Urological treatment and follow-up of patients with spinal dysraphism

(With a summary in English)

Pieter Dik

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Urological treatment and follow-up of patients with spinal dysraphism

Urologische behandeling en resultaten bij patiënten met spinale dysrafie (With a summary in English)

Proefschrift ter verkrijging van de graad van doctor aan de Universiteit Utrecht op gezag van de Rector Magnificus Prof. Dr. W. H. Gispen, ingevolge het besluit van het College voor Promoties in het openbaar te verdedigen op vrijdag 12 november 2004 des middags te 2u30

Door

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geboren op 10 augustus 1955
te Rotterdam

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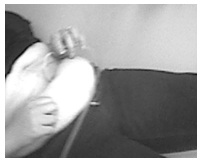
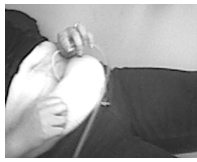
Contents



Introduction

I

Introduction



Spina bifida is a congenital defect of the spine in 1-3 out of 1000 live born children[1] and still is one of the most common serious congenital malformations. The spinal cord lesion in such patients is localised at variable levels. Many of the lesions are asymmetrical. At any level the motoric and sensitive lesions may occur and depending on the level of the lesion a variety of symptoms can be found.

Innervation of the bladder and pelvic floor is complex. Parasymptomatic and symptomatic autonomic nerves innervate the bladder neck and the detrusor muscle of the bladder. The somatic pudendal nerve innervates the pelvic floor.

Depending on the level of the lesion the bladder can be overactive or inactive, and pelvic floor and bladder neck can be overactive or inactive. According to odds, in a cross table this means that in 25% of the patients the bladder can be overactive in combination with an inactive sphincter complex and that in 25% both bladder and sphincter can be overactive. The other 50% of the patients will be incontinent as a result of inactivity of the sphincter, 25% of them even with overactivity of the bladder.

	detrusor inactive	**detrusor overactive**
sphincter inactive	25%	25%
sphincter overactive	25% = at risk	25% = at high risk

Overactivity of the bladder can result in damage of the kidneys due to high pressure in the urogenital system. Especially in combination with overactivity of the sphincter complex a high risk situation develops. Vesico-ureteral reflux, urinary infections and pyelonephritis form a continuous threat to the kidneys.

In many institutions it is still accepted as a fact of life that 25-40% of these patients develop pyelonephritic lesions or even end stage renal disease.[2,3]

In a study of 132 spina bifida patients from 1974-1986 in our institution[4] urodynamic investigation showed that the distribution of risk factors was

as follows:

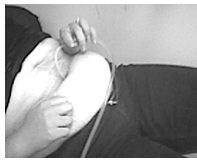
	detrusor inactive	**detrusor overactive**
sphincter inactive	35 (26%)	42 (32%)
sphincter overactive	13 (10%)	42 (32%)

In reality, the risk factors were even worse than was expected. In 42% (=10%+32%) the sphincter complex was overactive but in 32% also the detrusor was overactive, resulting in a high risk factor for upper urinary tracts.
For this reason high bladder pressure needed to be converted by means of drugs or by means of surgery in order to create a compliant bladder reservoir. Emptying of the bladder was done by cathetrization.[5,6,7,8,9,10,11,12,13] This rationale is further discussed in chapter 2.

Therefore from 1988 on, all patients with spina bifida, that were admitted to our institution, were treated with intermittent catheterization and antimuscarinic agents shortly after birth and surgical closure of the spinal defect.
In some patients suplementary surgical therapy was needed for treatment of vesico-ureteral reflux, incontinence, persisting high bladder pressures or for the creation of a continent vesicostomy.[14,15,16,17,18,19]

Aims of this thesis

1. Is hyperactivity of the detrusor muscle a result of compensation against an overactive sphinctermechanism or of pure neuropathic origin?
   Urodynamic studies were done in 15 spina bifida patients before and after stopping antimuscarinic agents (Chapter 3).
2. Is augmentation plasty of the bladder also feasible by surgical removal of a large part of detrusor muscle?
   Detrusorectomy was done in 35 patients, 19 patients because of



poor compliance and in 16 patients in an attempt to stop antimuscarinic agents (Chapter 4).

3. Is surgical treatment for continence a good option?
   In 24 girls and in 14 boys with pelvic floor paralysis a sling procedure was done (Chapter 5 and 6).
4. How were the results of the vesicostomies that were created?
   In a group of 36 patients the results of vesicostomies were studied (Chapter 7).
5. Is kidney function improved by lowering bladder pressures?
   From January 1988 untill June 2001 a group of 144 spinal dysraphism patients was treated by lowering intravesical pressure and regular evacuation of the bladder by means of clean intermittent catheterisation. Development of kidney function and continence was studied (Chapter 8).

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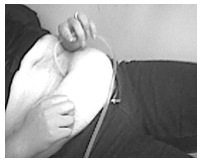

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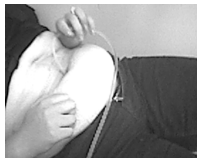

Bladder-sphincter dysfunction in myelomeningocele

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Pieter Dik
Tom P.V.M. de Jong

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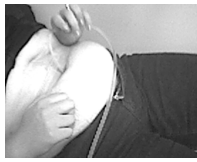
Incontinence and obstruction: structural problems?



Myelomeningocele (MMC) is one of the most common and serious congenital defects, with an incidence of 1 to 2 per 1,000 live births. Despite secondary prevention, by prenatal ultrasound and abortion of affected fetuses, and also despite primary prevention by prescribing folic acid preconceptually in women with an increased risk for neural tube defects[55], each year a predictable number of children are born with a seriously malformed central nervous system.
Clinically, apart from the well known lower limb paresis, the expression of MMC ranges from prenatal hydrocephalus, Arnold-Chiari malformation, and syringomyelia, to secondary tethering of the spinal cord at toddler age, and-too often-renal failure secondary to neuropathic bladder-sphincter dysfunction (NBSD) in adolescence or adult life. In an ongoing Scandinavian survey, started in 1990, almost 50% of all children born with MMC end up institutionalized, and the medical heritage of adult patients with MMC now outnumbers the newborns with a ratio of almost 10 to 1.[28]

In the past, urinary incontinence was judged to be the most obvious clinical problem in NBSD[44,28], and diagnosis and treatment were predominantly aimed at the detrusor muscle.
The first comprehensive cystometric study on children with MMC, from E. Durham Smith in Melbourne[44], confirmed these clinical impressions:

Table 1. Associated urinary tract anomalies in 64 patients with Spina Bifida (E. Durham Smith, 1965)44

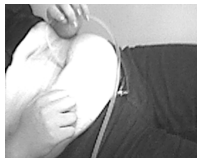
22	Upper tract dilatation, with vesicoureteral reflux
4	Upper tract dilatation, without vesicoureteral reflux
8	Vesicoureteral reflux, normal upper tract
3	Duplex system
1	Horseshoe kidney
1	Posterior urethral valves
2	Hypospadia
1	Exstrophia vesicae

incontinence and detrusor inactivity prevailed in almost every investigated child, and upper urinary tract problems were classified as renal anomalies associated with the neural tube defect (Table 1). In a later study, Smith reiterated the high incidence of upper tract problems in older children as a strong argument for urinary diversion in all children with MMC before the age of 3 years.[45]

Unfortunately, this drew attention away from studies that presented evidence for a different etiology of upper urinary tract problems in children with MMC. Wilcock and Emery investigated 4560 autopsies done at the Sheffield Children's Hospital between 1947 and 1966 for abnormalities of the urinary tract[58]: primary abnormalities (agenesis, hypoplasia, dysplasia, duplication, fusion, ectopia) were one category, dilatation deformities (hydronephrosis, hydroureter, bladder wall diverticula) a second, and the third one consisted of true anatomical infravesical obstruction with upper urinary tract dilatation. In 4120

Table 2. Distribution of urinary tract abnormalities in 404 children with myelomeningocele in relation to age at death (A.R. Wilcock & J.L. Emery, 1970)[58]

Age at death	Normal	Primary deformity	Dilatation deformity	Combined deformity	Total
Stillborn	12 (75%)	2 (12%)	1 (6%)	1 (6%)	16
0-1 mnth	139 (79%)	17 (10%)	16 (10%)	5 (3%)	177
2-3 mnth	62 (72%)	9 (10%)	12 (14%)	3 (3%)	86
4-12 mnth	48 (66%)	13 (19%)	7 (10%)	4 (6%)	72
1-2 yrs	15 (52%)	3 (11%)	8 (30%)	3 (11%)	29
3-4 yrs	10 (42%)	4 (17%)	8 (35%)	2 (9%)	24



autopsied children without MMC the three categories together had a prevalence of 5.3%, whereas in the 404 with MMC this prevalence was 29%. This high prevalence is due to the age-related increase of dilatation deformities in the 404 cases with MMC (Table 2).
Gordon Stark, at the Royal Hospital for Sick Children in Edinburgh, was the first to prove that detrusor areflexia was not the rule in MMC. Detrusor hyperreflexia correlated well with hyperreflexic pelvic floor activity (documented with electromyography and pudendal nerve blockade) in almost 40% of Stark's patients, validating the concept of functional infravesical obstruction by dyssynergic pelvic floor activity in children with NBSD47.

Functional approach: patterns of bladder-sphincter dysfunction

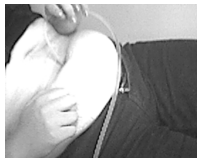
By aiming at incontinence first, the traditional management of NBSD in children with MMC was associated with significant renal morbidity and mortality: "It is disappointing to find, after doing surgery on the back, on the hydrocephalus, and on the limbs, that the child has developed chronic ill health because of renal damage".[59]
When this quotation was being published, neurourology and urodynamics had dramatically reduced morbidity and mortality in adults with traumatic spinal cord lesions. In this field, the concept of functional obstruction by detrusor-sphincter dyssynergia had been understood much earlier, and urodynamic assessment of detrusor and urethral sphincter function became pivotal role in the management of both urinary incontinence and functional bladder outlet obstruction. Direct results were a sharp decrease in mortality from renal causes[15,8,16], and a host of new treatment modalities. External sphincterotomy[13], clean intermittent (self)catheterization[27], α-adrenergic blocking agents[25], artificial-sphincter implantation[40], and reflex micturition by spinal cord stimulation[39] gradually replaced, in the early 1970's, the need for urinary diversion in adults with NBSD.

It took the development of pediatric urodynamics, in the late 1970's and early 1980's, to prove that children with MMC too may have detrusor-sphincter dyssynergia, or total paresis of bladder and/or sphincter muscles. In MMC, detrusor-sphincter dyssynergia creates the functional obstruction of the bladder outlet that is responsible for upper urinary tract dilatation and high-pressure vesicoureteral reflux (VUR), which increase in incidence with age (Table 2).[49,42,18] Incomplete bladder emptying adds recurrent UTI, which makes functional obstruction of the bladder outlet equivalent to anatomical obstruction in every aspect.

Pathophysiology

Urinary bladder and urethra form a functional unit. Storage and evacuation-mutually exclusive functions-are controlled and coordinated at different levels of the central nervous system, converging at the 'sacral micturition center'-which is structurally abnormal in almost every child with MMC.
Depending on level and extent of the lesion, the myelodysplasia in MMC may cause areflexia or hyperreflexia. At the level of the lesion, somatomotor and visceromotor output are absent or impeded (areflexia, lower motor neuron lesion), while sensory input is also affected. Below the level of the lesion, intact spinal cord segments will function without supraspinal control or coordination, much the same as in transsection of the spinal cord (hyperreflexia, upper motor neuron lesion).
Somatomotor neurons in the anterior horns can be affected while visceromotor neurons in the intermediolateral cell columns remain functional, and vice versa-the myelodysplasia does not necessarily affect somatomotor and visceromotor efferents in the same way.
The clinical expressions, areflexia and hyperreflexia of detrusor and/or pelvic floor muscles, are confounded when the neuronal lesions are mixed (upper and lower motor neuron) or incomplete.

A classification of neuropathic bladder-sphincter dysfunction can only



take into account the complexity of the neurological lesion when based on the assessment of both detrusor and urethral sphincter activity, the net results of visceromotor and somatomotor output.
Therefore, a descriptive classification, focussed on the urodynamic patterns of dysfunction of detrusor and urethral sphincter[56,17], serves clinical purposes better than the time-honoured neurological classifications[4] based on the level of the lesion.

Urodynamic studies in children with MMC[50] permit pertinent conclusions about the activity of both detrusor muscle and urethral sphincter mechanism, during bladder filling and bladder emptying. A urodynamic study records detrusor activity by continuously measuring detrusor pressure in the bladder with a size 4 F microtip transducer catheter; simultaneously, pelvic floor acivity is recorded as electromyographic activity, with skin electrodes placed perianally; whenever feasible, a recording of the urinary flow rate is added.[50]
Overactivity of the sphincter mechanism during emptying implies functional obstruction, while inactivity during emptying spells incontinence. To these two clinically relevant categories the classification of detrusor activity adds two more groups: detrusor overactivity and detrusor inactivity, reflected clinically in small or large volumes for cystometric bladder capacity, and high or low values for compliance, respectively.

Overactivity and inactivity of detrusor and sphincter muscles

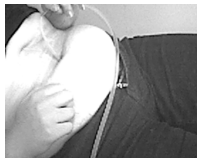
In children with MMC, inactivity or overactivity of either detrusor or striated urethral sphincter can occur in any combination, resulting in four possible categories, or patterns, of bladder-sphincter dysfunction. Table 3 shows the distribution of four main patterns of bladder-sphincter dysfunction found in a cohort of 188 children with MMC, followed from

Table 3. Distribution of 4 patterns of bladder-sphincter dysfunction in 188 children with myelomeningocele, followed from birth.[51]

	Detrusor inactive	Detrusor overactive	Detrusor normal	Total
Inactive sphincter	44	20	--	64
Overactive sphincter	26	85	--	111
Normal sphincter	--	--	13	13
Total	70	105	13	188

birth with serial urodynamic, uroradiological and neurological studies.[51] Between 1976 and 1995, each of these 188 children had on average 2.9 urodynamic studies.

The four patterns represent clinical expressions of the primary neurological lesion in MMC. Consequently, they tend to remain consistent at follow-up.[54,51] However, changes may occur in single urodynamic parameters, such as compliance of the bladder, cystometric bladder capacity, bladder pressure during emptying, and urine flowrate.
Changes in the urodynamic pattern itself occur too. They herald a change in the neurological lesion, such as secondary tethering of the spinal cord, or a late expression of associated lesions like hydromyelia or syringomyelia.[3,46,48] In patients with a low-level MMC and minor motor dysfunction, urodynamic changes often are the first signs of secondary tethering or progressive syringomyelia. They will show up as detrusor-sphincter dyssynergia in children with previously normal bladder-sphincter function, or as a decrease in activity of previously (over)active detrusor and/or sphincter muscles.
Pattern recognition is the main diagnostic modality to be gained with urodynamics in the assessment of NBSD. It differentiates between the clinically important categories of obstruction and incontinence[32,33,3,41,50], and the interpretation of urodynamic investigations in terms of activity of detrusor and striated urethral sphincter is the basis for the classification of NBSD.



Classification based on urodynamic data alone is unrealistic, and a voiding cystourethrogram should always complement the urodynamic study. Ideally, urodynamics and cystourethrography are performed simultaneously, as a so called video-urodynamic study.[38,5]

Incontinence

Incontinence is the main problem in the two patterns of NBSD with inactivity of the striated urethral sphincter, as judged by the electromyogram of the pelvic floor. The functional bladder capacity will ultimately depend on detrusor activity: extremely low values are to be expected with detrusor overactivity, low to near-normal values with detrusor inactivity (Figures 1a and 1b).
Due to the low resistance of the outflow tract, detrusor activity may be difficult to assess: cystometry with a closed bladder outlet will be necessary to rule out residual reflex activity. Also, electromyographical registration of pelvic floor activity on a slow-speed chart recorder may give a false impression of reflex activity of the pelvic floor: monitoring the electromyogram on an oscilloscope is mandatory for a decisive diagnosis.
Continence in this setting is difficult to achieve, because it depends on the passive resistance to flow of the bladder outlet; even incomplete lesions of the striated urethral sphincter will always cause some stress incontinence.

Obstruction

Functional infravesical obstruction due to detrusor-sphincter dyssynergia is the main problem in the two patterns with overactivity of the striated urethral sphincter (Figures 2a and 2b).
When combined with detrusor inactivity, sphincter overactivity will cause urinary retention, overflow at high opening pressures, and high values for functional capacity. However, a chronically overdistended detrusor may only appear to be inactive: careful slow-fill cystometry, starting with an empty bladder and with the bladder outlet closed, will detect residual reflex activity.

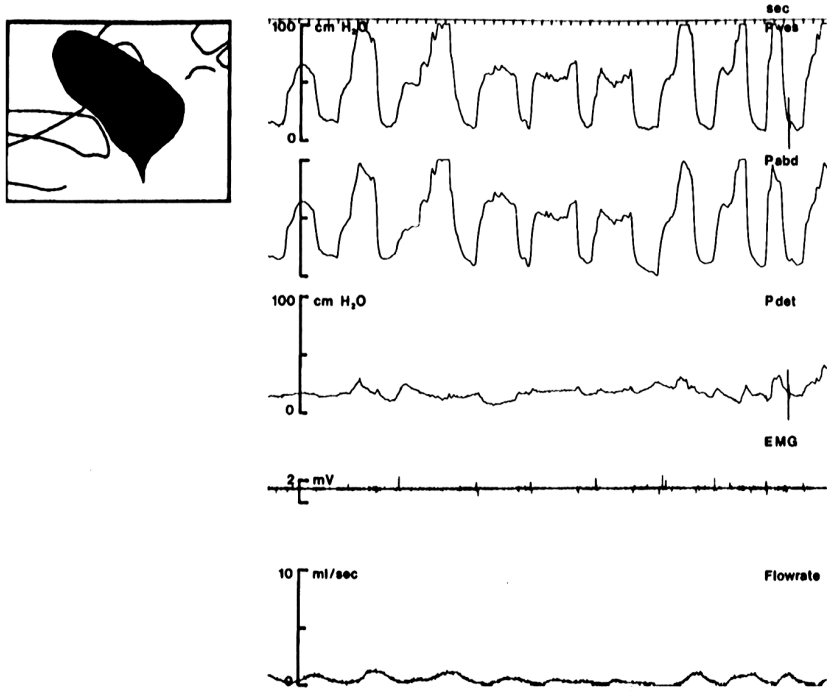
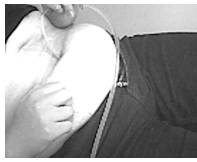


Figure 1a.
Pelvic floor inactivity with detrusor inactivity in a 10-year old girl with MMC. pves=bladder pressure, pabd=rectal pressure, pdet=bladder pressure minus rectal pressure (detrusor pressure), EMG=electromyogram of pelvic floor muscles. No detrusor activity could be detected, and the pelvic floor was electrically silent during filling of the bladder as well as during coughing and straining. In this registration the patient tries to empty her bladder by rhythmic increases in abdominal pressure (Valsalva's manoeuvre). As a result, the pelvic floor flattens out with each increase in abdominal pressure, causing movement artefacts in the electromyogram, and changes in the vesico-urethral angle that impede urinary flow.

Insert: VCUG characteristics for pelvic floor inactivity with detrusor inactivity. The bladder wall is smooth, bladder neck and proximal urethra open up V-shaped.



