSON LAS) at 27 weeks of age (n = 14 each). After 8 weeks of implantation (i.e. 35 weeks of age), brains of 4 animals per group were processed for histological assessment using Antibodies against Aβ40/42 (polyclonal; US BIOLOGICAL), glial fibrillary acidic protein (GFAP polyclonal, DAKO) and the microglial marker CD11b (monoclonal; BIOMOL). The remaining brains were used for Aβ40/42 ELIZA. N=7 35-36 weeks old Tg-mice provided the age-matched early-onset AD controls.

**Results:** Total counts of Aβ40/42 positively stained plaques assessed in the frontal cortex were reduced in the animals with GLP-1 transfected CellBeads® implants when compared to the “native” stem-cell group and the control: 107 ± 24 (GLP-1 hMSCs) vs. 165 ± 44 (“native” hMSCs) vs. 140 (control, n=1); p = 0.07 (t-test of GLP-1 vs. “native” hMSCs). Likewise, the number of reactive astrocytes (> three GFAP positively stained processes) measured in the dentate gyrus of the hippocampus showed a tendency towards a lower count in GLP-1 CellBeads® mice. Morphometric analysis of CD11b positively stained particles per cortical area (%) showed most striking evidence in group differences: animals with GLP-1 transfected CellBeads® showed a significant reduction of microglial immunoreactivity against age-matched AD control: 0.28 ± 0.14% vs. 0.58 ± 0.05% (p = 0.02, t-test). “Native” CellBeads® showed a reduced but not significant change in the microglial response.

**Conclusion:** GLP-1 producing stem cells encapsulated in alginate have lowered Aβ40/42 load in a mouse model of early-onset AD, which corresponded to a significant down-regulation of specific microglial-type changes in that model.

**Reference**


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### S16 Periventricular destabilization and ventriculomegaly in aging rats: implications for reduced neurogenesis and cognition

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**Background:** Cognitive deficits in aging, NPH and Alzheimer’s disease (AD) are exacerbated by compromised neurogenesis in the dentate gyrus (DG) and subventricular zone (SVZ). We previously found beta-amyloid (Aβ) retention in cortex and hippocampus of aged rats and diseased humans, due to greater RAGE and lesser LRP-1 expression of microvascular transporters for Aβ. Now we focus on the periventricular DG and SVZ that harbor stem cells convertible to new neurons in adults. Working hypothesis: Aβ retention in neurogenic zones harms neural stem cells, leading to reduced cognition.

**Materials and methods:** Brown-Norway/Fischer (B-N/F) rats (3, 12, 20 & 30 mo) were tested in a Morris water maze (following placement at 3 starting points along the periphery of a circular water tank) for the time to reach/climb a platform above water. In trials 1-15, we determined the latency (sec) required for rats to mount the platform following placement at the starting point. For trials 1-6, the platform was visible, while trials 6-15 involved the new challenge of finding the submerged platform in the same location. On the final day (probe trial), time spent in quadrant 4 (former location of platform) was measured in the platform absence. Latency was thus used to evaluate the extent of spatial memory recall. Animals were then injected with BrdU (50 mg/kg i.p. for 1 hr) and euthanized with pentobarbital to enable brain sampling for immunohistochemistry (IHC) and microscopy. Univariate statistics on latency for the cued (platform visible) and non-cued (platform hidden) trial hypotheses were done by J. Machan.

**Results:** There were significantly different (Holm-Bonferroni adjusted) slopes of mean log (latency) among age groups for several non-cued trials [p < 0.05 (103 df), 3 vs. 12; 12 vs. 30; 20 vs. 30 mo]. This then points to progressive decrements, with advancing age, in spatial working memory in B-N/F rats. In DG and SVZ, there was increasing amyloid burden (Aβ 42) and decreasing BrdU (mitosis) activity between 3 & 30 mo. Astroglial GFAP increased significantly between 12 & 20 mo. Microglial OX6 IHC was enhanced over 20 to 30 mo. Staining of nestin (neural stem cell marker) peaked at 20 mo, but was reduced at 30 mo. Ependyma dismantling and ventricle enlargement occurred at 30 mo.

**Conclusion:** Aged rat CNS at 30 mo resembles NPH/AD. DG & SVZ are stressed by Aβ burden and inflammation. The diminished spatial memory prompts potential CSF agent usage to stabilize neurogenesis.

**Acknowledgements**

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### S17 Abdominal catheter with resistance can be an alternative in hydrocephalic children, when shunt implantation is impossible due to prematurity or extreme hydrocephalus

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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S17

**Background:** Preterm infants have a risk of developing postnatal haemorrhage and secondary hydrocephalus. In these children and those with an extreme hydrocephalus shunting is a problem due to thin vulnerable skin and very wide sutures respectively. Tapping or external ventricular drainage is a
Materials and methods: Between 1977 and 2008 six hydrocephalic infants were shunted with a pre-bent ventricular catheter and an abdominal catheter with resistance. Four of the infants were prematurely born with a postnatal haemorrhage and secondary hydrocephalus and two born at term with a giant hydrocephalus. The medical records of these children were retrospectively reviewed with respect to gestational age and weight at first operation, ICP, length of catheters, complications and age at valve implantation.

Results: Four of the infants were prematurely born at 24 to 28 gestational weeks and the other two at 39 and 41 respectively. All children had thin and vulnerable skin at operation. The premature born were shunted at a weight between 700 g-1900 g and a corrected age of 28 to 36 weeks. The other two were shunted at the age of 43 and 40 weeks weighing 3800 and 4100 g respectively. At operation all infants had a bulging fontanel and the head circumference varied from +3 to +8 SD. ICP varied from 9-20 cm H2O. One prematurely born infant was not kept in supine position postoperatively and developed a subdural haemorrhage. It was treated conservatively. A real shunt was inserted at revision due to short ventricular catheter or desire to change the opening pressure at the age of 3.5 months to 6.5 years.

Conclusion: Pre-bent ventricular catheter and an abdominal catheter with resistance is a useful alternative, when a shunt is impossible to implant. It is important to follow fontanelle tonus and keep a supine position postoperatively in order to reduce rapid drainage and a risk for postoperative haemorrhage.

S18

An in vitro investigation of the antimicrobial activity of silver-processed catheters for external ventricular drainage

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Background: Ventriculitis is a serious complication of external ventricular drainage (EVD). Silver-processed catheters (S-PC) are available that are intended to reduce the risk of infection. Clinical results of use of S-PC in other settings have been mixed, with benefit limited to only short-term use [1, 2]. Little clinical experience of S-PC for EVD use [3], and no in-depth laboratory studies have been reported. We therefore examined the catheters to determine their antimicrobial activity in clinically relevant tests.

Materials and methods: Test bacteria were Staphylococcus epidermidis, Staphylococcus aureus (MRSA) and Escherichia coli. Catheters (Silverline®) were purchased from Forth Medical Ltd, UK. For comparison, an in-house processed catheter [4] was tested. Both contain nanoparticulate silver. Two tests were conducted, and scanning electron microscopy (SEM) was also carried out. tK100: This measures the time taken to kill 100% of bacteria when attached to the catheter material [5]. In vitro challenge$S$ determines the ability of the S-PC to resist colonisation in flow conditions when repeatedly challenged with bacteria (as in EVD). In addition, focused ion beam SEM (FIBSEM) investigated the distribution of silver in the catheter materials.

Results: At high bacterial inoculum (107 cfu/mL) both S-PCs failed to show any antimicrobial activity and they were also not able to resist colonisation. At low inoculum (104 cfu/mL) initial reduction in viability in the tK100 test was followed by resurgence after 2 days to control levels. Again, the S-PC became colonised. FIBSEM showed more silver nanoparticles in the in-house catheter material but it still did not show superior activity.

Conclusion: S-PC exhibit antimicrobial activity for a few days, after which they are ineffective in killing attached bacteria. This may be sufficient to reduce infection rates in very short-term EVD.

