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SUPPLEMENT PREFACE

S1
49th Annual Meeting of the Society for Research into Hydrocephalus and Spina Bifida

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S1

The 49th Annual Meeting of the Society for Research into Hydrocephalus and Spina Bifida was held in Barcelona, Spain, from 29th June to 2nd July 2005. We are especially grateful to Amparo Cuxart and Esther Pages who, together with their team, made us all very welcome.

The city of Barcelona has much to offer, from the medieval elegance of the Gothic Quarter, to the rather more idiosyncratic architecture of Antonio Gaudi. Nor should it be forgotten that Picasso who spent much of his working life in Paris, was a Spaniard, who lived for many years in Barcelona.

Barcelona is the main Catellan city, and we were treated to a feast of Catellan history, culture and language, as well as the more modern icons who play for Barcelona FC.

The scientific sessions, held in the comfortable venue of the Hospital Universitari Vall d'Hebron, produced a great variety of topics, from cutting edge scientific research on hydrocephalus to very valuable work on the functional problems of children with spina bifida. Undoubtedly the highlight of the scientific programme was the Casey Holter Lecture given by John Mazur. John treated us to a fascinating insight into the orthopaedic management of patients with spina bifida, and brought to the task a working lifetime of experience.

Finally a warm welcome was extended by Hugh Richards, to the 50th Annual Meeting which will be held in Cambridge, England from 30th August to 2nd September 2006.

ORAL PRESENTATION

S2
Progression and reversibility of gliosis due to hydrocephalus in the H-Tx rat

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S2

Background: Persistent gliosis, if present in shunt-dependent hydrocephalus, has the potential to alter the biomechanical properties of the brain, impair cerebral perfusion, and impede neuronal regeneration and plasticity. Determining the onset, progression, and reversibility of gliosis due to hydrocephalus is important in designing and implementing better clinical treatments for this disorder. Thus, gliosis was studied as the severity of hydrocephalus increased in five, twelve and twenty one day old untreated H-Tx rats with congenital hydrocephalus and control littermates. Previous clinical and experimental studies have suggested that gliosis may persist after shunting, but these findings have been based on relatively short post-shunt survival times.

Materials and methods: In an effort to determine the effects of post-shunt recovery time on hydrocephalus-induced gliosis, we placed neonatal low-pressure ventriculo-subcutaneous shunts in 15 day old H-Tx rats with severe hydrocephalus, and sacrificed these animals 1 or 3 weeks later. Tissue from different regions of the cerebral cortex was processed for routine immunohistochemistry and Western blot procedures, and probed for both microglial (Isolectin B4, ILB4) and astrocytic (Glial Fibrillary Acidic Protein, GFAP) proteins.

Results: Western blot analysis revealed a marked increase in GFAP protein in both the occipital and parietal cortices of 12 day old hydrocephalic animals, suggesting that an increase in pressure was the trigger for the onset of gliosis. The dramatic rise in GFAP expression continued to be seen in both 21- and 36-day old untreated hydrocephalic animals as well. Shunting these hydrocephalic animals in order to reduce the increased intracranial pressure had a significant effect; both short and long recovery periods were able to reduce the amount of gliosis present, indicating that shunting is an effective treatment for reversing persistent gliosis. Immunohistochemical examination of GFAP followed similar up-regulation trends as seen in the Western blot analysis.

ILB4 blots indicated that in young hydrocephalic animals (5 & 12 day animals) there was a trend toward up-regulation of microglia in response to hydrocephalus, but from day 21 and beyond, microglia levels *decreased* in response to injury. Shunted hydrocephalic animals exhibited microglia levels similar to those of control animals. On histochemical examinations, microglia appeared to be developmentally delayed in young

hydrocephalic animals, and in the older 21 and 36 day hydrocephalic animals, they exhibited an activated morphology. Morphologically, microglia in shunted animals appear to be in a state of recovery; i.e. they are not as activated as in hydrocephalic animals, but still show some signs of reactivity.

Conclusion: Overall, these results suggest that reactive astrocytosis and microgliosis are associated with progressive untreated ventriculomegaly, but that appropriately timed shunting can reverse most of these effects. It remains to be seen, however, if gliosis behaves the same with persistent shunt malfunctions.

S3
Myelomeningocele in fetal rabbit: effect of preterm delivery and corticosteroid treatment

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S3

Background: Damage of neural elements in myelomeningocele seems to be progressive during gestation because of amniotic fluid chemical contact. Corticosteroids administration and preterm delivery seem to improve the outcome in gastroschisis (bowel exposition to amniotic fluid) We studied the effect of preterm delivery and corticosteroid treatment in a model of myelomeningocele (MMC) in the rabbit fetus.

Material and Methods: Twelve New Zealand White rabbits underwent laparotomy and hysterotomy at 23 days of gestation. Fifty-nine out of 107 fetuses underwent lumbar laminectomy (3 to 4 levels). Dura was opened to expose the neural elements to the amniotic fluid. Six rabbits underwent caesarean section on gestational day 31 for fetal harvest; three of them had no treatment (group T) and three received costicosteroid treatment (group TC). The other six rabbits underwent caesarean section on gestational day 29 for fetal harvest (preterm delivery); three of them had no treatment (group P) and three received costicosteroid treatment (group PC). Alive newborns were clinically, neurophysiologically and histologically analyzed.

Results: None of mothers died during the procedure. After birth, newborns show lower weight and higher vitality in corticosteroids treated groups (TC and PC). Deformity of lower extremities was less important in groups TC (Term and Corticosteroids) and P (Preterm) and no deformity was observed in group PC (Preterm and Corticosteroids). Lower kyphosis was observed in group PC (Preterm and Corticosteroids). Pain related and spontaneous mobility of lower extremities was higher in groups treated with costicosteroids (TC and PC). Only newborns at term (T and TC groups) show response to evoked potentials (CMEP's). The response was early and higher in group treated with corticosteroids (TC). Histologically, we observed progressive lesion of the spinal cord. Groups treated with corticosteroids (TC and PC) show less inflammatory response. Arnold Chiari Malformation was present in all groups.

Conclusion: Preterm delivery and prenatal corticosteroid therapy seem to be an effective treatment to decrease neural injury in myelomeningocele fetuses. More studies in this line are required to obtain consistent conclusions.

S4
Gene alterations associated with closure of the cerebral aqueduct in hydrocephalic H-Tx rats

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S4

Background: To elucidate the pathogenesis of congenital hydrocephalus we utilized gene array technology as well as quantitative real-time PCR, to identify specific genetic components which act to influence the closure of the cerebral aqueduct in the H-Tx rat.

Materials and methods: Midbrain regions which contain the cerebral aqueduct were micro-dissected from hydrocephalic and control animals at 5 days of age (n = 5). After RNA extraction and purification, total RNA was subjected to PCR techniques to generate cDNA that was subsequently labeled and hybridized (one brain per array) to the Rat 230 A oligonucleotide array from Affymetrix. Hybridization intensity for each array was measured using a confocal scanner, and results were normalized and reported as fold change differences. Raw expression data were subjected to a Student's t-test as well as the Bayesian t-test, which is a method that helps control for variations resulting from small sample size. Only those transcripts passing both the fold change of 1.5 fold and t-test cut-offs ($p < 0.05$) were examined further.

Results: Forty-seven transcripts passed significance using our filtering criteria. Of these, 17 transcripts were up-regulated and 30 were down-regulated. These were grouped to a variety of different functional categories including transcription and translation, but also to other categories not typically associated with genetics such as vitamin transport, bone and tooth development. Some of the significantly altered genes correlated with literature found on earlier studies of hydrocephalus and were selected for further examination using quantitative real-time PCR. These were Cholecystokinin (Cck), a lectin (Lgals3), Tissue Factor Pathway Inhibitor 2 (Tfpi-2), Tumor Necrosis Super Family Member 4 (Tnfsf4), Pax-6 and Xanthine Dehydrogenase (Xdh). qrt-PCR results revealed significant changes in two genes Lgals 3 and Xdh while others failed to achieve statistical significance most likely due to sensitivity limits of the test.

Conclusion: These results suggest that gene alterations occurring in the midbrain region may act to cause aqueductal stenosis in this rat model. It is notable that out of nearly 7,000 predicted genes of the rat, only 47 transcripts were significantly altered in this gene array study. Of these, 8 already had known associations to hydrocephalus. Narrowing the entire genome down to 47 significant transcripts that may act to cause aqueductal stenosis greatly narrows the focus for future studies, and identification of these genes provides a first step in attempting to reduce the occurrence of this disorder in humans.

S5

In moderate communicating hydrocephalus of human fetuses, ependymal denudation is a common feature that may result in abnormal neurogenesis

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Background: Recent investigations carried out in natural and experimental mutant mice have provided strong evidence that a primary alteration of the ependymal cell lineage triggers a moderate foetal hydrocephalus [1, 2]. In human cases of hydrocephalus, however, ependymal loss has been regarded as resulting from the ventricular dilatation due to the accumulation of cerebrospinal fluid [3].
Materials and methods: The present investigation was carried out in 16–40 week old human foetuses with a communicating hydrocephalus and displaying a moderate dilatation of the ventricular cavities (n = 8), and foetuses of similar ages with no neuropathological alterations (n = 15). Paraffin sections throughout the walls of the cerebral aqueduct and lateral ventricles were processed for lectin binding and immunocytochemistry using ependyma, astroglia, neuroblasts and macrophague markers.
Results: Large areas of ependymal denudation were found in the aqueduct and lateral ventricles of all foetuses developing a communicating hydrocephalus. At variance, no ependymal detachment was observed in non-hydrocephalic foetuses. In the youngest foetuses with hydrocephalus, denuded areas were not covered by astrocytes or other organized cell elements, leaving the neuropile directly exposed to the ventricular lumen. The area devoid of ependyma increased as the foetus developed. In the oldest foetuses studied, the denuded areas of the lateral ventricles were lined by a dense plexus of astrocytes. Under the denuded surface the presence of ependymal rosettes was observed. In the denuded areas of the lateral ventricles of hydrocephalic foetuses it was found (i) a loss of the germinal ependymal zone, (ii) disorganization of the subventricular zone and, (iii) abnormal migration of neuroblasts into the ventricular cavity.
Conclusion: The early loss of ependyma in human hydrocephalic foetuses would be associated to both, the hydrocephalic process and an abnormal migration of neuroblasts.

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S6

Aging rat brain: a model for analyzing interactions among CSF dynamics, ventriculomegaly and the β-amyloid retention of alzheimer's disease

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S6

Background: Age-associated disruptions in brain barrier systems (including choroid plexus) lead to multiple problems for CSF turnover and brain interstitial fluid composition. Age is a great risk factor for Alzheimer's disease (AD). We have presented evidence that beta-amyloid (Aβ) retention in AD is linked to decreased CSF turnover and reduced Aβ transport out of human brain. It is also known that CSF formation is reduced in aged rats (Preston et al.).
Materials and methods: To extend this model, we sought evidence to confirm the postulated Aβ retention in the brain of old animals. Brown-Norway/Fischer (B-N/F) rats, at 3 mo (young adult) and 30 mo (advanced age), were used to characterize the presence of Aβ 1–42 fragments in various regions of CNS. Immunohistochemistry was used to assess the degree and localization of Aβ 1–42 both the cerebral cortex (CC) and lateral ventricle choroid plexus.
Results: In the young adult B-N/F animals, there was negligible Aβ 1–42 staining in the CC. In contrast, there was substantial amyloid staining, primarily in neurons, in the 30-mo-old CC. At the blood-CSF barrier, the choroidal epithelium displayed some Aβ 1–42 staining even at 3 mo, suggesting reabsorptive clearance transport of this peptide fragment from the CSF. However, in the 30-mo rats, there was increased staining of the amyloid 1–42 in the plexus.
Conclusion: These findings point to a greater burden of Aβ in the CNS as the result of advanced aging. Thus, this accumulating Aβ in cortical and choroidal tissues is consistent with the independent observations of a slower flow of CSF in older animals. The parallel findings of Aβ retention and CSF slowing, in aged rats vs. human AD subjects, encourage further mechanistic studies in B-N/F animals to delineate functional relationships among Aβ transport, CSF formation/volume, and Aβ retention in hippocampal and cortical regions.

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S7

The importance of cerebrospinal fluid on neural cell proliferation in developing chick cerebral cortex

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S7

Background: A key event in the development of mammalian cerebral cortex is the generation and differentiation of neuronal population during embryonic life. Cerebrospinal fluid (CSF) is produced by the choroid plexuses within the ventricles of the brain. The CSF circulates in a regular manner after the ventricular system and the choroids plexuses have developed, and the foramina in the 4th ventricle have opened to enable it to carry chemical information. CSF flows through the ventricular system passing over all regions of germinal activity. The central nervous system (CNS) of vertebrates originates from neuro-epithelial cells located within the embryonic neural tube. Several mitogenic and trophic factors have been implicated in the processes of cortical cell proliferation and differentiation. These include fibroblast growth factor (FGF), insulin growth factor (IGF) and other neurotrophic factors. FGF promotes the proliferation of stem cells isolated from the brain and direct them toward specific fates. Stem cells are highly plastic, with their proliferation and differentiation potential dependent on different growth factor treatments. It was shown *in vitro* that brain-derived neurotrophic factor (BDNF) and glial-derived neurotrophic factor (GDNF) have positive effects in promoting neural progenitor cell differentiation towards the dopaminergic phenotype. In the subset of progenitor cells, FGF2 is necessary in early G1 to promote commitment to a subsequent cell cycle.
Material and Methods: In this study chick embryos were used to show the importance of CSF on neural cell proliferation in the developing cerebral cortex. The chick embryos were cannulated *in situ* with a fine capillary tube to drain CSF out of the ventricular system. At the same time, BrdU was administered to the embryos. After surgery the embryos were incubated for another three days. All the CSF-drained and control embryos were collected, fixed in paraformaldehyde and cut on a microtome and stained with Methyl Green Pyronine and anti-BrdU antibody.
Results: Quantitative measurements showed that the thicknesses of the germinal epithelium and cerebral cortex in CSF-drained embryos were less than those in the control group at the same age (n = 20 for each group). The number of cells produced in the germinal epithelium of CSF-drained embryos was decreased when compared to the normal group.
Conclusion: This study provides confirmatory evidence that CSF is important for neural cell proliferation.

S8

An alteration of the subcommissural organ (SCO) leads to aqueductal stenosis and hydrocephalus

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S8

Background: In all species developing congenital hydrocephalus in which the SCO has been investigated, changes in the SCO-Reissner fibre (RF) complex have been reported. However, the question whether these changes precede hydrocephalus, or are a consequence of it, has not been fully clarified. We have reported that in the rat, the maternal transfer of antibodies against RF-glycoproteins to the foetuses and to the pups prevents RF formation and leads to aqueductal stenosis and hydrocephalus [1]. This finding gave support to the early hypothesis of Overholser et al. [2] who had proposed that a maldevelopment of the SCO may result in hydrocephalus. We have now designed new experimental protocols to further test this hypothesis.
Materials and methods: Since in the rat the first RF is formed around PN-7, we designed a protocol for the postnatal immunoneutralization of the SCO. Antibodies against RF-glycoproteins were perfused into the CSF at PN-2 and PN-5. At PN-30, 74% of these rats were devoid of RF, had aqueductal stenosis and had developed hydrocephalus. A different strategy has been the study of the SCO in two mutant species developing congenital hydrocephalus, the hyh mouse and the HTx rat. During the first postnatal week the SCO of normal hyh mice forms the first Reissner fibre whereas that of the hydrocephalic littermates does not; the absence of RF preceded the obliteration of the Sylvius aqueduct and the development of a severe hydrocephalus. Similarly, the HTx rat lacks a RF despite having an active SCO. Since the absence of RF appears as a key event in the development of hydrocephalus, studies were performed to clarify the mechanism responsible for the lack of formation of RF.
Results: It was found (i) that the SCO of hyh mice has a decrease expression of SCO-spondin, the main constituent protein of RF; (ii) an alteration in the pattern of the secretory proteins present in the SCO, suggesting an abnormal processing or degradation. We have succeeded to detect and identify, for the first time, the SCO secretory proteins present in the CSF. It was found that the SCO of the hyh mice and the HTx rats secretes abnormal CSF-soluble proteins, and in the case of the HTx rats these proteins were more abundant. This is surprising since in the HTx rat only the supracommissural portion of the SCO develops; this implies that only about 20–30% of the secretory cells present in this mutant account for the increased quantity of secretory proteins present in the CSF. In the HTx there are SCO secretory products that are present in the ventricular CSF and missing from the subarachnoidal CSF. Thus, the CSF of both hydrocephalic species presents abnormalities in the quantity and quality of the SCO secretory proteins. Preliminary evidence indicates that CSF of children with congenital hydrocephalus contains secretory proteins which are missing from the CSF of non-hydrocephalic children.
Conclusion: 1. A primary alteration in the SCO of the mutants hyh and HTx leads to: (i) a modification in the expression of its secretory proteins; (ii) an alteration in the processing of these proteins which, once released into the CSF, do not aggregate normally, resulting in the absence of RF and in the presence in the CSF of abnormal forms of such proteins. 2. The subarachnoidal CSF of HTx rats does not contain certain

SCO secretory products. 3. Detection in the human CSF of compounds that would correspond to SCO secretion may open a new field of research in human congenital hydrocephalus.