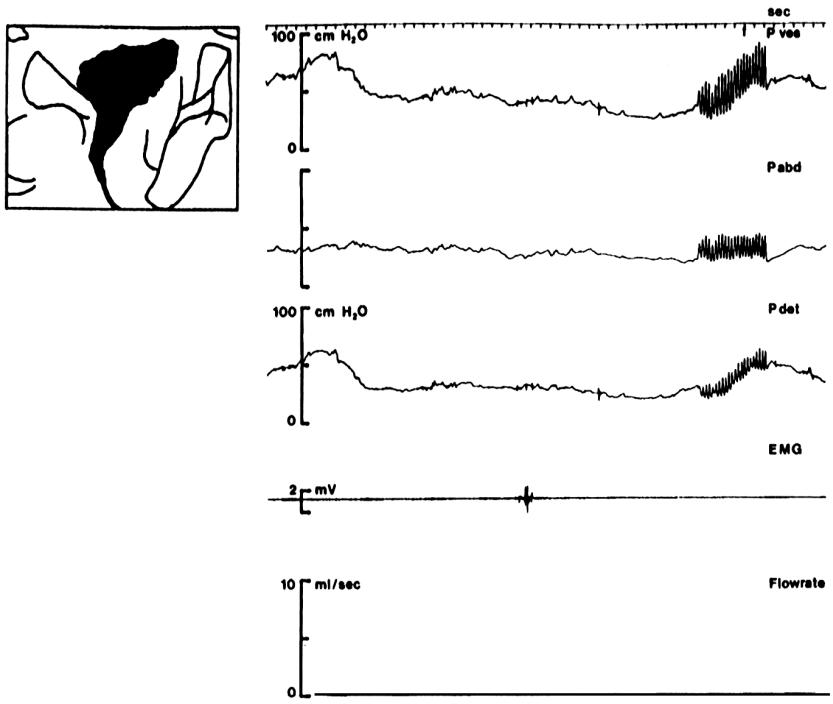


Figure 1b.
Pelvic floor inactivity with detrusor overactivity in a 7-year old boy with MMC, referred with continuous dribbling of urine and stress incontinence. pves=bladder pressure, pabd=rectal pressure, pdet=bladder pressure minus rectal pressure (detrusor pressure), EMG=electromyogram of pelvic floor muscles. There is weak but hyperreflexic detrusor activity, provoked with suprapubic tapping. Electromyographically and clinically, the pelvic floor muscles show complete inactivity, both with tapping and with the subsequent detrusor contraction. Cystometric bladder capacity is very small, and with each detrusor contraction urine is lost.

Insert: VCUG with detrusor overactivity and sphincter inactivity; the bladder wall shows some trabeculation due to hypertrophy, and the bladder neck opens actively with detrusor contraction (or passively, with any increase in abdominal pressure). The proximal urethra will be V-shaped during urine flow.

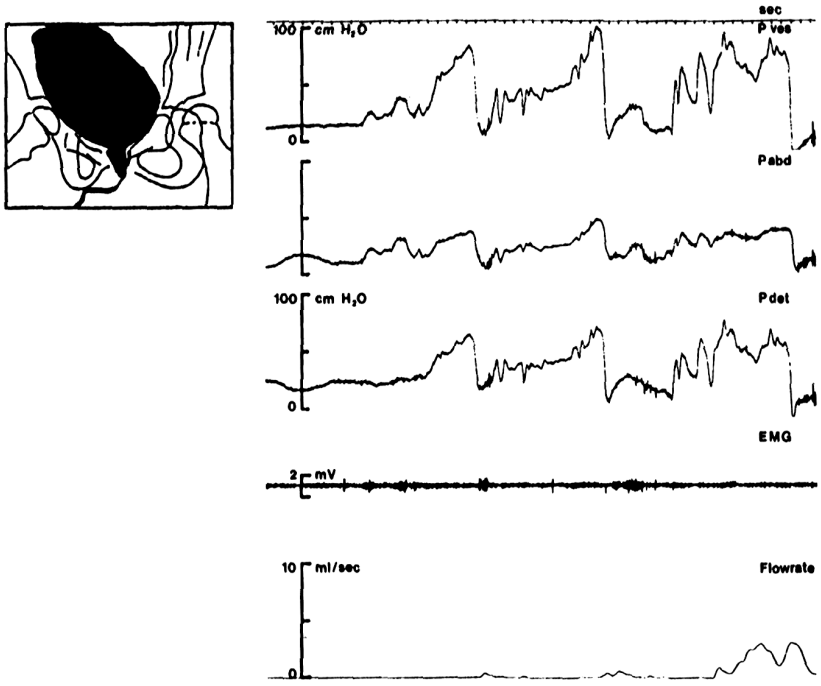


Figure 2a.
Dyssynergic pelvic floor activity with detrusor inactivity in a 14-year old boy with MMC, referred with overflow incontinence. pves=bladder pressure, pabd=rectal pressure, pdet=bladder pressure minus rectal pressure (detrusor pressure), EMG=electromyogram of pelvic floor muscles. During manual expression of the bladder, very high bladder pressures result in poor urine flow and incomplete bladder emtying, due to dyssynergic pelvic floor activity. Manual expression was discontinued, and with CIC complete continence was achieved.

Insert: VCUG characteristics for pelvic floor overactivity with detrusor inactivity. The bladder wall is smooth, bladder neck and proximal urethra are visible, U-shaped, with increased abdominal pressure only.

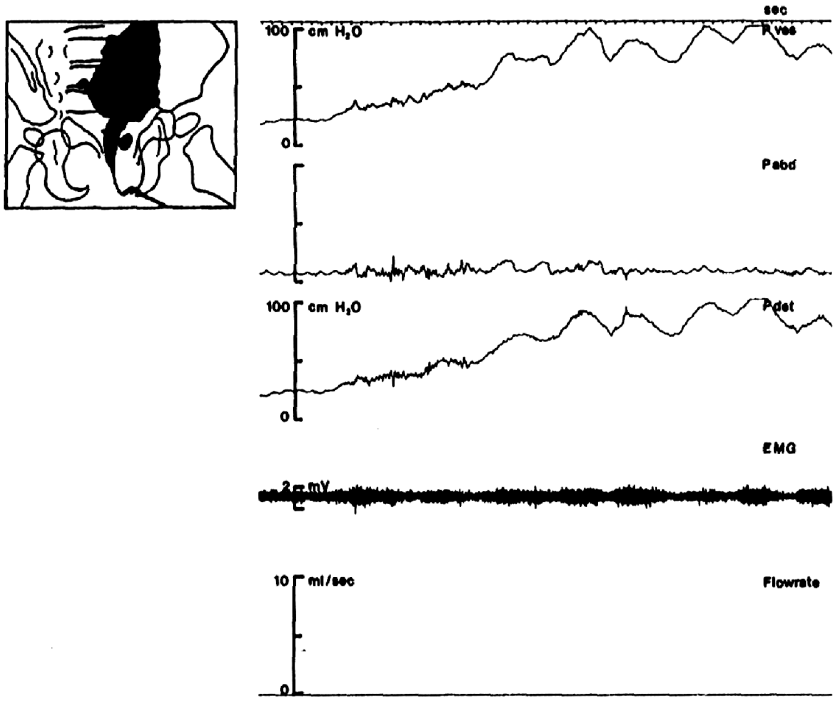


Figure 2b.
Detrusor-sphincter dyssynergia with detrusor overactivity in a 6-year old girl with MMC. pves=bladder pressure, pabd=rectal pressure, pdet=bladder pressure minus rectal pressure (detrusor pressure), EMG=electromyogram of pelvic floor muscles. Dyssynergic pelvic floor activity waxes and wanes with every detrusor contraction, during filling and during voiding, without any sensation of urge. Voiding occurs as a series of urine leakges at extremely high pressures, with dribbling incontinence as the clinical result.

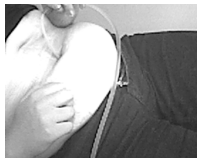
Insert: VCUG with detrusor overactivity and pelvic floor overactivity. The bladder wall shows marked trabeculation due to hypertrophy, and with each overactive detrusor contraction bladder neck and proximal urethra open up U-shaped, dilated down to the level of the striated urethral sphincter.

When both detrusor and urethral sphincter are overactive, the critical factor is the balance between the two overactive and dyssynergic muscle groups. For the pelvic floor muscles, the recorded electromyographical activity is not a measure of contraction force; voiding pressures can be normal, despite increased electromyographical activity of the pelvic floor. Also, detrusor overactivity as such is not always synonymous with a small bladder capacity-the neurological lesion may be incomplete for both the detrusor muscle and the urethral sphincter. This accounts for a wide range of values for cystometric bladder capacity and maximum voiding pressures in this group.
Bladder-sphincter function may remain compensated, at the price of detrusor hypertrophy, high bladder pressures and small functional capacity; decompensation and obstructive uropathy are heralded by increasing values for bladder capacity, the occurrence of post-void residual volumes, and by a high rate of UTI.[54,43]

There is mounting evidence that this pattern of NBSD will ultimately result in a small, low-compliance bladder, with continuously elevated pressures, both during filling and emptying. The underlying structural changes in the bladder wall-collagen deposition in the muscular layer[12,1]- are thought to be secondary to obstruction or infection, or both. Ultimately, in a number of cases with hyperactivity of both detrusor and sphincter, a surgical conversion of the low-compliance system to an inactive and compliant reservoir will have to be done, to protect the upper urinary tracts and to create sufficient functional bladder capacity for continence.

Management

In the first years of life, the kidney parenchyma is highly susceptible to backpressure and infection. In this period, emphasis will be on documenting the pattern of NBSD, and assessing the potential for functional obstruction and vesicoureteral reflux, preferably before the age of 3-4



months. Also in this period, the technique for clean intermittent catheterization (CIC) is to be taught to the parents, and children under age 3 years are prescribed low-dose chemoprophylaxis.[43]
Most children who need help to overcome fecal stasis and retention will also start with colonic lavage at this relatively young age.
At a later stage, when the pattern of NBSD has been established, management can be tailored to the specific problems of a child, and the strategy to gain continence can be developed.

Conservative management—first years of life

Clean intermittent catheterisation

Even with the combination of sphincter inactivity and detrusor inactivity, CIC remains the method of choice.[9,26,34,57,23,6,37,19] It always reduces the degree of incontinence, and offers much better control over UTI.[52]

CIC will not alleviate incontinence in children with a small bladder and detrusor overactivity. In these cases, pressures during emptying or filling will remain unacceptably high, and ultimately the bladder wall will show structural changes that lower compliance and capacity, especially when detrusor overactivity is combined with sphincter overactivity.
Pharmacological conversion of the overactive detrusor to an inactive reservoir has to be added to CIC. Oxybutynine chloride is the drug of choice to achieve this conversion, and it has a very high rate of succes in NBSD[34,11], in the normal dosage of 0.3-0.4 mg per kg body weight per day, divided over 3-4 doses. Side effects may be circumvented by instilling the drug, dissolved in water, directly into the bladder, after emptying by (clean intermittent) catheterization.[2,14,35]
Recently, the group from the University Children's Hospital in Leuven, Belgium, reported on a striking rise in detrusor compliance together with a high resolution rate of vesicoureteral reflux in infants with MMC and detrusor-sphincter dyssynergia, when treated with the combination of intravesical oxybutynine chloride and CIC.[7] This prompted many centers to start CIC with oxybutynine in all infants with urodynamically proven detrusor-sphincter dyssynergia, in the first few months of life.[11]

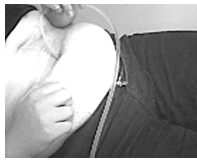
Urinary tract infections

UTI's seldom pose problems in patients with inactivity of the urethral sphincter, provided bladder emptying is complete. When the bladder is emptied by manual expression, recurrent UTI's will, however, be a problem. Manual expression may be an easy alternative to CIC in children with inactivity of the pelvic floor, but it almost never results in complete bladder emptying because of the caudad displacement and kinking of the urethra that occurs with each push on the lower abdomen (Figure 2a). UTI's are easily overlooked in children with MMC, because of the obvious absence of signs such as dysuria or frequency; this may cause considerable delay in proper treatment, especially in the very young.[43,52]

Incomplete bladder emptying is a hallmark of NBSD with overactivity of pelvic floor muscles. Residual urine will be contaminated with fecal flora, and the step from contamination to infection is a matter of time. The 20 years of experience with CIC, starting with Lapides' seminal paper[27], have taught us that the rate of UTI during CIC is significantly lower than without CIC, despite the textbook's approach of avoiding any catheterization for fear of contaminating the contents of the bladder: it is precisely the regular elimination of contaminated urine that prevents infection.[52]
Also, patient compliance with chemoprophylaxis will be enhanced by the concomitant improvement in incontinence. The number of visits to the hospital can be reduced by having urine samples for culture taken by catheter at home, and cultured with dipslides.

Vesicoureteral reflux and reflux nephropathy

In the children with inactivity of the pelvic floor muscles, VUR will tend to be low-grade, with a high rate of spontaneous resolution (Table 4). Detrusor-sphincter dyssynergia completely changes the characteristics of VUR.[22,20,49] High bladder pressures are generated, either by the detrusor contracting against a dyssynergic sphincter or by full-blown retention due to detrusor inactivity. In children with NBSD there is a very clear correlation between high-pressure VUR and the incidence of renal scars (Table 4). Early detection and treatment of functional obstruction are thus mandatory to prevent the progressive scarring of reflux



nephropathy. The combination of CIC with oxybutynine chloride has been proven invaluable in the management of MMC-children with high-pressure VUR, regardless of age.[2,7,11]

Table 4. Renal units with vesicoureteral reflux and reflux nephropathy versus urethral sphincter activity. In 174 children with MMC and bladder-sphincter dysfunctions[51]

	no VUR (RN)	VUR 1-2 (RN)	VUR 3-5 (RN)	Total (RN)
Inactive sphincter	108 (0)	15 (1)	3 (2)	126 (3)
Overactive sphincter	163 (0)	14 (1)	35 (19)	222 (20)

Vesicoureteral reflux (VUR) was graded 1-5; detection of reflux nephropathy (RN) was either by intravenous urography or 99mTc-DMSA-scintigraphy
¶The 14 patients with normal bladder-sphincter function from Table 1 are not included: no VUR was detected

Surgical management-final approach

CIC remains the mainstay for complete bladder emptying. In surgical management, as well as in conservative management, the emphasis is on conversion of high-pressure situations to low-pressure high-compliance reservoirs. In selected cases, urethral resistance to flowwill have to be increased. The age at which these procedures are best performed is difficult to advise on, as the full clinical expression of MMC takes time to develop. The psychomotor development in MMC depends heavily on the outcome of hydrocephalus, and in cases with associated cervical malformations, paresis of the upper limbs due to syringomyelia may develop around school age, impairing the ability to perform CIC.

Bladder capacity

Whenever hyperactivity and secondary fibrosis of the detrusor have rendered the bladder useless as a reservoir, functional bladder capacity has to be increased first, before CIC can be expected to give positive results. This can be done by neurosurgical denervation of the detrusor, or by a bladder augmentation procedure.[21] The primary goal is to convert the low-compliance, low-capacity bladder into an inactive reservoir, which usually makes the child dependent on CIC to achieve adequate emptying. Consequently, it is imperative to test the acceptance of CIC with both the parents and the child before resorting to augmentation procedures. For special cases (wheel-chair dependent children) techniques have been developed that provide both a high-compliance reservoir and an easy-access conduit for catheterization, such as appendicovesicostomy.[24,10]

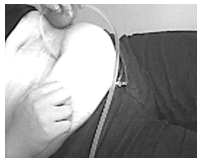
Urethral resistance to flow

If stress incontinence remains a problem with CIC, and bladder capacity is sufficient, then the passive resistance to flow of the bladder outlet can be increased by surgical procedures such as colposuspension, a 'sling-procedure', or, in selected cases, by implantation of an artificial sphincter.[29,31]

Unanswered questions

Detrusor matrix and smooth muscle

Experimentally, obstruction-induced hypertrophy is associated with de-differentiation of detrusor muscle cells. De-differentiation is associated with changes in the extracellular matrix of the detrusor, analogous to what happens in obstructed blood vessels: the ratio type III/type I collagen increases and compliance decreases.[36,1] In the end, contractility of hypertrophied detrusor muscle is impaired, but in the early phases of obstruction the detrusor muscle is markedly overactive. With afferent blockade (capsaicin, dorsal rhizotomy) as well as efferent blockade (anticholinergics), this obstruction-induced overactivity disappears and



hypertrophy decreases.
It is tempting to postulate that early treatment with CIC and anticholinergics will prevent the deposition of abnormal collagen in the detrusor matrix, preserving normal compliance and capacity, in children with MMC and detrusor-sphincter dyssynergia. However, we do not know how long to continue treatment with anticholinergics, and we lack prospective controlled studies assessing the ratio type III/type I collagen in full-thickness bladder wall biopsies.

Efferent innervation of striated pevic floor muscles

Detrusor-sphincter dyssynergia presumably is caused by defective supraspinal coordination of the micturition reflex: without such coordination, contraction of detrusor and relaxation of striated sphincter do not occur simultaneously. However, there still is discussion about the exact efferent pathways to the striated urethral sphincter and pelvic floor muscles, and both somatomotor (pudendal nerve) and visceromotor (plexus pelvicus) neurons seem to be involved.[30] Isolated and uncoordinated reflex activity of striated pelvic floor muscles occurs in spinal cord transsection and MMC, but also in Duchenne's muscular dystrophy, where striated muscle cells degenerate progressively, and in spinal muscular atrophy, where progressive degeneration occurs of somatomotor anterior horn cells with the striated muscle cells they innervate.
A common denominator that could possibly explain the occurrence of isolated pelvic floor activity (detrusor-sphincter dyssynergia) in patients without sacral somatomotor activity is the nucleus of Onufrowicz, a small group of sexually dimorph motor neurons in the anterior horns of the sacral spinal cord, anatomically and functionally different from the adjacent somatomotor neurons.[53]

Acknowledgements

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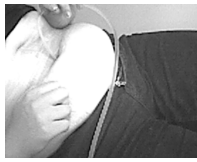

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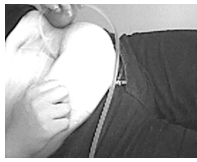

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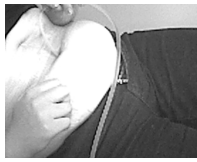

Detrusor overactivity in spina bifida, how long does it need to be treated?

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Jan D. van Gool
Tom P.V.M. de Jong

(The study is a by-product from a pharmaceutical multicenter trial that has been conducted to obtain FDA approval for pediatric use of oxybutynin. That study was financed by the ALZA company)

3

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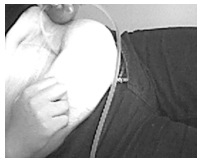
Abstract

Aims To determine whether a lasting therapeutic effect can be expected from long-term antimuscarinic therapy for neurogenic detrusor overactivity in spina bifida and to answer the question whether detrusor overactivity in spina bifida children with detrusor/sphincter dyssynergia is primarily based on the neuropathy or, in part, can be a secondary detrusor reaction to the functional urethral obstruction.
Patients and methods Fifteen spina bifida patients, aged between 1 and 12 years, all on a regime of clean intermittent catheterisation (CIC) and oxybutynin since shortly after birth, underwent 3 consecutive urodynamic studies (UDS). One prestudy UDS for treatment control, one UDS after withdrawal of oxybutynin for 3-5 days and one UDS after reinstallment of oxybutynin treatment. Urodynamic results were compared concerning detrusor overactivity, cystometric bladder capacity and compliance.
Results Overactivity of the detrusor was seen in 2 patients on the prestudy UDS. After several days of withdrawal of oxybutynin overactivity was seen in 11 patients. After oxybutynin withdrawal, bladder compliance was within safe margins for 2 patients only, after reinstallment safe vesical pressures were seen in 11 patients.
Conclusion The functional obstruction based on detrusor/sphincter dyssynergia has been by-passed chronically in all these children by cic and oxybutynin. From the fact that after long-term treatment with oxybutynin detrusor overactivity recurs immediately after withdrawal of medication, one can conclude that no long-lasting therapeutic effect of pharmacological suppression is to be expected. Apparently, in children with detrusor/sphincter dyssynergia, detrusor overactivity is primarily of neuropathic origin. This conclusion obviates the life-long use of antimuscarinic therapy in spina bifida patients with detrusor overactivity. Research must focus on finding alternatives for chronic pharmacological suppression of the detrusor.