References

S19

The importance of being vertical - hydrostatic valves and angle of inclination at implantation

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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S19

Background: In recent publications the performance of gravitational valves for shunting hydrocephalus is reported to be influenced significantly by the angle of inclination in sagittal plane at implantation. But there are other well known reasons for under- and over-drainage like etiology, opening pressure of plane at implantation. But there are other well known reasons for under- and over-drainage like etiology, opening pressure of valve, intra-abdominal pressure, size of patient or obesity. Therefore we evaluated the effect of valve inclination in a series of patients treated with retroauricular implantation of proGAV and compared the influence with other possible parameters.

Materials and methods: In 128 adult patients (130 cases) with various etiologies treated with a V-P-shunt, the angle of inclination of the gravitational unit, part of the proGAV, in relation to the vertical to the German Horizontal was measured on lateral projections of X-rays or scout-views of CT and correlated with primary over- and under-drainage, also taking...
into account the primary opening-pressure, size and weight of the patient.

Results: In 78 cases (60%) the angle of implantation was in the acceptable range +/- 10° relative to the ideal vertical position. 29 patients (22.3%) revealed a posterior inclination of >10° theoretically predisposing to over-drainage and 23 cases (17.7%) an anterior sagittal inclination in danger for under-drainage. But of our 20 cases with over-drainage, only four demonstrated a posterior, whereas five had an anterior inclination of >10°. On the other hand out of our 33 cases with clinical and radiological signs of under-drainage only nine presented with anterior, but 11 with posterior distinct inclination of >10°. There was also no unequivocal correlation between the occurrence of these “complications”, and the opening pressure of the valve.

Conclusion: The results of our series do not support the critical reports pointing out the necessity of strict vertical implantation. In our opinion the posture and individual position of the head in daily life is more important. Nevertheless, because the function of gravitational valves depends on the inclination relative to the vertical, it should be implanted to ensure horizontal position of the gravitational unit in the lying and vertical in the standing position of the patient as accurate as possible, bringing up the question of superiority of thoracic implantation.

S20
Implantation failures and suboptimal positions of gravitational valves - with massive impact on shunt dysfunction
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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S20

Background: The function of gravitational (g)-valves is strictly dependent on the angle of verticalization. For even minor axis-deviations have a significant impact on the functional pressure, a strict orientation parallel to the longitudinal body axis is important. Despite the decisive role only 1/166 g-valve-papers (incl. running studies) investigated systematically g-valve-deviations (= failure angles) to the body axis. Furthermore, the more frequent implantation site on the lateral head yet has not been compared to the thoracal site.

Materials and methods: Each 50 consecutive g-valve patients with retroauricular and thoracal implanted gravitational devices were randomly extracted from our medical records of about 650 g-valve-implanted patients. On scout-scans/x-rays the deviations to the body axis were measured. The impact on g-valve-function and additionally the effect of a head elevation of 30 degrees were calculated.

Results: Only 22% of retroauricular vs. 28% of thoracal implanted devices were correctly placed (<10 degree). Valves placed on the head showed anteverision in 84% and retroversion in 16%. The mean deviation was 21 degrees implying a valve-offset of 72 (126) mm H$_2$O in a 200 (350) mm H$_2$O-g-valve, the maximum was 43 degrees (valve-offset: 136 (239) mm H$_2$O).

A nocturnal head elevation of 30 degrees may result in a mean valve-offset of 156 (272) mm H$_2$O calculated with the mean deviation angle and 191 (335) mm H$_2$O in the worst case. In the thoracal position the mean counted 10 degrees in lateral and 16 degrees in anteroposterior direction, implying a valve-offset of 55 (96) mm H$_2$O in 200 (350) mm H$_2$O-valve. Maximal deviation was 52 degrees resulting in valve-offset of 158 (276) mm H$_2$O.

Conclusion: Position failures are common in our series and may declare malfunction of g-valves. The thoracal implantation site is clearly superior to the head position and should therefore be preferred in adults.

S21
An in vitro study to evaluate the antimicrobial activity of a shunt catheter against Propionibacterium acnes
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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S21

Background: Infection is the major complication of shunt placement for hydrocephalus. Propionibacterium acnes is an anaerobic Gram positive rod-shaped skin bacterium, and a recognised cause of shunt infections. The clinical presentation in P. acnes shunt infections is delayed, and is under-diagnosed due to lack of anaerobic culture conditions and the need for laboratory incubation periods of at least 14 days. As the evidence supporting antimicrobial prophylaxis for shunt infections is weak, antimicrobial catheters have been developed. This project aimed to evaluate the protective effect of an antimicrobial shunt catheter, Bactiseal® (Johnson & Johnson Professional Inc., Raynham, USA), against P. acnes and to monitor the development of resistance by this bacterium.

Materials and methods: Bactiseal® shunt catheters were supplied by Codman. Three methods were used to evaluate the antimicrobial activity of the catheter. The Serial Plate Transfer Test (SPTT) is a screening test for the duration of antimicrobial activity and to monitor resistance. Catheter segments were placed onto agar plates seeded with P. acnes and incubated anaerobically. Every 7 days, segments were removed and placed on fresh plates and reincubated. The inhibition zone was measured across the short axis. This was repeated until no inhibition zones were seen. In the second method, time taken to kill 100% of P. acnes attached to catheter segments was determined by allowing P. acnes to adhere to plain and antimicrobial catheter segments and incubating them. Three samples were retrieved daily, sonicated to remove the adherent bacteria, and the sonicate cultured quantitatively to detect P. acnes growth. Thirdly, a simulated in vitro model was used to determine the ability of the antimicrobial shunt catheters to resist successive P. acnes challenges every 14 days under constant perfusion, designed to mimic the CSF flow.

Results: The SPTT showed duration of antimicrobial activity for 70 days. The tK100 showed that it takes 96 hours to kill all the P. acnes attached to the catheter. The in vitro model showed that the catheters protected against P. acnes colonization after 5 successive challenges (ie up to 70 days). Also, no resistance was found.
Conclusion: This is the first in vitro study to evaluate the antimicrobial activity of Bactiseal® against *Propionibacterium acnes*. The findings of this study indicate that the antimicrobial catheter is likely to reduce shunt infections caused by *P. acnes*.

References

S22
Adjustable gravitational valves. From the conception in 1996 to first implantations 2008
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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S22

Background: In 1975 Hakim conceived and Schulte constructed the first gravitational (g)-valve, which used implemented balls for a position-dependent automatic adjustment of the valve-resistance, in order to compensate for the hydrostatic overdrainage in the upright position. In spite of excellent tests in vitro the Hakim-Lumbar was rarely used and had no commercial success, probably due to an exclusive design for lumboperitoneal shunts. In addition the obligate vertical orientation was difficult to achieve because of the round valve body. In the early 90's the forgotten concept was rediscovered simultaneously by Richard/Block, Affeld/Miethke, Aschoff, Sophysa and Chhabra and let to numerous new g-valves with a superior handling.

In 1991 the combination of g-with adjustable valves was proposed and realized in 1993 (Aschoff). Since 1994 they were routinely implanted by an increasing number of users. Actually about 40 g-valve-studies show reduced quotes of clinical relevant shunt infections of cerebrospinal fluid shunts. In the early 90's the forgotten concept was rediscovered simultaneously by Richard/Block, Affeld/Miethke, Aschoff, Sophysa and Chhabra and let to numerous new g-valves with a superior handling.

In 1991 the combination of g-with adjustable valves was proposed and realized in 1993 (Aschoff). Since 1994 they were routinely implanted by an increasing number of users. Actually about 40 g-valve-studies show reduced quotes of clinical relevant overdrainage; subdural requiring evacuations were 20-30% only compared to conventional valves. However an inappropriate selection of pressure ranges with consecutive g-valve revisions remained a problem. In 1996 the author suggested adjustable g-valves and developed 2000/1 seven detailed technical solutions. The idea was picked up by Miethke, who patented the first ProSA in 2000 and an improved version, which passed the CE-tests in 2008.