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S9
Clinical and neuropathological evolution of the hydrocephalus developed by the mutant mouse hyh

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S9

Background: The hyh (hydrocephalus with hop gait) mutant mice develop inherited hydrocephalus. A key feature in this mutant is that there is a foetal-onset ependymal denudation which precedes cerebral aqueduct obliteration and hydrocephalus [1]. Recently, a point mutation in alpha-SNAP protein has been identified as responsible of the hyh phenotype [2]. However, preliminary findings from our laboratory have suggested clinical and pathological heterogeneity in the expression of hydrocephalus, indicating that other (nongenetic?) factors may influence the degree of severity of this pathology. This is in accordance with findings in other hydrocephalic mutant strains [3, 4]. The present investigation was designed to (a) study the clinical evolution of hydrocephalic mice in order to evaluate wether or not clinical heterogeneity does actually occur, (b) identify nongenetic factors (maternal age, multiparity) that may affect such an evolution, and (c) identify neuropathologic events underlying clinical heterogeneity.

Materials and methods: Mice of the hyh strain (B6C3Fe-*a/a-hyh*) were used in this investigation. The expression of hydrocephalic phenotype was studied in 1690 hyh mice (231 litters). The clinical evolution of hydrocephalic mice was achieved following up 79 postnatal (PN) hydrocephalic mice, from PN-1 to PN-180. Brain samples of hydrocephalic and non-hydrocephalic mice were studied at different developmental stages with several methods, including light microscopy, immunocytochemistry and scanning electron microscopy.

Results: In agreement with a monogenetic mendelian recessive disease, 22.4% of newborns developed the hydrocephalic phenotype. The male:female ratio was 1 in non-hydrocephalic mice and 2 in hydrocephalic mice. Multiparous females, as compared to primiparous, had litters with a significant reduction of both, frequency of hydrocephalus and sex ratio. Maternal age did not affect these parameters. Two mortality profiles were identified: (i) 70% of hydrocephalic mice died during the first 8 postnatal weeks and (ii) 30% died during the following months with more than 10% still surviving up to 7 months. The degree of severity of the pathology, as evaluated by the rates of body weight increase and mortality, was higher in males than in females. These results lead us to identify two major forms of clinical evolution, namely (a) rapidly progressive, and (b) slowly progressive. The neuropathological analysis showed that during the first 2 PN months the severity of hydrocephalus was variable ranging from moderate (communicating) hydrocephalus to a very severe (non-communicating) hydrocephalus. A common feature to all pathological groups was ependymal denudation. However, these groups differ in several aspects such as (i) precocity of the onset of aqueductal obliteration; (ii) nature and degree of alterations of periventricular structures, such as the hypothalamus; (iii) presence or absence of spontaneous communications between ventricles and subarachnoid space; (iv) intraventricular haemorrhages and (v) mesencephalic compression. Aspects i, iv, and v showed a high correlation with early mortality, whereas spontaneous ventriculostomies together with the absence of ventricular haemorrhages were associated with a less severe or arrested pathological process leading to a long-term hydrocephalus.

Conclusion: It is concluded that (1) there are nongenetic (epigenetic) factors related with maternal multiparity (hormones? lactation?) that influence the expression of the mutation, (2) there are sex-related factors (genetic? hormonal?) that determine a higher frequency and severity of the disease in males, (3) there is a correlation between early or late mortality and the nature of the CNS alterations, and (4) the hyh mutant appears as a unique animal model to investigate long-term hydrocephalus.

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S10
Bridging health care gaps for new survivors – a total population study of young persons with MMC

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S10

Background: Since the number of newborns with myelomeningocele (MMC) is decreasing a national network of neuropaediatricians with long experience of MMC has been founded in Sweden. Our first task was to identify the areas of medical concern in adolescents with MMC.

Materials and methods: A total national population study has been performed. The first analysis concerns those born 1986–89 and is based on review of medical records.

Results: 175 adolescents born 1986–89 were living in Sweden on July 1st 2004, 86 females and 89 males. Their special medical characteristics are presented in Table I. Single symptoms and

Table 1 (abstract S10)

Individuals with MMC	No	%		No	%
Mental retardation (MR)	46	26	Recurrent urinary tract infections	27	15
Active epilepsy	24	14	CIC	149	85
Hydrocephalus	150	86	Anticholinergic medication	70	40
- Shunts	145		Surgery (eg Mitrofanoff)	42	24
- Ventriculocisternostomi	5		Incontinence pads	125	71
Tethered cord syndrome (Op)	62	36	Reduced kidney function	3	1,7
No independent walking indoors	92	53	Anal water irrigation	103	59
Walking with aids	35	20	MACE	17	10
Walking independently indoors	47	27	Gastrostomy	6	3,5
Orthopedic surgery/ortoses	128	73	Respiratory aids	5	3
Scoliosis (operated 44)	74	42	Recurrent bedsores	34	19

signs specifically/not specifically related to the MMC were recorded but not presented here.

Conclusion: In Sweden approximately 40 adolescents with MMC will yearly reach adulthood the next decennium. A majority of them will have medical problems with need for a multidisciplinary team approach in order to supply the best care in adulthood.

S11
Survey of individuals with spina bifida in Maryland, USA, 2004

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S11

Background: The Chesapeake-Potomac Spina Bifida Association (CPSBA) conducted a survey of individuals with spina bifida (SB) in Maryland during the first half of 2004 in order to assess their current status and unmet needs. The survey was sponsored by the Maryland State Office of Genetics and Children with Special Health Care Needs (OGCSHCN). The findings of this survey are to be used to inform programs and services and to identify the most important self-perceived challenges faced by individuals with spina bifida in the areas of health, education, daily living and employment and to determine areas of unmet service need.

Materials and methods: A survey questionnaire composed of structured and semi-structured questions was developed with input from CPSBA, two regional SB centers, and OGCSHCN. Surveys were to be completed by the individual with SB or a caregiver. Prospective survey participants were identified using merged contact data from the two SB centers, two local chapters of the Spina Bifida Association of America and CPSBA (a regional affiliate), and OGCSHCN. Surveys were mailed to 644 potential survey participants. Of those, 125 (19.4%) returned the survey.

Results: Of respondents, 49.6% were female, 73% were White, 7% Hispanic, 15% African-American, 2.4% Other. Mean age was 17.2 years with 15% aged birth to 5 years, 22% were 6–12 yrs, 34% were 13–21 yrs, and 22% were 22–59 yrs. Self-reported diagnosis was myelomeningocele in 80%, 81% were shunted, and 33.6% were totally wheelchair dependent for mobility. The top 3 problems across all age groups were lack of control of bowels (74%), lack of control of bladder (72%), and public ignorance about SB (71%). Other problems reported by more than 50% included lack of recreation/sports activities, inadequate social life, emotional stress among family members, lack of information about resources, cost of medical equipment and supplies and cost of health care services not covered by insurance. Of individuals 18 years and older (N = 54), 68% completed high school, 24% went on to some college, and 11% obtained a college degree, yet 39% were totally unemployed. Common health problems included pressure ulcers, depression, and obesity. Self-perceived overall quality of life was excellent in 31%, good 48%, fair 17%, and poor 1%.

Conclusion: Individuals with SB are aging. Most have good or excellent quality of life yet there are a number of common challenges that have not yet been overcome including continence, social and community integration.

S12
Long term prognosis of fetal hydrocephalus

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S12

Background: In japan, 55% of the patients with congenital hydrocephalus are diagnosed prenatally as fetal ventriculomegaly, as result of advances in prenatal imaging techniques. However the clinical and ethical problems of fetal hydrocephalus continue to be unsolved. The aim of this paper is to clarify these problems.

Materials and methods: forty three patients(25 males and 18 females) with fetal hydrocephalus underwent surgery from 1982 to 2005 in our department. The patients were classified based on the basic disease and associated anomaly.

Results: The result of the classification were, 6 patients with simple hydrocephalus, 11 patients with myelomeningocele(MMC), 5 patients with X-linked hydrocephalus, a patient with Dandy-Walker syndrome, 4 patients with holoprosencephaly, 5 patients with encephalocele, 5 patients with arachnoid cysts, 2 patients with atresia of Monro's foramen, a patient with after hemorrhagic hydrocephalus, 3 patients with hydrocephalus accompanied with fetal brain tumors. The outcome showed a wide variation, with normal 19%, slightly delayed 16%, moderately delayed 16%, severely delayed 23% and peri and postnatal death 19%. This variation seems to be determined by the basic disease and associated anomaly.

Conclusion: A guideline for the diagnosis and treatment of fetal hydrocephalus is urgently required, which should be based on the analysis of the clinical data of each disorders and critical

appraisal of reviews. The number of adult patients with congenital hydrocephalus is now increasing. Therefore, the new issue of medical and social problems surrounding adult patients with congenital hydrocephalus should be discussed.

S13
Follow up of neonates with progressive hydrocephalus who were managed at the Royal Hospital for Sick Children

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S13

Background: This audit looked at the management and disabilities of neonates born between 1989–1999 who were admitted to Ward 2B at the Royal Hospital for Sick Children with hydrocephalus. Patients with spina bifida were excluded from this study.
Materials and methods: Names and hospital numbers of 135 patients who matched the inclusion criteria were obtained from the hospital ward database. Information on 105 of these patients was extracted from their medical records. Of these, insufficient statistics were available for 2 patients. Patient demographics, management and follow-up were studied and the subsequent data was analysed.
Results: 103 of the 135 patients (76%) were included in the study. Of these, 29 (28%) had primary congenital hydrocephalus and 74 (72%) had hydrocephalus secondary to acquired obstruction. In the latter category, the majority were secondary to intraventricular haemorrhage. However, 5 were a result of meningitis, and 2 were due to other causes. 85% survived (16 died). About half of these patients (7–44%) died before their first birthday. Of the 103 patients, 22 (21%) did not require shunting for their hydrocephalus. 31 of the remaining 81 patients (38%) have had no shunt problems till date, and 6 have required elective revisions to peritoneal catheters only.
Detailed notes on follow up were not available for 8 of the patients as they were followed up elsewhere. Disabilities were common in the remaining population, with majority having learning difficulties. 41 (43%) have visual problems, 31 (33%) have epilepsy and 21 (22%) have some degree of cerebral palsy. However, 10 (11%) of these patients have had no problems and are attending mainstream schools, 5 (5%) have visual problems only, and another 5 (5%) have only mild learning difficulties.
Conclusion: Severe disabilities are common in this group of patients. Most have significant visual problems, a third have epilepsy, and 22% have some degree of cerebral palsy. Further studies on this cohort of patients need to be carried out to identify their needs in the community.

S14
Chiari II malformation and myelomeningocele

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S14

Background: Chiari II malformation has been reported in 60–95% of patients with myelomeningocele. Many theories have been proposed to explain the origin of Chiari II malformation, the best of them is the lack of expression of surface molecules on neurons in the developing neural tube, with failure of posterior neuropore closure. Multiple anomalies involving the hindbrain, spinal cord and supratentorial compartment can be seen in this complex malformation, developing hydrocephalus, syringohydromyelia, and other anomalies that have influence in therapy and prognosis.
Materials and methods: Patients with myelomeningocele are operated on shortly after birth, but they usually need surgical therapy again afterwards, consisting of posterior fossa decompression, once they are evaluated following a clinical and imaging protocol. A retrospective review of all patients with myelomeningocele and Chiari II, diagnosed in our pediatric hospital since 1991 until now, is presented.
Results: Our series include 81 patients with Chiari II malformation, mostly associated with previous myelomeningocele.
Conclusion: Authors emphasize the clinical, imaging, and other procedures required to diagnose and evaluate these patients, in order to safely indicate surgical decompression. An explanation about the different surgical methods used in our department is given, with correlation with overall reported results.

S15
A review of 173 cases of myelomeningocele seen in a tertiary referral fetal management unit over a 12 year period

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S15

Background: 173 pregnant women with a myelomeningocele (MMC) affected fetus were referred to St Mary's Hospital between January 1991 and December 2002. The number of cases referred each year was greatest in 1993 and 1998 and least in 1995. The termination rate increased from a low of 43% in 1994 to a high of over 90% in 2000, 2001 and 2002.
Materials and methods: The Cortical Index (BPD-2xVA) was calculated for the fetuses from data collected at the time of the anomaly ultrasound scan carried out at 18 to 20 weeks of gestation.
Results: The majority of cases had a Cortical Index of less than 32 (mean value for fetuses without a MMC). There was a trend for the higher vertebral level MMCs to have the smallest Cortical Indices but there were many exceptions.
Conclusion: Of the 173 cases only 23 (13%) developed hydrocephalus, i.e. progressive increase in the ventricular atrium size with a concurrent disproportionate increase in the head circumference. There was no correlation between the vertebral level of the MMC and hydrocephalus.

S16
The problems of hydrocephalus and CSF shunt in the patients with myelomeningocele in their adolescence and adulthood

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S16

Background: Hydrocehalus with myelomeningocele (MMC) is generally considered to be a problem in their early life.

Few discussions have been made about the management of hydrocephalus with MMC after adolescence. Furthermore in Japan about 20 years ago closure of myelomeningocele was sometimes performed by orthopedists or pediatric surgeons and very little concerns about hydrocehalus were paid for. Therefore the process of the management of hydrocehaus varies widely among the patients with MMC in the adulthood, some patients are left untreated or long-term malfunctioned or others are intensively followed-up. The aim of this paper is to evaluate the intellectual and social outcome between various management and to report six cases who are underwent VP shunt in the adulthood because of their symptoms due to intemittently increased intracranial pressure are revealed after long-standing so called arrested hydrocephalus.

Materials and methods: A total of 24 (11 male and 13 females) patients with MMC associated hydrocehalus who had been followed over ten years after the initial closure are included in this study.

Results: The patients are classified into three groups. We defined the patients who are intensively followed after the initial CSF shunt and VP shunt are also functioning yet as class1.Class 2 includes the patients whose VP shunt is not functioning and who are considered as a shunt independent and arrested hydrocephalus. The patient in Class 3 has been performed no CSF drainage but show ventricular dilatation. We evaluated intellectual outcome using Wechsler adult intelligence scale(WAIS).

Conclusion: We conclude hydrocephalus associated MMC is not only the problem in their early life but also the life-long issue.

S17
Management of pregnancy, delivery and postpartem care of mothers with ventriculoperitoneal-shunted hydrocephalus and review of literature

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S17

Background: Since the introduction of cerebro spinal fluid (CSF)-shunt implantation in 1971 at the University Hospital of Innsbruck the number of hydrocephalus patients reaching reproductive age has increased in recent years. Our main aim was to attend these patients throughout pregnancy, delivery and maternity. These patients have been in our care from the beginning of their disease to adulthood and we have reviewed their outcome with other reported patients in literature.

Materials and methods: Follow-up data were obtained either from our own clinical notes or from charts of the obstetrics unit and anaesthesiology unit.

Results: We present three patients with four pregnancies out of our cohort of 365 CSF- shunted patients. Indications for shunt placement were twice postmeningitis hydrocephalus occlusus (at the age of three months and at the age of two months after premature birth of 34 gestational weeks) and once congenital hydrocephalus of undetermined origin. There were no shunt malfunctions during all four pregnancies. Pregnancy outcomes were three vaginal deliveries, one using vacuum extraction. One woman refused vaginal delivery for her second child and had a primary low transverse cesarean in spinal anaesthesia with likewise no shunt malfunction.

We built up a multidisciplinary team with clearly defined roles, including an obstetrician, a neurologist and an anaesthetist. Because of different correlated mentally impairment of these patients intensive follow-up and special aspects after delivery have to be addressed in order to ensure the quality of care like medical consultation and educational matters concerning the baby, social welfare work, vocational guidance and vocational training to improve their independence.

Conclusion: Based on our few cases we could not experience complications regarding maternal shunt dependency contrary to literature. All these patients being now „mother patients" are well integrated in society and their families. We suggest that proper care of these patients can lead to normal pregnancies, deliveries and maternity.

S18
Malformations of the fetal spine using in utero MR imaging

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S18

Background: The detection of spinal cord malformations *in utero* remains a challenge for clinicians involved in antenatal diagnosis. No imaging method can make accurate predictions as to the neurological/developmental functional outcome in an individual case but having the most anatomical detail of the malformation gives the best chance of accurate counselling. In this paper we report our experience of the first 50 cases in which we performed *in utero* magnetic resonance (MR) imaging for expected fetal spine pathology.