Introduction



Spina bifida patients with a neurogenic bladder, characterised by overactivity of both detrusor and sphincter, are usually treated with oxybutynin and clean intermittent catheterisation (CIC) to lower vesical pressures and by-pass the functional obstruction that is created by the detrusor/sphincter dyssynergia. When not treated adequately, detrusor-sphincter dyssynergia leads to a low compliant and low capacity bladder, with high pressures that will finally damage kidney parenchyma.[1,2,3] Oxybutynin pharmacologically suppresses detrusor overactivity and gives adequate storage capacity at low vesical pressures. As a consequence, the bladder must be emptied with CIC to by-pass the functional outlet obstruction.[4]

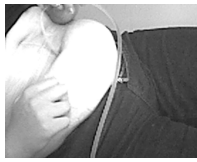
In patients with spina bifida, detrusor overactivity combined with sphincter overactivity is seen in almost 40% of the cases. The cause of overactivity is thought to be a defect in supraspinal management of urine storage and bladder emptying, due to myelodysplasia at the level of the anatomical malformation. Detrusor overactivity is also seen in patients with an anatomical bladder outlet obstruction due to posterior urethral valves. In these patients detrusor overactivity mostly disappears after valve ablation, with or without the temporary help of antimuscarinic therapy and/or CIC.[5] In the spina bifida patient with detrusor/sphincter dyssynergia the functional obstruction is by-passed by oxybutynin and CIC, taking care of storage and emptying at low pressures. Thus, one could hope that after long-term treatment bladder overactivity will disappear. Every clinician dealing with spina bifida patients knows that in non-compliant patients the detrusor returns to baseline overactivity when medication is not well taken. No literature exists reporting systematic research into this subject. The aim of this prospective stop-start study is to evaluate whether detrusor overactivity in patients with a neurogenic bladder is primarily caused by abnormal neuro-anatomy or by changes in the bladder secondary to the functional outlet obstruction. If detrusor overactivity in spina bifida patients is secondary to the functional outlet obstruction, one would expect that pharmacotherapy is only needed temporarily, as it is in patients with PUV or in some cases of urge urinary incontinence. In case of a primarily neuropathic origin of detrusor overactivity, the overactivity must recur during a stop-test of oxybutynin.

Patients and methods

This prospective stop-start study was approved by the Ethical Committee of the University Medical Center Utrecht and conducted according to the guidelines of Good Clinical Practices. All parents signed informed consent. Fifteen children with a neurogenic bladder due to spina bifida participated in this analysis. They were randomly selected out of the 225 patients form the pediatric spina bifida group that is under control in our hospital. For inclusion, patients had to be on treatment with oxybutynin and intermittent catheterisation for a longer period from shortly after birth. Oxybutynin dosage was 0,4mg/kg /day in 3 oral gifts or in 2 intravesical instillation.[6] Twelve of the patients had been diagnosed neonatally with neurogenic overactivity of the detrusor, one with areflexia that changed into overactivity 3 months after back closure and for two detrusor activity was uncertain because they were on oxybutynin at the first UDS. Twelve patients had been diagnosed with bladder/ sphincter dyssynergia. At the start of the present study, all patients were tested urodynamically (prestudy-UDS). Oxybutynin was discontinued for 3-5 days and a second urodynamic study was performed (study UDS-1). A last urodynamic study was performed within 6 month after restarting of the medication (study UDS-2). All patients were seen twice each year by a physical therapist, orthopaedic surgeon, neurologist and rehabilitation specialist to rule out changes in neurological function by

Table 1

Patient characteristics		
Patients (n)	Male	12
	Female	3
Age (yr.)		**1-12**
Level of spina bifida lesion (n)	Thoracic	4
	Lumbar	10
	Sacral	1
Duration of medication use (months)		**14-105**
Neonatal diagnosed with (n)	Detrusor overactivity	12
	Areflexia, later overactivity	1
	Unknown	2
	Dyssynergia	12



tethering of the cord. None of the patients had any suspicion for tethering or changes in the neurologic lesion when they were in the study.

Urodynamic studies (UDS)

The standard filling cystometries were carried out after exclusion of urinary tract infection. All studies were done in the morning, in case of antimuscarinic therapy 2-3 hours after medication was given. Vesical pressure was recorded with a 6 Fr. transurethral microtip catheter with filling lumen, abdominal pressures with a 6 Fr. microtip catheter in a small rectal balloon. Activity of the striated pelvic floor muscles is monitored by skin electrodes on the perineum. The bladder is filled with NaCl 0.9% between 20 and 30o Celsius at a rate of 5-20 ml/min, adjusted to a maximum of 10% of expected bladder capacity for age per minute. Expected bladder capacity for age is calculated by the formula: 30+ (30 x age in years), that is commonly used for children with normal bladder function.[7] Bladder compliance is calculated during filling of the bladder at two thirds of maximum bladder capacity by dividing volume in ml's and pressure in cm water. Maximal cystometric bladder capacity is defined by the maximum volume instilled at 40 cm's water pressure, or by the volume instilled before the start of urinary leakage. Detrusor overactivity is diagnosed when repeatedly contractions over 15 cm water pressure are seen. All patients had 2 or more bladder fillings for each urodynamic study. When 2 consecutive fillings produced identical data these were used for analysis.

Results

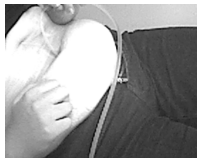
Detrusor/sphincter activity

Of the spina bifida patients selected for this stop-start study, 12 had been diagnosed neonatally with detrusor overactivity, 1 with areflexia after birth and overactivity at 3 months of age and of 2 patients it was

unknown because treatment had been installed before the first UDS. Pre-study UDS showed that detrusor-sphincter dyssynergia was present in 12 patients, no dyssynergia in 2 and of one the status was unknown. At the start of the study, oxybutynin had been used, orally or intravesically, between 14 and 105 month. During this treatment overactivity of the detrusor was seen in 2 patients (Table 2, prestudy UDS). After 3-5 days of discontinuation, overactivity reappeared in 11 patients (Table 2, UDS 1). After reinstallment of oxybutynin treatment the overactivity disappeared in all patients, except two, one of which showed overactivity in the prestudy UDS and the other did not (Table 2, UDS 2).

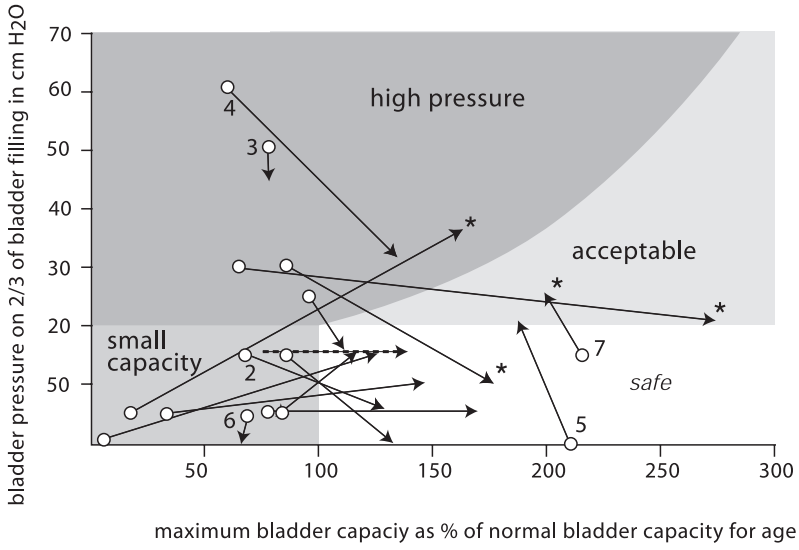
Table 2 Overactivity (* = positive urine culture)

patient	Neonatal Overactivity	Neonatal detrusor-sphincter dyssynergia	Month treatment with oxybutynin	Prestudy UDS with oxybutynin Overactivity	UDS 1 without oxybutynin Overactivity	UDS 2 with oxybutynin Overactivity
1	+	+	82	-	+	+
2	+	+	105	-	-	-
3	+	+	87	-	+	-
4	+	+	74	-	-	-
5	?	+	43	-	-	-
6	+	+	61	+	+	-
7	?	?	52	-	-	- *
8	+	+	21	-	+	-
9	+	+	47	-	+	-
10	+	+	48	-	+	-
11	+	+	27	-	+	-
12	-	+	14	-	+	- *
13	+	+	57	-	+	- *
14	+	-	35	-	+	- *
15	+	-	36	+	+	+



Compliance: pressure and capacity

Figure 1 is a graphical representation of the changes in end-filling vesical pressure and cystometric capacity upon re-administration of oxybutynin for each individual patient. The cystometric capacity, expressed as % of normal capacity for age, is plotted versus the pressure upon 2/3 bladder filling. For each patient two data sets are plotted, one from the 3-5 day period of oxybutynin withdrawal (arrow origin) and one after resumption of oxybutynin administration (arrow head).
Maximal cystometric capacity was below normal in 13 patients during withdrawal. In two of these patients (3+6) capacity remained unchanged and below normal after restart of oxybutynin. The other 11 patients showed strong elevation of capacity to values above normal. In the two patients with a large cystometric capacity during oxybutynin withdrawal (5+7), a small decrease of capacity was seen after resumption of oxybutynin treatment to values around 200% of the normal capacity for age. Patient 5+7 had areflexia in both urodynamic studies, as did patient 2+4.
Pressure was measured upon 2/3 of bladder filling. Figure 1 shows the median pressure arrow of all fifteen patients (dotted arrow). Although we know from literature that oxybutynin has pressure lowering effect we



can not conclude that from our data.[1]
Figure 1 also shows a distinction in different area's. A safe white area, in which the bladder pressure is below 20 cm H_2O and the bladder capacity is normal or above normal for age.[8] The grey area with "acceptable" in it is also thought to be safe, because if capacity is above normal a higher pressure can be accepted. Besides these two area's, there are two other grey area's that cannot be accepted as safe in daily practice. One has a capacity for age below normal and the other is an area in which vesical pressures are too high for safe renal function. Figure 1 shows that the number of patients that are in the safe or acceptable area increases from two to eleven upon re-administration of oxybutynin.

Discussion

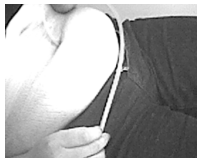
Our data show that 11 out of 15 patients have de novo detrusor overactivity shortly after discontinuation of oxybutynin. Long term CIC and oxybutynin has by-passed the possible secondary effect of functional outlet obstruction on the bladder during voiding in all these patients. The first conclusion that can be drawn is that no lasting therapeutic effect can be expected from long-term antimuscarinic therapy. Second conclusion is that secondary detrusor overactivity based on the functional urethral obstruction does not play a significant role in spina bifida and that the detrusor overactivity is of primary neuropathic origin in the vast majority of the patients.
Comparing bladder capacity in the situation without and with oxybutynin, an important enlargement of capacity is seen in most patients. In the UDS after withdrawal of oxybutynin adequate bladder filling was often impossible because of urinary leakage during detrusor contractions. This in contrast with patients 5+7, who both did not have overactivity in the withdrawal phase and both had no significant enlargement of bladder capacity after reinstallment of oxybutynin. In retrospect one can conclude that these 2 patients had no detrusor overactivity from the start although they were diagnosed with detrusor/sphincter dyssynergia.

This explanation does not hold true for patients 2+4 who both had a significant enlargement of capacity but did not have overactivity in both situations, also not for patients 3+6 because they had similar capacities with and without detrusor overactivity. Capacity also depends on urethral resistance. It is of interest that, because of the good urodynamic results of patients 5 and 7 in the oxybutynin withdrawal period, we agreed to stop the oxybutynin. Both patients had to resume oxybutynin within weeks. One because of abdominal pains and recurrent urinary tract infections, the other started losing urine after years of continence. Both recovered after reinstallment of oxybutynin.
Looking at the median arrow there is no significant difference in detrusor pressure with and without oxybutynin. Given the enlargement of capacity and status quo of pressure we can conclude that detrusor compliance is better with oxybutynin. The following questions remain: Can compliance be measured accurately in the presence of detrusor overactivity and is the improvement of compliance with oxybutynin due to disappearance of overactivity or is there a direct effect on the bladder wall tension?
One may point at the favourable results of urethral dilatation on detrusor function as reported in literature.[9] Careful reading of that manuscript shows that no effect of dilatation was seen in patients with a high pressure overactive detrusor.

Conclusion

Our results prove that detrusor overactivity in detrusor/sphincter dyssynergia is primary of neuropathic origin and that no lasting treatment effect can be expected from long-term antimuscarinic therapy. This confirms the well-known facts from daily practice. The consequences of these facts are, to ensure kidney function on the long run, that life-long pharmacological therapy by antimuscarinics or other means is needed for nearly all spina bifida patients with detrusor/sphincter dyssynergia and also for a selected group of patients without dyssynergia. We have to

accept this while looking at other possibilities to treat detrusor overactivity. We have had some success in surgical treatment of detrusor overactivity by partial detrusorectomy in patients that had surgery to obtain urinary continence.[10] Results of botulinum toxin injection into the detrusor muscle are promising.[11] Other pharmacological and neurosurgical options must be considered in the future.



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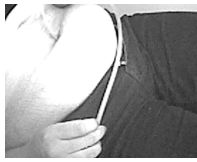

Detrusorectomy for neuropathic bladder in patients with spinal dysraphism

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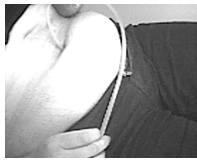
Abstract

Purpose To assess the outcome of detrusorectomy in 35 patients with spina bifida who were incontinent due to poor bladder volume or poor compliance.
Materials and Methods Of 51 patients requiring bladder augmentation 35 underwent detrusorectomy. In 3 patients ileocystoplasty was later performed as a secondary procedure because of failure of the detrusorectomy.
Results A total of 35 patients (17 males, 18 females) underwent detrusorectomy. Mean patient age at operation was 9.9 years (range 0.4 to 17.8). Mean followup was 4.9 years (range 1 to 10.5). A continent catheterizable vesicostomy was constructed in 14 patients and ureteral reimplantation was performed in 8. Twenty-five patients also underwent sling and/or Burch cystourethropexy during detrusorectomy, of whom 19 are continent and 5 have some leakage between clean intermittent catheterizations. In 1 girl the sling procedure was not successful, and she was subsequently treated with bladder neck closure.
Bladder compliance after operation was improved in 9 cases and unchanged in 10. Of the 16 patients in whom compliance was already acceptable before the operation and was unchanged after detrusorectomy 7 were able to stop antimuscarinic therapy. Compliance became poor in 4 cases, of which 3 required ileocystoplasty. Bladder volume (as a percentage of normal volume for age) was increased after detrusorectomy in 13 patients, unchanged in 11 and decreased in 11. Complications of detrusorectomy included bladder leakage in 2 cases. One patient needed a laparotomy because of urinary ascites shortly after the operation.
Conclusions Detrusorectomy may be combined with other procedures such as ureteral reimplantation, slingplasty and continent vesicostomy. Of 35 treated patients compliance improved in 16 (46%),volume improved in 13 (37%), 3 had no change in parameters, and 3 had a slight decrease in volume and compliance. Four patients had poor results, of whom 3 needed a secondary ileocystoplasty. Therefore, it may be concluded that detrusorectomy is a safe and probably useful procedure for improvement of bladder volume and compliance in patients with neurogenic bladder dysfunction, and may obviate the need for ileocystoplasty in a limited number of patients.

Introduction



In patients with spina bifida bladder compliance and bladder volume can be impaired as a result of recurrent urinary tract infections and detrusor sphincter dyssynergia.[1] Ileocystoplasty, colocystoplasty and even gastrocystoplasty can be helpful but these patients need continuous urological followup because of unknown risks of neoplasm and stone formation.[2,3,4] Since 1989 bladder augmentation by partial detrusor excision has been reported in literature with various success rates.[5] It seems that after detrusorectomy the augmented bladder can shrink, probably by contraction of the scarred denuded mucosa.[6,7] Therefore, demucosalized gut segments have been used in combination with autoaugmentation (detrusorectomy) with variable results.[8,9,10]

At our institution bladder autoaugmentations by detrusorectomy have been done since 1990. During autoaugmentation other procedures have been performed simultaneously, including slingplasty, ureteral reimplantations and formation of continent vesicostomies. To determine the outcome of this management, we assessed bladder compliance, bladder volume, continence, reflux and stoma quality in patients treated by detrusorectomy.

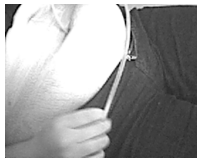
Patients and Methods

Of a cohort of 250 patients younger than 18 years with spina bifida 35 with neuropathic bladder were treated by detrusorectomy or autoaugmentation of the bladder between 1990 and 1999. Mean age at operation was 9.9 years (range 0.4 to 17.8) and mean followup was 4.9 years (range 1 to 10.5). Seventeen patients were male. All patients were evaluated preoperatively with at least 2 urodynamic studies conducted with oxybutynin. Patients with neuropathic sphincter insufficiency underwent at least 1 urodynamic study that included filling the bladder while the bladder neck was occluded with a balloon catheter, to measure the true bladder volume and to predict bladder behavior after applying therapy to increase outlet resistance. In 25 patients a bladder neck sling

and/or Burch colposuspension was also done. Fourteen patients received a continent vesicostomy and 10 underwent ureteral reimplantation. Indications for autoaugmentation were poor compliance and oxybutynin dependent detrusor overactivity.

Surgical procedure

Using a transverse or a midline abdominal approach, the rectus fascia is opened longitudinally in the midline. The operation starts with meticulously opening the adventitial layers of the bladder in the midline until only bare detrusor muscle is left. These layers are marked with a suture to allow their identification and closure at the end of the procedure. In previously unoperated bladders the detrusorectomy starts at the pubic bone and passes widely around the dome of the bladder. Throughout this procedure the bladder is maintained at a filling pressure of 30 cm H_2O and a small patch of detrusor is left at the urachal remnant. Redundant detrusor is excised to create a large diverticulum of the bladder. Finally, the adventitial layers of the bladder are closed in the midline and the urachal remnant is fixed to the anterior abdominal wall at the level of the umbilicus. Small leaks from the mucosa that sometimes occur during surgery can be sealed using a 2-component collagen solution (Tissuecol, Immuno, Heidelberg, Germany), as efforts to suture the hole usually cause more leakage. After the operation bladder drainage is done over an elevation of 20 cm above the level of the bladder, and as soon as possible, usually on postoperative day 2, the transurethral catheter is clamped off every 2 or 3 hours to challenge the bladder volume and prevent shrinkage. When performing a sling procedure in these patients, a 2 cm wide strip of rectus abdominis fascia is prepared for use as a sling around the bladder neck.[11]
In patients undergoing colposuspension the technique according to Burch was used. If ureteral reimplantation was required, the ureters were reimplanted according to the Lich-Gregoir technique. However, it also proved feasible to use the Cohen technique—following closure of the bladder detrusorectomy could be done laterally on both sides of the midline. Continent vesicostomy was done using the appendix, while a bladder tube was used in patients with a large bladder.[12] In 1 patient a patent urachus could be used as a continent vesicostomy, and 1 patient



requiring a salvage procedure received a vesicostomy that was formed out of labial skin. At followup all patients were assessed by urodynamic studies, all received low dose antibiotics (2 mg/kg trimethoprim daily) and oxybutynin (0.3 mg/kg daily in 3 doses), and all used clean intermittent catheterization 5 times daily.