Materials and methods: The ProSA implies an excenter fixed on a magnetic rotor, which varies the tension of a spring counteracting the weight of a gravitational ball. The opening pressure in vertical can be changed stepless between 0-40 cmH₂O. A brake excludes unintentional readjustments by magnets and MRI up to 3 T. The implantation is possible on the sternum or lateral head. Like all g-valves, a strict vertical orientation to the longitudinal body axis is essential. The ProSA can be combined with any simple DP- or adjustable valves.

Results: From Dec 2008 until now 15 implantations were clinically successful (actualized data follow in June). Three of them with decompenstating complicated hydrocepalus had a perioperative ICP-measurement; all showed physiological ICPs in upright and horizontal.

Conclusion: Adjustable g-valves are a consequent further development of shunt technology and verifiable effective in vivo. A prospective multicenter trial has been launched (Kehler/Kiefer 08).

S23
Modelling, estimation and optimal control issues in cerebrospinal fluid dynamics
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Background: Mathematical models have proved useful in studying the pressure-volume compensation of patients suffering from hydrocephalus, a condition caused by excessive accumulation of cerebrospinal fluid (CSF) in the brain. A standard approach to managing hydrocephalus is through implantation of a shunt. Two important issues in mathematical research on hydrocephalus remain unaddressed—the effect of noise on the nonlinear CSF dynamics and the optimal shunt design for managing hydrocephalus.

Materials and methods: Natural physical analogies between CSF compensation and an electrical circuit lead to a nonlinear differential equation describing the nature of pressure-volume compensation in CSF dynamics. Physiological measurements of intracranial pressure (ICP) using a constant rate infusion test shows deviations from the deterministic differential equation due to fluctuations caused by noise. These fluctuations raise two fundamental research problems—modelling the effect of noise on CSF dynamics and estimating the resulting model. Furthermore, to improve shunt design, we need an optimal controller that takes the nonlinear dynamics of CSF dynamics into account.

Results: Visual examination of the noise pattern in the data shows that a Markov process driven by Brownian motion can capture the effects of fluctuations. Such a Markov process finds its mathematical representation in a nonlinear stochastic differential equation (SDE). We solve this nonlinear SDE and estimate its parameters through a Kalman filter. We use techniques of modern nonlinear control theory to derive a controller that will keep the patient's ICP at an ideal target level. Theoretically, such a controller can be used to significantly improve existing shunt design.

Conclusion: We offer the following methodology to advance the state of the art in hydrocephalus research—a nonlinear stochastic differential equation to facilitate theoretical analysis of shunting in hydrocephalus by capturing CSF dynamics more realistically than before, an estimation method based on a sophisticated Kalman filter and an optimal nonlinear controller to stabilize and maintain the patient's ICP at any desired target level.

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Association for Spina Bifida and Hydrocephalus, ASBAH House, 42 Park Road, Peterborough PE1 2UQ, UK for suggesting the research area and introducing him to researchers studying Hydrocephalus through mathematical modelling.

**S24**

**Preparation for adult participation, starting at the beginning**

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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S24

**Background:** Improvements in medical care have dramatically improved the survival rate to adulthood of children born with spina bifida (SB). In the United States, many of these adolescents and young adults encounter the following challenges: difficulties in transitioning from pediatric to adult health care and enrolment in health insurance plans as well as self-management of their special health needs; reduced sensitivity to learning differences and psychosocial needs; changes in the type and level of formal supports and access to services; changes in individual decision making; a change in the role of parents; obstacles in establishing adult relationships; and finding vocational success.

SB-specific guidelines to make this journey from diagnosis at birth to a maximized level of independence and participation as an adult have not been clearly delineated. This presentation will describe a lifespan approach to foster the successful transition to adulthood.

**Materials and methods:** Centers for Disease Control and Prevention professionals, U.S. clinicians, researchers, and individuals living with SB have collaborated in structured work-groups to identify crucial areas of preparation for adult independence and participation. Three domains of a transition pathway model from early childhood to adulthood were targeted: Self Management/Health, Personal and Social Relationships, and Employment/Income Support. Components of the transition pathway model include: identification of key developmental milestones and measures, and the use of assessment tools intervention strategies and referral resources. The resulting Transition Pathway Model serves as a lifespan template for professionals and families to better prepare children and youth for adulthood in the three domains and serves as a record of milestones and measures, and the use of assessment tools.

**Results:** Preparation for Adult Participation” logic model

- Key developmental milestones and associated indicators in the areas of:
  - Self Management/Health
  - Personal and Social Relationships
  - Employment/Income Support
  - Interventions recommended to assist in milestone achievement

**Conclusion:** Much work has been done in the area of transition for young people with chronic disabling conditions such as SB. Many individuals with SB are less likely to finish high school, pursue secondary education, get and keep jobs, and live independently. This presentation describes a life-span oriented framework to potentially improve these outcomes for youth with SB.

**S25**

**Quality of life of African children with spina bifida: results of a validated instrument**

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**Background:** There are significant ethical issues in the management of children with spina bifida (SB), especially in resource-poor settings. The arguments often center on quality of life (QoL) issues - yet there are no objective QoL studies from Africa to date. Our purpose was to determine QoL in these patients using a validated instrument, and correlate the QoL to the degree of symptoms and defects.

**Materials and methods:** SB children from Bethany Kids at Kijabe Hospital (BKKH) and its mobile clinics throughout Kenya were interviewed regarding their QoL using the validated Schedule for the Evaluation of Individual Quality of Life - Direct Weight (SEIQoL-DW). This instrument can transfer well across cultures by using open questions clustered in 6 domains chosen based on the study group responses. Symptoms and defects caused by SB were obtained from medical records. These included SB type, motor level, hydrocephalus, urinary incontinence, use of clean intermittent catheterization (CIC), and fecal incontinence. The same instrument was applied also to a group of age-matched healthy controls.

**Results:** The study included 166 children: 102 SB patients and 64 controls, aged between six months and 18 years. In 44 children the parents were also interviewed. The main defect was myelomeningocele (68%), 59% had hydrocephalus, and CIC was used by 67% of 64 controls, aged between six months and 18 years. In 44 children the parents were also interviewed. The main defect was myelomeningocele (68%), 59% had hydrocephalus, and CIC was used by 67% of 49 incontinent children older than 2.5 years. The SEIQoL score of children with SB was 65.1 (scale 0 - 100), as compared to 78 in the controls (p < .001). SB children scored significantly lower than healthy controls in three domains: “health and disease”, “development” and “basic needs”; yet both groups identified “self-actualization” and “development” as the most important domains. There was no significant difference in the total SEIQoL scores whether the children or their parents were interviewed, and no single SB-related determinant made a significant difference in the score.

**Conclusion:** As expected, the QoL of African children with SB is lower than that of healthy controls, but remains surprisingly acceptable. No SB-related clinical factors appeared to influence significantly the QoL. The domains health and disease, development and basic needs differed significantly in the two groups. These domains need more attention in the future.

**S26**

**Independency in daily living of adult patients with myelomeningocele (MMC)**

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Background: MMC children's daily living is followed closely in most of the western world, however correspondingly little is known about adults' daily living. In this study we aim to find data on everyday life of adult MMC patients and correlate these to independent living.

Materials and methods: In our clinic at the Neurosurgical department, University hospital in Aarhus, we established contact to all our 46 known adult MMC patients (Birth 1961-1982) and invited them to fill out a questionnaire concerning everyday living, educational level, employment and housing facilities. One patient did not participate, 45 accepted.