Materials and methods: Cases were referred from five fetal assessment units in the North of England and Midlands. Antenatal fetal anomaly ultrasound scans had shown some variety of vertebral or spinal abnormality. A phased array flexible surface coil was used in all cases and single shot fast spin echo sequences were used (5 mm and 3 mm-thick slices). Detailed follow up was obtained in all the cases examined consisting of post mortem procedures or clinical and radiological follow up. The results of those studies were taken as the reference standard. The diagnoses made independently on the basis of ultrasound and MR were compared with the reference standards.

Results: Normal MR examinations were found in 8/50 cases that were suspected to be abnormal on ultrasound. All of these cases were shown to be normal postnatally. Open dysraphic processes, mainly myelomeningocoele, were found on MR and confirmed on post mortem studies or post natally. Two had been misdiagnosed on ultrasonography. In a further 15 cases developmental spinal abnormalities were correctly characterised by MR an two of those were misdiagnosed on ultrasound. Six other pathologies were shown (sacral teratoma) all of which were correctly diagnosed by ultrasound.

Of the 21 cases of myelomeningocoele 13 were lumbro-sacral, 3 thoracic, and 4 sacral. One case of hemimyelomeningocele was correctly diagnosed. 13/21 had low cerebellar tonsils and 8 had normally placed tonsils at the time of scanning. In all 13 with low

cerebellar tonsils the extra-axial CSF spaces of the brain were effectively not visualised. 5/8 of the patients with normally placed tonsils had a normal amount of extra-axial CSF. Absence of the extra-axial CSF space was not seen in any closed spinal dysraphic pathologies.

Conclusion: In utero MR contributes to the accurate diagnosis of developmental spine pathology before 24 weeks gestational age. Its major contribution appears to be in confirming or refuting the presence of an abnormality although it does contribute to the anatomical diagnosis. Absence of the intracranial surface CSF spaces are a frequent accompanying factor of open dysraphic processes, particularly those associated with Chiari 2 deformaties.

S19
Symptomatic cerebellar tonsillar ectopia in lipomyelomeningocele patients

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S19

Background: To study the incidence of cerebellar tonsillar ectopia and Chiari type symptoms in a population of LMM patients.

Materials and methods: The records of patients with a diagnosis of LMM between the years of 1978 and 2003 (130 patients) at Children's Hospital and Regional Medical Center (CHRMC) in Seattle, Washington were reviewed. The presence and degree of tonsillar ectopia was determined by reviewing total spine and brain MRIs (sagittal T1 sequences) from these patients. We defined significant ectopia as greater than 5 mm below the foramen magnum. We limited the study to the 46 out of 130 patients who had previous MRIs. Clinic notes from yearly clinic visits were also reviewed in order to determine the presence of symptoms such as headaches, shoulder pain and bulbar symptoms. We used Fisher's exact test of proportions.

Results: We identified cerebellar tonsillar ectopia greater than 6 mm in 14/46 (30%) of the patients. The degree of tonsillar ectopia ranged from 6 to 13 mm below the foramen magnum. Review of the medical records of all 46 patients which included a yearly clinic visit until the age of 21, revealed that 6/14 patients with significant tonsillar ectopia had frequent headaches associated with cough or valsalva, while only 1/32 patients without significant ectopia had headaches (P = 0.002). Patients with significant ectopia were not more likely to have multiple detethering operations (4/14 (29%) in the ectopia subgroup versus 5/32 (16%) in patients without significant ectopia) (P = 0.3). There was no correlation between the number of detethering operations and degree of tonsillar ectopia within each group. Also, no correlation between the age of the patient at initial repair and the degree of tonsillar ectopia was observed.

Conclusion: This study has revealed a 42-fold increase in the incidence of pathologic cerebellar tonsillar ectopia in LMM patients in comparison with historical controls. In addition we have identified symptoms suggestive of Chiari type I malformation in greater than half of the patients within this subgroup.

S20
Skin covered myelomeningoceles do not exist: What are these lesions?

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S20

Background: The author reports a clinical experience of congenital midline skin covered lesions and discusses the diagnostic approach, neuro imaging, operative management, and follow-up, with particular emphasis on patients with terminal myelocystocele.

Materials and methods: During the period of August 1977 through December 2004, the author evaluated children with skin covered spinal lesions, and made the diagnosis of: meningocele (6), lipomas and lipomeningoceles (42), hamartomas (9), teratomas (6), and terminal myelocystocele (8).

Neuro Imaging: The patients were initially diagnosed by either spinal high resolution ultrasonography, spinal computed tomography (CT), or spinal magnetic resonance imaging (MRI). All the patients with terminal myelocystocele underwent preoperative and postoperative spinal MRI.

Operative Findings: All patients underwent operative confirmation of the clinical diagnosis at the time of corrective surgery for the underlying disease. The patients with terminal myelocystocele underwent release of the tethered cord, radical but subtotal resection of the lipoma, and myelotomy and drainage of the syringocele with microlaser neurosurgery.

Results: Of the 8 patients with terminal myelocystocele, 4 had associated abdominal wall defects (i.e., bladder exstrophy) and 4 did not. Patients without abdominal wall defects were diagnosed earlier in life and underwent operative intervention sooner than those with abdominal defects. The former had better neurological outcome and less operative interventions. These findings will be presented.

Conclusion: There is a wide variety of congenital midline skin covered lesions in the dorsal medial embryo. Correct diagnosis enables an earlier and more effective management. Terminal myelocystoceles are a distinct clinical entity that is at risk of having a late diagnosis and consequently a delay in treatment.

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S21
In utero MR for ventriculomegaly

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S21

Background: MR is being used increasingly for the diagnosis of fetal abnormalities in utero, both in research studies and in the clinical environment. It is perceived that in some situations MR may have a higher diagnostic accuracy than ultrasound in detecting some conditions, particularly brain and spine

abnormalities. In this paper we present our current data concerning the assessment of diagnostic accuracy of in utero MR compared against ultrasound when investigating fetuses with ventriculomegaly.

Materials and methods: The study consists of two referral patterns, firstly fetuses from any gestational age after 19 weeks where the referring ultrasonography considered the examination to be difficult or there was some debate about the presence of abnormalities other than ventriculomegaly. This group consisted of 40 fetuses in which the primary referral problem was ventriculomegaly. The second consists of the first 15 cases from an ongoing study in which 20–22 week fetuses are recruited only if the referring ultrasonographer is sure that the fetus had ventriculomegaly only. The results of the ultrasound and MR examinations were compared with the final clinical, radiological or post-mortem examination as appropriate.

Results: The MR examinations in the forty cases in group 1 ('difficult ultrasound cases')

a) Complete agreement 19/40 (48%)

b) MR gave extra information but unlikely to have affected management 1/40 (2%)

c) MR gave extra information likely to affect management 2/40 (5%)

d) MR changed the diagnosis and affected management 18/40 (45%)

In group 2 (high confidence of ventriculomegaly)

a) Complete agreement between ultrasound and MR 14/15 (92%)

b) MR changed the diagnosis and affected management 1/15 (8%)

Conclusion: The improvement in diagnostic accuracy of MR over ultrasound when investigating 2nd trimester ventriculomegaly is exceptionally dependant on referral patterns and a wide variation of figures between different studies is to be expected.

S22

The ideal approach to back closure; Are we closing the backs properly? Is laminectomy always necessary?

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S22

Background: The surgical approach to primary 'back-closure' of meningomyeloceles differs, based on which specialist performs the closure. If the Neurosurgeons tend to be a bit overaggressive and perform more laminectomies than seems necessary, the Pediatric surgeons can be over cautious and tend to sometimes leave the intraspinal abnormality unattended. We believe that a golden mean is the best approach.

However, till date we had not evaluated the results of our back-closures and whether our approach had resulted in a successful morphological correction of the entire lesion – and not just a cosmetically satisfying outcome.

The retrospective study aims to evaluate the morphological results of our back closures and assess whether the post-operative neurological outcome had any relation to the morphology. The complications of the repair were also analysed and correlated to the surgical technique.

Materials and methods: Fourteen patients whose back lesions were closed more than an year ago were included in the study. Their present ages ranged from 1 1/2 years to 8 years. The follow up period corresponded to the age group i.e., 1 1/2 to 8 years as most of the lesions were closed in the first month of life.

All patients underwent a recent detailed postoperative MRI scan of the entire spine and skull. These MRI findings were compared with the pre-operative MRIs (wherever available) and the morphologic result was judged as an 'incomplete' or 'complete' correction.

The patients' neurological development was tracked and correlation to the postoperative morphology made. Surgical complications if any in these cases were recorded.

Results: 9 patients have so far undergone their recent MRI scans and 5 more will get their scans done in this month. The morphology of the operated cases will be presented with the pictures. In 7 of the 9 cases studied so far the repair has been complete. In one patient the laminectomy performed was retrospectively deemed as unnecessary – and the patient had a CSF leak in the postoperative period – which could be due to the overaggressive approach. On the other hand in one patient some of the intraspinal lipoma was left behind and may require removal.

Conclusion: The paper aims to discuss the optimal surgical approach for the back closure especially vis-à-vis the judicious use of laminectomies. The paper suggests that it is not necessary to perform a laminectomy in every patient.

S23

Occult ventriculo-atrial shunt infection: a forgotten condition

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S23

Background: For some time after introduction of the Holter valve, shunting for hydrocephalus was ventriculo – atrial (VA). Features of infection in ventriculoperitoneal (VP) and VA shunts differ considerably, and lack of familiarity of the latter has led to inappropriate referral and incorrect diagnosis and treatment. We present a recent illustrative case with new microbiological findings and re – emphasise the diagnostic criteria.

Materials and methods: Case report: F, 51 yrs, VA shunt following benign space – occupying lesion 1979. Discharged well from follow-up 1986. Generally well until referred September 2004 to the Respiratory Medicine unit c/o productive cough and tiredness 9 months. She also had generalized aches and pains, fever and night sweats. Differential diagnoses were tuberculosis, cardiac valvular disease or intracerebral abscess.

Results: She had haematuria. Blood cultures grew *S epidermidis* – "contaminant". Shunt infection was ruled out as "it was too long after insertion". Trans – oesophageal echocardiogram revealed no cardiac vegetations or thrombus on the catheter. Investigations for shunt infection (ASET) revealed an antibody titre of >40,000. When the shunt was eventually removed the ventricular CSF was normal with no growth. The removed shunt grew *S epidermidis* but in SCV form, ie easily missed. Details of relevant investigations will be presented in full. There was immediate=improvement post – operatively and the patient was well at follow – up with no further shunting.

Conclusion: Features of VA shunt infection often mimic those of other conditions, and definitive treatment is often delayed while various specialists investigate. This case is a recent example with a VA shunt inserted 27 yrs ago. Delay in treatment resulted from lack of familiarity with the features of VA, rather than VP, shunt infections. The lessons (people with VA shunts still present for diagnosis; VA shunts are still being inserted; it is important to recognize the symptoms of VA shunt infection promptly to avoid permanent damage from immune complex disease; and finally, thought here are clinical pitfalls, there are well – established simple diagnostic tests for VA shunt infection. These lessons apply to all specialties, including neurosurgery and microbiology.

S24
Impact on sexuality and urinary incontinence in adults with spina bifida

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S24

Background: The aim of this study was to examine the impact of urinary incontinence on sexual activity in adult patients with spina bifida.
Materials and methods: A total of 82 patients (61% male, 39% female) of average age: 30.5 (19–48) affected by spina bifida were available for interview. A questionnaire was administered to determine data related to patient neurological level, management of bladder dysfunction, aspects of their sexual activity and the possible interference with urinary incontinence, among others. The questionnaire also included a section for male patients able to sustain erection, SHIM (Sexual Health Inventory for Male), to determine the degree of their erectile dysfunction. Bivariable and multivariable statistical analysis valued the most common factor interfering the sexual activity of this highly statistically significant population.($p < 0.05$).
Results: Out of 82 patients tested, only 32.9% had sexual contact, and most of these had a partner. Urinary incontinence significantly interfered with their sexual activity ($p < 0.05$). Most males used sheaths and most women used intermittent catheters. Data showed males had less frequent sexual activity than females ($p < 0,05$) but masturbated more often. (p: 0,001). Analysing patients according to the degree of their lesion showed most patients able to have sexual activity, intercourse and erection, had a statictically significant low lumbar neurological level or sacrum ($p < 0,05$).
Conclusion: The study determined that patients with spina bifida have low sexual activity and their urinary incontinence affects their sexual relationships.

S25
Bladder mucosal cuff urethral lengthening – a modification of Kropp procedure

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S25

Background: Management of urethral incontinence in patients with a neuropathic bladder remains a surgical challenge. If surgery is deemed necessary then the ideal procedure achieves dryness with the ability to perform urethral catheterisation either as the chosen route for bladder drainage or as an alternative to stoma catheterisation. The Kropp procedure and its modifications is difficult and has varied reported results. We describe our experience with bladder mucosal cuff lengthening of the urethra at the time of augmentation.
Materials and methods: The bladder is opened in the saggital plane. Adrenaline 1:100,000 is infiltrated under the mucosa that lies distal to the ureteric orifices down to the bladder neck. This mucosa is elevated as far as the upper urethra. The funnel shaped cuff is implanted under the mucosa between the ureteric orifices and distally is covered by a wrap of detrusor muscle.
Results: We have performed this procedure in 10 patients (6 females and 4 males) with a mean age of 11 years (range 6 y 9 m–15 yr 3 m). The neuropathic bladder was secondary to spina bifida in 8 cases, and transverse myelitis in 2. Preoperative urodynamics revealed a poorly compliant bladder in 9 with leakage at a mean filling volume of 138 mls (15–390). In all patients an augmentation procedure was performed, and in 8 cases a Mitrofanoff stoma was established. At a mean follow-up of 14.9 months (2–26 months), 9 patients are dry urethrally (1 with an indwelling stoma catheter overnight). All the patients are on intermittent catheterisation 3–4 hourly. Two patients catheterise urethrally by choice. One boy developed problems with stoma catheterisation and relief was achieved by the urethral route. In 1 patient the procedure failed to achieve continence.
Conclusion: Bladder mucosal cuff lengthening of the urethra may be superior to the Kropp procedure for achieving urinary continence in patients with a neuropathic bladder. Catheterisation by the urethral route remains possible and for some patients may be the route of choice.

S26
Relation between sacral sparing and long term urological outcome in open spina bifida

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S26

Background: The Cambridge Cohort of 117 patients born with open spina bifida provide information on causes of death and outcome to age 40 with no loss to follow up. We previously showed survival and long term prognosis were related to sensory level.
Aims: To examine the influence of sacral sparing on urological outcome. Sacral sparing was defined as intact sensation to pinprick in at least one dermatome in the saddle area S2–S4.
Design: Prospective cohort study.
Materials and methods: The cohort comprises 117 consecutive individuals with open spina bifida who were treated unselectively from birth in the Neurosurgical department at Addenbrooke's Hospital, Cambridge, England between 1963 and 1971. They have been reviewed six times by the same independent observer. Based on the results of meticulous neurological examination in infancy, we divided the group into those with and without sacral sparing and looked at the relation with long term outcome.
Results: 33 (28%) of the 117 individuals had sacral sparing. 10 (30%) of them have died compared with 57 (68%) of the 84 without sacral sparing ($p < 0.001$). None of those with sacral sparing died of renal causes compared with 19/57 (33%) of those with no sacral sparing ($p < 0.001$). Urological admissions during the teenage years were commoner in those with no sacral sparing:

19/42 (45%) compared with 2/26 (8% p = 0.001). Urinary continence was closely related to sacral sparing at mean ages 4, 9 and 25. Thus at age 25 16/25 (64%) of those with sacral sparing were continent compared with 1/36 (3%) of the remainder.

Conclusion: Although urological management has improved, it is likely that babies with open spina bifida who have sacral sparing will have a better long term outcome than those without in terms of overall survival, renal deaths, urological admissions and urinary continence.

S27

Efficacy and safety of propiverine in comparison to oxybutynin in children with neurogenic detrusor overactivity: an observational study

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S27

Background: Assessment of efficacy and safety of propiverine (prop.; Mictonetten™) and oxybutynin (oxy.) in children with neurogenic detrusor overactivity (NDO) aged 1–18 years.

Materials and methods: In a comparative cohort study 255 children with NDO (199 myelomeningocele (MMC), 46 spinal cord injury), were treated with anticholinergics for 2.5 years on average at 14 centers and were evaluated retrospectively. 127/255 children were allocated to prop., 128/255 to oxy.; median age at diagnosis and treatment initiation were 2.08 and 7.18 (prop.) vs. 3.37 and 7.98 (oxy) years, respectively.

Results: Primary efficacy outcome, max. detrusor pressure at micturition, was on average reduced to a significantly larger extent in the prop. than in the oxy. group. Correspondingly, clinically relevant reductions of detrusor pressure (below 40 cm H_20 or reduction by > 50%) resulted significantly more often in the prop. than in the oxy. group (74% vs. 50%). Urodynamic results are in agreement with clinical findings (tab. 1).