Urodynamic studies.

The standard 5-channel urodynamic tests were carried out after exclusion of urinary infection using computerized testing with a microtip catheter with filling channel. The bladder was filled with saline at a temperature of 37C at a rate of 15 to 30 ml per minute, adjusted to age related expected bladder volume. A simultaneous pelvic floor electromyogram was recorded with skin electrodes attached to the perineum. All recordings took place under oxybutynin treatment to exclude intrinsic bladder wall tension by a baseline detrusor contraction. Bladder wall compliance was determined during filling of the bladder at two-thirds maximum capacity (volume/pressure). Compliance was considered poor if the value was less than 10. Maximum bladder capacity was defined by the maximum tolerable bladder filling or by the volume instilled before occurrence of an estimated urine loss exceeding 20% of the instilled volume.[13]

Results

Nineteen patients had poor compliance preoperatively, of whom 9 regained normal compliance after detrusorectomy and 10 remained unchanged (fig. 1). Sixteen patients had normal compliance preoperatively, of whom 7 were able to stop oxybutynin because of low pressures throughout the filling phase. Maximum bladder capacity was increased in 13 of 35 patients, unchanged in 11 and decreased in 11. Figure 2 demonstrates age related bladder volume before and after surgery in 35 patients.[14]

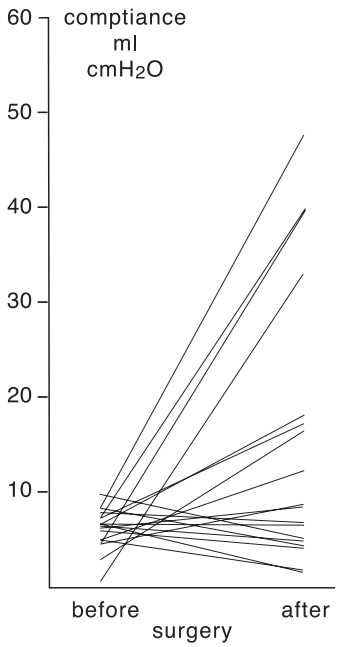


Fig. 1.
Compliance before and after bladder augmentation by detrusorectomy in patients with poorly compliant bladder preoperatively.

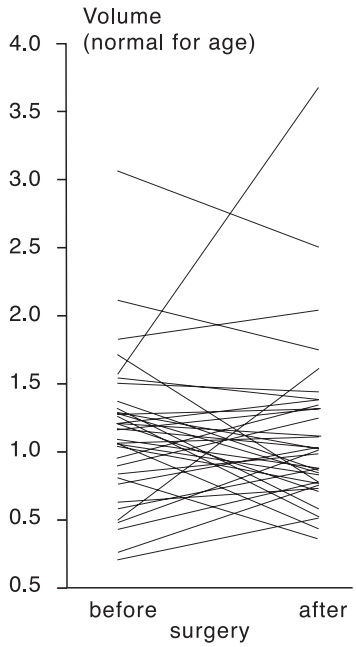
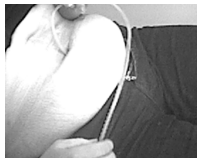


Fig. 2.
Bladder volume before and after bladder augmentation by detrusorectomy. Values are calculated as percentage of normal for age in all patients.

Of 25 patients undergoing a bladder neck procedure to enhance urinary continence 19 became continent, 5 currently have daytime wetting (1 severely) and 1 needed bladder neck closure. Of 14 continent vesicostomies 8 patients had an excellent result, 3 stomas were leaking, 2 stomas needed temporary dilation because of stenosis and 1 patient later refused to use the stoma. Of 10 ureteral reimplantations 3 were done bilaterally. In 1 patient subostial injection of a bulking agent (polydimethylsiloxane) was used. All ureters became nonrefluxing after these procedures.

Complications occurred in 4 patients. Two had postoperative bladder



leakage that was treated by drainage. These 2 patients later needed another type of bladder augmentation. Secondary cystoplasty was needed in 4 patients, of whom 3 underwent enterocystoplasty (2 because of small volume and 1 because of incontinence) and 1 ureterocystoplasty because of small volume of the detrusorectomized bladder.

Discussion

Detrusorectomy for bladder augmentation was first reported in dogs and humans in 1989.[15] In the following years only small series of patients were reported. With the use of early oxybutynin treatment and clean intermittent catheterization as standard procedures bladder compliance and volume remain adequate in most patients with myelomeningocele.

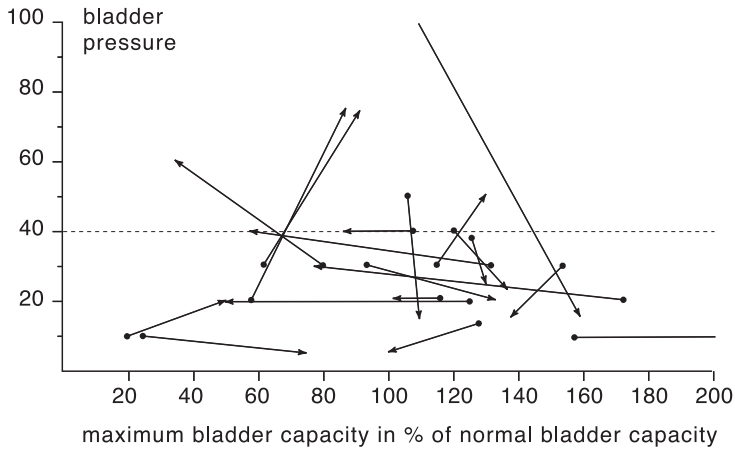


Fig. 3.
Closed circles indicate bladder pressure (cm H_2O) before operation in relation to bladder capacity (as percentage of normal for age expected bladder volume). Arrows indicate capacity after detrusorectomy in patients with poorly compliant bladders preoperatively. Most patients had good volume and safe bladder pressure after operation.

Tabe 1. Table. Age related bladder volume, end filling bladder pressure and compliance before and after surgery in 19 patients with poorly compliant bladder

Compliance (vol/pressure)		**Pressure (cm H_2O)**		**Vol (% age predicted)**	
Preop	Postop	Preop	Postop	Preop	Postop
4.5	8.8	38	25	127	130
6.7	1.7	30	60	80	35
6.0	4.3	30	40	132	58
0.5	33.3	200	15	50	160
6.7	6.7	30	45	62	72
7.5	17.4	40	23	120	137
8.5	4.5	20	20	125	51
7.5	40.0	10	5	25	75
5.0	12.5	10	20	20	51
8.0	7.0	30	50	115	131
8.5	48.0	10	5	156	363
3.0	16.7	50	15	106	110
6.3	8.8	40	40	108	87
5.0	1.8	20	30	171	78
6.6	4.7	20	20	116	143
4.6	40.0	13	5	129	101
10.0	5.3	20	74	58	87
5.3	22.5	30	20	95	134
6.7	18.3	154	138	154	138

However, in some patients bladder compliance deteriorates nevertheless. Bladder autoaugmentation in our series was performed in 19 patients to try to improve poor bladder compliance. Compliance remained unchanged in 10 patients (53%). Better results were achieved if patients were operated on at a younger age. Figure 3 and the table indicate age related maximum bladder volume before and after surgery in these 19 patients in relation to end filling pressures. If we agree that pressures up

to 40 cm and postoperative bladder volume of 80% of ideal expected volume could be tolerated, the end results are relatively good, with only 3 of 19 patients failing treatment.
Sixteen patients with preoperatively normal compliance underwent detrusorectomy to try to stop antimuscarinic treatment. This treatment failed in 9 patients (56%) and oxybutynin could not be stopped.

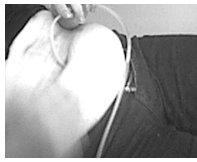
Maximum bladder volume (as a percentage of normal for age expected volume) was decreased in 11 of 35 patients (31%). In these cases we were not successful in achieving all of our goals. However in 17 of 31 patients with a strict indication for enterocystoplasty an autoaugmentation by detrusorectomy obviated the need for primary ileocystoplasty.
In approximately 50% of the cases true success was achieved with a relatively minor operation that did not require bowel preparation. Operating time for detrusorectomy was never more than 1.5 hours, and patients could leave the hospital within 6 days, or on postoperative day 4.

Detrusorectomy can be combined with other techniques such as ureteral reimplantation, formation of a continent vesicostomy and bladder neck procedures such as sling and Burch colposuspension. In the literature only 1 report of detrusorectomy in combination with a Mitrofanoff stoma was found.[16]

During the last decade many variations on detrusorectomy have been developed to prevent shrinkage of the denuded mucosal area. [17,18,19,20] Careful preparation and preservation of adventitial layers of the bladder, and closure of these layers over the denuded area prevented contraction and shrinkage of the bladder. Moreover, postoperative challenge of the bladder by elevated drainage and early intermittent clamping contributed to better development of bladder volume. In our series it appeared that in bladders with hyperactive detrusor postoperative volume was eventually better than in hypoactive bladders (Levene's test, $p = 0.14$). Remaining active detrusor probably enhances further expansion of the augmented bladder. In 9 patients with preoperatively atonic detrusor compliance became worse after the operation.

Conclusions

Detrusorectomy is a relatively simple procedure that can be used in selected cases to avoid enterocystoplasty, and shows promise in deteriorating bladders. Detrusorectomy can be done in combination with other procedures such as ureteral reimplantation, bladder neck surgery and continent vesicostomy. In case of failure a secondary operation such as an enterocystoplasty can be done without problems. Moreover, other necessary procedures such as vesicostomy, antireflux procedures and sling procedures are already done during the first operation so that the patient still benefits from the initial operation.



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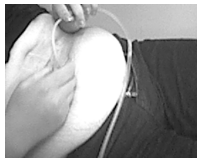

Transvaginal sling suspension of bladder neck in female patients with neurogenic sphincter incontinence

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5

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Abstract

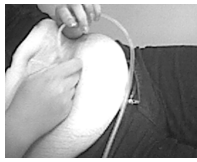
Purpose Many surgical options exist to enhance bladder neck closing pressure in women. Most procedures are relatively large with a success rate of between 70% and 90%. Sling procedures with the sling placed between the anterior vaginal wall and bladder neck cause a risk of traumatic lesions of the bladder neck at operation and of postoperative erosion of the sling into the urethra. We evaluated the results of surgical treatment for neurogenic pelvic floor paralysis in girls with spina bifida by transvaginal rectus abdominis sling suspension.

Materials and Methods Between 1991 and 2001 we treated 24 girls with a pubovaginal sling placed through the vagina. Patient age at operation was 1 to 17 years (mean 9). After identification of the bladder neck and anterior vaginal wall 2 small holes were made into the vagina left and right of the bladder neck. The sling was taken through these holes and fixed to the contralateral pubic bone. The sling procedure has been combined with ileocystoplasty, auto-augmentation, a continent catheterizable stoma and ureteral reimplantation when needed.

Results Of the 24 patients 19 were dry after the initial procedure and 3 others became dry after a total of 4 additional injections of a bulking agent into the bladder neck via suprapubic needle introduction under transurethral endoscopic guidance. A patient underwent bladder neck closure after a vesicovaginal fistula developed from the ileal bladder and another primarily elected bladder neck closure for persistent urinary incontinence. No infectious complications occurred that were related to the procedure. Clean intermittent catheterization was possible in all patients.

Conclusions Transvaginal sling suspension is safe, relatively easy to perform and cost-effective compared with most alternative procedures. It appears to be as successful as other more complicated procedures to achieve urinary continence in girls with spina bifida.

Introduction



Many different surgical options exist to treat neurogenic sphincter incontinence. The literature reports successful treatment with bladder neck lengthening procedures[1,2], artificial sphincter implants[3], bladder neck suspension[4] and slings.[5–9] Most reported procedures have a urinary continence success rate of between 70% and 92%. Reports of the success rate of rectus abdominis sling suspension of the bladder neck generally praise the results. However, it can be technically difficult to explore the plane between the bladder neck and anterior vaginal wall, especially in patients with spina bifida with severe vertebral column anomalies and hip fixation. It can result in a vesicovaginal fistula or in sling erosion into the urethra. We have adopted the policy of bringing the fascial sling around the bladder neck through the vagina.

Material en methods

A total of 24 female patients with spina bifida and neurogenic sphincter paralysis underwent surgery to cure urinary incontinence. Patient age was 1 to 17 years (mean at operation 9). Mean followup was 3 years (range 0.6 to 11). The patients were recruited from a cohort of approximately 225 patients younger than 18 years with spina bifida.

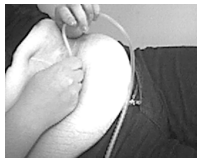
The indication for operation was urinary incontinence in the majority of cases. In a few young patients high bladder pressure with vesicoureteral reflux was the primary reason for bladder augmentation with or without ureteral reimplantation and the incontinence procedure was done as an adjunct. All patients were considered to be depending for life on clean intermittent catheterization (CIC). In 5 girls the sling procedure was combined with ileocystoplasty because of a low compliant, low capacity bladder. A total of 11 girls were treated with detrusorectomy, partly for a low compliant, normal capacity bladder and partly in an attempt to stop the need for antimuscarinic therapy. Eight wheelchair bound patients received a catheterizable stoma in the umbilicus combined with the sling procedure.

All patients were treated with surgery under antibiotic prophylaxis with amoxicillin/clavulanic acid and gentamycin. Vaginal preparation was done by flushing the vagina with 10% povidone/iodine solution. In most patients a transverse lower abdominal incision was made with longitudinal opening of the rectus abdominis fascia in the midline. In patients who also underwent ileocystoplasty a longitudinal lower abdominal midline incision was made. A 10 to 15 x 2 cm paramedian strip of rectus abdominis fascia was made, leaving the caudal end fixed to the pubic bone. In patients who had had an earlier transverse incision of the rectus fascia a 2 cm strip of externus abdominis fascia was harvested, running from the pubic bone to the anterior superior iliac spine.

The bladder neck and anterior vaginal wall were identified with a transurethral balloon catheter and freed, comparable to the preparation done for Burch-type colposuspension. A metal clamp introduced into the vagina was used to lift the anterior vaginal wall left and right of the bladder neck. Using electrocautery 2 small holes were made into the vagina and a vessel loop was passed around the bladder neck through the holes. Because most patients were prepubertal and none had given birth before the operation, there was not enough room in the vagina to attempt to create a submucosal tunnel in the anterior vaginal wall.

The fascial sling was fixed to the vessel loop and passed through the holes. The sling was passed bluntly through the contralateral rectus abdominis muscle and fixed tightly to the tubercle of the pubic bone with strong polyglycolic acid sutures. In most patients the sling operation was combined with other procedures, including ileocystoplasty in 5, detrusorectomy in 13, a continent catheterizable stoma in 8 and extravesical ureteral reimplantation in 3. Patients were treated with low pressure suction drainage before the bladder for 2 to 4 days. Bladder drainage was done by a transurethral catheter for 7 days combined with a suprapubic catheter in ileocystoplasty cases. Hospitalization for patients without ileocystoplasty was 3 days. Those with no catheterizable stoma resumed CIC after 7 days. Special attention was given to teach the patients the changed direction of the urethra when transurethral CIC was resumed.

Results



Mean follow-up was 3 years (range 0.6 to 11). Of the 24 patients 19 (79%) were dry immediately after the operation and they remained dry during followup. Three patients became dry after subsequent injection of the bulking agent Macroplastique (Uroplasty, Minneapolis, Minnesota) into the bladder neck, 1 of whom those needed 2 injections. Injection was performed by putting the rigid needle suprapubically into the bladder neck under transurethral endoscopic guidance. In 1 patient a vesicovaginal fistula developed when CIC was forgotten at school 6 weeks after ileocystoplasty and transvaginal sling placement. She was treated with bladder neck closure. Another patient with a catheterizable stoma in the umbilicus elected bladder neck closure as primary treatment for persistent incontinence after the sling operation. A total of 22 patients (91%) became dry, including 3 with extra endoscopic procedures. Two failures were treated with bladder neck closure and these girls perform CIC through an umbilical stoma. Morbidity of the open vaginal wounds was limited to minor vaginal discharge in all except the patient with a late vesicovaginal fistula. No infections were related to the vaginal procedure.

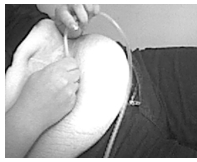
In a few patients further surgery after the sling procedure provided the opportunity for endoscopic vaginal examination. Although no attempt had been made to cover the sling with mucosa during the first operation, the vaginal epithelium had entirely covered the sling in all cases and the sling could not be identified except for the sharp angle in the anterior vaginal wall. In all patients the urethra was patent. We did not suspect sling erosion in any case. Notably many patients passed through puberty after the sling suspension without changes in urinary continence and without obstruction. Apparently the sling grew with the patient without negative side effects.

Conclusions

Transvaginal sling suspension of the bladder neck is an operation that is easy to perform and learn with results comparable to those of other types of surgery to achieve urinary continence in patients with spina bifida. Technically it is superior to many other procedures because it is relatively simple and without the need to open the bladder or pass between the bladder neck and anterior vaginal wall. No negative side effects of the transvaginal pathway were noted except for a vesicovaginal fistula in 1 case. The result appears to be permanent, in contrast to Burch-type colposuspension, which we performed in earlier patients and which in our hands had no long-lasting effect in many of them. It is an inexpensive operation compared with sphincter devices because no material costs exist and only a short hospital stay is needed for the procedure when it is not combined with ileocystoplasty. The procedure can similarly be done in other groups of female patients who need bladder neck suspension because of nonneurogenic structural incontinence. In this nonneurogenic group of patients the sling should not be tightened under tension to retain the possibility of normal voiding, in contrast to the patients with spina bifida patients in this report, who depend on CIC.

Editorial comment

The authors report a series of 24 girls treated in a 10-year period in whom sling cystourethropexy was performed via the vaginal approach for urinary incontinence. The authors make several important points. Most patients reported on were prepubertal and nulliparous and, therefore, vaginal access was limited, making placement of the sling more difficult than it would be in the older incontinent female population, who are typically multiparous patients with good vaginal access. To minimize the amount of vaginal dissection the authors made no attempt to cover the sling with mucosal flaps or a mucosal tunnel and yet the vaginal epithelium covered the sling in all cases when assessed at subsequent examination. The second point, which deserves emphasis, is the fact that the authors tied the sling under some tension in patients with a postoperative expectation of clean, intermittent catheterization. In patients in whom the possibility of normal voiding is entertained the sling is not tied under any significant tension. The experience that we now have with older women undergoing sling cystourethropexy supports the fact that



virtually any tension on a sling frequently leads to postoperative voiding dysfunction.