Results: Age range was 20-42 years of age. Mean 29.7. We found significantly correlation to independency in daily living if patients could walk (RR = 1.6 (95% CI = (1.2;2.1)), if patients did not receive disablement pension (RR = 3.1 (95% CI = (1.7;5.8)), or if they successfully graduated from primary school or higher level of education (RR = 1.47 (95% CI = (1.1;2.0))). Independency was most frequent if patients had or have had employment at some point (RR = 1.2 (95% CI = (0.94;1.6)), did have a partner (RR = 1.5 (95% CI = (0.89;2.4)) or had children (RR = 1.8 (95% CI = (0.63;4.9))), though not statistically significant.

Conclusion: Preservation of walking ability into adulthood, useful education, contact to the labour market and good family conditions seem important for the independency of MMC patients.

S27
Decompensation of ‘arrested hydrocephalus’ - 2 case studies
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Background: A significant proportion of spina bifida (SB) children have a ventriculo-atrial or ventriculo-peritoneal shunt inserted in the neonatal period for hydrocephalus. Those felt to be non-shunt dependent may develop active hydrocephalus in later life. Symptoms can include headache, cognitive decline, and drowsiness. We present 2 cases of unusual presentations of raised intracranial pressure (ICP) in SB patients in their 5th and 6th decades.

Materials and methods: Review of charts and investigations.

Results: Patient A initially attended our Clinic in 1990, aged 39. In 2004 she developed oozing from her previously surgically closed defect site, which continued intermittently for 7 months. She received several courses of antibiotics, and magnetic resonance imaging (MRI) failed to reveal a track for CSF; or evidence of soft tissue infection. In 2006 she had an episode of loss of consciousness, associated with headache and a recurrence of the discharge. CT scans bore the appearance of chronic arrested hydrocephalus, but no evidence of raised ICP. Following consultation with the neurosurgeons, infusion studies confirmed elevated ICP and a shunt was inserted, with symptomatic improvement.

Patient B also first attended in 1990, and was reviewed regularly without evident neurological deterioration. In 1994, aged 44, she experienced a low-impact road traffic accident. Following this she complained of slurred speech, reduced hearing, and bilateral facial weakness. CT confirmed ventriculomegaly without signs of raised ICP; and over several months the symptoms improved. In 1997, the symptoms gradually recurred, and progressed. CT was unchanged, but MRI suggested raised ICP, and Neurosurgical referral was made. Infusion studies confirmed raised ICP and the patient received a shunt with improvement in symptoms.

Conclusion: Previously arrested hydrocephalus may become active, without features of raised ICP on CT scan. Presenting features may be subtle and seemingly transient, and where there is a high index of suspicion, MRI and/or infusion studies may be diagnostic. Symptoms may be reversible on insertion of a shunt, with corresponding improvement on quality of life.

S28
Palliative care: recognition of changing need in a children’s spina bifida service in Northern Ireland
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Background: The regional Spina Bifida (SB) service for Northern Ireland is organised through two multi-professional teams based in Belfast, one for children and the other for those of older teenage years and beyond who transfer to an adult service. Although the incidence of SB is lower in comparison to earlier decades, more children are living longer with complex problems requiring support and remediation. This study examines the palliative care needs of children and young people with SB attending the children’s service that were recognised as having a life-limiting dimension; required symptom control; and there was an expectation of early death.

Materials and methods: Eighteen children were recognised from the clinic database by the paediatrician as fulfilling the inclusion criteria. The case notes were examined and key features identified in relation to neurological, urological and developmental status; symptom complexes; interventions; and outcome.

Results: Of the 18 children (5 M:13 F) 13/18 had thoracic level lesions. All had shunt dependent hydrocephalus and neuropathic bowel/bladders and 7/18 severe learning difficulty. None had severe renal impairment. Of those born 1984 - 1991 (group 1) 5/9 died and they were more likely to have had back lesions not surgically closed, to have died after recurrent pneumonias and less frequently had severe pain. Of those born from 1994 (group 2) 2/9 died. Symptom complexes related to infanlile Chiari were more frequently recognised and remediated; tracheostomy and tube feeding was more prevalent and late neurological effects, including neuropathic pain more problematic.

Conclusion: Some children with SB require an active and total approach to care embracing physical, emotional, social and spiritual elements. This palliative care approach may require specialist management of pain/ventilation, in support of a community team trained up to deal with an array of symptom complexes and interventions within a community setting.
**S29**

**Journey into the unknown: a survey into the effects of ageing on the health of people with spina bifida and/or hydrocephalus in the West Midlands area**

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*Cerebrospinal Fluid Research* 2009, 6(Suppl 2):S29

**Background:** This study looked at the effects of ageing on the health of 42 adults with spina bifida (SB) and/or hydrocephalus (H) over the age of 35 years, living in the West Midlands Region of the United Kingdom, and known to the authors, who are employed as Advisers with ASBAH. Of the 14 males and 28 females who took part, 9 had SB, 27 SB&H, 4 H and 2 spina bifida occulta. The focus of the project was identified in preliminary exploration with a group of service users and emphasis given to general health, mobility, continence and hydrocephalus.

**Materials and methods:** An initial simple questionnaire about health issues was sent to 180 people of whom 42 volunteered to take part in a more detailed study. Confidentiality was assured. A questionnaire was devised and the interviews conducted by the authors. The results were collated into a database for study. At the request of the focus group an attempt was made to identify feelings about the effects of ageing.

**Results:** Participants revealed widespread concern related to general health; for example 26/42 had experienced skin problems, 31/42 were concerned about weight and 17/42 had 2 spina bifida occulta. Depression was a significant feature in over half of the respondents. The psychological and physical impact of deteriorating mobility was a key finding: 18 were wheelchair users as children but this figure had risen to 26 in adulthood. A review of bladder and bowel continence management showed little evidence of access to modern methods. Shunting remained the main treatment of hydrocephalus but a few revisions were reported. Tables and charts illustrating the results, and quotes from participants are included in the text.

**Conclusion:** The project provided a snapshot of the health challenges faced by 42 adults living with SB and/or H and offered an opportunity for them to have a voice, to inform debate among themselves, carers and professionals, in order to make a positive contribution to the understanding of their condition during the ageing process. It also provoked ideas for further research into the world of living with this complex condition; e.g. exploring the capacity of those with SB/H to consider change in continence management, or an assessment of the impact of adopting wheelchair use during adulthood. Comparative studies with other age groups i.e. 18-35 yrs and 10-18 yrs might also provide a valuable insight into how changing treatments and attitudes might result in different outcomes for today’s young people with SB and/or H.

**S30**

**A survey of bowel washout practice in children with neuropathic bowel in the UK and Ireland**

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*Cerebrospinal Fluid Research* 2009, 6(Suppl 2):S30

**Background:** Most children with spina bifida require medical intervention to achieve social faecal continence. Bowel washouts can be delivered retrogradely (per rectum) or via an Antegrade Continence Enema (ACE) stoma. We wished to ascertain the spectrum of practice nationally, and if there was an optimum regimen.

**Materials and methods:** Continence Nurse Specialists from a broad sample of paediatric tertiary-referral units completed an on-the-spot questionnaire on their bowel washout programme.

**Results:** Eleven units across England, Scotland, Wales, Northern Ireland and the Republic of Ireland were surveyed. Each department supervised between15-350 (mean = 83, total > 910) children on bowel washouts for various conditions, of which spina bifida was the commonest. Some units employed a washout volume of 20 ml/kg body weight and others a fixed volume for all children, which ranged from 100 - 1000 ml. Almost all departments added salt to tap-water to approximate an isotonic solution. The vast majority of units also prescribed in the washout a laxative (bisacodyl, macrogols/polyethylene glycol, phosphate, sodium citrate, sodium picosulphate, or liquorice-root in reducing order). Some departments omitted the laxative, or lowered its dose, when starting a child on a washout programme, in an attempt to reduce offsetting side-effects. A selection of devices were used to administer rectal washouts, the commonest being a graduated-coupe with gravity-feed irrigation-bag, or the Peristeen balloon-catheter system (Coloplast).