Both propiverine and oxybutynin demonstrated a resolution or downgrading of vesico-uretero-renal reflux (tab. 2).

Table 1 (abstract S27) Efficacy

	Prop. pre	Prop. post	Oxy. pre	Oxy. post
Max. detrusor pressure at micturition (cm H_20)	59.81	36.74	65.16	54.95
Compliance (ml/cm H_20)	18.94	27.56	9.99	15.64
Max. bladder capacity (ml)	145.93	242.28	221.82	309.97
Continence (%)	7,69	31,62	20,80	50.41
Catheterization frequency/24 h	2.52	1.87	2.46	2.87

Table 2 (abstract S27) Reflux

	Prop. pre	Prop. post	Oxy. pre	Oxy. post
Reflux left side (stage III–V) (N)	14	5	13	5
Reflux right side (stage III–V) (N)	12	4	13	4

Propiverine was better tolerated than oxybutynin (9.40 vs. 17.46% adverse events), in those children suffering from MMC significantly better.

Conclusion: Comparative studies of efficacy and tolerability of anticholinergics in NDO of children were missing so far. This cohort study demonstrates a more effective reduction of the max. detrusor pressure at micturition with prop. in comparison to oxy. Prop. was better tolerated than oxy. Urodynamic effects are correlated with improvement of reflux, indicating possibly more favourable long-term outcomes of the upper urinary tract.

S28

Bone Mineral Density in patients with Myelomeningocele

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S28

Background: Identification and quantification of osteoporosis in patients who have myelomeningocele has been limited until now but it should be useful in order to improve their general care and prevent fractures in the future. The aim of this study was to examine bone mineral density in patients with myelomeningocele (MMC).

Patients and methods: Eighty patients with myelomeningocele were randomly chosen from a roster of >500 patients with (MMC) followed at a multidisciplinary spina bifida unit in a third-level public university hospital, which serves as the referral centre for these patients in our country. Patients with known metabolic acidosis, renal insufficiency, or other metabolic bone disease (i.e., hyperparathyroidism) were excluded from this study. We measured Bone Mineral Density (BMD) with total-body DXA scan with subregional areas values and the biochemical markers of bone mineral metabolism in blood and urine. To study relationships among the variables, the Chi-squared, ANOVA and lineal regression tests were applied.

Results: The mean total body BMD was 1.1591 (range 0.9–1.38). Fifty two per cent of the patients were in the normal range of BMD, 31.6% were osteopenic and 15.8% were osteoporotic. The bivariate analysis demonstrated that the body mass index (p = 0.033) and hip flexion contractures (p = 0.024) were related with pelvis T-score. Neurological level (p = 0.038), functional ambulation (p = 0.024) and hip flexion contractures (p = 0.024) were related with leg T-score. Hip flexion contractures (p = 0.027) was related with leg Z-score. The only determinant for leg BMD in the multivariate approach was type of gait (p = 0.012; 95% CI 0.042–0.229); When we use total-body BMD as dependent variable, the model showed as determinants: type of gait (p = 0.003; 95% CI 0.031–0.88) and sex (p = 0.044; 95% CI 0.003–0.155).

Conclusion: Fatter MMC (body mass index >25) patients had less osteopenia or osteoporosis than normal or thin patients. The higher neurological level, the worse BMD. Although type of gait is determinate by neurological level, this study suggests that the type of gait is the most important determinant leg and total-body BMD.

S29
Spondylolisthesis in myelomeningocele

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S29

Background: The absence of important posterior elements in myelomeningocele (MMC) seems to justify a higher prevalence of spondylolisthesis among these patients regarding the normal population. The aim of this study was to analyze the prevalence and the degree of slippage of spondylolisthesis in myelomeningocele patients.
Patients and methods: One hundred and thirty patients with myelomeningocele were randomly chosen from a roster of >500 patients with myelomeningocele followed at a multidisciplinary spina bifida unit in a tertiary university public hospital. A cross-sectional study was done collecting data from patient records and X-rays archives. X-rays measurements of sacral slope and grade of listhesis were standardized with AutoCad System. To study relationships among the variables, the Chi-squared, ANOVA tests were applied.
Results: The mean age of this series was 24 years (range 2–53). 64 were male and 69 were female. 71,4% of patients had mid-lumbar, low-lumbar or sacral neurological levels. 16% had spondylolisthesis. The mean slippage was 21.6% (range 9–44), being 68,2% grade I and the remaining 31,8% grade II. The more frequent level for slippage was L5-S1. All the patients with spondylolisthesis were ambulators. The risk of spondylolisthesis was related with ambulation ($p = 0.012$). Ambulatory type ($p = 0.035$), functional ambulation type ($p = 0.007$) and lumbar hyperlordosis ($p = 0.018$) were also statistically related with the presence of spondylolisthesis.
Conclusion: Prevalence of spondylolisthesis in MMC is greater than in normal population (16% vs 5.8%). Gait related variables and hyperlordosis were related with the presence of spondylolisthesis.

S30
Neuroepithelial denudation in the hyh mutant mice with congenital hydrocephalus produces agenesis of corpus callosum and alteration in the cerebral cortex

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S30

Background: *Hyh* mutant mice suffer a congenital hydrocephalus triggered by ependyma denudation [1]. Additional pathological events have been observed: the absence of corpus callosum (ACC) and the reduction in the thickness of the cerebral cortex in this mutant. These two alterations frequently appear associated with human and animal hydrocephalus. Crossing the midline by callosal axons requires the presence of three types of midline glial cells (glial wedge, glial sling and indusium griseum glial cells) and also the correct guidance provided by pioneering axons. This crossing occurs about E-16.5 and pioneering axons appear around E-15.5 [2]. Development of cerebral cortex begins at E-12, continues until postnatal life, and requires proliferation and migration of progenitor cells from subventricular regions.
The aim of this work is to clarify the nature of the relationship between hydrocephalus and ACC and abnormal neurogenesis.
Materials and methods: Control and hydrocephalic *hyh* mice (Jackson Lab., USA) were used. To study the ACC mice from E-15.5 to PN-1 were used. Antibodies against NCAM (callosal axons), GFAP (midline glial cells) and β-III tubulin (neuroblast) were used. DiI tracing at E-17.5 were used to show crossing of midline by callosal axons. Alteration of the cerebral cortex was studied from 1 to 120 postnatal days. Digital photographs were taken and Noesis Visiolog software was used to measure the thickness of the cerebral cortex. Data obtained were statistically processed using Microsoft Office Excel and Sigmastat32 software. The ventricular surface was studied at E-15.5 by scanning electron microscopy. Organotypic slice culture and DiI labelling at E15.5 were used to analyze growth of pioneering axons and migration of neuroblast [2, 3].
Results: At PN-1 hydrocephalic mice, corpus callosum is missing. In these animals, however, other commissural formations are present and the lateral ventricles are collapsed, indicating that the ACC is a phenomenon preceding lateral ventricles dilatation. In addition, DiI tracing at E-17.5 shows that in hydrocephalic animals callosal axons do not cross the midline. This led us to study the midline glial cells and pioneering axons. It was found that in E16.5 hydrocephalic mice, the midline glial populations are altered and alterations appear to be associated with the denudation of discrete areas of the lateral ventricles. In hydrocephalic mice, pioneering axon elongation, labelled with DiI at E15.5, has a wrong direction and do not cross the midline. In hydrocephalic mice, cerebral cortex shows a statically significant reduction of its thickness that is especially significant at PN-3, when dilatation on lateral ventricles is not yet apparent. In addition, neuroblast-like cells are detected on the ventricular surface of hydrocephalic mice by use of immunochemistry, scanning electron microscopy, and DiI labelling of organotypic slice culture.
Conclusion: i) Denudation of the ependyma would alter the midline glial cell populations associated with the crossing of callosal fibres, and subsequently alter the direction of the pioneering axons, resulting in the absence of corpus callosum. ii) The denudation of the ependyma layer would result in the disorganization of the germinal areas leading to abnormal neuroblast migration and, probably, to a reduction of the thickness of the cerebral cortex. iii) Detachment of the neuroepithelial cells in hydrocephalic foetuses should not only be associated to the pathogenesis of congenital hydrocephalus but also to abnormal neurogenesis and agenesis of corpus callosum.

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S31
Differential permeability to horseradish peroxidase in affected and non-affected ventricular walls during postnatal development of normal and hydrocephalic *hyh* mice

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S31

Background: *Hyh* mutant mice suffer a congenital hydrocephalus triggered by ependyma denudation [1]. The ventricular surface in non hydrocephalic newborn mice is lined by the immature ependyma, which is characterized for being vimentin (-) and S100β (-), at variance in the adult animals the mature ependyma expresses vimentin and S100β [2]. On the other hand, in the hydrocephalic mice the ependyma begins to denudate on the 12th day of gestation, and at PN8 only some areas of lateral ventricle are still endowed with ependyma. In parallel, astroglia starts to cover the denuded surface forming a new cell layer, the glial scar, which lines the damaged ventricular surface. We have studied the permeability to horseradish peroxidase (HRP) of these four regions at the ventricular wills: mature ependyma, and denuded areas with or without glial scar.
Materials and methods: Control and hydrocephalic *hyh* mice (Jackson Lab., USA) at 3rd and 30th day of post-natal life were injected into a lateral ventricle with 3% HRP. 15 min after the injection the animals were sacrificed under anesthesia. HRP was detected by immunocitochemistry with specific antibodies. Inmunocitochemistry for PCNA (to label proliferating cells) and GFAP, S100β and vimentin was used.
Results: In non-hydrocephalic mice the immature ependymal layer was impermeable to HRP, whereas the mature ependyma was permeable. In hydrocephalic animal the areas where the ependyma had detached and the glial scar had not yet form were permeable to HRP, diffusing through the parenchyma. The glial scar was recognized for being GFAP positive and surprisingly, vimentin positive. When this barrier was fully developed at PN-30, it was apparently impermeable. However, the presence in the neuropile of cells labelled with HRP might indicates that some HRP has passaged through the glial scar. In adult hydrocephalic animals, there are zones where the ependyma is not denuded. This ependyma and the neighbouring glial scar appear impermeable to HRP. However, the HRP labelling of subventricular structures in these levels suggest that some tracer has passed through.
Conclusion: The different permeability properties between mature and immature ependymal layers suggest that differences exist in cell adhesion features and permeability. In hydrocephalic mice, denudated areas devoid of glial scar are very permeable to HRP. Thus, ependymal denudation implies the loss of CSF-parenchyma barrier, which could influence the CNS development. In adult hidrocephalic mice there are ependimal patches that do not detach. This particular ependyma, as the glial layer lining the denuded area, prevents partially or completely the passage of HRP. The HRP labelling of subventricular structures in this two regions could be an indication that some HRP has passed through the non-detached ependyma and through the glial sheath by an as yet unknown mechanism. This suggests that these ependymal areas could correspond to an specific ependyma population that in the normal animal would be a tight ependyma, and that such an ependyma would have the same barrier properties as those of the glial scar. What actually are these barrier properties are being further investigated in our laboratory.

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S32
Brain amyloid accumulation in senescent rats with kaolin-induced hydrocephalus

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S32

Background: NPH patients have a high rate of Alzheimer's disease (AD) on cortical biopsy. 30–50% of shunted NPH patients show amyloid (Aβ)plaques and neurofibrillary tangles. It is postulated that Aβ accumulates in AD and NPH due to decreased Aβ clearance via CSF and blood-brain barrier (BBB). The present study investigates Aβ accumulation and Aβ transport in aged hydrocephalic rat brains.
Materials and methods: Kaolin-hydrocephalus was induced in senescent (12 months) SD-rats. Untreated age- matched rats served as controls. Aβ accumulation was investigated by specific Aβ(1–40) and Aβ(1–42)antibody immunohistochemistry performed 2 weeks (short-term), 6 and 10 weeks (long-term) after hydrocephalus induction. Each group consisted of five animals. Also, specific BBB Aβ receptors were labelled: LRP-1, which transports Aβ from the interstitial fluid (ISF) into the plasma,

and RAGE, which transports Aβ from the plasma into the ISF. Both receptors are located on the capillary endothelium.

Results: After 2 weeks of hydrocephalus, both Aβ 42 and Aβ 40 showed increased staining of the arachnoid and ependyma compared to controls. Cortical and hippocampal CA3 pyramidal neurons displayed Aβ 42 cytoplasmic staining in some animals. At 6 weeks, cortical and hippocampal endothelial and perivascular Aβ 42 and 40 accumulations were observed, most prominently with Aβ 42. Importantly, interstitial Aβ 42 and Aβ 40 accumulations were observed, and periventricular plaque-like formations were found in all animals. At 10 weeks, the observed plaque-like formations were increased, whereas cortical perivascular accumulations varied and were either increased or identical to the 6 weeks animals. LRP-receptor staining was decreased in cortical and subcortical vessels at two weeks. However, the decrease was most prominent after 6 weeks. After 10 weeks, LRP-1 receptor staining was restricted to large dilated capillary vessels. RAGE receptor staining showed diametrically opposite changes to those seen for the LRP-1 receptor.

Conclusion: In a rat model of chronic hydrocephalus, perivascular, interstitial and periventricular accumulations of Aβ 42 and 40, both of which play a major role in AD-plaque formation, are observed, with Aβ staining increasing the longer hydrocephalus exists. BBB receptor staining indicates impaired Aβ clearance from the ISF into the plasma. These preliminary studies indicate that Aβ accumulation in hydrocephalus is, in part, due to a failure of brain amyloid clearance as it is in AD. Reduced CSF turnover seen in AD, NPH and rat kaolin-hydrocephalus, and reduced Aβ net transport at the BBB appear to be involved. Perivascular Aβ accumulation, known to be a potent vasoconstrictor, may also play a role in the white-matter ischaemia seen in both human NPH and in rat chronic hydrocephalus.

S33

Resistance to CSF outflow depends upon duration of symptoms in patients with Normal Pressure Hydrocephalus

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S33

Background: Cerebrospinal Fluid (CSF) pressure-volume compensatory parameters may change over time under pathological and normal circumstances. Normal ageing may affect CSF compensation: the resistance to CSF outflow increases and the formation of CSF decreases with age. In acute hydrocephalus after subarachnoid haemorrhage, baseline intracranial pressure (ICP) and resistance to CSF outflow acutely increase but they may return towards baseline over the next few weeks. Idiopathic Normal Pressure Hydrocephalus (iNPH) awaits longitudinal studies. Is NPH always the late (compensated) stage of acute hydrocephalus? Are the CSF compensatory parameters invariant in time (counting from the onset of clinical symptoms) or do they change with time?

Materials and methods: We have investigated 73 patients presenting with NPH (mean age 73; 45 males and 28 females). They all presented with ventricular dilatation and gait disturbance, with memory deficit in 72% and urinary incontinence in 52%. All patients underwent computerized CSF infusion studies.

Results: Mean ICP was 10.1 +/− 5.1 mm Hg and mean resistance to CSF outflow was 17.3 +/− 5.2 mm Hg/(ml/min). 34 shunted patients were available for follow up and their improvement was expressed using NPH score. Mean duration of symptoms was 25 +/− 22 weeks (range from 2 to 144 weeks).

Conclusion: Neither baseline ICP nor brain compliance nor improvement after shunting exhibited any dependence on the duration of symptoms. The resistance to CSF outflow decreased with the duration of symptoms but only for a duration greater than 0.5 year (longer than 27 weeks; $R = -0.702$; $p < 0.005$). Hence it is inappropriate to use absolute threshold to distinguish normal from abnormal Rout: such value must be adjusted for age and duration of symptoms.

S34

The relative contribution of cerebrospinal fluid malabsorption and obstruction in the development of hydrocephalus in human neonates with spina bifida

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S34

Background: The pathogenesis of hydrocephalus in human neonates with spina bifida (SB) is incompletely understood. In HT-x rats, a model for congenital hydrocephalus, initial cerebrospinal fluid (CSF) malabsorption and CSF obstruction seemingly interplay in the pathogenesis. In human hydrocephalic SB neonates, assessment of CSF biomarkers may help to distinct between the relative contribution of CSF malabsorption and obstruction in the development of hydrocephalus. In this respect, concentrations of aminoterminal propeptide of type I collagen (PINP), a biomarker for arachnoideal fibrosis, has been shown to relate to CSF malabsorption in human hydrocephalic neonates. Additionally, high concentrations of transforming growth factor β1 (TGFβ1, involved in cellular proliferation and migration) are associated with CSF malabsorption (mice), whereas low TGFβ1 concentrations are associated with congenital CSF obstruction (HT-x rats). In human hydrocephalic SB neonates, it is unclear how PINP and TGFβ1 relate to the development of hydrocephalus. Elucidation of the pathogenesis of hydrocephalus in SB neonates may be important for the timing and optimalization of therapeutical strategies.

Objective: To determine the relative contribution of CSF malabsorption and obstruction during the development of hydrocephalus in SB neonates.