The authors report that 91% of the 22 patients became dry, of whom 3 required additional endoscopic procedures. Unfortunately there are no urodynamic studies preoperatively or postoperatively reported and it is somewhat difficult to determine what the effect of the sling was in achieving continence since most patients also underwent procedures to improve bladder compliance, which in and of itself may result in continence without any bladder neck treatment.

I think that this procedure is worthwhile even given the fact that vaginal access in these patients is limited because abdominal dissection of the urethra is an even more formidable task. With some experience the vaginal approach for sling placement should result in a shorter and safer procedure.

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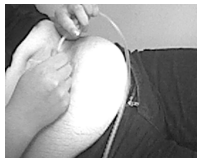

Urinary continence and erectile function after bladder neck sling suspension in male patients with spinal dysraphism

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6

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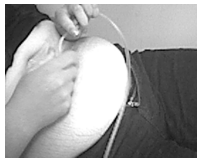
Abstract

Objective To assess the outcome of using sling suspensions combined with clean intermittent catheterization (CIC) in patients with spina bifida, of whom a third are incontinent through pelvic floor paralysis.
Patients and methods Between March 1992 and April 1997, 14 male patients (mean age at surgery 11.7 years, range 6.5–15.2) with spina bifida and neurogenic sphincter incontinence underwent a puboprostatic sling suspension as a primary treatment. The procedure, via an abdominoperineal approach, consists of suspending the bladder neck by placing a simple U-shaped rectus abdominus fascial sling. The perineal approach is used to develop the plane between the rectum and Denonvillier's fascia, and to prepare the passage of the sling alongside the prostate. Apart from the sling procedure, eight of the 14 patients underwent autoaugmentation of the bladder and two underwent ileocystoplasty during the same operation. All patients used CIC daily. Erectile function was assessed by reports from the patients and their parents, and continence by report and urodynamic studies.
Results Of the 14 patients, 13 achieved urinary continence with no additional procedures; one required a subsequent submucosal injection at the suspension site with silicone particles in povidone (Macroplastique®) to become continent. Two patients reported slight leakage at night. Before surgery, all but one patient reported having spontaneous or mechanically manipulated erections; none had erections on psychological stimulation. After surgery, erectile function was preserved in 13 of the 14 patients; in one there were problems establishing the right dissection plane between the rectum and prostate, but spontaneous erections returned a year after surgery.
Conclusion In males, the abdominoperineal puboprostatic sling suspension using rectus abdominis fascia appears to be a successful treatment for sphincter incontinence in patients with spina bifida, and safely maintains erectile function.

Introduction



Sphincter incontinence is common in patients with spina bifida, occurring in about a third.[1] There are several techniques to achieve continence in these patients, e.g. bladder neck procedures[2,3,4], intravesical flap-valve procedures[5,6,7] and the AUS.[8,9,10] Our primary choice is the puboprostatic sling procedure, using an abdominoperineal approach, to treat sphincteric incontinence in these patients.[11,12,13,14] When urodynamic studies indicate clear bladder dysfunction (low capacity or compliance), surgery on the bladder is undertaken at the same time.[15] For bladders with low compliance and a relatively good capacity for age, autoaugmentation (detrusorectomy) is the first choice of procedure. When the bladder capacity is low for age, independent of bladder compliance, ileocystoplasty is combined with the sling procedure. To determine the outcome of this management, we assessed the continence and erectile function of patients undergoing these procedures.

Patients and methods

Between March 1992 and April 1997, 14 male patients with spina bifida and neurogenic sphincteric incontinence were treated (mean age at surgery 11.7 years, range 6.5–15.2). All patients were evaluated with at least two urodynamic studies, one of which included filling the bladder while the bladder neck was occluded with a balloon catheter, to predict bladder behaviour after applying therapy to increase the resistance. Seven patients had poor detrusor compliance, four of whom also had a low capacity for their age. The other seven patients had normal bladder compliance, but three also had a low capacity for their age. All patients had leak-point pressures of <40 cmH_2O and they were all stress-incontinent, both day and night. Four of the patients had a normal or near-normal bladder capacity for their age and required no additional bladder surgery. In all other patients, a detrusorectomy was initiated after the sling procedure, although this was deemed inappropriate in one and he underwent ileocystoplasty.

Surgical procedure

Using an abdominoperineal approach, a 2-cm wide strip of rectus abdominis fascia is prepared for use as a sling around the prostate, at the level of the bladder neck, posterior to Denonvillier's fascia (Fig 1.). The sling is harvested through a lower abdominal midline incision. Starting at the level of the umbilicus the fascial strip is freed from the medial margin of the rectus fascia. The strip remains based at the pubic bone with the pyramidalis muscle attached to the fascial strip. Through a pre-anal inverted U-incision, the centrum tendineum is identified and opened,

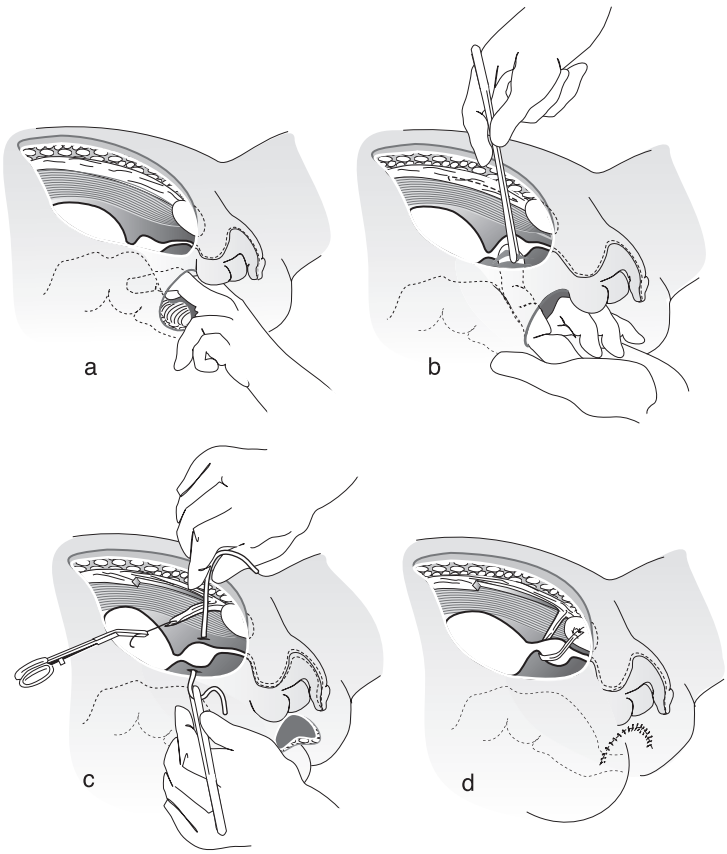
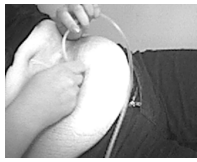


Fig. 1.



providing access to the posterior prostatic surface. With a balloon catheter as a landmark, the preparation is continued to the level of the bladder neck (Fig 1a). The endopelvic fascia is perforated on either side of the prostate by blunt finger pressure (Fig 1b) and a temporary silicone band passed around the bladder neck (Fig 1c). The fascial sling is then attached to the silicone band, passed around the bladder neck, and fixed to the contralateral pubic bone with 1/0 polyglycolic acid sutures (Fig 1d). The tension on the sling is adjusted to allow easy passage of a 14 F catheter into the bladder before and after fixing the sling. Intraoperative urethral pressure profiles were not recorded; in earlier patients there was a poor correlation with operative success. Recently, in two patients with a wide bladder neck, the sling was wrapped around the bladder neck by one full turn before fixing it to the pubic bone.

Eight of the 14 patients also underwent bladder autoaugmentation (detrusorectomy); this is initiated with a meticulous opening of the midline adventitious layers of the bladder. These layers are marked with a suture to allow their identification and closure at the end of the procedure. In previously unoperated bladders, the detrusorectomy starts at the pubic bone and passes widely around the dome of the bladder. The bladder is maintained at a filling pressure of 40 cmH_2O throughout detrusorectomy and a small patch of detrusor is left at the urachal remnant, with redundant detrusor excised. The adventitious layers are closed in the midline and finally the urachal remnant is fixed to the anterior abdominal wall at the level of the umbilicus. Any small leaks from the mucosa occurring during surgery can be sealed using two-component collagen solution, as efforts to suture the hole usually cause more leakage. In two patients, the sling procedure was combined with an ileocystoplasty because of fibrosis of the mucosa. One of these had undergone a failed detrusorectomy 3 years earlier and the other had recurrent UTIs.

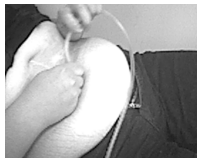
The patients were followed for a mean (range) of 3.8 (1.5–6.5) years, during which all were assessed using urodynamic studies, all received low-dose antibiotics and oxybutynin (0.3 mg/kg daily in three doses), and used CISC five times a day.

Results

Ten patients immediately achieved day-time continence and two complained of mild nocturnal incontinence. One patient with persistent daytime incontinence required a subsequent injection with silicone (Macroplastique®) at the suspension site and became dry, and the other became continent spontaneously after 2 months. Two other patients remain mildly incontinent day and night, and use pads; one is incontinent only when performing CISC through the stoma when the bladder is at maximum capacity. The other patient seems to be incontinent during unstable bladder contractions, although urodynamic studies suggested that the bladder volume and compliance were normal. These last two

Table 1 Age related bladder volume before and after surgery in 14 patients

Treatment / Patient no.	Bladder volume (% expected for age)	
	Before	After
Detrusorectomy		
1	15	112
2	29	52
3	35	65
4	41	74
5	63	129
6	99	71
7	135	151
8	140	111
No detrusorectomy		
1	86	122
2	94	129
3	102	136
4	117	100
Ileocystoplasty		
1	35	119
2	62	98



patients were those treated using a full turn of the sling around the bladder neck rather than a U-shape.
All the patients were evaluated with urodynamic studies at least one year after surgery; the age-related bladder capacity improved in 11 patients (Table 1) and all patients had good compliance with low end-filling pressures. One patient with grade 1 VUR underwent a sling procedure with no augmentation, developed grade 5 VUR on the right side and lost kidney function (23% by DMSA scintigraphy) by 5 years after surgery. Because his bladder was of good capacity and he was completely continent, he failed to comply further, and stopped using CISC and prophylactic drugs. Twelve of 14 patients reportedly had unchanged erections after surgery; one had reported having no erections previously and one (aged 15 years) had impaired erections for more than a year. In this patient the sling was initially placed in the posterior wall of the prostate instead of posterior to Denonvillier's fascia; a year after surgery his erectile function gradually returned to normal, and at age 19 this wheelchair-bound patient with asymmetric lesions claimed to be capable of intercourse and ejaculation. Two patients had mechanical problems with CISC because of a false passage into the prostatic urethra that developed after surgery. In one the false passage was caused by a faulty (sharp-edged) catheter and in the other there were persistent problems in inserting the catheter past the suspension site. Both patients required a continent catheterizable stoma using the appendix.

Discussion

Prostatic sling procedures for male neurogenic incontinence were reported by Elder in 1990[11] but no account of erectile function after such procedures was given in previous reports. However, some reports[16,17] describe good erectile function after implantation of an AUS around the bladder neck. However, at the level of the bladder neck the neurovascular bundles run more dorsolaterally and are not closely associated with the bladder neck. The risk of injury to the neurovascular

bundle may be higher in the present type of sling procedure because the fascial sling is brought around the prostate, with extensive development of the plane between the rectum and prostate. The preservation of erectile function after such surgery was therefore unpredictable when we first used this procedure.[18] Thus we initially restricted the operation to patients who were considered unlikely to have an active sexual life.[19,20] The perineal approach enables the development of the plane dorsal to Denonvillier's fascia; when the first results were favourable, the operation was offered as the first choice.

The structure of the pelvic floor in these patients differs from that in normal individuals; because of paralysis, the muscles are degenerate and fatty, providing few typical landmarks. However, the plane posterior to the prostate can be developed relatively easily in the fatty surrounding tissue and the endopelvic fascia opened laterally to the prostate to avoid damaging the neurovascular bundles. The nerves appear to be spared in this procedure by leaving Denonvillier's fascia on the prostate and by passing the fascial sling laterally away from the prostate. (Fig 2). Thus, using the abdominoperineal approach it is easier to establish the plane between Denonvillier's fascia and rectum to allow the passage of the

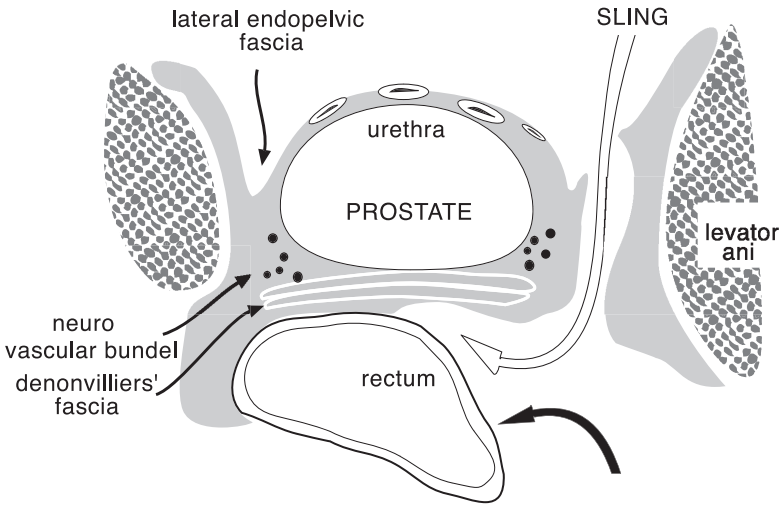
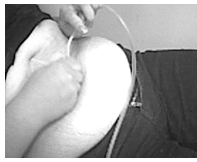


Fig. 2.



sling, and to preserve the neurovascular bundle, than is possible with the suprapubic approach.

The continence attained after the simple sling procedure was better than predicted from existing reports. This is attributable to the relatively easy and exact positioning of the sling at the bladder neck with the perineal approach. Because of recent reports of poor results using the U-shaped sling in patients with a wide bladder neck, we wrapped the sling around the bladder neck by one full turn before fixing it to the contralateral pubic bone. Surprisingly, two of the present patients with this type of sling remain incontinent. Growth does not appear to be an important factor in maintaining continence and the ability to perform CISC; several of the present patients who underwent surgery before puberty have no problems with CISC after pubertal growth.

None of the present patients had erectile dysfunction after surgery, although one had temporary impotence (and currently reports antegrade ejaculation). It is accepted that the patients' and parents' reports are a relatively poor indicator of erectile function, but more accurate information[19,20] cannot be obtained in this group of patients.

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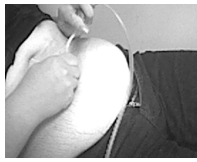

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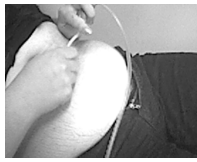

Disappointing results in continent vesicostomies

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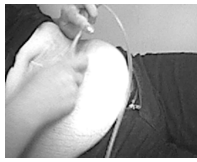
7

submitted

Abstract

Objective To evaluate the percentage of problems and complications because of stenosis and leakage of a catheterizable vesicostomy.
Patients and methods In a retrospective study data were collected from the records of 36 patients that had a continent vesicostomy operation. This operation was done in 3 patients with bladder exstrophy, 27 with neurogenic bladder, in 2 encephalopatic patients and in 4 with overextended valve bladders.
Results Mean follow-up was 38,5 months (10,9-73,8 months). The vesicostomy has been constructed using the appendix in 18, a patent urachus in 1, an ileal tube (Monti procedure) in 3 and a flipped detrusor (Boari flap) tube in 11 patients. Three ureters were used as a continent stoma. Twenty-one patients needed secondary operative procedures. Ten incontinent stomas were treated with injection of a bulking agent (Macroplastique®) leading to continence in only 5. In one patient the Monti tube stoma was too wide and the tube was tapered with improved result. Of 9 stenoses 8 patients ended up with a patent vesicostomy after a mean of 1,2 secondary procedures. In 1 patient the stoma was lost due to recurrent stenosis and one patient had a complete new vesicostomy (Monti tube). At the time of evaluation in 6 patients (16%) still some discomfort exists because of leakage or stenosis.
Conclusion In preparing a patient for a continent catheterizable bladder stoma we have to warn for the expected 58% complication rate after surgery. After several interventions a remaining 16% still has problems with leakage or stenosis.



Introduction

Now that the Mitrofanoff principle[1] is well known in reconstructive urology with large series[2,3,4], modifications are made to simplify and reduce long-term complications such as stomal stenosis.[5,6,7] If the appendix as catheterizable tube of choice is absent, has been removed, used in other reconstructive procedures[8] or is unsuitable for morphological reasons, surgeons must have other options.[9]
Multiple techniques were described so far for achieving continence in urinary diversion and reconstruction. This indicates that to date a universally applicable, reliable procedure with a low rate of complications has not yet been found.[5,6]
Over the past 6 years 39 continent vesicostomies were constructed in 36 patients in our institution. Several techniques were used. It appeared that in a number of these patients problems arose because of stenosis and leakage of the vesicostomy.

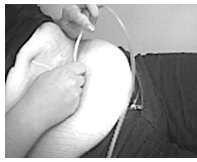
Methods

In a retrospective study data were collected from the records of 36 patients that underwent a continent vesicostomy operation. Multiple indications for such reconstructive surgery exist. Wheelchair bound female patients that need a transfer for catheterization were candidates. And also parents requested a continent stoma for their children because of heavy weight of the children and back problems of the parents. School-going children, that need to be catheterized by other caretakers, requested the vesicostomy for privacy reasons. In one case the vesicostomy was needed after problems with CIC because of a false-route in the prostatic area.
Mean follow-up was 38,5 months with a range of 10,9 - 73,8 months. Diagnosis was 3 bladder exstrophy, 27 neurogenic bladder, 2 encephalopatic patients and 4 with overextended valve bladders. Five techniques were used to create the catheterizable tube: appendix tube, flipped detrusor tube, ileal tube[10,11], ureter and a patent urachus was used. A Lich-Gregoir type of antireflux procedure was used with appendix,

ileal tube, ureter and urachus. A Kropp-like submucosal formation of a tunnel[12] was used in the Boari flipped detrusor tube stoma.
Postoperatively an indwelling stent was left in the vesicostomy for 2 weeks. After removal of the stent intermittent catheterization was started after instructions by a nurse practitioner in the outpatient clinic.
Complications like leakage and stenosis were recorded and treatment modalities are described. When stenosed, first step was dilatation and insertion of a 2,5 cm long 14 French teflon blunt nail in the stoma between catheterization cycles.

Results

In a total of 36 cases, the vesicostomy has been constructed using the appendix in 17, a patent urachus in 1, an ileal tube (Monti procedure) in 4 and a flipped detrusor (Boari flap) tube in 11 patients. Three ureters were used as a continent stoma.
Twenty-one patients needed secondary operative procedures, 9 based on stomal stenosis, 10 because of incontinence and 2 because of a false route.
Stomal stenosis was a skin problem in 7 cases, a distal tube stenosis in 1 and proximal stenosis at the level of passage into the bladder in 1. Of 9 stenoses 8 patients ended up with a patent vesicostomy after a mean of 1,2 secondary procedures. In 1 patient the stoma was lost due to recurrent stenosis.
Ten incontinent stomas were treated with injection of a bulking agent (Macroplastique®) leading to continence in 5. Conversion into a sigmoidocystoplasty with colon "Monti" tube was done in 1 patient with an appendix stoma after several unsuccessful interventions. Also a Monti procedure was done in another patient with an incontinent appendix stoma. One other patient with an incontinent Monti tube received a Boari stoma made of the wall of his ileocystoplasty. The patient with the failed and stenotic urachus stoma also had a poor compliant bladder. She was treated with an ileocystoplasty and Monti tube vesicostomy.