The most frequently reported side-effect was abdominal cramping, which tended to occur more often with bisacodyl or phosphate, especially at higher doses or if very constipated. The estimated time spent on the toilet after administration of the washout varied from 30 - 90 (median = 45) minutes, and seemed to be independent of the washout volume or composition. All units started with a daily washout, and most gradually lengthened the interval between washouts to every other day, or even to twice per week, until soiling recurred. There was a general impression that bisacodyl was the most productive aperient.

The most commonest complaint from children (regardless of age) and parents alike was the time commitment. However, most users felt that this was balanced by the time saved no longer having to deal with faecal incontinence.

**Conclusion:** A diverse range of regimens was reported, suggesting that no ideal one exists for all children. Bisacodyl appears to cause more cramping; but is probably the most efficacious laxative additive, so may reduce the weekly-time spent on the toilet, which is the biggest issue for families.

**S31**

**Effectiveness and independence - different treatments of neurogenic bowel dysfunction in children with myelomeningocele**

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*Cerebrospinal Fluid Research* 2009, 6(Suppl 2):S31

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**Conclusion:** A diverse range of regimens was reported, suggesting that no ideal one exists for all children. Bisacodyl appears to cause more cramping; but is probably the most efficacious laxative additive, so may reduce the weekly-time spent on the toilet, which is the biggest issue for families.
Background: Constipation is a major problem in children with myelomeningocele and may result in a range of problems from impaired growth to faecal incontinence. Treatment regimes differ between countries and comparisons between the different methods are rare. Apart from effectiveness aspects as time needed and factors related to possibilities of independence are also important. Dominating treatment regimes are oral laxatives, transrectal irrigation (TRI) and different kinds of irrigation via appendicostomy.

Materials and methods: A questionnaire was sent to all children with myelomeningocele aged 7-16 years living in the south eastern health region and the region of Skåne in Sweden (n = 96) and in the south and east regions of Norway (n = 84). The questionnaire covered several areas including, bowel and bladder emptying, urinary infections and independence at the toilet and had separate parts for the child and parents. The quality of life instrument PedsQL® was also used. A total of 180 questionnaires were sent out and 106 (59%) answers were received. Distribution between genders was equal. Analysis of drop-outs showed no significant differences according to age, gender and regime of bowel emptying.

Results: Distribution according to regime of bowel emptying was: spontaneous 18 (17%), TRI 52 (49%), appendicostomy 32 (30%) and other regimes 4 (4%). Of the 106 children 13 used some oral treatment to improve bowel function in most cases combined with one of the regimes above. Children using appendicostomy as well as their parents reported higher satisfaction compared to children using TRI. On the other hand parents to children using appendicostomy reported longer time on toilet compared to those of children using TRI. Faecal incontinence was reported lower quality of life than those with appendicostomy. The children with myelomeningocele reported lower quality of life than the normal population.

Conclusion: Transrectal and appendicostomal irrigation are the dominating methods of bowel treatment in children with myelomeningocele in at least parts of Sweden and Norway. Higher parent and child satisfaction was associated with use of appendicostomy, compared to TRI, but there was no significant difference in quality of life. Faecal incontinence was significantly less frequent in the appendicostomy group, but it takes longer time for this group to empty the bowel. Furthermore, the parents reported no difference in the need of support between the two methods of bowel emptying. Families should be included in choice of bowel regime.

S32 Spend a penny independent - a multidisciplinary project
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Background: Today children with long-lasting state of illness including children with myelomeningocele (MMC) reach adulthood to an entire larger extent than before and will set an entitled requirement on participation in the society. A mapping of treatment regimes for children with neurogenic bladder - and bowel disturbances shows that independence in the toilet situation is quite rare despite intensive actions at the hospital and that incontinence is common. A multidisciplinary project to evaluate the obstacles to independence in the toilet situation has been running. The general aim was to develop a strategy, based on the outcome of four of altogether nine studies, to give a possibility for the growing child to gradually take responsibility for itself that may create improvement in quality of life, decrease in costs for continence aids, assistance and healthcare.

Materials and methods: A pilot study has been performed including 16 children, 5-17 years (mean 11 years) with MMC. After consent a visit at the child’s home was performed by an urotherapist and occupational therapist together. After observation of the toilet visit the child was asked to choose to train either the bladder - or the bowel emptying and to set step by step goals to increase independence.

Evaluation: Observation of toilet activity by a standardized manual, COPM (Scale 0 very bad to 10 excellent), CICOPA (Cards with additional pictures showing the CIC) and GAS (goal setting). A timetable for growing up http://www.rbu.se was given to the family together with some questions about the child’s own knowledge about his/her disability. The child’s time perception ability was observed.

Results: After a median of two visits, 8 children reached their goals (+2) and another 5 more than the agreement (+3). The goals were not reached by two children. Participating families emphasized the difference in focussing on the situation at home compared with discussing it in hospital environment.

Conclusion: Actions with an urotherapist and occupational therapist working together in a home setting to reach independence for the child with MMC had better outcome than traditionally performed in the hospital setting. Further children will be included in the study.

S33 The double dutch technique: split ileal graft and double Monti tube in ileocystoplasty
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Background: We introduce a modification of ileocystoplasty combined with double Monti tube. This modification prevents the dog ear of the ileum during detuberalisation and also the Monti tube is supported by the surrounding mesenterium of the ileal augment.

Materials and methods: In 5 patients that needed ileocystoplasty the new technique has been used. Four patients had a small neuropathic bladder, one patient had a small contracted bladder without neurological disorder.

The surgical technique is as follows: 30 or 40 cm ileum is isolated without neurological disorder.

A 16 mm wide strip of ileum is then cut from the top of the right ileal part, and a similar strip is cut from the bottom of the left ileal part. The strips are cut near the mesentery to form the Monti tubes. The small strips are tuberalised and joined in the
middle to form a catheterisable tube. The ileal segments are opened antimesenterially. These ileal flaps are closed over the Monti tube in the middle. The lower part of the Monti tube is implanted with a submucosal tunnel in the bladder wall and the ileal patch is then anastomosed with the bladder. The Monti tube is anastomosed to the umbilicus in an ordinary way without any traction.

Results: All patients have umbilical stomas without leakage or strictures. Intermittent catheterisation is very easy. It seems that the Monti tubes are strait and well supported by the surrounding tissues so that kinking is not possible. The augmented bladders show excellent volume and compliance.

Conclusion: Although we treated only a small number of patients we are convinced that this modification provides advantages during the procedure and produces better results in the future.

S34
Fractures in children and adolescents with spina bifida - experience of a Portuguese tertiary care hospital
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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S34

Background: Some decades ago, patients with myelomeningocele were damned to a short and distressing existence, but nowadays, with medical advances, their life has been prolonged. However quality of life is far from expected in many cases.

The aim of this study was to examine the occurrence and pattern of bone fractures in paediatric Spina Bifida (SB) patients. A literature review about the state of the art of treatment and prevention of secondary osteoporosis in patients with SB was also done.

Materials and methods: We reviewed data of all SB patients, aged 0-18, who have been followed in our SB Nucleus in the last two years. Once the eligible population of patients with SB had been assembled, chart reviews were conducted to abstract data from the health records. After that, each family was contacted, either directly or by telephone call. The parameters examined were: date of birth, sex, level of neurological lesion, type of paralysis, shunted hydrocephalus, shunt revision, syringomyelia, history of prolonged immobilization, the number of fractures and their location, age of occurrence of each fracture and the type of provoking stress. We used MATLAB software (Version 7.1) for all statistical analyses.

To examine the current recommendations regarding osteoporosis and prevention of fractures in paediatric SB patients we searched the Cochrane database, MEDLINE/PUBMED, EMBASE and CINAHL.