Materials and methods: CSF concentrations of PINP (radio isotope assay) and TGFβ1 (ELISA) were assessed in hydrocephalic SB neonates (n = 10), and compared with PINP and TGFβ1 concentrations in hydrocephalic neonates with aqueduct stenosis (CSF obstruction (n = 4)), and with fetal intraventricular haemorrhages (CSF malabsorption (n = 4)). Interleukin-6 concentrations (IL-6; ELISA) in CSF were determined in all samples to estimate the proinflammatory state.
Results: In CSF from SB-hydrocephalus patients, concentrations of PINP and TGFβ1 were ~80% and ~50% lower than in malabsorption hydrocephalus (median values: PINP 181 ng/ml vs. 1074 ng/ml, resp., p = 0.002; TGFβ1 104 vs. 277 pg/ml, resp., p = 0.03). CSF PINP and TGFβ1 concentrations did not significantly differ between SB-hydrocephalus and obstruction hydrocephalus. Median IL-6 CSF concentrations did not differ between the groups.
Conclusion: Present data on CSF biomarkers strongly indicate that CSF obstruction contributes more to the development of hydrocephalus in SB neonates than arachnoideal CSF malabsorption. These data in hydrocephalic SB neonates are compatible with the concept that low CSF growth factor concentrations and CSF obstruction to the cortex may relate to cortical impairment.

S35
The efficacy of antibiotics against *Propionibacterium acnes* biofilm infections on spinal implant material

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S35

Background: *Propionibacterium acnes* (*P. acnes*), a common anaerobic skin commensal, has been implicated in delayed infection after implantation of spinal instrumentation. Biofilms of this organism have not been demonstrated previously. Spinal instrumentation is used to correct scoliosis in spina bifida.
We investigated the susceptibility of *P. acnes* growing within mature biofilms on titanium discs to Penicillin G alone, and to a combination with Rifampicin. Biofilms were exposed to therapeutic doses of antibiotics modelled on currently recommended treatment regimens.
Materials and methods: Biofilm group: Surgical titanium discs (6 mm dia) were exposed (1 hr) *to P. acnes*, washed and immersed in fresh culture medium at 37°C. The attached bacteria to titanium were allowed to mature for 6 days (biofilms). Subsequently, the discs were retrieved, sonicated and the number of viable bacteria counted by chemiluminiluminesence and culture.
Treated groups: One group of mature biofilms was exposed to Penicillin G alone and the other with combination of Penicillin G with Rifampicin for 96 hrs respectively. Again, the discs were retrieved, sonicated and the number of viable bacteria were counted by chemiluminiluminesence and culture.
Results: All *P. acnes* biofilms responded to treatment with a significant reduction in bacterial numbers. Combination therapy was more effective and produced greater reductions (96.6%) of viable bacteria populating the biofilms than penicillin alone, 93.3% ($p < 0.01$). Complete eradication of the biofilm was not achieved in any cases.
Conclusion: *P. acnes* develop as a biofilm on spinal implant materials.
Antibiotic therapy significantly reduced the bacterial numbers. It remains to be determined whether longer periods of treatment will successfully eradicate the biofilm.

S36
Hydrostatic valves in treatment of paediatric hydrocephalus

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S36

Background: The pathological patterns of overdrainage like subdural haematoma or effusions are not so often in treatment of paediatric hydrocephalus. Slit ventricle, secondary premature suture synostosis and the lost of elasticity and compliance of the brain are specific paediatric problems of overdrainage and have frequently been observed following shunt insertion. In cases with clinical symptoms these complications can be difficult to treat. Hydrostatic valves minimise this risk of overdrainage. This study aims to evaluate the initial experience with a hydrostatic valve system, with emphasis on overdrainage associated complications.
Material and methods: 20 children receiving a PAEDI-GAV valve from 4/2003 till 1/2005 in our hospital were included in a prospective study. The valve is a combination of a conventional ball in coin differential pressure unit and a gravitational unit. The pressure levels were individually defined for the patients ranging from 4/14 up to 9/24 cm H_2O. In addition to the analysis of clinical parameters, radiological measurements and shunt revisions we focussed on overdrainage related complications. The developing of the size of the ventricle system was also taken into consideration.
Results: In 6 older children with shunt blockage we replaced a differential pressure valve with a PAEDI-GAV device during shunt revision. 14 newborns and babies with hydrocephalus of different aetiology were treated with a PAEDI-GAV system as a primary v-p shunt. In this group the average CSF protein level at shunt insertion was 0.78 g/l (0.12–1.349 g/l); mean CSF cell count was 4 per 1/3 ml (1–15 per 1/3 ml). Two pre-term newborns with posthaemorrhagic hydrocephalus were treated previously with DRIFT. None of the infants suffered a subdural effusion or haematoma after shunting, but 2 from 6 newborns with devices at a pressure level of 4/14 cm H_2O developed slit ventricles without clinical symptoms. The frontal and occipital horn width ratio decreased from an average of 0.611 to 0.488 at first follow-up. We had to perform 9 revisions in 6 children. Here are included 3 revisions in a newborn with a large interhemispherical arachnoid cyst and 2 revisions in a premature newborn with severe liver cirrhosis-associated ascites. The main cause for revisions was blockage of the ventricle catheter. We did not encounter any valve failure. There were no shunt infections in both groups.
Conclusion: The intra-operative handling of the PAEDI-GAV valve is good. The small dimensions of the device make it

suitable for the use in newborns and infants. Selection of pressure levels should be adapted to age and the individual characteristics of the dynamics of the ventricular system.

S37
Shunting of hydrocephalus with the new adjustable gravitational proGAV – advantages compared to other devices

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S37

Background: The new proGAV represents the combination of a new adjustable differential-pressure unit in series with a gravitational device. By its construction principle the proGAV should be capable to avoid the main disadvantages of other so-called "programmable" valves: The burden of the necessity for repeated X-ray-controls, the sensitivity to irregular adjustments in MR, the ongoing danger to overdrain of other adjustable differential-pressure-valves and the high probability of obstruction in adjustable valves with Anti-Siphon-Units.
Materials and methods: From February 2004 we conducted a series of shunting 32 adult patients with different etiologies. In all cases the proGAV was implanted in ventriculo-peritoneal drainages with frontal boreholes. Primarily we were interested in the security to determine the adjusted opening pressures by avoiding the burden of continuous repeated X-ray-controls, in the capability to adjust the valve transcutaneously safely and in the ability to avoid irregular adjustments, for instance by MR-studies, by its "brake". We focused secondarily on the radiological and clinical results and the possibilities for improvement by readjustments.
Results: After a follow-up of at least 3 months the clinical and radiological results of our small series give evidence for the reliability of the proGAV to avoid most of the disadvantages of other hydrostatic and/or adjustable devices. In 8 patients we saw an indication to change the opening-pressure. In 6 cases we lowered the opening pressure because we suspected functional underdrainage, but was followed by unequivocal improvement in only 3 patients. In 2 cases narrow hygromas developing postoperatively resolved after increasing the opening pressure. 2 patients succumbed due to complications not related to the valve. Thus the final clinical outcome proved excellent and good according to the Black-outcome-scale in 82%. The radiological and clinical final outcome of our little series up to now seems to prove the ability of the new construction principle to achieve change of pressure-settings and its control easily and with safety avoiding the necessity of surgical exchange of the valve. Not one case of unintended adjustment has to be registered in all the controls, but only 2 patients have been exposed to MR up to now.
Conclusion: The series is too small and the outcome represents only preliminary results, thus a comparison to series with other adjustable valves is obsolete up to now. But the new theoretical concept and the first clinical results give evidence of the proGAV to be superior to other devices and may inaugurate a new era of shunting hydrocephalus.

S38
Obesity and BMI in myelomeningocele

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S38

Background: We have analyzed 5033 visits for 663 patients to assess the most appropriate measures to determine obesity and overweight status for patients with myelomeningocele (MM) age 2–20 years of age.
Materials and methods: We recorded height or body length (Ht) (from head to hip and knee joints to sole in the presence of contracture), weight (Wt) and arm span (As) at yearly examinations (14,828 measures) and immediately before and after spinal fusion for 21 patients (126 measures). Ht, wt and all BMI calculations were compared by T tests to standards published by the National Center for Health Statistics of the US Government (NCHS). BMI was calculated with Ht and As. These two measures of BMI were also compared to each other by T tests. Multiple cell Chi Square tests were utilized to compare different levels of paralysis Lesion Level 1 (LL 1, L2 and above), LL 2 (mid-lumbar L3-5) and LL 3 (Sacral). We will show examples of Ht, Wt and DMI charts using the restricted calorie diet as recommended by Manenica (1982) demonstrating its effectiveness.
Results: Analysis of before and after scoliosis surgery height measures demonstrated the shortening effect of scoliosis on Ht and altered BMI calculated using Ht. ($P = < 0.0001$) Neither Wt nor Ht of patients with MM could be approximated to take into consideration lower limb hypoplasia. BMI of MM patients measured using As more closely approximated "normal" for age than BMI calculated using Ht. For example, females BMI calculated by Wt/As^2 was not significantly different from NCHS data ("T" Test; $P = 0.8$) but calculated by Wt/Ht^2, $P = 0.006$) BMI by Chi Square comparison between younger and older male patients with MM in our series are: LL1 and LL2 patients age 2–12 years are more obese (>95%ile) than those age 13–20 ($P = 0.03$ and 0.01). Age has no effect on the distribution of obesity amongst LL3 males ($p = 0.3$) and for female LL1, ($P = 0.6$), LL2 ($P = 0.9$), and LL3 ($P = 0.2$). BMI between different levels of lesions are insignificant between male and female LL1 ($P = 1.0$) and LL 2 ($P = 0.9$). LL1 ($P = 0.02$) and LL2 ($P = 0.0$) male and female patients are more frequently obese compared to LL3, ($P = 0.04$ and 0.007 respectively for females). Samples of these analyses will be shown.
Conclusion: Calculations of BMI using As for patients with MM are more appropriate for estimating overweight and obesity status for patients with MM than using Ht. Fewer children with MM in our series are overweight or obese than expected based on USA data for "normals" and published data about Spina Bifida Patients. BMI decreased following implementation of the Dietz regimen suggesting that it is an important adjunct in managing obesity.

S39
Attention functions in children with spina bifida with and without hydrocephalus

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S39

Background: This study is part of the multidisciplinary research program "Prognosis of Spina Bifida" of the Radboud

University Nijmegen (The Netherlands). Recent studies indicate that children with hydrocephalus have difficulty on attention and memory tests. However, it remains unclear whether these problems stem from deficits in the attentional system or from the perceptual and motor requirements of the task. The purpose of the current study is to investigate attention functions in children with spina bifida and hydrocephalus (SBH) as compared to those without hydrocephalus (SB) by administering a neuropsychological test procedure that takes into account the different task demands.

Materials and methods: 55 children between 6 and 15 years of age were recruited from the spina bifida team of the Radboud University Nijmegen, Medical Centre. All children underwent a neuropsychological assessment which consisted of tests on a wide range of cognitive functions, comprising speed of information processing, selective and sustained attention, simultaneous and sequential memory. Of the whole group of children, 36 were included for further analysis on the criteria documented presence or absence of hydrocephalus and total IQ at least 70. By comparing computerized reaction time tasks with paper-and-pencil tasks we can distinguish between attentional problems due to impaired motor speed or due to attentional deficits.

Results: Results reveal that hydrocephalic children are impaired on certain paper-and-pencil attention subtests of the WISC-III and the Bourdon-Vos Concentration Test compared to normative data of healthy controls. SBH children show deficits concerning the 'freedom from distractability factor' of the WISC-III in contrast to children without hydrocephalus. However, there were no differences between SBH and SB concerning computerized attention tasks (sutained and focused attention, impulsivity), and the Stroop-Color-Word Task (distractability).

Conclusion: When motor demands are minimized, children with hydrocephalus do not display attention problems. From this, we conclude that SBH children are not impaired in attention in general, but perform poorer on attentional tasks due to the motor demands inherent to the tasks. Therefore, it is important to assess attention in SBH with computerized simple reaction time tasks, which measure the different aspects of attention. More research is needed among individuals with SBH before the use of computerized diagnostic as a stand-alone tool apart from adjunctive cognitive assessment instruments is valid.

S40

Pressure sores in adult spina bifida (SB) patients – a questionnaire based interview of the norwegian population

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S40

Background: In a previous study we found that 35% of the adult SB population in Norway have sores [1], corresponding with other studies [2]. In this study we focused on sores and risk factors, i.e. sensory, motor, autonomous and cognition deficits, associated neurological diagnoses and lifestyle factors.

Materials and methods: Of the 193 SB patients (112 women, 81 men) registered in august 2003 at TRS, 87 (57 w, 30 m) completed a questionnaire. Associations between sores and risk factors were analysed by Pearson Chi-Square tests. Patients were categorised in three groups: (a) sores at the time of interview, (b) sores in the last five years and (c) without sores. A p value less than 0.05 was considered significant.

Results: In group (a) there were 26 patients (30%), in (b) 45 (52%) and (c) 16 (18%). In group (a) 10 had several sores. 12 sores were localised on toes, 10 on feet and 8 on buttocks. Other localisation was seldom. Sores were associated with sensory deficit (p = 0,04). Regions with normal sensibility had no sores, with reduced or missing sensibility 7 and 19, respectively. Memory deficit was the only cognition deficit associated with sores (p = 0.02). Among 44 patients, 16 were in group (a), 25 in (b), and 3 in (c). 14 patients with both tethered cord and operated Arnold Chiari malformation had higher risk for sores (8 in group (a), 6 in (b)) than patients with none or one of these diagnoses (p = 0.02). Hydrocephalus and syringomyelia were not associated with sores. Nutrition, BMI, smoking, training, job and living together were not associated with sores. Only 20 (23%) were inspected by others.

Conclusion: Totally, 82% of SB patients reported sores at time of interview or during the last 5 years. Occurrence of sores was associated with sensory function, memory deficits and with a combination of tethered cord and Arnold Chiari malformation. Surprisingly, few patients reported skin inspection by others.

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S41

Shortened silent period suggests inhibitory deficits in children with spina bifida

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S41

Background: This study is part of the multidisciplinary research program "Prognosis of Spina Bifida" performed at the Radboud University Nijmegen (The Netherlands). From a macroscopic point of view, spina bifida is a congenital malformation of the central nervous system in which both spinal cord and the brain are involved. However, from a microscopic point of view, little is known about how spina bifida affects the cortical and spinal interneuronal network. Assessment of the silent period (SP) following Transcranial Magnetic Stimulation (TMS) allows the opportunity to investigate inhibitory deficits in this network. Our aim was to investigate if inhibitory deficits are involved in the pathophysiology of spina bifida. Therefore, we studied the SP in children with spina bifida.

Material and methods: TMS was performed in 37 children with spina bifida (mean age 11.2 years, SD 2.8). Of these, 24 subjects were diagnosed with open spinal dysraphism and 13 with closed spinal dysraphism. Motor evoked potentials (MEPs) and SPs were bilaterally recorded from the biceps brachii muscle.

Results: Measurable MEPs and SPs could be obtained in all subjects. The mean durations of the SPs (right mean 66.8 ms, SD

25.3 and left mean 67.6 ms, SD 26.1) were shorter than reference values from the literature (mean 94.0 ms, SD 10.1[1]). The mean duration of the SP did not differ between subjects with open spinal dysraphism and subjects with closed spinal dysraphism. No differences were found in mean duration of the SP between subjects with and without hydrocephalus, Chiari malformation or corpus callosal dysgenesis.

Conclusion: Although the mechanisms for TMS induced silent periods are poorly understood, both cortical and spinal factors appear to be involved. Therefore, a shortened SP in children with spina bifida suggests deficits in the cortical and/or spinal inhibitory mechanisms, even in children with closed spinal dysraphism and in children without macroscopic cerebral malformations. We suggest that these deficits are more likely to be congenital rather than to be a result from secondary damage.

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S42

An Instrument to Measure the Health Status of Children with Hydrocephalus: The Hydrocephalus Outcome Questionnaire

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S42

Background: The measurement of clinical outcome in pediatric hydrocephalus frequently ignores the substantial effect that the condition can have on a child's physical, emotional, cognitive and social health. Therefore, our group developed a quantitative health status measure, called the Hydrocephalus Outcome Questionnaire (HOQ), designed specifically for children with hydrocephalus. This was designed as a simple questionnaire to be completed by the child or child's parents.

Materials and methods: The standardized steps in the development of a health status measure were followed. Item generation involved health professionals and focus groups with parents of children with hydrocephalus. This created a comprehensive list of 165 unique health status items. To reduce this list, questionnaires were sent to 69 sets of parents to assess what they felt were the most important of these health issues. The 51 most important items were then selected to represent the following health domains: Physical, Social-Emotional and Cognitive Health. The 51-item questionnaire was then tested for reliability and construct validity, in another cohort of 90 sets of parents, against the following independent measures of specific components of health: Health Utilities Index (HUI-2), Wide Range Achievement Reading Test (WRAT), Strengths and Difficulties Questionnaires (SDQ), Functional Independence Measure for Children (WeeFIM).