A false route near the bladder was treated with 3 weeks of indwelling catheter in 1 patient.
Fifteen patients did not need secondary procedures.
Of the 36 patients, 30 eventually ended up with a continent and catheterizable stoma.

Table type of vesicostomy, complications and reoperations

36 patients	n	stenosis or fausse route	leakage	redo operation	
appendix	17	6	5	revision	2
				monti	2
boari	11	4	2	revision	1
ureter	3	0	0	-	0
monti	4	0	3	reïmplatation	1
				revision	1
				boari	1
urachus	1	1	0	monti	1

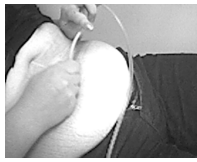
Discussion

After a decade of enthusiastic reports in literature more recently problems with continent vesicostomies are being published.[13,14] In many cases the complications of this surgery leads to a temporary episode of frustrating attempts by parents and children to come to clean intermittent catheterization. We have not been able, in our series, to find predictors for success or failure besides the fact that obese patients run a greater risk for stenosis of the tract. Temporary intubation of the distal 2,5 cm's, between catheterizations, with a silicon or teflon plug enables to overcome a shrinking skin anastomosis. The problem of stomal stenosis probably can be diminished by leaving the stomal catheter longer in place for at least 3 weeks. In some institutions 6 weeks is advocated. The circular wound has a better opportunity to heal so that stenosis can be avoided.

Meanwhile we have observed that injecting bulky agents (Macroplastique®) in the wall of a leaking stoma is of use in only 50%. Probably the material is pushed away after some time by repeated catherizations. Leaking stoma's need to be repaired by elongation of submucosal tunnels in the bladder rather than by endoscopic procedures.

Conclusions

In preparing a patient for a continent catheterizable bladder stoma we have to warn for the true expected 58% complication rate after surgery. After several interventions a remaining 16% still has problems with leakage or stenosis.



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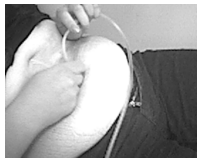

Urologic follow-up of patients born with spinal dysraphism

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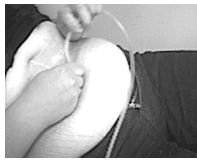
8

submitted

Abstract

Objective Renal scarring and renal failure remain a major problem in spina bifida children, even with reported death in the first year of life of more then 20% of cases. Data are presented to show that optimal treatment of the neurogenic bladder from birth on can preserve kidney function in most spina bifida patients.
Patients & Methods Data of all newborns with spinal dysraphism admitted at our institution from January 1988 till June 2001 were reviewed. From admission and during follow up, start and type of treatment (antimuscarinic agents, clean intermittent catheterization, antibiotic prophylaxis) as well as renal (ultrasound, DMSA scan, serum creatinin, creatinin clearance: Schwartz formula) and bladder function (urodynamic studies) was monitored.
Results Data of 144 children out of 176 could be evaluated by the end of the study: 109 patients with spina bifida aperta and 35 with occult spinal dysraphism. Of the remaining 32 patients 25 died shortly after birth due to causes not related to the urinary tract. Five of the 144 had pre existing renal abnormalities. Seven patients were lost to follow-up because of reallocation. Of 109 aperta patients 60 patients had an overactive sphincter. Twelve of them had reflux and three of them renal scars. Of 35 patients with occult spina bifida only 9 had an overactive sphincter. Of 26 patients with normal to inactive sphincter 7 had vesico-ureteral reflux and 3 of them had renal scars. Twenty-four out of 29 children with spina bifida occulta and 44 out of 53 patients with spina bifida aperta were continent at school age (6 years). None of all patients currently is developing end stage renal disease. All 3 patients with renal scars in the occulta group started therapy with intermittent catheterization and antimuscarinic therapy after one year of age. In the aperta group only one of three renal scar patients followed a late onset therapy.
Discussion/Conclusion Compared to literature children born with spina bifida, if adequately treated urologically, can probably last a lifetime with their own kidneys. To ensure protection of the upper urinary tract, low intra-vesical pressure is necessary. Early start of clean continuous intermittent catheterization is the treatment of choice and administration of antimuscarinic agents to counteract detrusor instability is indispensable in most cases. Pro-active treatment of risks for upper tract deterioration results in neglectable loss of renal function, even when early urinary continence is included in the treatment protocol.

Introduction



The incidence of children born with meningomyelocele (MMC), worldwide, varies from 0.3 to 4.5 per 1000 births.[1] In the Netherlands this is 0,38 per 1000-life births.[2] Though in time survival chances for babies born with a MMC have risen enormously[3], renal failure is still accepted in many institutions as a long-term complication and remains a major cause of death.[4,5,6] Recent literature[7] reports series of kidney transplantation in children with MMC illustrating the reality of development of end stage renal failure. The incomplete innervation of the urinary bladder and pelvic sphincter, due to the neural tube closing defect, can cause problems in the storage and emptying function of the bladder, which in time can lead to renal failure.[8,9] Vesico-ureteral reflux (VUR) and recurrent pyelonephritis are the important reasons of renal failure in early and later life.[10, 11, 12] Complications of urinary tract infections especially occur in the first year of life.[13]
We try to prove that with adequate preventive measures and early onset treatment of these complications, bladder function can be optimized and kidney function may be preserved for life.

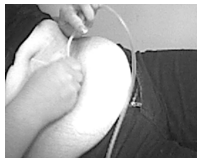
Patients and Methods.

Starting in January 1988 new spina bifida patients that were presented at our hospital were treated with clean intermittent catheterization (CIC), antimuscarinic agents and antibiotic chemoprophylaxis from birth on in order to prevent obstructive uropathy and to preserve renal function. Exclusively non-latex catheters were used in patients with MMC because of the high risk of latex allergy in this group. Starting in 1991, all patients were treated latex free during all interventions and during CIC.[14,15] To secure low intra-vesical pressure antimuscarinic agents were administered (oxybutynin or sometimes, if needed, replaced by tolterodine). For evaluation of effects on bladder function urodynamic studies (UDS) were done starting at the age of 3 months.
From January 1988 till June 2001, 176 children with a (myelo-) meningocele (MMC) were admitted to our hospital. The development of kidney and

lower urinary tract function was followed. At first presentation an ultrasound of the urinary tract was done and serum creatinin level was measured. All patients were followed in the spina bifida outpatient clinic at regular intervals with controls by a pediatrician, orthopedic surgeon, neurologist, neurosurgeon, rehabilitation specialist and physical therapist and with support of a nurse and a social worker. UDS were done at the age of 3-4 months with yearly control UDS during follow-up. Intercurrent urinary tract problems were dealt with in the pediatric urology outpatient clinic. Surgery for urinary continence was in most cases offered starting at school age. Surgery for vesico ureteral reflux (VUR), recurrent infections and high detrusor pressures was done when indicated regardless of age. Female wheel-chair patients were offered a continent catheterizable stoma. For the current study, results of ultrasound studies were evaluated to detect renal parenchymal scarring, serum creatinin levels and body length. In renal ultrasound was looked for parenchymal scars, dilatation, difference in kidney length, or other signs of renal damage. Patients suspected for scarring had a DMSA-scan for further evaluation. A DMSA-can was also done when US of the kidneys was not reliable in cases of renal position anomalies with major scoliosis. In case of suspicion for renal anomalies the creatinin clearance was calculated with the Schwartz formula: creatinin clearance in ml/min = (k* body length/serum) creatinin μmol/l. In our clinic and during this study a value of k of 38 was used for both boys and girls. Furthermore continence in both groups of patients was studied in operated and non-operated patients.

Results

Of 176 children, 25 newborns died due to reasons not related to the urinary tract. Seven children were lost to follow-up because of reallocation to another region or country. Of the 144 included patients, 70 were boys (49%) and 74 were girls. Thirty-five patients (24,3%) had occult spinal dysraphism, 109 (75,7%) a spina bifida aperta. The follow-up ranges from



5,4 to 162,2 months (mean 77,4 months) for the aperta group and 11,3-160,5 months (mean 94,6 months) for the occulta group. None of the children had abnormal serum creatinin level shortly after first presentation.

Ultrasound at presentation

Results of early ultrasound investigation of the kidneys are summarized in table 1. A total of 7 renal units had low-grade dilatation (3 unilateral and 2 bilateral) and 4 units showed gross dilatation (grade 4-5 reflux in 4 patients that were referred to our institution at later age and were untreated so far). One patient had a left multicystic dysplastic kidney and one other patient a very small dysplastic kidney on the right side. A horseshoe kidney was found in one patient and an upper pole cyst in two.

Table 1 Ultrasound findings in 144 spina bifida patients at first presentation

ultrasound 144 patients at first presentation	minimal dilatation unilateral	minimal dilatation bilateral	gross dilatation unilateral	MCKD or dysplastic	upper pole cyst	double system	horse-shoe kidney
spina bifida aperta	2	1	1	2	2	1	1
spina bifida occulta	1	1	3	-	-	-	-

Ultrasound during follow-up

During follow-up low grade dilatation was found in 10 renal units in 7 patients: 3 patients had minimal bilateral dilatation and 4 had a minimal unilateral dilated kidney. One patient had high-grade unilateral dilatation. Six children have currently grade I-II vesico ureteral reflux (VUR). One girl had grade 4 bilateral VUR and had a bilateral implantation,

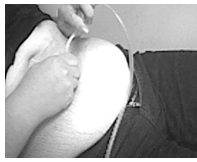
combined with a detrusorectomy after closure of the study episode.
One girl later had left ureteric obstruction, due to an orthopedic surgical complication. After reanastomosis of the obstructed ureter, a DMSA scan showed left side renal function of 20%.
Unilateral parenchymal scars were suspected in 10 patients on ultrasound, but only in 6 (all girls) confirmed by DMSA renal scan as is shown in table 2.

Table 2 Ultrasound findings in 144 spina bifida patients at follow-up. Renal damage was confirmed with DMSA scan in 6 patients.

ultrasound 144 patients during follow-up	minimal minimal unilateral	minimal dilatation bilateral	gross dilatation unilateral	suspicion for renal scar	DMSA scar or function loss
spina bifida aperta	3	2	1	6	3
spina bifida occulta	1	1	-	4	3

DMSA study

DMSA scintigraphy was done in patients that were suspected for renal damage by ultrasound (table 2). In the occulta group one patient had 34% function in the right kidney, one 16% the left and one 30% in the right kidney. Parents of the girl with the left 16% scarred functioning kidney admitted that they did not always comply with the catheter regimen. Three patients with spina bifida aperta showed poor remaining function in their left-sided kidneys: 17%, 21% and 20%.
The loss of kidney function in the girl with left sided 20% kidney was due to obstruction as result of an orthopedic surgical complication. A vesico-vaginal fistula was made and ureteric reimplantation was done. In the girl with the poor functioning left kidney (17%). Her parents refused an augmentation and also did not comply with the catheter regimen. Two



patients had a pre-existing parenchymal lesion: one boy with a left sided multicystic dysplastic kidney and a girl with a small dysplastic right kidney. In the aperta group of 109 patients with 216 evaluable renal units, 3 units had parenchymal damage: 1,4%. In the occulta group of 35 patients 3 of the 70 evaluable renal units showed parenchymal scars. All three patients had dilating reflux and started CIC and antimuscarinic therapy more than six months after birth.

Table 3 Detrusor and sphincter behaviour in 109 patients with spina bifida aperta.

109 patients spina bifida aperta 52 males, 57 females

		DETRUSOR	
		Inactive	Active
SPHINCTER	Inactive	**33** 6 VUR	**16** 2 VUR
	Active	**22** 4 VUR (1 with renal scar)	**38** 8 VUR (2 with renal scar)

Table 4 Detrusor and sphincter behaviour in 35 patients with spina bifida occulta.

35 patients spina bifida occulta 18 males, 17 females

		DETRUSOR	
		Inactive	Active
SPHINCTER	Inactive	**21** 5 VUR (2 with renal scar)	**5** 2 VUR (1 with renal scar)
	Active	**7**	**2**

Table 5 109 patients with spina bifida aperta: overactive sphincter least frequently seen in cervical and low lumbal meningomyeloceles.

109 patients spina bifida aperta localisation of lesion		overactive sphincter complex
cervical	2	0
thoracic	20	13
lumbal	68	16
sacral	19	9

Urodynamic study

Results of urodynamic studies are summarised in table 3 and 4. Overactivity of the sphincter was found in 60 of 109 aperta patients and in only 9 of 35 occulta patients. VUR occurred in the aperta group in 20 patients, 12 of them had an overactive sphincter and three of them showed eventually renal function loss. In the occulta group VUR was seen remarkably not in patients with overactive sphincter. However, even with inactive sphincters seven patients had VUR and three of them had dilating reflux and renal function loss on DMSA scan.
In the aperta group an overactive sphincter complex was found more often in sacral and thoracic lesions. Lumbal lesions had more often paralytic sphincters and incontinence as is shown in table 5. However further analysis shows that in 25 lesions in the region of Th10-L2 (the area where sympathetic afferentes and efferentes registrate and regulate bladder compliance) 16 patients had an overactive detrusor and 14 also had overactivity of the sphincter.

Surgery

The ureter was reimplanted into the bladder (5 bilaterally) in 14 girls and a left ureteral reimplantation was done in one boy.
To provide social urinary continence and to improve bladder compliance

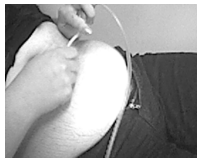


Table 6 53 patients with spina bifida aperta, older than 6 years of age: 7 still incontinent, 4 will still receive a sling and augmentation plasty

53 patients spina bifida aperta

older than 6 years: continence		overactive detrusor	inactive sphincter	received sling and augmentation	will need sling and augmentation
continent	39	12	18	18	0
pads	7	1	5	4	0
incontinent	7	3	3	2	4

an auto-augmentation of the bladder was done in 37 patients (detrusorectomy), in 22 patients also combined with a sling procedure.[16] In a group of 53 patients older than 6 years of age with spina bifida aperta continence was evaluated. The results are summarised in table 6: 39 patients are continent, 7 are minimal incontinent and use pads and 7 patients are still incontinent, three because of an overactive poor compliant bladder and three because of an inactive sphincter. Two patients already received a sling but are still incontinent and 4 patients will receive a sling and bladder augmentation in next future. One patient still prefers to be incontinent and will be followed.

Table 7 shows the continence of 29 out of 35 patients in the occulta group that were evaluated at school age (6 years of age): in patients with spina bifida occulta continence seems not to be related to sphincter overactivity but rather to inactivity of the detrusor muscle. Four patients with overactive detrusor and inactive sphincter became continent with antimuscarinic therapy. Five patients are incontinent, two of them need only pads for mild incontinence. In one of them recently an ileocystoplasty, bladder neck sling and vesicostomy was done, three other patients are on the list for bladder augmentation plasty. Table 8 shows continence in the total group of 35 patients with spina bifida occulta and their neurological diagnosis.

Table 7 29 out of 35 patients with spina bifida aperta that were older than 6 years of age (schoolage): 3 still incontinent, 2 patients use pads. Continence is not related to sphincter overactivity in patients with spina bifida occulta. Four patients with overactive detrusor and inactive sphincter became continent with antimuscarinic therapy.

29 patients spina bifida occulta, 14 males, 15 females

		DETRUSOR	
		Not over-active	Over-active
SPHINCTER	Not over-active	**17** 16 continent 1 incontinent (5 sling & augment)	**4** 4 continent
	Over-active	**7** 4 continent 2 incontinent 1 pads (4 sling & augment)	**1** 1 pads (1 sling&augment)

Follow-up creatinin level

Follow-up creatinin level of 103 children was recorded. The patient's history, clinical and urodynamic follow-up was not suspect for renal deterioration in the other 41 patients. With the Schwarz formula the Creatinin clearance was calculated. Out of these 103 children 2 had a creatinin clearance (Ccr) under 80 ml/min. One girl has a Ccr of 54 ml/min but has a length that deviates more than 2.5 times the standard deviation under normal. She is currently three and has a normal UDS with no signs of VUR. Another girl has a Ccr of 70 ml/ min and her left ureter was reimplanted because of grade 5 left VUR, she is currently without VUR , but a DMSA-scan showed a left kidney functioning of 17%, as was suspected by ultrasound. All other patients had a Ccr well above 80 ml/min (mean 133ml/min). A girl with a pre-existing right renal scar had a calculated Ccr of 84ml/min.

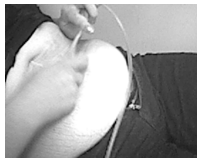


Table 8 35 patients with occult spina bifida: 6 incontinent (2 with only pads); 3 on list for augmentation, 1 recently had augmentation

35 patients spina bifida occulta				
localisation/diagnosis		Continent	Continent and spontaneous micturation	Incontinent
cervical occulta	1	1		
diastematomyely	1		1	
lipo myelomeningocele	9	3	6	
L4-5 occulta	4	1		3
lumbal meningocele	4	1	3	
L4-5 lipomyeloschizis	1	1		
sacral skin covered myelomeningocele	3	3 (2 after sling and augmentation, having renal scars)		
sacral occulta	8	3 (1 after sling and augmentation, having renal scar)	3	2
tethered cord lesion	3	2	1	
caudal regression Th10	1			1

Antimuscarinic medication and catheterization

Antimuscarinic drugs are still used by 94 patients (65,3%) with an equal male to female ratio. Intermittent catheterization eventually could be stopped in 22 patients (15,3%), because of near normal findings with UDS at follow-up. Fourteen of these 22 patients had an occult spina bifida (table 8).

Discussion

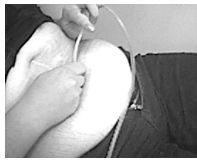
Dyssynergia causes bladder outlet obstruction, which, if left untreated, will in time cause renal damage. The rationale for protection of the upper urinary tract therefore lies in controlling both bladder functions: 1) ensuring safe intra-vesical pressures during urine storage, and 2) establishing adequate emptying of the bladder at low pressures. In order to prevent complications of obstructive uropathy clean continuous intermittent catheterization (CIC) was started, in most cases combined with oxybutynin to prevent high intra-vesical pressures.[17, 18, 19]

Not all patients with a MMC will develop neurogenic lower urinary tract dysfunction, leading to detrusor-sphincter dyssynergia.[9] In a new-born child with MMC, it is not yet possible to predict later pelvic floor behavior. We have chosen to start CIC and antimuscarinic agents as soon as possible and decide later, based on UDS findings, what therapeutical strategy will be the best for each particular patient. Definitive choice of therapy in our series was made after an early UDS in the first 4-6 months after birth. Patients with detrusor overactivity received oxybutynin, if they had combined sphincter overactivity, CIC was continued.