Results: The sampling process for this study began with 152 patients; however the inclusion criteria were fulfilled by only 113 patients, who sustained 45 fractures (in 25 patients). These involved predominantly femur or tibia. Statistically significant differences were found between the occurrence of fractures and the clinical ambulation and motor level. The inciting events that lead to fractures are commonly unidentified or are associated with relatively minimal traumas.

Conclusion: Despite the decline of SB in the western world, with consequent lesser scientific demand, we still have to treat patients with this condition. The importance of prevention and treatment of SB-induced osteoporosis is highlighted by our report. The safety and efficacy of drugs to treat osteoporosis in adults have not been evaluated satisfactorily in children with SB. There needs to be a common effort to provide the opportunity to solve this problem through rigorously randomized and controlled designed trials. It isn’t enough to give years of survival, without improving the quality of life.

S35
Urinary calcium excretion in children with spina bifida: correlation to level of lesion, mobility and frequency of fractures?
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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S35

Background: There are numerous methods to measure bone density, all of them are time consuming and expensive. The purpose of this study was to find an easy method to correlate mobility, risk of fractures and level of lesion in patients with spina bifida by using a simple urine test for calcium excretion.

Materials and methods: We collected clinical data and urinary calcium (and creatinine) in 42 and the serum calcium level in 36 patients with spina bifida. We correlated the lab findings to the clinical data (using a standardized questionnaire).

Results: We could not find a correlation between the urinary calcium excretion, the level of lesion, the mobility parameters (ability to stand upright, gait distance) and the frequency of fractures. There is a positive correlation between the serum calcium level, the Hoffer criteria, gait distance and the ability to stand upright in patients with spina bifida.

Conclusion: The urinary calcium cannot be used as an easy method to predict the risk of fractures due to osteopenia. The correlation of serum calcium levels mobility parameters has to be explained by further investigations with more patients and refinements of investigation methods (e.g. additional examination of parathyroid hormone).

S36
Review of cumulative diagnostic radiation exposure during childhood in patients with spina bifida
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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S36

Background: Diagnostic imaging using ionizing radiation is a crucial tool in the management of patients with spina bifida, starting almost directly from birth. During childhood, a patient with spina bifida will have multiple CT scans of the head, Voiding cysto-urethrogram, and X-rays of the limbs and spine. Hence, the patient with spina bifida will have a much greater exposure to
radiation than the average person throughout their lifetime. For a child, the radiation exposure to their immature and developing body can have significant consequences. Experts such as the International Commission on Radiation Protection have described a risk of cancer due to imaging studies that increases with increasing radiation dose. This study describes the magnitude of the exposure to diagnostic radiation in children with spina bifida. Understanding this should help the clinician caring for children with spina bifida to be prudent with the ordering of radiologic studies. It will also help clinicians caring for children and adults with spina bifida to be cognisant that their patients have a significant risk factor for the development of malignancies, especially those known to be related to radiation exposure such as leukaemia and lymphoma. They then can provide timely screening for early detection for these conditions.

Materials and methods: The spina bifida program at Children’s Hospital of Los Angeles cares for well over 600 patients. Out of the portion of the clinic population that is presently 18 years old or older, 30 were chosen randomly as subjects for the study. Inclusion criteria were that they had myelomeningocele and hydrocephalus, and had been receiving their care at CHLA since at least one year of age. Exclusion criteria included any other significant illness not related to myelomeningocele and hydrocephalus, e.g. cystic fibrosis, cancer, congenital heart disease, chronic lung disease etc. The radiologic records for each of the 30 subjects were reviewed and the total number of imaging studies involving ionizing radiation was noted. Using standard values for the amount of radiation involved in each study, each recorded study was converted into a radiation dose, e.g. one CT of the head equals a dose of 4 mSv of radiation. Then the total radiation dose for a patient’s childhood was determined by adding up all of the individual doses. The total dose per patient was then averaged among the 30 subjects, determining the average total dose of ionizing radiation during childhood for a patient with myelomeningocele and Hydrocephalus.

Results: Children with myelomeningocele and Hydrocephalus are exposed to significantly high amounts of ionizing diagnostic radiation, averaging about 50 mSv over 18 years.

Conclusion: Children with myelomeningocele and Hydrocephalus are exposed to large amounts of radiation as part of their medical care and management. Ionizing radiation has been identified as a risk factor for the development of cancer. Children are especially vulnerable due to increased sensitivity of growing tissues, possible long latency period, and smaller cross-sectional areas are exposed. Clinicians should be aware of the magnitude of radiation exposure during childhood for their patients with spina bifida so that they can exercise prudence in ordering studies and screen for possible malignancies.

S38
Fetal operation followed by Caesarean section may have a beneficial effect upon neuromuscular function in spina bifida aperta

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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S38

Background: Spina bifida aperta (SBA) is associated with neurological dysfunction cranial and caudal to the meningomyelocele (MMC). Fetal surgery may ameliorate cranial abnormalities, but effects upon neuromuscular function caudal to the MMC are unclear. SBA myotomes cranial to the MMC are additionally influenced by the MMC. SBA myotomes caudal to the MMC are influenced by cerebral dysfunction, whereas myotomes caudal to the MMC are additionally influenced by the MMC. Increased muscle ultrasound density (MUD) reflects neuromuscular damage. By the intra-individual difference in MUD (dMUD = [MUDcaudal] - [MUDcranial]) the effect by the MMC upon neuromuscular integrity is derived. In the present study, we aimed to compare dMUD and neuromuscular function between fetally and postnatally operated SBA patients.

Materials and methods: We compared dMUD and neuromuscular function in 6 (age- and MMC-) matched pairs of fetally and postnatally operated SBA patients [age 0-3.5 years; lumbar (6) and lumbar-sacral (6) MMC]. In all patients, quadriceps muscle was innervated cranial- and calf muscle caudal- to the
Hypoventilation and sleep apnoea syndromes are

Background: Hypoventilation and sleep apnoea syndromes are associated with increased body mass index (BMI) and Chiari malformation, both of which are common in the spina bifida (SB) population. Despite a number of published case reports, recent literature on the management of SB does not specifically mention such conditions. We discuss the presenting symptoms, aetiology, investigation and outcomes of our affected patients.

Materials and methods: Chart review of patients considered for ventilatory support (n = 6) identified from the database.

Results: Patients complained of a combination of problems, including respiratory symptoms, resistant lower limb oedema, and persistent erythrocytosis. Episodes of unresponsiveness and headache were also noted, and hydrocephalus/shunt malfunction was considered a differential in some cases. Five patients had shunts in place, and four patients had undergone scans confirming Chiari malformation.

Following appropriate investigation, including pulmonary function testing and sleep studies, three patients were commenced on nocturnal ventilatory support, with symptomatic improvement. The remainder are under regular review by the respiratory physicians with a view to future treatment.

Conclusion: A low threshold for further investigation and referral should be employed in SB patients with symptoms suggestive of respiratory dysfunction. Those felt appropriate for nocturnal ventilatory support can have significantly improved Quality of Life and symptom resolution with treatment. Both investigation and treatment are non-invasive and widely available. This is particularly important where symptoms could be attributed to Chiari malformation or decompensation of arrested hydrocephalus, as the patient may avoid the risks attendant to neurosurgical procedures.