Results: The HOQ took approximately 10–15 minutes for the parents to complete and demonstrated excellent test-retest reliability (0.93, 95% confidence interval (CI) 0.88–0.96), inter-rater reliability (0.88, 95% CI 0.79–0.93), and internal consistency (Cronbach's alpha 0.94). Construct validity was demonstrated by very good Pearson correlations of domain scores with their respective independent measures. The child-completed version of the HOQ also demonstrated very good reliability properties.

Conclusion: The HOQ for children with hydrocephalus has been developed and has demonstrated excellent reliability and validity properties. This will provide a valuable measurement tool for a wide range of clinical research projects in pediatric hydrocephalus. Using the HOQ, our group has begun a large-scale study to explore the determinants of health outcome in this population of children.

S43

The quality of primary relationships in families of children with spina bifida

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S43

Background: This study was part of the multidisciplinary research program "Prognosis of Spina Bifida" of the Radboud University Nijmegen, The Netherlands. Based on a family systems perspective, mothers and fathers of children with spina bifida were examined in comparison to non-clinical samples of parents across different levels of family functioning (individual, marital, parental, and familial). Two questions were addressed: (1) To what extent do families of children with spina bifida differ from regular families; and (2) Do child characteristics (severity of spina bifida, IQ, and/or behavioural problems) predict the divergent family characteristics?

Materials and methods: Mothers and fathers of children with spina bifida (n = 70; age Mean = 8.6, SD = 4.4; 43 girls) filled out questionnaires for which norm data were available including the Child Behaviour Check List, Coping Orientation of Problem Experience Inventory, Dyadic Adjustment Scales, Parenting Stress Index, and Family Environment Scales. Severity of Spina Bifida was assessed by a child neurologist and through parent reports. A neuropsychologist assessed the child's IQ by use of the WISC-III.

Results: On individual level, index mothers and fathers did not diverge from parents of able-bodied children in their problem-focused coping efforts. However index mothers reported to seek significantly less social support and index fathers reported significantly less avoidant ways of coping than their counterparts. On dyadic level, both index parents reported to experience significantly less marital satisfaction in comparison to other parents. Within the parent-child dyad, index parents reported to experience more child-rearing satisfaction than parents of able-bodied children, but at the same time they also reported significantly more parenting stress, i.e. more depression, less feelings of parenting competence, more role restrictions, more health problems, and more social isolation. On family level, index families scored significantly higher on the Family Relations Index than norm groups, indicative of more cohesion, expressiveness, and less conflicts. Preliminary linear regression analyses showed that the severity of spina bifida predicted avoidant coping negatively and family structure (organization and family norms) positively. The child's low IQ predicted less marital satisfaction, less child rearing satisfaction, and more family structure. Internalization problems of the child predicted less marital satisfaction and more parenting stress.

Conclusion: The meaning of the current results will be discussed in the perspective of family systems and quality of life. The paradoxical results on the parenting dyad will be discussed along the parenting dimensions of affection, responsiveness, and control.

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S44

POSTER PRESENTATION

S45
Post-operative complications associated in patients with spina bifida: an analysis of shunted patients

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S45

Background: All Spina Bifida patients with Myelomeningocele require specialty care from Orthopaedics, Neurology, Urology, GI and Plastics. A high percentage of these patients require surgery as a treatment modality. This outcome research study illustrated increased compilations post surgery in Myelomeningocele patients with VP shunts compared to the general Spina Bifida population with non-existing VP shunts. The special focus is on VP shunt placement for Hydrocephalus and/or Arnold Chiari Malformations. Although this specific patient population may require surgical intervention, it is crucial for surgeons to recognize and anticipate the potential complications involved.
Materials and methods: 70 patients with Spina Bifida and shunted hydrocephalus were evaluated who had undergone GU, GI, Neurosurgical and Orthopaedic procedures.
Results: There are 44 patients with complications that had undergone procedures involving the abdominal cavity and/or spinal corrections. The lower extremity cases did not have postoperative complications. The majority of the complications −80% were shunt related.
Conclusion: Often the shunt malfunction or infection is not readily appreciated by caretakers outside the medical center and may be subtle such as malaise, poor appetite, low grade temp, etc. At times a shunt function test may not be abnormal. It is statistically significant to appreciate the potential for shunt malduction early in these patients and treat them accordingly to prevent morbidity such as herniation, and death.

S46
Distal obstruction in shunted children after bladder perforation

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S46

Background: The commonest reason for shunt dysfunction is proximal or distal obstruction due to short or disconnected catheters. Infection with an abdominal cyst can also give a distal obstruction.
Materials and methods: Between 1998 and 2003 five children (7–16 years) were operated for bladder perforation. One of the children was augmented with ileum, three with colon and one underwent detrusor myectomy.
Results: Two children had a laparotomy due to bladder perforation with urine in the abdominal cavity. Two–five days later they developed headache, lethargy and signs of high intracranial pressure. The distal catheters were externalised for 1–5 weeks before successful replacement into the abdominal cavity. The third child perforated during a renography and two days developed signs of shunt-dysfunction. The distal catheter was externalised and later the shunt was converted to a ventricular-atrial system. The fourth patient had an iatrogenic lesion of the bladder with urine leakage during abdominal surgery. Ten days later there were signs of distal obstruction and after externalisation, the shunt was converted to an atrial system. The fifth patient had a neonatal perforation and after augmentation several episodes with abdominal pain believed to be due to local abscesses. There were signs of shunt-dysfunction on one occasion, thus the distal catheter was externalised and later replaced into the abdominal cavity. During a later episode a bladder perforation to a localised cavity was found at laparotomy.
Conclusion: Ventriculo-peritoneal shunted children with bladder perforation and urine free in the abdominal cavity can develop distal obstruction due to a temporary resorbtion difficulty of CSF. Careful observations of signs of shunt dysfunction are therefore recommended. Following externalisation of the distal catheter it is possible to replace it into the abdominal cavity.

S47
An independent 40 year review of mortality in open spina bifida

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S47

Background: The mortality in young children with spina bifida has fallen since 1963 when the Cambridge study began. Studies in older children and adults show a considerable loss at follow-up, and incomplete data on causes of death.
Materials and methods: The Cambridge Cohort consists of 116 cases born between 1963 and 1971. The causes of death up to 2005 are recorded. Information came from hospital records and the Office of National Statistics. Further information was obtained from autopsy reports and from doctors and carers.
Results: 67 (57%) of the patients have died. Most deaths in the first 20 years were caused by hydrocephalus and CSF infections. In the second 20 years deaths were more commonly cardio-respiratory and renal. Mortality was greater where the sensory level of the lesion was higher.
Conclusion: The overall death rate compared with other centres. Patients with a high sensory level have twice the mortality of those with a low sensory level.

S48
Increased cooperation for children with spina bifida in performing clean intermittent catheterisation (CIC) – a client centred, goal attained, intervention study

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S48

Background: Children with spina bifida often have urinary incontinence and therefore use Clean Intermittent Catheterisation (CIC) to empty their bladders. The children initially are helped in performing the CIC but later they are expected to manage this procedure by themselves. The task is not an easy one and the children might get too much assistance in toileting procedures too long a period.
The aim of this study was to examine and describe if and how a client-centred, goal attained intervention with specific sequential measurable objectives (short-term goals) could increase the children's co-operation in CIC.
Eight children with spina bifida living in two geographic areas were identified for purposes of this study.
Materials and methods: The data collection was inspired by case study format and contained field observations on two different occasions per child and a knowledge inventory with the parents and staff in question were utilised. Also assessments of caregiver assistance and film/photo/video of the different environments were incorporated into the study. Individual, specific objectives for the intervention jointly were established by the children, parents and therapists. The intervention was performed by the occupational therapist and the urotherapist together with the children, the caregivers and consisted of adaptation of routines, equipment, environment and practice.
Results: The results of this study describe the problems that occurred when the children performed the CIC and the content of the intervention. The results of the six children were presented in parallel categories and differences between the first and the second observation were identified.
The results indicated that the goal attained and client-centred work was successful. As much as 31/39 and 37/39 of the objectives were fulfilled totally or partly. Half of the children increased their co-operation after intervention and also made progress in related areas. The results also indicated that there was unawareness *if* and *how* the children were allowed to participate in CIC. Parents and children kept CIC-routines from early childhood and did not change them as the children grew. Change in CIC routines occurred during intervention and an increased understanding of the importance of co-operation in CIC emerged. The working position was individual and was together with the environment of great importance for a successful occupational performance. In order to become increasingly involved, the toilet often had to be adapted in different ways. Some children were in need of specially designed equipment during the initial stage. Equipment that was gradually removed as the child increased his/her competence. Other children needed new equipment and some children a refurnished bathroom to increase their co-operation.
Conclusion: Occupational therapy and urotherapy in combination are successful when the focus is increased co-operation in CIC for children with spina bifida. This study revealed that children could become increasingly involved in CIC due to intervention and co-operation of the occupational therapist, urotherapist, parents and caregivers.

S49
Exercise tolerance, level of physical activity and muscle strength in independent ambulators with Sacral Myelomeningocele

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S49

Background: In previous studies we investigated functional outcome in children with sacral level (lipo) myelomeningocele. Although 89% of them were community or normal walkers, most (90%) of them had balance problems, such as hopping into squares, jumping and standing on one leg. This might interfere with regular sporting activities, which are often limited in these children.
In this study we want to investigate the causal link between muscle strength, balance problems, endurance, level of everyday and sporting activities, and self-perceived motor competence in two groups of ambulant children with lumbosacral level paralysis: myelomeningocele (MMC) versus lipomyelomeningocele (LMMC)
Materials and methods: Currently (from February to April 2005) a cross-sectional study is carried out at the Spina Bifida outpatient clinic from the University Medical Hospital Utrecht. Thirty three children met the inclusion criteria (lesion level below L4, IQ > 80, aged between 6-18 years, being able to ambulate for 500 metres or more).
Muscle strength is measured with a hand-held myometer in upper and lower extremities in the following muscle groups: shoulder abductors, wrist extensors, grip strength, hip flexors, hip abductors, knee extensors, knee flexors, ankle dorsiflexors and calf muscles. Endurance is measured with the 6 minute walking test. The patients are instructed to walk at their own chosen walking speed from one side of the corridor to the other, turn and walk back. The total distance covered in 6 minutes is calculated. Exercise capacity is measured using a maximal exercise test on a treadmill ergometer and an expired gas analysis system (VO2 peak). The level of everyday physical activity is measured with a diary. Self-perceived motor competence is measured with the Dutch adaptation of the Harter Self-Perception Profile for Children. Data are analysed using independent samples T-tests.
Results: Currently we are collecting all data and the results will be discussed. A sample of 17 children with MMC and 6 children with LMMC are willing to participate in the study. Their mean age (SD) is 10.3 (3.3) and 10.6 (3.1) years respectively. All results will be corrected for known confounders such as age, gender, body mass index, body fat. The results will be compared with reference values of the normal population. In addition, we will compare the outcome in children with myelomeningocele with associated hydrocephalus and Chiari II malformation, with that of those with lipomyelomeningocele, without those associated central nervous system

abnormalities. Causal relations between muscle strength, the level of everyday physical activity, endurance and self-perceived motor competence, will be calculated.

S50
Hydrocephalus and myelomeningocele; series and results

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S50

Background: Following different reported series, myelomeningocele presents in 1–2 per 2000 live newborns. Hydrocephalus occurs in approximately 80–90% of all them.
Materials and methods: Authors present their personal experience in patients diagnosed of having myelomeningocele, seen in their Pediatric Neurosurgery Department since 1991 to 2004.
Results: During this period of time, a total of 396 patients were diagnosed of having myelomeningocele, and 352 of them have developed associated hydrocephalus. All these 396 patients were treated with CSF diversion.
Conclusion: Algorithm mostly used for diagnosis and follow-up in these patients, the different optional CSF diversion methods, the malfunction problems due to obstruction or infection, the better therapeutic approach to shunt malfunction, as well as the protocols used for following-up these children during the neonatal, infant and pubertal ages, will be presented in this paper. A comparative study between the reported series and our own experience is also made.

S51
Biochemical markers of bone metabolism in patients with Myelomeningocele

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S51

Background: Biochemical markers of bone turnover provide a means of evaluating skeletal dynamics that complements static measurements of bone mineral density (BMD). This study was designed to examine biochemical markers of bone metabolism in myelomeningocele (MMC) patients.
Patients and methods: Eighty patients with myelomeningocele were randomly chosen from a roster of >500 patients with myelomeningocele followed at a multidisciplinary spina bifida unit in a public tertiary university hospital. Patients with known metabolic acidosis, renal insufficiency, or other metabolic bone disease (i.e., hyperparathyroidism) were excluded. The methods used in the study were clinical interview and examination, measurement of total-body bone mineral density (BMD) with subregional values and estimation of biochemical markers of bone turnover (formation: osteocalcin, bone specific alkaline phosphatase (BSAP); resorption: urinary deoxypyridinolines, type I collagen cross *linked* N-telopeptide (NTx)) and the main parameters of calcium phosphate metabolism in blood and/or urine. To study relationships among the variables, the Chi-squared, ANOVA and lineal regression tests were applied.
Results: The formation bone markers were into the normal values while the resorption bone markers were higher than normal values. The bivariate analysis showed statistically significant relationships between bone mineral markers and age, body mass index, hip flexion contractures, intake of calcium, and abnormalities in menstrual period. Bone resorption markers were related with pelvis BMD. Bone formation markers were related with trunk, spine and total body BMD. PTH was related with trunk and total body BMD. The multivariate approach demonstrated that BSAP levels were determinate by body mass index ($p = 0.002$), urinary deoxypyridinolines ($p = 0.002$) and neurological level ($p = 0.013$). Osteocalcine levels were determinate by calcium intake ($p = 0.001$) and sex ($p = 0.008$). Urinary deoxypyridolines levels were determinate by urea ($p = 0.001$) and hip flexion contractures ($p = 0.009$). Finally, NTx levels were determinate by calcium intake ($p = 0.001$).
Conclusion: Biochemical markers of bone mineral metabolism in myelomeningocele could be a good tool to evaluate the bone metabolism although it is necessary have a prolonged follow-up in order to conclude their real value in the current practice.

S52
IIIrd Ventriculostomy: Data from the UK Shunt Registry

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Cerebrospinal Fluid Research 2005, **2(Suppl 1):**S52

Background: Although the UK Shunt Registry is concerned primarily with shunt performance, we hold data on IIIrd Ventriculostomies performed in the British Isles.
Materials and methods: We have identified 819 patients where IIIrd Ventriculostomy was the primary procedure. The median age of these patients was 11.9 years. The most common reasons for IIIrd Ventriculostomy were given as congenital aqueduct stenosis (28%) and benign and malignant tumours (29%).
The effectiveness of IIIrd Ventriculostomy was estimated using a Kaplan-Meier statistical model, with failure as the insertion of a valved shunt. 10 patients died before any valve insertion.
Results: 77% of patients were shunt free at one year and 71% at five years. Of these patients, 17 received a second IIIrd Ventriculostomy and one patient had a third.
Conclusion: These figures compare favourably with the shunt valve survival rate in children of 72% after one year and only 56% after 5 years.

S53
Detrusor sling bladder neck closure – follow up results

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Introduction: There are a number of procedures which aim to prevent urethral leakage of urine in patients with a neuropathic bladder performed in combination with reconstruction operations. We have previously reported our initial

experience using a sling created from detrusor muscle[1]. This presentation gives longer follow up results of the procedure.

Methods: The technique was described previously[1]. An incision is made in the anterior wall of bladder muscle and a detrusor flap is raised. This strip is wrapped around the upper urethral mucosa and sutured with 3/0 polygalactamin before closure of urethral muscle over strip.

Results: We have performed this procedure on 5 patients (2 males and 3 females) with a median age of 7 years 3 mo (range 5–17 yrs). The neuropathic bladder was secondary to pelvic tumour (n = 2), spina bifida, following treatment of Hirschsprung's disease and anorectal anomaly (n = 1 each). At a median follow-up of 4 years (range 3–5 years), 3 patients remain dry on intermittent catheterisation via their Mitrofanoff stomas and one is damp. One patient remained urethrally incontinent from early failure of the procedure on transfer to adult services. No patient has achieved urethral catheterisation.

Conclusion: Our results suggest that the detrusor sling bladder neck closure can achieve lasting continence with results comparable to bladder neck division. Urethral catheterisation following this procedure is unlikely to be achieved. In patients who have had previous surgery at the bladder neck this procedure is unlikely to be feasible.

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S54

Clinical and histological outcome of fetal spinal surgery in a chronic sheep model

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Background: Fetal surgery is a treatment modality for open spina bifida. However, the value of in-utero spina bifida repair is questionable [1, 2]. Therefore we tried to improve the surgical procedure in an animal experiment and also explored the original motive of in-utero treatment, i.e. the so-called two-hit hypothesis [3].