Looking at the calculated creatinin clearance (Ccr) all our patients, even the 6 with renal scarring, still have normal renal function. But the use of the Schwartz formula for Ccr calculations has its restrictions: children with a MMC have less body mass and less muscle mass and they are smaller than normal children. Moreover, serum creatinin will be normal as long as the contralateral kidney function is intact or even is down to 20% function. We doubt whether Ccr gives adequate reflection of kidney function in spina bifida follow-up. However in recent literature even simple serum creatinin is regarded to be a good choice for evaluation of renal function in children with neuropathic bladder.[20]

Three kidneys of a total of 216 evaluable units in the spina bifida aperta group had a scar and partial loss of function, i.e. 1, 4% of all units. However one of these three patients was first treated in another hospital without antimuscarinic medication nor intermittent catheterization while having VUR grade 4-5.

In the group of 35 occult spina bifida patients also 3 renal units showed parenchymal loss. These patients however, all started urologic treatment at later age. In other hospitals their urological complications were not recognized and dealt with and not until referral intermittent

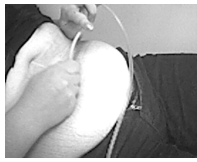


catheterization and antimuscarinic therapy was started. Therefor it is clear that of all 144 patients that started urologic treatment shortly after birth only 2 patients developed renal scars. All other scars proved to be caused by temporary non-compliance of the parents with the CIC program.
Early onset of therapy seems therefore to be useful in order to prevent renal damage.
A low percentage (1, 2%) of "renal function deterioration" was earlier reported in literature by Hopps and Kropp[21] in a retrospective study of 83 evaluable patients of a total of 188: all “high risk” patients (retention and hydronephrosis) were treated with incontinent vesicostomy or CIC. In that study however, by making a vesicostomy, no attempts were made to preserve compliant bladder reservoirs and to achieve continence in contrast to our series. Remarkably also 29 of 65 initially "low risk'' patients later were converted to high risk at a mean age of 3,1 years, and only after an episode of pyelonephritis or other complications proper action was taken. We advocate a more pro-active attitude towards imminating urological problems in children with spinal dysraphism.
Follow-up by means of ultrasound investigations of the kidneys is reliable.[22,23] It seems unnecessary to subject all MMC patients to invasive DMSA scans if serum creatinin and ultrasound investigations are perfectly normal especially in case of low bladder pressures in UDS. Indeed, the chance of renal failure grows with age. In the past cortical damage has been described in 13, 3% of children with MMC under the age of 2, while 27, 3% of MMC patients over 10 years old has renal parenchymal damage.[24] Muller et all reports up to 40% evidence of renal damage in a literature review.[25] In recent literature exact data of progression to ESRD in patients with MMC are not provided, though in a recent study of Lawrenson et al[6] the ratio in patients with a neural tube defect compared to normal patients (age 10-69) for developing renal failure (14/10000) was 6,8-9,0 for males and 9,2-11,5 for females.
Lapides[26] postulated that "maintenance of a good blood supply to the renal pelvis, ureter, bladder and urethra by avoiding high intraluminal pressures and over distension is the key to prevention of urinary tract infection". We owe him much gratitude for his insights.
The importance of continuous follow-up of patients with MMC in a

multi disciplinary team has already been stressed in several studies.[6,27,28,29,30] Patients and parents visit all the specialists in one day. A patient may not need to visit all specialists every time and can even be dismissed for control from specific specialties, but we like to stress once more the importance of urological follow-up even in adult life.

Conclusions

Children born with a MMC, when adequately treated urologically, can probably last a life-time with their own kidneys. To ensure protection of the upper urinary tract, low intra-vesical pressure is necessary. Early start of therapy is essential. Continuation of intermittent catheterization, whether or not combined with anti-muscarinic agents, should be based on repeated urodynamic studies. As deterioration of renal or bladder function still can develop during adolescence, a long-term follow-up is essential. Preservation of renal function and continence are end targets also in high-risk patients. Pro-active treatment of risks for upper tract deterioration results in neglectable loss of renal function, even when early urinary continence is included in the treatment protocol.



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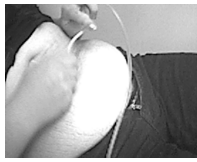

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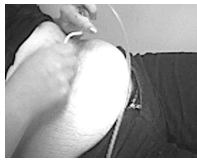

History of the use of catheters in spinal cord lesions.

Pieter Dik, MD, pediatric urologist
Fons Ypma, urologist
Jan D. van Gool, pediatric nephrologist

Historical overview

9

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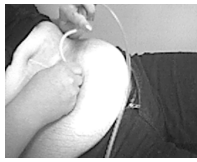
Introduction

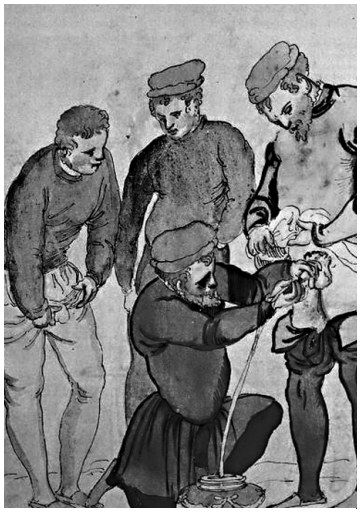


It is interesting to observe how many years it took to understand that intermittent catheterization could be applied as a permanent solution for patients with spinal cord lesions and spina bifida. Not until after the second world war and Korean war spinal cord lesion patients with neuropathic retention bladder were treated on a large scale with intermittent catheterization. It still took many years until Lapides propagated in the 70's to use clean intermittent catheterization in females with recurrent urinary tract infections and later also in paraplegic patients. In the 80's this idea was first applied to spina bifida patients and today it is used on a large scale.

The history of catheterization

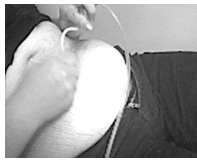
The development of the modern catheter has a history of 5000 years. In ancient times catheterizations of overfilled bladder were reported with curled-up palm leaves and hollow onion leaves. Babylonians[1,2] and Egyptians may have used gold to make catheters. Because it is soft and malleable, gold was ideally suited for the purpose. The Greek Erasistos (310-250 BC) of Kos used an S-shaped catheter. The word catheter is a Greek word, meaning "to lower into": Καθητερ.

Catheter found in Pompei



"Tour de Maitre"

In excavations of Pompeii, Roman metal catheters were discovered. Galen (131-210 AD) also demonstrated an S-shaped metal (lead) catheter.
In mediaeval times (Ambrose Paré, 1564) silver catheters became more popular. At the hospital St. Louis in Paris, the catheter, that was developed by Auguste Nelaton (1807-1873, physician to Napoleon III) and thanks to Goodyear's vulcanisation process of rubber, was used to produce what is still known and used as the Nelaton type of catheter of red rubber, with a solid tip and one eye.
Intermittent catheterization was used as a method to empty the bladder in patients with prostatism. In a rare case it was also used in a patient with neuropathic bladder. Glass catheters, stainless steel, silk-woven and rubber catheters were used. Lubrication was done with sweet oil, saliva, butter or other substances. Catheters were carried around in devices like walking sticks, umbrellas, but also in hats, caps and belts.
Urinary catheters were improved and perfected in the following years by men with great names like Benjamin Franklin (1752) who copied the Van Solingen device.[3] Van Solingen, a 17th century Dutch physician made a catheter from a flat silver wire, wound spirally and covered with waxed threadbound parchment.[4]
Later silver catheters were produced with the natural curve of the prostatic urethra and with larger apertures for better drainage. Mercier (1811-1882) introduced the flexible rubber coudé catheter in 1836 although this catheter was invented by Emile Coudé.[5] Charrière, the Parisian instrument maker (1803-1876) developed a sizing system that became known as the French scale in progressive diameter. Bilroth (1829-1894) the famous German surgeon explained a technique for negotiating urethral stricture "by introducing of elastic sounds (called bougies because they were formerly made of wax) of gradually increasing thickness".[6]
George Tiemann patented a vulcanised curved rubber catheter with a tapering tip in 1881.[7] In 1872, J.J. Wright, a surgeon from Halifax in Yorkshire (England), designed a rubber catheter with flexible shoulders.[8] It was not until 20 years later that De Pezzer[9] gave an account of his mushroom-ended catheter at the Congrès Français de Chirurgie (1890). Two years later, in 1892, Malecot, a senior intern of Felix Guyon described the 'sonde se fixant d'elle-même à demeure dans la vessie', a



wing-tipped catheter known by his name.[10] Numerous other self-retaining catheters were described during the early part of the 20th century.
The balloon catheter has been developed by Zorgniotti. Foley (1891-1966) an American urologist, devised a balloon catheter for hemostasis in prostatic surgery.[11]

The development of clean catheterization.

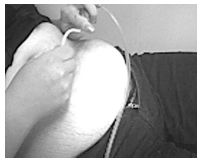
Joseph Lister (1827-1912), professor of surgery in Glasgow, experimented with urine purification and found that it was normally sterile. Meanwhile the Germ Theory was developed and sterile gloves were introduced for use during instrumentation and catheterization although originally the gloves were used to protect the hands of the physician and nurse.[12]
In 1901 Morton suggested that patients with spinal fractures should empty the bladder by catheterization with aseptic instruments. In 1913 Elsberg wrote one of the first textbooks on neurosurgical techniques and recognised the likelihood of bladder dysfunction after laminectomy.[13]
He advocated a program of intermittent catheterization with "most rigid surgical cleanliness… The bladder should never be permitted to become overdistended, but should be emptied every 8 hours or oftener. If cystitis develops, the bladder should be washed out with boric acid solution or 1-10.000 solution of nitrate of silver. The cystitis will sometimes improve rapidly after a permanent catheter has been introduced". This was an unusual point of view since suprapubic catheterization was the preferred way of managing chronic bladder dysfunction at that time and was often applied to spinal cord injured victims of World War I. Also other methods of bladder evacuation were tried in those days. Many physicians feared that intermittent catheterization would introduce infections and other methods were popularised. Straining, suprapubic tapping, Bethanecolchloride and Crede manoeuvre. In 1937 Helmholz reported on sulphonamide for urinary tract infections and 10 years later penicillin became available. Since World War II, the majority of centres in the United States practised bladder training with an indwelling catheter and tidal drainage. Over the years however, most of the centres abandoned tidal drainage in favour of other procedures, such as Bors blocking

procedures, which expedited the return to an upper motor neuron type of bladder. While in the United States bladder training has been performed since 1947, intermittent catheterization with a 'non-touch' technique was being practised at the Stoke Mandeville Spinal Injuries Centre in England by Ludwig Guttmann. The non-touch technique must be performed by a physician who is surgically scrubbed and dressed; intermittent catheterization by that technique is performed every 6 h.

Guttman, one of the first specialists in spinal cord injury realised that an indwelling catheter or a suprapubic cystostomy tube did not prevent urosepsis. He noted that sterile intermittent catheterization was preferable to chronic intubation.[14]

Guttman visited the clinic (An Arbor) where Lapides worked in the late 1960's, Lapides believed that high intraluminal urinary tract pressures and bladder distension were the cause of most urinary tract infections.[15] Lapides applied clean intermittent self-catheterization technique to a 30-year-old woman with diurnal incontinence and urinary tract infections. The catheter was sterilised between applications by benzalkonium chloride soaks for 20 minutes and she was additionally treated with oral propantheline bromide. She became completely continent and without urinary tract infection.[16] The young woman found out that sterility of her catheter was not important at all. It should be performed atraumatic and clean but not aseptic (although we must admit that urinary infections nowadays can occur in patients on "clean"intermittent catheterization protocol). Lapides expanded the clean intermittent catheterization program to other patients with neurogenic bladder dysfunction, including men and children.

This meant an impulse for development of a new concept of single-use catheters. These catheters were made of plastic or PVC and were atraumatic. Later low friction catheters were introduced in 1983. When this type of catheter is immersed in water, the hydrophilic layer attracts a gentle liquid surface that completely covers the catheter. The water reduces the friction between the urethra and the catheter by 90 to 95% in comparison with ordinary catheters with or without gel. This considerably reduces the risk of patient discomfort and minimises the risk of trauma and complications.[17] The hydrophilic surface is made of a polymer - PVP (polyvinyl pyrrolidone), and sodium chloride (salt). The PVP



binds water, while the sodium chloride acts to retain the water layer on the catheter. All materials used are latex-free, non-toxic and non-pyrogenic. The tips and eyes of the catheters are rounded to reduce risk of trauma. The osmolality of the catheter should equalize the osmolality of human urine in order to prevent that catheters dry out during catheterization due to the osmotic gradient.[18,19] This might prevent damage to the urethra. The concept of a high osmolality catheter is called: urotonic surface technology.

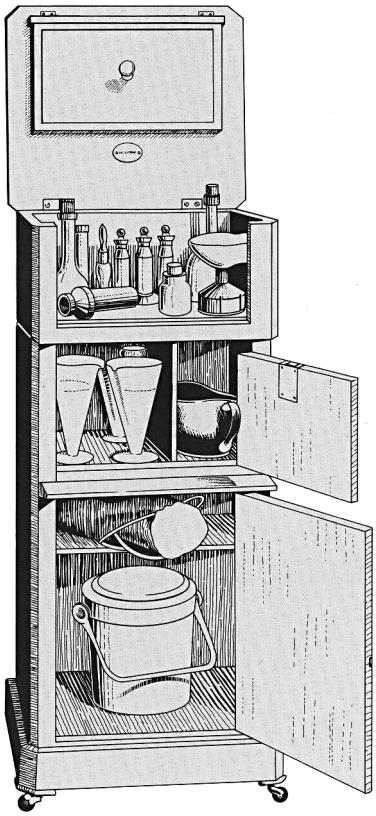
Patients with spina bifida and spinal cord lesions will have to cathetrize for the rest of their lives. A safe catheter is a prerequisite. It has been suggested that repetive injury of the urethra might even enhance cancer of the urethra.[20] Longterm follow-up studies of intermittent catheterization programs are requested.

The hydrophilic-coated PVP catheters are also very suitable to introduce into Mitrofanoff channels. In 1980 Mitrofanoff published his paper about a continent cystostomy in the management of the neurogenic bladder.[21] Since then many physicians have constructed thousands of these catheterizable stomata and meanwhile many modifications have been invented.

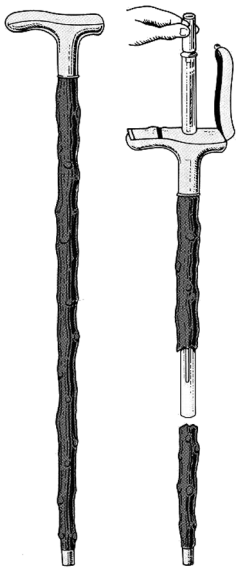
Daily routine of intermittent catheterization

Conclusion

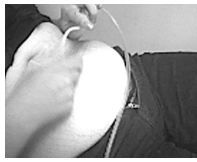
Physicians tend to believe that present day knowledge is the gold standard and that all that was done in the past is inferior to modern techniques. This historical overview[22] proves that this is a wrong concept. Intermittent catheterization has been applied for many centuries for many reasons. However, the indications for the use of clean intermittent catheterization have certainly improved because of new insights that were shown to us by great men[23] in the past.



Cabinet with requisites for self-catherization



Hollow cane, glass-covered, for storage of catheter



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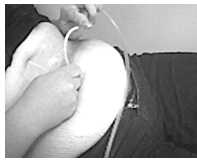
Intermittent catheterization:

what is new?

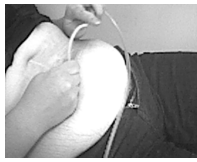
In order to understand present and future developments of urological therapy of patients with neuropathic bladder, one needs to know the history and facts in the past.
The application of intermittent catheterization was used in patients with neuropathic bladder on a large scale since Lapides introduced it in he 70's. Was this a new concept?
My grandfather Gerard Dik, who served as a captain on a cargo ship, broke his lower spine, by falling off a gangway in between his ship and quay. This accident happened in Denmark, near Copenhagen, in 1913. During the rehabilitation process in a local hospital he appeared to have a permanent cauda syndrome and he was unable to void. The Danish doctors taught him to catheterize four times a day and he was taught how to flush his bladder with antibacterial solutions (AgNO3). With this protocol he survived until 1953.
This was a true example of good medical practice "avant la lettre".



Summary, discussion, conclusions and future perspectives.

10

Outline of thesis.



This thesis focuses on the treatment of neuropathic bladder-sphincter dysfunction. Targets of outcome are preservation of bladder- and kidney function and achievement of continence in children with spinal dysraphism.

Approximately 50% of all patients with spinal dysraphism have overactivity of the sphincter complex, which consists of sphincteric and/or pelvic floor muscles.[1,2,3]

Patients with a weak, paretic sphincter complex are continuously incontinent, but have little risk for upper renal tract damage. Even if they have overactivity of the bladder, all urine will be expelled through the incompetent urethra and will not flow back into the kidneys. However, in these patients urinary tract infections still may occur based on incomplete emptying. At school age these patients are offered urinary continence by means of a fascial sling underneath the bladder neck. Sometimes this operation is combined with antireflux surgery, detrusorectomy for eliminating detrusor overactivity and creation of a continent vesicostomy which facilitates intermittent catheterization without the necessity for transfers. A vesicostomy also improves privacy and independence of the patient.

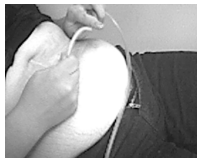
Patients with an overactive sphincter complex are, when untreated, also incontinent based on high detrusor pressures. Besides this, they have a high risk of developing upper renal tract deformities such as vesico-ureteric reflux, renal dilatation and loss of renal function as a result of high pressures and recurrent pyelonephritis. Not the functional infravesical obstruction but the abnormal innervation leads to overactivity and higher bladder pressures. Overactivity of the detrusor needs treatment with antimuscarinic agents such as Oxybutynin and Tolterodine. Also surgical conversion by means of detrusorectomy or augmentation ileocystoplasty may be done if needed. This operation can be combined with an antireflux procedure, sling bladder neck elevation and creation of a continent vesicostomy. Keeping detrusor pressures low during the filling phase is the cornerstone for preservation of kidney function..

Recurrent urinary tract infections need to be treated, especially in case of high bladder pressures in combination with vesico-ureteric reflux or in case of recurrent pyelonephritis.[4,5,6,7]

Shortly after birth reliable urodynamic studies cannot be done, as the spinal cord may be in an instable situation like spinal shock. After 3-4 months a first urodynamic investigation is done. In the meanwhile the patient is on intermittent catheterization in combination with antimuscarinic agents. One cannot distinguish accurately a child with an overactive sphincter complex from a low risk inactive pelvic floor patient at that time just by observing the amounts of residual urine after a wet diaper.
Therefore all patients are being catheterised 4-5 times a day and they all receive antimuscarinic agents and antibiotic chemotherapy starting shortly after birth.

It is remarkable that it took so many years before the concept of intermittent catheterization was adopted in order to preserve bladder- and kidney function. After the Second World War many patients with spinal injuries died of renal failure. After the Korean and Vietnam War victims with spinal cord lesions were treated with clean intermittent catheterization (CIC) because of residual urine and recurrent urinary tract infections.[8] Less urinary infections and pyelonephritis occurred and patients became continent. Kidney failure became a rare complication in these patients. Several years after publication of these results in spinal cord lesion patients, the concept of intermittent catheterization was adopted by spina bifida teams in a few institutions.[9,10,11,12] Nowadays a CIC protocol is being used in many institutions world-wide. In contrast, in literature still recent reports exist on renal function loss and end stage renal disease in the follow-up of patients with spinal dysraphism.

Preservation of kidney function and bladder function are important targets in the treatment of patients with spina bifida. For these patients continence is also an important issue. Quality of life is still insufficient if a patient survives with excellent renal function being incontinent for both urine and faeces.