[Page 18 of 22]
Expression of p73 in the developing human subcommissural organ

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Background: The subcommissural organ (SCO) is a cerebral structure, formed by an ependymal differentiation of the third ventricle and is composed of two layers of cells: the ependymal layer in contact with the ventricular light and the hypendymal layer just below the posterior commissure (PC). The subcommissural organ (SCO) functions are associated with the circulation and composition of the CSF, which secretes glycoprotein into the CSF where the greater part is condensed and forms Reissner’s fibre (RF), and the other soluble minor part in the CSF. In the human, the development of SCO is greatest during fetal life and also produces glycoprotein but does not form RF. Variations and alterations in the secretion in the SCO have been described in hydrocephalus. p73 is a complex protein with a variety of isoforms, the transactivating isoforms (TA) are able to transactivate p53 gene target and induce apoptosis, whereas the N-terminally truncated isoforms (N) have anti-apoptotic activities. Immuno-blotting of the choroid plexus and cerebrospinal fluid revealed an N-glycosylated form of TAp73, which suggests that p73 may be secreted. The aim of the present work is to analyze the importance of the p73 expression during the SCO development.

Materials and methods: Brains from 10, 12, 21, 22, weeks of gestation, three months postnatal and a 27 year old human, from the collection of the Department of Anatomy of University of La Laguna, were used. Brains were processed using the following standardized form: fixation in formaldehyde, post fixation in Bouin’s fluid for 24 hours, dehydration, and paraffin embedding, thereafter were cut in three (A, B, and C) coronal and sagittal sections 10 μm thick. The A series were stained with Cresyl Violet or Klüver-Barrera. B and C series were immunohistochemically processed using p73 as primary antibody.

Results: The immunoreactive material for anti-p73 was observed at the fetal ages, and the reaction was more intense at 12 weeks in the ependymal layer. At 22 and 24 weeks of gestation the p73 immunoreactive material was observed in both cellular layers and even in the peripheral prolongation, but the intensity of the reaction decreased with respect to the first ages. At three months and 27 postnatal years the reaction is weaker than prenatal ages.

Conclusion: The greatest intensity of the reaction was observed at 10 weeks of gestation which coincides with the moment of the greatest development of the human SCO.

S42

Choroid plexus differences in rats with spontaneous and induced hydrocephalus

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Cerebrospinal Fluid Research 2009, 6(Suppl 2):S42

Background: In hydrocephalus alterations of the brain structures have been described, among them: cortical displacement, cerebrospinal fluid composition alterations and circumventricular structure variations are described and many of these variations could be cause or consequences of the hydrocephalus. The protein p73 is a member of a family of transcription factors and equilibrium between p73 isoforms is necessary for the normal development of the brain and the maturation of the neuroepithelium. On the other hand, the p73 deficiency produces many alterations in the brain that include hydrocephalus. The purpose of this work was to analyze the alteration of the choroid plexus (CP) in different types of hydrocephalus.

Materials and methods: Ten control male rats and ten male rats with spontaneous and induced hydrocephalus were used. The control group was composed of rats sacrificed at 26 and 50 weeks of age and the hydrocephalic rats (6 kaolin-induced hydrocephalus, 4 spontaneous hydrocephalus) rats were sacrificed at the same ages as control. The rats were fixed by vascular perfusion with Bouin’s fluid, dehydrated and embedded in paraffin under standard conditions. Brains were cut into four serial coronal sections. One of the serial coronal sections was stained by the Klüver-Barrera method. The other sections were immunohistochemically processed using anti-p73 and anti-transinthetin (TTR) as primary antibodies.

Results: We found, in the induced hydrocephalus, structural alterations and a decrease in the p73 immunoreactive material when compared to control group. In spontaneous hydrocephalus we did not find great structural variations of the CP however changes in the intensity of anti-p73 reaction were found with respect to the control. The TTR expression varied with the hydrocephalus, in control rats it was clearly observed in the CP and was increased in spontaneous hydrocephalus.

Conclusion: The obstructive hydrocephalus causes CP morphology alterations and a decrease in the p73 and expression, contrarily the CP, significant structural variations in the spontaneous hydrocephalus were not found. Furthermore, some changes in the intensity of anti-p73 and anti-TTR were found and these variations could precede the onset of the hydrocephalus.
S43
A Swedish national follow-up programme for children and adolescents with myelomeningocele
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Background: In 1998 a Swedish national follow-up programme for children and adolescents with myelomeningocele (MMC), with focus on neurogenic bladder and bowel dysfunction was launched. In 2004, 600 children and adolescents with MMC from 0 - 18 years of age were included in the programme and the needs for further medical follow-up after transition into adulthood for the cohort born 1986 - 89 has been presented (Olsson et al 2007). A subgroup of 39 children with MMC in the south-east region of Sweden born 1993 - 2003, was evaluated (Wide et al 2007), showing a high success in preventing renal damage when keeping to the proactive follow-up programme. The programme was evaluated and revised, now enlarged to include also other areas for follow-up e.g. neonatal care, gastroenterology, orthopedics, neurosurgery, endocrinology, cognition, sexuality, latex allergy, transition etc, also including guidelines for physiotherapy and occupational therapy. The programme will also include a national MMC-register. The aim is to get standardize evidence based national recommendations for the follow-up of children and adolescents with MMC from birth into adulthood.

Materials and methods: A network of professionals working with children with MMC has presented guidelines as far as possible evidence based, for the different areas of follow-up. Editors are neuro-pediatricians from the six university hospitals in Sweden. Regular cohort studies are planned for every 3-4 year period to follow the future development of the total MMC-population in Sweden.

Results: The first chapters are available on Internet (blf.net; neuropediatrik, vårdprogram) on the site of the Swedish Neuro Pediatric Society, SNPF. A national register is under construction.

Conclusion: The Swedish national follow-up programme from 1998 for children and adolescents with neurogenic bladder and bowel dysfunction is after evaluation and revision, enlarged to include all aspects of follow-up for children and adolescents with MMC. The programme was launched January 2009 and is available on the Internet.

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S44
A 50 year natural history of an untreated myelomeningocele - a rare case
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Case report: An almost 50 year old woman, admitted to our clinic very recently, born with a small lumbo-sacral myelomeningocele (MMC), bilateral pes equino-varus and paralysed feet. The father refused any treatment. However, she survived, grew up, became able to walk with crutches and to bicycle. Bladder emptying was by means of abdominal pressure, later by means of a Bricker-bladder. She went through ordinary school and further education, but lost gradually walking ability and became wheelchair-bound. She became married and had two healthy children by Caesarean section. She is now employed as leader of the secretariat in an educational institution on normal conditions. In the meantime the MMC has grown slowly to the actual size of approximately 60 × 40 × 30 cm. She can lie on both sides, but most of her life is in the sitting position. She now asks for surgical treatment. Because of time, we haven’t done surgery yet, and because of contractures in hips and knees and the size, we will have to drain the MMC before MR scan to plan the operation that will take place in April. Subsequently we will have to deal with the potential hydrocephalus (VP-shunt? 3rd ventriculostomy?).

S45
Changing needs for children and adults with spina bifida and hydrocephalus in Northern Ireland
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Background: The needs of persons born with Spina Bifida (SB) and/or Hydrocephalus (H) may change with age. ASBAH has in response to this sought the views of persons with Spina Bifida (SB) and/or Hydrocephalus (H) on its Northern Ireland database, to identify what the different needs may be. The results indicate that with the transition from childhood to adulthood there is a change in the perceived need.

Materials and methods: Postal questionnaire sent out from ASBAH to all persons with SB and/or H on its Northern Ireland database.

Results: 770 questionnaires were distributed and 134 (17%) were returned. 98 adults (M:F 45:51) and 36 children (M:F 18:18) responded. The main issues raised by the adults were, personal care and support (12.5%), problems with accessibility (12.5%), increased benefits/better income (15%), transport difficulties (20%), finding employment (5%), help socialising (12.5%) and adaptations and equipment (10%) Within the children’s responses, the main issues identified were personal care and
Support (17%), problems with accessibility (17%), increased benefits (17%), transport (17%), better medical care (10%), lack of friends (10%), help socialising (6%), and adaptations and equipment (6%). In both groups, these needs were identified as areas where study days would be of benefit to both children, their parents and to adults.