Table 1 (abstract S54) Findings at full term age, according to type of surgical procedure

Procedure	Clinical outcome	Histologic features
Biomatrix closure (7)	No impairment (6) Died after birth (1)	Minor cord abnormalities (4) No cord anomalies (3)
Closure using skin (3)	No impairment (2) No data available (1)	Considerable cord abnormalities (1) No cord abnormalities (2)
Unclosed defect (6)	Major paraparesis (4) No impairment (1) Died after birth (1)	Major cord abnormalities (6)

Material and methods: Study subjects were fetal lambs with an, at 79 days gestation, surgically created opening of the spinal canal. Biomatrix covering, applied immediately after creation of the spinal defect, was taken as a tool for surgery improvement. The clinical and pathological findings at full-term age were taken as outcome measures. For comparison, two procedures were used, i.e., spinal canal opening without closure; and closure using skin.

Results: See table 1

Conclusion: Our findings indicate that intra-uterine biomatrix closure is feasible, but as for spinal cord sparing, is not superior over closure using skin. However, due to its simplicity, biomatrix closure might imply less surgery inherent complications, including immature birth and still-birth. Further studies are necessary before definite conclusions can be drawn. The same applies to the two-hit hypothesis. With respect to this issue, our findings are supportive but not decisive.

S55

Utilization of medical care among children with spina bifida

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Background: Children with spina bifida are at risk for developing multiple medical problems that often lead to hospital care. During 2003 we performed a retrospective study including all children with spina bifida, born between 1984 and 1991, and living in Uppsala county. The aim of the present study was to investigate the occurrence and nature of all events of hospital care during the study period. We also analyzed risk factors associated with a high utilization of medical care.

Materials and methods: The study population consisted of 15 children (6 girls and 9 boys) with a median age of 16.8 (14.0–18.9) years. Five children were ambulant and 10 were non-ambulant. Fourteen children had hydrocephalus and 11 of these had a shunt inserted. All except one child had some degree of impaired urinary bladder function. Two children had mental retardation. For all patients medical records were reviewed from all inpatient departments at University Hospital, Uppsala. Data were also collected regarding perinatal problems and other medical and functional problems.

Results: During the study period the children with spina bifida had been hospitalized for a mean number of 200 (43–491) days. The most frequent causes for admission were neurosurgical, urological and orthopedic. High number of days in hospital was associated with non-ambulation, complication affecting the shunt, high-pressure urinary bladder and scoliosis, but not with increasing age of the child. For the group of children the mean number of operations was 14 (2–32). The most frequent cause for operation was neurosurgical, including one or more shunt revisions (11 children), decompression operation (4 children) and release of a tethered cord (3 children). Analysis of perinatal riskfactors showed that both high medical consumption (more than 300 days) and a high number of operations (15 operations or more), were strongly associated with complicated primary closure of the cele.

Conclusion: Although the health of children with spina bifida has steadily improved, many continue to have frequent and

severe complications, requiring hospitalization and also often operation. Complicated primary closure of the cele might be a risk factor for a later high utilization of medical care.

S56

Effects of hydrocephalus and ventriculoperitoneal shunting on afferent and efferent connections of the feline sensorimotor cortex

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Background: Previous reports have suggested that connectivity of the cerebral cortex may be irreversibly altered by hydrocephalus, but very few studies have examined this possibility directly. Therefore, an axonal tracer study was initiated in a feline model of infantile hydrocephalus that was amenable to ventricular shunting.
Materials and methods: Obstructive hydrocephalus was induced in 10-day old kittens by intracisternal injections of kaolin; saline-injected animals served as controls. Hydrocephalic kittens received low-pressure ventriculoperitoneal (VP) shunts 10–14 days post-kaolin. Unilateral injections of wheat-germ agglutinin-conjugated horseradish peroxidase (HRP) were made into the sensorimotor cortex (Brodmann's areas 4, 6 and 3) in hydrocephalic animals (n = 5) at 9–15 days post-kaolin to represent the pre-shunted condition. Shunted animals (n = 5) received HRP injections at 1, 2 and 4 weeks post-shunt. Control animals (n = 5) received HRP injections at set time-points between 12–47 days of age to broadly match the sacrifice times of the shunted animals.
Results: VP shunting reversed all behavioral abnormalities, including spastic movements, extensor rigidity, and lethargy. Reduction of anterograde and retrograde HRP labeling was most profound within the contralateral cortex and portions of the midbrain, and considerable in the thalamic relay nuclei, especially the ventrolateral nucleus. Labeling within cell bodies of the ventral tegmental area (VTA) decreased greatly in untreated hydrocephalus. Untreated hydrocephalus reduced retrograde labeling in the locus coeruleus but did not affect the raphe nucleus. Shunting increased both anterograde and retrograde labeling of contralateral motor cortex to near normal. Thalamic relay nuclei recovered retrograde labeling, but anterograde labeling did not return to control levels. Shunting restored cellular label to the VTA and locus coeruleus. Surprisingly, recovery of labeling occurred as early as 7 days after shunting, suggesting that functional deficits in axoplasmic flow, rather than structural deterioration of axons, were responsible for at least some of the changes associated with untreated hydrocephalus.
Conclusion: Collectively, these data suggest that (1) cortical connectivity involving both afferent and efferent pathways was impaired in untreated hydrocephalic animals, and (2) shunting improved both cortical afferent and efferent connectivity, but (3) complete re-establishment of the cortical efferent pathways did not occur. Dysfunction in cortical pathways, if permanent, could be responsible for many of the motor and cognitive deficits seen clinically in afflicted hydrocephalic children.

S57

Determination of risk factors & evaluation of the outcome of patients with spina bifida aperta

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Introduction: Spina Bifida is a term used for all forms of open spinal defects from myeloschisis to meningocele. The etiology & pathogenesis is still not yet clear. The risk factors and treatment aspects are still under review and debate. We have assessed several possible risk factors including; Birth order, sex, maternal age, maternal obesity, consanguinous marriage, miscarriages, occupation, geographical area of residence and also followed the outcomes after surgical treatment.
Methods: Prospective study of patients of all ages presenting to the neurosurgical department from 1998 to 2002. Patients and parents fully assessed and investigated for risk factors and any abnormalities. All data was collected and analysed for etiological and predisposing factors. Patients treated had surgical repair carried out in standard five layer closure with patients discharged on day eight. The surgical outcome was assessed at six months.
Results: 34 patients. Mean age 2.1 yrs (range 1 day to 25 yrs old). 13 females, 21 males. Location of spina bifida aperta were 10 lumbar, 13 lumbosacral, 9 dorsolumbar and 2 dorsal. Defects were 4 meningocele, 21 myelomeningocele and 9 lipomyelomeningocele. 29 patients underwent surgical repair, 10 of which were shunted for hydrocephalus, 9 of these 10 were myelomeningoceles and 1 meningocele. 5 patients had csf collections at repair site. 2 deaths due to meningitis occurred preoperatively. 4 patients had improved neurologically post operatively the rest showed no improvement in any existing neurology. No patients deteriorated in neurological function. 8 patients were 1st born and 17 were 4th & higher order. Maternal age mean 28.6 (range 16 yrs to 40 yrs). 8 patients were from consanguineous marriages, and 8 from mothers who had previous miscarriages. 90% of mothers were housewives with a Mean Body Mass Index of 23.9. 15 out of 34 families lived in hilly areas.
Discussion: Risk factors found from this study were, consanguineous marriages, first born and high birth order, teenage birth and high maternal age. A higher incidence in males was found. Meningoceles had the best outcome, whilst myelomeningoceles outcome varied. Most common complication being hydrocephalus requiring a shunt. Neural tube defects have a multifactorial origin and further research and education is required for establishing associated factors and improving treatment.

S58

The neural tube and heart defects: our experience

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Background: The most common forms of congenital anomalies are spina bifida and cardiac anomalies. It is known that they can occur together, although the reason for this is not clear.

Materials and methods: Four patients were reviewed in our unit with combined spina bifida and cardiac lesions. We reviewed clinical data to evaluate the type of spina bifida and cardiac lesion.
Results: Two cases of spina bifida were associated with complex cardiac anomalies. One patient with spina bifida occulta also had complex cardiac anomaly. The fourth patient had a terminal lipoma and died in cardiac failure.
Conclusion: Spina bifida and complex congenital heart disease may co-exist in the same patient, but no clear evidence exists as to the etiology

S59
Tragic as a boundary experience by parents of a child with spina bifida

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Background: This study is part of the multidisciplinary research program "Prognosis of Spina Bifida" of the Radboud University Nijmegen. In the framework of this program both a prospective and a retrospective study on children with different types of spina bifida and their parents has been conducted; the disciplines involved were child neurology, neuropsychology, child & family studies and empirical theology. The empirical theological part of this programme investigates the moral and religious orientations of parents of a child with spina bifida while confronted with the diagnosis and ongoing difficulties during childhood.
Materials and methods: This presentation will focus on 'boundary experiences', in particular the specific boundary experience of tragic. Boundary experiences can be regarded as confrontations with the contingency of human existence. These experiences fundamentally call into question the meaning of life. In the empirical theological project the four following boundary experiences were studied on the basis of theological conceptualisation and are subsequently studied empirically: tragic, suffering, guilt, and death. This presentation will focus on the boundary experience of tragic which refers to the experience of a tension between an *'I should'* and an *'I can't'*. The following questions will be raised: 1. Which attitudes towards tragic are present among the parents of a child with spina bifida? 2. Is there a difference in support of these attitudes when some neurological and neuropsychological characteristics are taken into account?
Results: With regard to the first question three attitudes (on the basis of factor analysis) towards the experience of tragic were found among parents (n = 103) of a child with spina bifida. Hereby a distinction is made between religious and non-religious parents. The average score at a 5-points-scale (1 = 'very weak', 5 = 'very strong') of the three attitudes indicate that the parents are uncertain about the model of physical tragic, and disagree with the models of personal and religious tragic. Preliminary results with regard to the second question cannot be given yet, because of the fact that the analysis is still well under way.

ORAL PRESENTATION

S44
Casey Memorial Lectureship: Adult consequences of spina bifida

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I am honored to be the Casey Holter Memorial lecturer. All of us in the Society miss John Holter very much! The Casey Holter Memorial Lecture was established and funded to preserve the memory of Casey, John's son who was born with hydrocephalus. The purpose of the Casey Holter Memorial Lecture is to encourage original thinking in a way to improve the care of individuals with spina bifida and hydrocephalus. Having kept this purpose in mind, I have chosen the title "The Adult Consequences of Spina Bifida" with the intent to review the outcome studies documenting our successes, and unfortunately in some cases our failures. By looking at these outcome studies, it is hoped that we can recognize areas of potential improvement in the treatment of children so they may have more fruitful lives as adults. In this review I have included the work of neurosurgeons, neurologists, orthopaedists, psychologists, sociologists, educators as well as physical and occupational therapists.
Unfortunately no one has a great deal of experience treating adults with spina bifida. The patients who were born prior to 1950 would not have benefited from the shunts we have today for hydrocephalus. Very few adults born with spina bifida prior to 1950 are alive today, as most of those infants would have died in childhood from complications of hydrocephalus. Those individuals born between 1950 and 1970 would have benefited from having their hydrocephalus shunted, however, urological care was not as sophisticated as it is today. Urodynamic monitoring of bladder function and intermittent straight catheterization had not been developed. Obstruction and reflux lead to chronic pyelonephritis. Unfortunately many of those individuals died in their late teens or early twenties because of renal failure. This group, like those born before 1950, is small with few survivors and little is known about them.
The children born after 1970 have benefited from both the shunts for hydrocephalus and modern urological care. This group has survived to adulthood and represents a growing population, which will present new challenges to us as caregivers. I will attempt to summarize some of the outcome studies dealing with adults who are in their second, third and fourth decades of life [2, 3, 8, 9, 10, 13].
The major question is "how often are adults with spina bifida leading successful and productive lives?" There are several studies addressing the quality of life, level of independence and self-determination. [4, 7, 9, 11, 13, 14, 16, 20, 21, 22, 23, 24, 27]. Using the Objective Checklist – ACL Autonomy scale, the Days of Coping Checklist – WCC Problem Focused Coping Scale and the Denver Self Care Aging Journal, Monsen [5] showed that adolescents and young adults with spina bifida are less independent than a matched comparison sample of adolescents and adults without spina bifida. A few intervention studies

(18, 19) have shown some promise in improving the independence and self care of these young adults through mentoring, coaching and peer support groups. One measure of success and independence would be the ability to seek and gain employment [3, 26]. Bomalaski, Teague and Brooks looked at the employment records for individuals with spina bifida. As urologists they were looking at the long-term impact of urological management on the quality of life in individuals with spina bifida. Their study showed that only 17% of individuals with spina bifida were fully employed and 14% were part-time employed. Fourteen percent of the adults were still in training while 6% could not find a paying job and volunteered as unwaged workers. The unfortunate statistic is that 49% were clearly unemployed and had no hopes of ever finding jobs. There are many reasons why adults with spina bifida may have difficulties in finding a job. The average IQ for an individual with spina bifida is 80, with 10% of this population having an IQ less than 70 [26]. Many have difficulties getting the level of education necessary for a highly technical job. Many are still socially incontinent and remain continuously wet with urine [3]. Being wet with urine gives them a foul odor making finding a job difficult, as they are not accepted socially. Motivation is key to any occupation. Unfortunately many of our adults with spina bifida have developed a passive co-dependency with their parents making the break from family difficult. Training opportunities may not be available to this group, depending on their community. Mobility and transportation can also be issues depending upon how independent they are with their walking or wheelchairs. Communities can vary a great deal with regards to wheelchair accessibility. Looking at all these factors that adversely affect employment, we can make some changes to improve the situation. More diligent neurosurgical monitoring of shunts can prevent shunt failures that may adversely affect cognitive function. Urologically we can strive to make them more continent. Newer advances in urology will undoubtedly improve the statistics on urinary incontinence. The antigrade colonic enema procedure has been a great advance in bowel continence. Early recognition of psychological problems can lead to early counseling to hopefully improve their motivation for independence. We can encourage our communities to provide training for our children with spina bifida. We can always work harder to help them gain mobility, either with wheelchairs or with walking. Hopefully over the next decade, we will be able to present data showing improvement in the employment statistics.

Getting married is another sign of independence from parents [17]. Twelve percent of the thoracic and high-lumbar level men, and 33% of the low lumbar and sacral level men were married. There was a slightly greater tendency for the women to be married. Thirty three percent of the thoracic and high-lumbar level women, and 75% of the lower lumbar and sacral level women were married. An obvious obstacle to marriage would be sexual dysfunction related to their spinal cord abnormalities and paraplegia. Despite their paraplegia, however, surveys of men with spina bifida found that 72% were able to achieve an erection with 54% being able to have an ejaculation. Thirty-one percent of the men were sexually active. The women have less of a problem in this area. Forty-nine percent of the women were found to be sexually active [6]. Looking at the population who are sexually active, 8% of the men were able to father a child and 34% of the sexually active women were able to get pregnant and deliver either vaginally or by Caesarian section [17].

Mobility is also important for independence. There are varying statistics between studies but overall there is general agreement that the low lumbar and sacral level individuals are more likely to walk than the thoracic and high lumbar level individuals [1]. Looking at adults with the low lumbar and sacral levels [5], we find 65% of this population are community ambulators while 20% can walk at home but use a wheelchair for long distances. Five percent are non-functional walkers who can walk for exercise, but walking serves no purpose or function for them. Ten percent of this group are wheelchair ambulators completely. Of the thoracic and high lumbar level patients, only 10% are able to walk in the community, 10% are domestic ambulators, 10% are nonfunctional ambulators and 70% are wheelchair ambulators [25].

For those adults with significant weakness in the legs, wheelchair ambulation is definitely more efficient and preferred by most adults with high-level spina bifida. The wheelchairs offer more speed, take less energy and are more convenient. It is much easier to get in and out of a wheelchair than to put braces on and to take them off. Walking may not be worth the extra effort. Walking does have some advantages for those adults that have maintained the ability and motivation to walk. Walking allows you to be accessible to more places. It gives you more exercise, which could help with weight control. Walking and weight bearing may help prevent osteoporosis and prevent fractures. Adults with spina bifida who walk tend to have fewer serious pressure skin sores than those confined to a wheelchair.

Musculoskeletal pain will be one of the reasons why adult patients with spina bifida will seek medical care. Thirty-five percent of the adults surveyed complain of upper extremity pain and most of these have either elbow or wrist pain from overuse. The overuse is most likely from using crutches for support in walking. Treatments consist of modifying their activity, physical therapy, orthotics and anti-inflammatory medication.

Back pain is common and requires extensive work up. The differential diagnosis for back pain includes tethered cord, scoliosis, spondylolisthesis as well as mechanical problems related to their abnormal gait.

Pain is extremely rare in the hip and the ankle but very common in the knee. I was able to find only one case report in the world's literature where a total hip replacement was performed on a patient with spina bifida. This patient was a woman with L4-L5 level spina bifida who had right hip pain from avascular necrosis. There was no mention as to why she developed avascular necrosis. With this being the only documented case of a patient with spina bifida and hip pain, the prevalence of painful arthritic hips must be extremely low in this population. I, therefore, believe we are correct in not being very aggressive with the treatment of hip dysplasia in children with spina bifida.

Degenerative arthritis of the knee, on the other hand, is turning out to be a major problem affecting the adult with spina bifida. Williams et al. [29] in 1993 studied 72 community ambulators, aged 23 to 39. Painful degenerative arthritis of the knee occurred in 24% of adults with spina bifida who walked. There are two main causes of arthritis of the knee in adults with spina bifida. The knee arthritis is related to (1) muscle weakness about the hip and (2) weak plantar-flexion of the ankle. The weak hip muscles lead to a gluteus medius lurch causing the trunk to lean laterally beyond the knee on the coronal plane. This causes a valgus force at the knee. This in turn leads to medial instability and eventual arthritis. The second cause of arthritis is the weak

calf muscles. Gait analysis [12, 28] has shown that the weak or nonexistent calf muscles leads to a poor push-off at the end of stance phase in the gait cycle. The patient, in order to move forward, must externally rotate the foot and tibia. The femur tends to rotate inward as the tibia rotates outward. The knee then becomes a fulcrum about which the body twists. This external rotation, valgus force leads to medial instability and eventual osteoarthritis of the knee. Three treatment plans for knee arthritis have been proposed. (1) Williams and Menelaus [29] recommend the use of a knee orthosis for prevention and treatment of the knee instability. (2) Vankoski [28] recommends forearm crutches and (3) Lim [12] suggests that a tibial osteotomy be considered to correct the external tibial deformity. Lim feels that these derotational osteotomies will delay if not prevent knee instability and later painful arthritis.

The most frequent, costly and worst problem seen in adults with spina bifida is skin breakdown. David Shurtleff [23] found that 85% of adults with spina bifida have had problems with skin sores at least one time in their lives. Some of course suffer from chronic skin ulcers. The cause of the skin sores is insensate skin and deformity, either from scoliosis, kyphosis, pelvic obliquity or contractures. Prevention and treatment must include the correction of deformity, patient education and wheel-chair modifications in addition to treating the skin ulcer with wound care.

In order to improve upon the results we have seen from our adult outcome studies, we need to start the rehabilitation process while the children are still young. I will briefly summarize our rehabilitation goals and treatment plans that we set up for children beginning in the newborn nursery. Much of what we do now in Orthopaedics is attributed to the work of Malcolm Menelous and John Sharrard.

Malcolm Menelaus was a member of this society from 1960 until his death, September 12, 2000. Malcolm gave the Casey Holter Memorial Lecture in 1976. The title of his lecture was "Orthopaedic Management of Myelomeningocele. A Plea for Realistic Goals and Minimum of Surgery." I was very close to Malcolm as he was my mentor when I did my fellowship at the Royal Children's Hospital in Melbourne, Australia. Malcolm was known throughout the world because of his interest in the care of severely disabled children, in particularly children with spina bifida. His book "The Orthopaedic Management of Spina Bifida Cystica", was published in Edinburgh in 1971 by E&S Livingston. Now in its third edition, it will stand as a monument to Malcolm's industry and dedication to the care of his patients. Malcolm was influenced a great deal by the work of John Sharrard who was also a member of this Society and died in 2001. John was known as one of the world's outstanding orthopaedic surgeons. He was an orthopaedic consultant in Sheffield where he participated in the multispecialty clinic established for the orthopaedic management of children with myelomeningocele. John Sharrard published well over 100 papers and 30 textbook chapters, many concerned with the paralytic diseases of children. There is no question that this Society will clearly miss John Sharrard and Malcolm Menelaus.

John Sharrard and Malcolm Menelaus taught us the importance of first evaluating the child's neurological status. We don't just concentrate on the spinal cord lesion created by the spinal defect but look at the total neurological picture. With the advent of the MRI we certainly recommend imaging of the brain and the entire spinal cord. We are looking for other associated anomalies such as a syringohydromelia, tethered cord and the Arnold-Chiari malformation. This slide demonstrates a synringohydromelia in a child with spina bifida. The next slide reminds us of the association of the Arnold – Chiari malformation with spina bifida. My main goal as an orthopaedic surgeon is try to determine whether or not I am dealing with a flacid paralysis or possible dealing with a spastic component to the child's neurologic picture. Once I determine this, I then try to determine the lesion level in the spinal cord. Before the spinal defect is closed, I recommend a manual muscle test to determine the spinal cord level of lesion. This manual muscle examination is repeated 5–7 days after surgery and then every 3 months. The manual muscle testing is limited and therefore inaccurate in the newborn period. We are restricted on positioning the patient after surgery as the infants need to be kept prone to protect the surgical wounds. The infant state itself makes the examination inaccurate as the infant is obviously not going to follow commands. Despite those limitations, we try to determine the presence or absence of muscle function with a simple grading system. We record an "X plus" if the muscle appears strong and an "X minus" if the muscle contracts but appears weak. A zero is recorded if the muscle does not function at all. If they have no muscle control of the lower extremities, we classify the child as a thoracic level patient. Lumbar one level (L1) would have hip flexion. Lumbar two (L2) level would have hip adduction and flexion. All of these patients (thoracic and upper lumber) would have the same functional capabilities and therefore we would put all of these patients into one group. This thoracic and upper lumbar group would have no sensation in the lower extremities, and are prone to develop skin sores. The patients with the Lumbar 3 level of lesion have some quadriceps function but the strength is weak and may not support weight bearing without long braces. The patients with the Lumbar 4 level have strong quadriceps and hamstrings. The patients with the Lumbar 5 level lesion have all of the functioning muscles as those with the Lumbar 4 level with the addition of strong dorsiflexors of the ankle. The patients with Sacral level lesions have all the functioning muscles as do the patients with the Lumbar 5 level of lesion with the addition of the strong plantarflexors.

Once we determine the level of lesion and come up with reasonable goals and expectation for the infant we begin parental education as soon as they can handle the emotional impact of having a child with spina bifida. Many times the parental education is delayed because of the grief that sometimes is initially overwhelming to the parents. Physical and occupational therapy is started immediately to begin range of motion and stretching exercises to prevent joint contractures. The parents are warned that motor development is normally delayed and they can not compare their infant to a child without spina bifida.

Most infants with myelomeningocele learn to belly crawl as their first means of mobility. Infants with strong voluntary hip flexion and knee flexion may creep on all-fours (assume the all-four creep). Children with low lumbar and sacral level lesions learn to walk by two years of age with or without bracing at the ankles. Children with high-lumbar level of paralysis often require crutches and bracing up to the hip. Children with thoracic and high lumbar paralysis may eventually stand upright and walk but need support of the hips, knees and ankles. This support must be provided by extensive bracing and mobility devices such as a

parapodium, reciprocal gait orthosis (RGO) or hip-knee-ankle-foot orthosis(HKAFO) used in combination with crutches or a walker. As a result, children with the thoracic and upper lumbar levels are unlikely to walk before the age of three or four.

The sacral level patients should have no problems walking and they require little intervention. Orthotically they may require an AFO if the plantarflexors are weak, a supramalleolar AFO if there is a flexible ankle deformity, or a foot orthosis (insert) for some minor foot deformity such as a cavus or flat foot. Many times they require no bracing at all.

The low lumbar (L4 and L5) level patients should be able to walk but usually function better wearing ankle foot orthoses (AFO). Several studies have been performed assessing the ability to walk with various orthotic devices. In children with low level lesions, AFO's are helpful. Velocity of walking is improved with better mechanics of walking using an AFO. The AFO is used if the quadriceps strength is grade 3 or better. The AFO prevents foot drop and allows foot clearance during gait. We would anticipate 75% of our children with low lumbar levels to maintain the ability to walk as adults. Patients with L-3 spinal cord level of paralysis need long braces or wheelchairs as their quadriceps are usually weak even if they show some innervation. For the high lumbar and thoracic level individuals, HKAFO's or RGO's are needed to maintain hip and knee extension. The velocity of walking seems to be faster with HKAFO's than RGO's if a swing to gait is used. If a reciprocating gait is used, the RGO seems to be superior. Ambulation with either the HKAFO or the RGO offers some physiological and psychological benefits. These benefits include improved bone density, better bladder emptying and improved self-esteem. These benefits, however, have not been proven with random trials. A recommendation for the future would be do a randomized controlled study looking at the benefits, costs and functional outcomes of walking versus using a wheelchair. We need to look at outcomes such as getting around in the home, school, or community. Elements of such a study should also include: bone density, incidence of decubitus ulcers, upper extremity function, activities of daily living, incontinence, employment, marriage and participation in recreational activities like sports.

As the children with thoracic and high lumbar lesions approach adolescence, most rely increasingly on wheelchairs for mobility. This occurs for several reasons. As the children get taller and gain weight, mobility becomes more difficult. A lot of energy becomes necessary to walk and mobility using a wheelchair becomes more efficient and faster than walking. Because most children with myelomeningocele will not become effective community ambulators, the supplemental or primary use of the wheelchair should be considered in children. Wheelchairs offer the advantage of speed, efficiency and are now socially more accepted. Motorized wheelchairs can be used as early as 2 or 3 years of age if the child is mentally normal with normal hand function. In addition to the severity of muscle weakness, impaired hand functioning, decreased IQ and motivation may affect the ability to walk. Walking may not be a realistic goal and wheelchair training should be started early for those children with a combination of a high level lesion, spinal deformity, joint contracture, and cognitive impairments.

It has been controversial as to whether or not we should immediately prescribe wheelchairs for these patients or make an attempt on trying to teach them to walk with braces. Our outcome studies show that even if these patients can learn to walk as children, they will definitely choose a wheelchair in adulthood. In Australia where walking was strongly encouraged, an outcome study there showed only 10% of the high level adult patients were able to remain community ambulators, only 30% retained the ability to walk but used a wheelchair in the community for long distances, 15% became domestic ambulators walking only in the home and 45% used a wheelchair everywhere. Walking is not the most important aspect of life to these individuals. Self care may be the most important priority for our children as they go into their teenage and adulthood years. Communication skills is the second priority and ambulation would be the third priority. Included in self care is the need to be continent of stool and urine. Our urologists work diligently to evaluate bladder function with urodynamic studies early in life and work hard to keep these children dry. I mentioned earlier in this talk, staying continent of urine and stool is crucial for social integration. Success in adulthood as in getting a job, having friends and getting married is a function of staying dry from urine and staying clean.

Orthopaedically for the children with high level paralysis, we primarily concentrate on preventing contractures so they can better fit into their braces or wheelchairs. We try to encourage the use of the wheelchair early in childhood. We do have the occasional parent who insists that their child with spina bifida be given the opportunity to walk. In these cases we do prescribe standing devices like this parapadium. The parapadium is particularly useful if the sitting balance is poor and there is a spinal deformity. For the older children and young adults we can use this type of standing device called a swivel walker. Propusion in the swivel walker is initiated with a lateral and somewhat forward weight shift using the abdominal, arm and upper trunk muscles to rotate forward advancing the brace. This allows them to be at eye level with their peers, possibly stand at a table or a blackboard at school. Standing could have some psychological benefits. In some isolated cases with highly motivated parents and children, we do prescribe the reciprocating gait orthosis (RGO). Forward propulsion with RGO is initiated with a lateral weight shift and trunk extension causing hip flexion on the non-weight bearing side. We would prescribe an RGO around age 4. A prerequisite is that they have good head and trunk control. Most of our children who walk with these devices will still need a wheelchair for long distances. There may be some benefit from a walking program. The adults who walked as children seen to be more independent in their activities of daily living than the adults who never walked. The adults who walked as children are more independent in their transfers to and from a chair. I would not recommend this for everybody and would only offer it to people who actually ask for it and show the motivation. If the motivation is not there, the patients, parents and caregivers end up wasting a lot of time and money in a process that is doomed from the beginning.

To switch gears, I would like to discuss some Orthopaedic management issues.

The clubfoot is the most common orthopaedic deformity seen in children with spina bifida. We begin treatment of the clubfoot with serial casting to try to stretch out the deformity. We do know this could possibly lead to skin sores because of the lack of sensation, however, we have not had any significant problems with pressure sores in the infants as long as we change the cast frequently. We consider surgical intervention if the casting is unsuccessful. Surgery is delayed until age 2 or 3 years of age

when the children begin to show signs of walking. We usually make a fairly long incision on the back of the foot. We release all the ligaments and tendons. We then pin the foot in the corrected position. A cast is used for 2 to 3 months post operatively. Afterwards, the children are given AFOs to maintain the correction. The rear entry floor reaction AFOs with solid ankles are the most appropriate short leg brace for children with spina bifida. This type of brace helps with proprioception as well as helps support the ankle. As the children walk, the brace vibrates with each stride and the vibration can be felt near the knee where they have sensation. By having the plastic touch the skin on the proximal tibial area, the vibrations are felt from the foot through the brace to the knee. This will substitute for their lack of propioception at the ankle. Hopefully, this will prevent ankle problems such as a Charcot joint.

The children who have excessive dorsiflexion of the ankle or calcaneous deformity can have significant problems. Their feet become deformed because the anterior tibial muscle is strong and has no muscle working against it. This leads to a prominent calcaneous and a cavus deformity as seen in this x-ray. This foot deformity is particularly problematic by the fact that there maybe no sensation over the heel. The deformity can lead to a severe heel sore especially in children with no sensation on the bottoms of their feet. Prevention is key. We recommend releasing the anterior tibial muscle or transferring it to the calcaneous in early childhood. Afterwards these children benefit from wearing the floor reaction AFO as previously described.

The sacral level patients have very few orthopaedic problems. Clawing of the toes can occur from intrinsic foot muscle weakness. The clawed toes can be treated surgically by releasing the long toe extensors and transplanting them into the lateral cuneiform bone of the foot. The big toe is corrected by transferring the long toe extensor into the first metatarsal and fusing or tenodesing the interphalangeal joint. The tendon transfer to the little toes is called the Hibbs procedure and the operation for the great toe is the Jones procedure. The postoperative results are usually quite good.

Hip surgery has been an area of controversy over the years. We have in the past recommended surgical management of the dislocated and subluxed hips. There are essentially four situations as described by this two dimensional Punnet square. We can have a high level patient requiring high braces and crutches with bilateral hip dislocations. In this situation we would never reduce the hip. In the low level patient with one hip dislocated, we would always recommend reducing the hips. In the case where you have a high level patient and a unilateral hip dislocation, the hip is reduced only if the other leg is good or there are contractures that need released. If there are bilateral dislocated hips in a low level patient, we would treat them again only if contractures need to be released. The treatment includes varus osteotomies with internal fixation and tendon transfers to help balance the muscles around the hip joint.

As we have gained more and more experience with children with spina bifida, we have come to realize that surgery around the foot is the most beneficial. Knee surgery may play a bigger role in the future. Hip surgery is rarely indicated except in the low level patients who can walk without support. Of course, spinal surgery preventing scoliosis is necessary in both the high and low level individuals.

In summary, I have presented the results from some of the available outcome studies dealing with adult patients with spina bifida. I have presented a summary of the Orthopaedic management of these patients. It is hoped that our treatment plans will improve the quality of life of our patients. The adults with spina bifida will present new challenges to the medical community. We must be there to help these adults with the quality of life issues such as employment, recreation and social integration. The babies born today with spina bifida will survive. We must try to improve their quality of life as caregivers and scientists involved with the research and treatment of individuals with spina bifida. In adults, the most common problems will be skin sores, back pain and knee arthritis. We will be prescribing braces for walking or wheelchairs for mobility. We will be performing surgery for correction of deformity and contractures.

Before concluding, I would like to pay tribute to John William Holter who established for this Society, the Casey Holter Lecture and the Casey Holter Essay Prize. John was an engineer and successful businessman. In 1955 his son Casey was born with hydrocephalus. John Holter devoted his professional skills to the development of shunting systems for the treatment of hydrocephalus. Working with Dr. Spitz, the first one-way valve was inserted at the Children's Hospital of Philadelphia in March of 1956. British surgeon George MacNab visited Dr. Holter, brought his device to England and started to use it at the Hospital for Sick Children, Great Ormond Street. This eventually led to its worldwide use. In 1963 John Holter was made an honorary member in the Society for Research into Hydrocephalus and Spina Bifida, becoming its first nonmedical member. He was a vigorous participant at the society's annual meetings, which he attended regularly. In 1976, Sheffield University conferred an Honorary Doctor of Science degree for him. In 1998 he was invested as an Honorary Commander of the Order of the British Empire, an honor of which he was immensely proud. John Holter was a dear friend to all of us in the Society. He remained active in the Society attending its meetings until his death in December of 2003.

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