**Conclusion:** This survey confirms that as persons born with SB and/or M move from childhood to adulthood there is a perceived change in their needs that has to be addressed. The changing need is a reflection of the difficulties in maintaining a position within society when born with Spina Bifida and/or Hydrocephalus. It identifies areas where services should meet this changing need.

**S46**

**Tethered cord - a new animal model**

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**Background:** Children with myelomeningocele (MMC) are at risk of losing skills if they develop tethered cord syndrome. It’s an ongoing discussion to do prophylactic tethered cord release or wait until the child develops symptoms. To learn more about tethered cord, we have developed a novel tethered cord model in pigs.

**Materials and methods:** Four 20 kg pigs (approximately 8 weeks old) underwent hemi-laminectomy on the 2nd segment of the sacral bone. Microsurgical dura opening was done in 1 sham pig and medulla was tethered in the remaining three. All four pigs underwent MRI using a clinically available 1.5 T magnet prior to surgery 2 weeks postoperatively.

**Results:** At follow-up all pigs were asymptomatic. MRI demonstrated no structural or pathological changes in the sham pig. In all three operated pigs, the spinal cord was tethered at the 2nd segment of the sacral bone. Furthermore, MRI revealed subclinical constipation in two of our pigs.

**Conclusion:** The result of this study supports our view that a porcine animal model with tethered cord may be useful in investigation of tethered cord in MMC.

**S47**

**A single-unit survey of bowel washout practice in children with neuropathic bowel**

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**Background:** The majority of children with spina bifida require medical assistance to eliminate socially disabling faecal incontinence. Having recently surveyed units across the UK and Ireland on their practice of bowel washouts (see abstract S30), we wished to evaluate our own (largely traditional) programme in more detail.

**Materials and methods:** Patients receiving bowel washouts were captured from the regional departmental database of 165 children (aged 0-18 years) with spina bifida, and a database of others attending the Continence Nurse Specialists. Parents were then contacted by telephone, and/or the child’s records reviewed, to complete a questionnaire on their individual practice.

**Results:** Ten patients with spina bifida, and six with other “neuropathic” conditions (anorectal malformation, Hirschsprung’s disease and chronic constipation) were identified. The mean age at which bowel washouts were instituted was 11.0 (range 4-18) years, and the mean interval since was 3.1 (range 0.3-8) years. An initial washout volume of 500 ml was prescribed for all children and, in some cases this was titrated according to effect. Salt was added to tap-water to approximate an isotonic solution for all washouts. In the washout solution twelve children required a laxative (sodium citrate in 11, and bisacodyl in one), while four did not. Rectal washouts were all administered via a balloon-catheter (Coloplast’s Peristeen system in 7 children), and most ACE washouts via a “gastrostomy” button-device (7 children).

The most common side-effect was abdominal cramping, particularly with bisacodyl or if the previous washout had been omitted. The time spent on the toilet after administration of the washout varied from 30-90 (mean = 53) minutes, with a tendency to be longer in those with larger washout volumes. All children were established on a daily washout, and then the interval between washouts was gradually increased, unless incontinence returned: 13 children still required once-daily washouts, but three other children remained socially clean with a washout every other day, three-times per week, and twice per week respectively (the latter on bisacodyl).

The chief difficulty for both children and parents was the time commitment, although this was more than offset by the improved quality of life.

**Conclusion:** Bowel washouts are a very effective treatment for neuropathic bowel. Although our numbers are small, the increased tendency to abdominal cramps seen with bisacodyl appears to be justified if it reduces the weekly-time spent on the toilet, which is the main complaint by users.

**SESSION REPORTS**

**S48**

**Experimental Hydrocephalus Pre-meeting 24th June 2009**

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This was the 9th session on animal hydrocephalus held since they were initiated in Atlanta, USA in 2000. The aim has been to give researchers who are presenting animal studies at the main meeting, the opportunity to present their work in an informal atmosphere with time for feedback and useful discussion from the audience which usually amounts to 20 - 40 people. This year the first talk was from Pat McAllister (University of Utah) on
“CSF and Capillary Pulsatility in Hydrocephalus” in which he described some MRI experiments to measure the CSF stroke volume in the aqueduct of hydrocephalic rats using a 9.4 Tesla magnet. He went on to report measurements of the capillary pulse index in normal and hydrocephalic rats, using a 2-photon laser scanning microscope through a cranial window with promising results. The second talk was by Dorte Clemmensen, Neurosurgery, Aarhus University Hospital, on “Experimental Tethered Cord - a New Model”. Tethered cord is a big problem in children with myelomeningocele and this group has been working to produce a pig model for future study. Using kaolin injections into the spinal cord they have been following the effects with MRI and are on the verge of success. The third talk was by Agustin Castaneyra-Perdomo, Universidad de La Laguna, Tenerife, on “Arterial Hypertension Effects on Choroid Plexus brain barriers”. He described experiments to identify CSF and choroid plexus changes in the spontaneously hypertensive rat (SHR). Some proteins, S100β, transthyretin and α1 antitrypsin were increased in hydrocephalus but many others were decreased. He suggested that the proteins behave similarly to Alzheimer’s disease markers and that the SHR rat has disturbances of the blood brain and blood CSF barriers.

After a coffee break, Conrad Johanson, Brown University, spoke on “Molecular, Cognitive and Epigenetic Profiling for Aging Models: Implications for Hydrocephalus and Neurodegeneration”. He explored the idea that changes in the CSF with aging may threaten ongoing neuroregeneration in the subventricular zone and dentate gyrus, particularly in relation to changes in Aβ, the transporters RAGE and the glial markers, GFAP and OX6 increased with age whereas BRDU, the marker for cell division decreased. Aging rats performed less well on the Morris water maze test. He argued that there is a case for early intervention to prevent the cascade leading to Alzheimer’s disease. Pat McAllister gave the next talk entitled: “Neuro-inflammation in Neonatal Hydrocephalus”. In a rat model with communicating hydrocephalus induced by kaolin, inflammatory cytokines were found in the cerebral cortex only. Using a more extreme model of hydrocephalus by induction at 1-2 days, they studied gene expression in the cerebral cortex using micro arrays and unique probe sequences. They found that out of 41,012 sequences 1,824 were changed at least 1.5 fold. Further analysis identified specific gene categories and individual genes that were affected. This was followed by the last talk by Janet Miller, Central Michigan University, “In Hydrocephalus, do Protein Levels Correlate with Gene Expression?” Janet has followed up her previous study using the H-Tx rat with inherited hydrocephalus where a number of genes had been shown to be linked to hydrocephalus. She argued that a more direct and potentially useful approach would be to study protein expression and using blotting techniques investigated the protein products of the altered genes found in the expression study. Interestingly, the direction of protein expression was often either opposite to the gene expression or showed no change.

Overall, this proved to be a most interesting morning provoking much discussion and we hope useful feedback for the presenters.

S49
Long-term management of children with spina bifida: commentary on the nurses break-out session, June 26th
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The breakout session was aimed to be an informal networking opportunity for nursing staff and other health care professionals, aiming to improve the care of children with spina bifida. The session went very well and the evaluations were very positive. The first session was from Marie McGonnell, our local ASBAH advisor. She gave an outline of her invaluable role as a support for the families especially prenatally. Following coffee, Mary White gave a talk on catheterisation in schools. This was very interesting and provoked a lot of discussion on how each centre managed their children with neuropathic bowels with regard to catheterisation. Marie McGrogan (the Coloplast representative for Peristeen), Laura Connolly and Emma Kelly gave a presentation and case discussion on Peristeen rectal irrigation system. This preceded a discussion on the management of neuropathic bladders. To conclude the session, one of the senior Physiotherapists in RBHSC, Finola Beattie gave a presentation on how children with spina bifida are managed their physiotherapy and mobility. Finola had video footage of children in the gym which provided the nursing staff a great insight into the invaluable role of the physiotherapy. All in all, the session was very well received and provided a forum for discussion and learning.