Fifteen years ago we started colonic wash outs with tap water 3-4 times a week in these patients and we observed complete evacuation of faeces out of the rectum and subsequent faecal continence, without adversary effects or complications in the majority of patients.[13,14]
In some patients supplementary surgical therapy was needed for urinary incontinence. We always try to combine this with other surgical procedures such as treatment of vesico-ureteric reflux, augmentation cystoplasty[15,16,17] or the creation of a continent vesicostomy. We have chosen for fascial sling techniques[20,21,22] instead of, at that time, fashionable artificial sphincter prosthesis.[23,24,25] Important reasons for this choice were the fact that sphincter prostheses cannot be applied to young patients[26] and the fact that the majority of MMC patients still need to be catheterized when they have an AMS sphincter prosthesis. We have excellent results for urinary continence with sling procedures that are relatively simple and cheap.

Summary and discussion

Chapter 2

Pediatric urodynamics taught us that detrusor-sphincter dyssynergia creates a functional bladder outlet obstruction in about 50% of any population of children with myelomeningocele. This functional obstruction causes renal damage[4,27,28,29] because of high intravesical pressures with secondary changes in the upper urinary tract, exactly comparable to upper tract changes in congenital anatomical urethral obstruction. Pediatric urodynamics also taught us that in children with myelomeningocele pelvic floor activity and detrusor activity can be abnormal (hyperactive or inactive) completely independent from each other. These insights have changed the management of myelomeningocele. Children with overactivity of the pelvic floor can be singled out at infant age, and started on clean intermittent catheterization, to prevent obstructive uropathy and preserve renal function. Children with detrusor

overactivity can be singled out too at very early age, and treated with anticholinergics (=antimuscarinic agents), to prevent irreversible structural damage to the detrusor and preserve normal bladder capacity and compliance.[30]

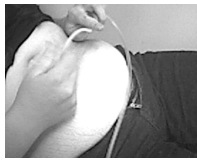
Some years after the publication of Baskin (1990) we now know that not only functional obstruction causes high pressure in a bladder. Also a true disturbance of neuronal innervation leads to neuropathic bladder behaviour as is described in chapter 3. Therefore all patients need not only intermittent catheterization but also antimuscarinic therapy to prevent high bladder pressures and upper tract deterioration.

Chapter 3

Urodynamic studies were done in 15 spina bifida patients before and after stopping antimuscarinic agents. Eleven patients showed almost immediately reappearance of overactive contractions of the detrusor muscle with high bladder pressures. The functional obstruction in these patients had been by-passed chronically by CIC and antimuscarinic agents. This did not reduce detrusor overactivity. Therefore, it was concluded that detrusor overactivity must have a neuropathic origin in these 11 patients. Although this seems a logical conclusion from daily clinical practice, and that this was always assumed in literature[31], it had never been specifically investigated or published before. Furthermore, this study underscores the fact that life-long suppression of detrusor overactivity is needed in all patients with neuropathic bladders and overactivity. This implies the need to search for alternatives to treat detrusor overactivity.

Chapter 4

Detrusorectomy was done in 35 patients, in 19 cases because of poor bladder compliance and in 16 in an attempt to stop the need for antimuscarinic therapy.
The outcome of detrusorectomy in 35 patients with spina bifida who were incontinent due to poor bladder volume or poor compliance was assessed. Of 51 patients requiring bladder augmentation 35 had primarily a



detrusorectomy. In 3 patients ileocystoplasty was done later as a secondary procedure because of failure of the detrusorectomy.
A total of 35 patients (17 males, 18 females) had a detrusorectomy. Mean patient age at operation was 9.9 years (range 0.4 to 17.8). Mean follow-up was 4.9 years (range 1 to 10.5). A continent catheterizable vesicostomy was constructed in 14 patients and ureteral reimplantation was done in 8. Twenty-five patients also had sling and/or Burch cysto-urethropexy during detrusorectomy, of whom 19 are continent and 5 have some leakage between clean intermittent catheterization. In 1 girl the sling procedure was not successful, and she was subsequently treated with bladder neck closure. Bladder compliance after operation was improved in 9 cases and unchanged in 10. Of the 16 patients in whom compliance was already acceptable before the operation and was unchanged after detrusorectomy 7 were able to stop antimuscarinic therapy. Compliance became poor in 4 cases, of which 3 required ileocystoplasty. Bladder volume (as a percentage of normal volume for age) was increased after detrusorectomy in 13 patients, unchanged in 11 and decreased in 11. Complications of detrusorectomy included bladder leakage in 2 cases. One patient needed a laparotomy because of urinary ascites shortly after the operation.
We conclude that detrusorectomy may be combined with other procedures such as ureteral reimplantation, sling plasty and continent vesicostomy. Of 35 treated patients compliance improved in 16 (46%), volume improved in 13 (37%), 3 had no change in parameters, and 3 had a slight decrease in volume and compliance. Four patients had poor results, of whom 3 needed a secondary ileocystoplasty. Therefore, it may be concluded that detrusorectomy is a safe and probably useful procedure for improvement of bladder volume and compliance in patients with neurogenic bladder dysfunction, and may obviate the need for ileocystoplasty in a limited number of patients.

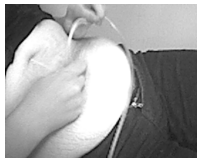
Most reports in literature on detrusorectomy describe disappointing results. In literature[16,32] and in discussions at scientific meetings the subject is still of current interest. Several authors have tried to cover the bladder mucosa with demucolised colon patches.[33,34] Our relatively high success rate is probably due to the meticulous closure of the adventitial

layers of the bladder over the bladder dome combined with immediate cycling of the bladder after the operation (that means: clamping off the catheter every 2 or 3 hours). However in certain cases the operation was not successful for unknown reasons. In the near future bladder augmentation can be done with a tissue engineered bladder template inlay procedure.[35,36]

Which surgical treatment for continence is the best option? In 24 girls and in 14 boys with pelvic floor paralysis a sling procedure was done (Chapter 5 and 6).

Chapter 5

Many surgical options exist to enhance bladder neck closing pressure in women.[37] Most procedures are relatively large with a success rate of between 70% and 90%. Sling procedures with the sling placed between the anterior vaginal wall and bladder neck carry a risk for traumatic lesions of the bladder neck at operation and of postoperative erosion of the sling into the urethra. We evaluated the results of surgical treatment for neurogenic pelvic floor paralysis in girls with spina bifida by transvaginal rectus abdominis sling suspension.
Between 1991 and 2001 we treated 24 girls with a pubovaginal sling placed through the vagina. Patient age at operation was 1 to 17 years (mean 9). After identification of the bladder neck and anterior vaginal wall 2 small holes were made into the vagina left and right of the bladder neck. The sling was taken through these holes and fixed to the contralateral pubic bone. The sling procedure has been combined with ileocystoplasty, auto-augmentation, a continent catheterizable stoma and ureteral reimplantation when needed.
Of the 24 patients 19 were dry after the initial procedure and 3 others became dry after a total of 4 additional injections of a bulking agent into the bladder neck via suprapubic needle introduction under transurethral endoscopic guidance. One patient underwent bladder neck closure after a vesicovaginal fistula developed from the ileal bladder and another primarily elected bladder neck closure for persistent urinary incontinence. No infectious complications occurred that were related to the procedure.



Clean intermittent catheterization was possible in all patients.
Transvaginal sling suspension is safe, relatively easy to perform and cost-effective compared with most alternative procedures. It appears to be as successful as other more complicated procedures to achieve urinary continence in girls with spina bifida.

The 92% continence rate after this procedure is comparable with the best literature reports. This simple and effective procedure is easier to perform then other surgical options.[38,39] Also in adult patients with stress incontinence this operating technique can be used, but patients should always be aware of the chance that intermittent catheterization may need to be continued.

Chapter 6

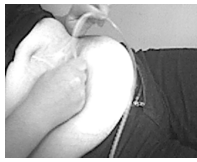
The outcome was studied of using sling suspensions combined with clean intermittent catheterization (CIC) in male patients with spina bifida, of whom a third are incontinent through pelvic floor paralysis.
Between March 1992 and April 1997, 14 male patients (mean age at surgery 11.7 years, range 6.5-15.2) with spina bifida and neurogenic sphincter incontinence underwent a puboprostatic sling suspension as a primary treatment. The procedure, via an abdomino-perineal approach, consists of suspending the bladder neck by placing a simple U-shaped rectus abdominis fascial sling. The perineal approach is used to develop the plane between the rectum and Denonvillier's fascia, and to prepare the passage of the sling alongside the prostate. Together with the sling procedure, eight of the 14 patients had an autoaugmentation of the bladder and two an ileocystoplasty during the same operation. All patients used CIC daily. Erectile function was assessed by reports from the patients and their parents, and continence by report and urodynamic studies.
Of the 14 patients, 13 achieved urinary continence without additional procedures; one required a subsequent submucosal injection at the suspension site with silicone particles in povidone (Macroplastique(R)) to become continent. Two patients reported slight leakage at night. Before surgery, all but one patient reported having spontaneous or mechanically manipulated erections; none had erections on psychological stimulation. After surgery, erectile function was preserved in 13 of the 14 patients; in

one there were problems establishing the right dissection plane between the rectum and prostate, but spontaneous erections returned a year after surgery.
In males, the abdomino-perineal puboprostatic sling suspension using rectus abdominis fascia appears to be a successful treatment for sphincter incontinence in patients with spina bifida, and safely maintains erectile function.

Regarding the plain of dissection during this procedure it is markable that erectile nerve fibres were spared with the male sling operation.[40] Sexuality in spina bifida patients was, when we started these operations not yet regarded as an issue. Since patients survived with reasonable quality of life scores and excellent kidney function, sexuality became an interesting subject to focus on, especially when boys appeared to have normal erections after sling procedures. During the procedure the sling is brought around the bladder neck on a safe distance from the erectile nerve fibres. We know from other observations that remarkably the sling grows as the child grows and that later in adolescence the nerve fibres still were not compromised.
Nowadays, more attention is paid to sexuality as a routine subject in the continuous follow-up in spina bifida patients.[41,42]

Chapter 7

How were the results of the vesicostomies that were created in our institution? In a group of 36 patients the results of vesicostomies were studied.
It appeared that in a high percentage of our patients with a so-called continent vesicostomy problems arose because of stenosis and leakage of the vesicostomy.
In a retrospective study data were collected from the records of 36 patients that underwent a vesicostomy operation. This operation was done in 3 patients with bladder exstrophy, 27 with neurogenic bladder, in 2 encephalopatic patients and in 4 with overextended valve bladders. The vesicostomy has been constructed using the appendix in 18, a patent urachus in 1, an ileal tube (Monti procedure) in 3 and a flipped detrusor



(Boari flap) tube in 11 patients.[18,43,44,45] Three ureters were used as a continent stoma. Mean follow-up was 38,5 months. Twenty-one patients needed secondary operative procedures. Ten incontinent stomas were treated with injection of a bulking agent (Macroplastique®) leading to continence in 5. In one patient the Monti tube stoma was to wide and the tube was tapered with improved result. Of 9 stenoses 8 patients ended up with a patent vesicostomy after a mean of 1,2 secondary procedures.
In 1 patient the stoma was lost due to recurrent stenosis and one patient received a complete new vesicostomy (Monti tube). At the moment of evaluation in 6 patients (16%) still some discomfort exsists because of leakage or stenosis.
Conclusion: In preparing a patient for a continent catheterizable bladder stoma we have to warn for the expected 58% complication rate after surgery. After several interventions a remaining 16% still has problems with leakage or stenosis.

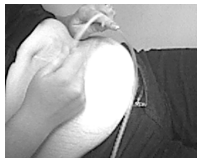
We have reached the conclusion that stomal stenosis can be diminished by leaving the stomal catheter longer in place for at least 3 weeks. In some institutions 6 weeks is advocated. The circular wound has a better opportunity to heal so that stenosis can be avoided.
Meanwhile we have observed that injecting bulky agents (Macroplastique®) in the wall of a leaking stoma is of little use. Apparently the material is pushed away by repeated catheterizations. Leaking stoma's need to be repaired by elongation of submucosal tunnels in the bladder rather than by endoscopic procedures. If, after sometimes a frustrating period of leaking or stenosis has been overcome, patients and parents are very satisfied with the possibility of a "Mitrofanoff".[46]

Chapter 8

Is kidney function adequately preserved by lowering bladder pressures? Renal scarring and renal failure remain a major problem in spina bifida children[47], even with reported death in the first year of life of more then 20% of cases. Data are presented to show that optimal treatment of the neurogenic bladder from birth on can preserve kidney function in most spina bifida patients.

Data of all newborns with spinal dysraphism admitted at the Wilhelmina Pediatric Hospital from January 1988 till June 2001 were reviewed. From admission and during follow up, start and type of treatment (anti muscarinergic agents, continuous intermittent catheterization, antibiotic prophylaxis) as well as renal ultrasound[48,49], DMSA scan[50], serum creatinin[51], creatinin clearance: Schwartz formula) and bladder function (urodynamic studies) was monitored.
Data of 144 children out of 176 could be evaluated by the end of the study: 109 patients with spina bifida aperta and 35 with occult spinal dysraphism. Of the remaining 32 patients 25 died shortly after birth. Three had renal abnormalities: 1 dilated kidney and 2 patients with absent left kidney. Seven patients were lost to follow-up because of moving to another city or hospital.
Of 109 aperta patients 60 patients had an overactive sphincter. Twelve of them had reflux and three of them renal scars. Of 35 patients with occult spina bifida only 2 had overactive sphincter. Of 26 patients with inactive sphincter 7 had vesico-ureteral reflux and 3 of them had renal scars. None of all patients currently is developing end stage renal disease. All 3 patients with renal scars in the occulta group started therapy with intermittent catheterization and antimuscarinic drugs after one year of age. In the aperta group only one of three renal scar patients followed a late onset therapy.
Compared to literature children born with a MMC, if adequately treated urologically, can probably last a lifetime with their own kidneys. To ensure protection of the upper urinary tract, low intra-vesical pressure is necessary. Early start of clean continuous intermittent catheterization is the treatment of choice and administration of antimuscarinic agents to counteract detrusor instability is indispensable in most cases.

Additional remarks
Recently a new evaluation of spina bifida patients was done concerning renal outcome. DMSA scan was done in 38 patients because of suspected renal deterioration or positional or torsion anomalies of the kidneys with unreliable ultrasound results. In 10 patients renal scars were found. In three patients pre-existing deformities were confirmed. One girl with a left small refluxing kidney with 7% function, also has a pre-existing



dysplasia of the right kidney.
The longer this difficult group of patients is being followed, more possible problems can be found. Next follow-up message is up in 10 years.

In a study of 132 spina bifida patients from 1974-1986 in our hospital was shown that with urodynamic investigation the distribution of risk factors was as follows:

Table 1 Distribution of activity and inactivity of detrusor and sphincter in 132 patients with spina bifida aperta in 1974 to 1986.

132 patients spina bifida aperta 1974-1986

		DETRUSOR	
		Not overactive	Overactive
SPHINCTER	Not overactive	**35** (26%)	**42** (32%)
	Overactive	**13** (10%)	**42** (32%)

In this present study of 144 spina bifida patients from 1988-2001 the distribution of risk factors is summarised in Table 2 and 3:

Table 2 Distribution of activity and inactivity of detrusor and sphincter in 109 patients with spina bifida aperta in 1988 to 2001.

109 patients spina bifida aperta 1988-2001

		DETRUSOR	
		Not overactive	Overactive
SPHINCTER	Not overactive	**33** (30%)	**16** (15%)
	Overactive	**22** (20%)	**38** (35%)

Table 3 Distribution of activity and inactivity of detrusor and sphincter in 132 patients with spina bifida occulta in 1988 to 2001.

35 patients spina bifida occulta 1988-2001

		DETRUSOR	
		Not overactive	Overactive
SPHINCTER	Not overactive	**21** (60%)	**5** (15%)
	Overactive	**7** (20%)	**2** (5%)

Compared to earlier data from the series of 1974-1986 the sphincter behaviour of the aperta group has not improved. In the occulta group totally different percentages are observed, like in other studies.[52,53,54,55,56] Of 35 occulta patients 24 are continent and 20 have a normal or inactive pelvic floor. Which is a remarkable finding. Posture and detrusoractivity probably play a more important role in continential in these patients.

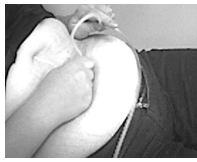
Chapter 9

History of intermittent catheterization.

In order to understand present developments and future adjustments of urological therapy of patients with a neuropathic bladder, one needs to understand the history and the course of events before we are able to arrive to where we are at the moment.

Not until after the second world war and Korean war spinal cord lesion patients with neuropathic retention bladder were treated on a large scale with intermittent catheterization.[57] It still took many years until Lapides propagated in the 70's to use clean intermittent catheterization in females with recurrent urinary tract infections and later also in paraplegic patients.[8] In the 80's this idea was first applied to spina bifida patients in a few institutions and today it is used on a large scale.

Conclusions



Spina Bifida is one of the most common and most invalidating congenital defects. Patients now can survive after initial closure of the spine and creating low intracranial pressures if needed by placing ventricular peritoneal drains. Scoliose operations and tendon reallocation operations may follow in order to keep the patient in an upright position, or if possible, to enable the patient to stand or to walk. Urological operations may follow in order to preserve kidney function and to enhance continence. Even after several operations many problems remain to be solved in most cases. Quality of life becomes now more and more an issue.

The concept of early onset intermittent catheterization in combination with antimuscarinic agents and antibacterial chemotherapy yields a tremendous improvement of kidney function preservation compared to other concepts. A vesicostomy is a useful option in a selected group of patients.

The concept of fascial sling bladder neck suspension appears to be very effective to enhance continence in children with neuropathic bladder. Major advantage of this procedure over sphincter prostheses is the fact that the procedure can be done at any body size and remain functioning with growing body length. It is cheaper then most comparable procedures. Moreover in boys this procedure does not compromise the function of erectile nerves that run close to the bladder neck.

The procedure that is used for bladder augmentation plasty by removal of a large part of detrusor muscle, appears to be effective in 50% of the cases. In case of failure a standard bowel patch cystoplasty still can be performed. However, the presence of bowel tissue in the bladder may produce complications like mucous retention, stone formation, recurrent infections, electrolyte and pH disturbances and possible malignant degeneration in later life. Therefore it seems justified to try another option like detrusorectomy first. Patients need careful urodynamic follow-up for assessment of bladder pressures and bladder compliance after detrusorectomy.

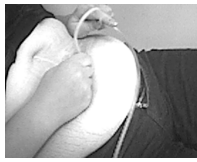
All these operations can be done combined in one session.

Future perspectives

1. Alternatives need to be found for antimuscarinic agents because these drugs can cause many side effects. Dryness of the mouth provokes caries. Dryness of the skin enhances overheating of the patient in hot environments. Many patients have psychological side effects like concentration weakness.
   Less side effects are reported if the antimuscarinic agents are flushed directly into the bladder.[58,59,60] Also other substances can be applied intravesically such as Capsaceine.
   Promising results of local injections in detrusor muscle of Botox (Botuline toxine) is reported.[61,62,63,64] We also treated a limited number of spina bifida patients with Botox with excellent results that seem to last for more than 9 months.
   One future possibility for definitive denervation of detrusormuscle would be a ventral root rhisotomy of S2-3 during primary closure of the spina bifida. This would eliminate the need for antimuscarinic agents or other substances, because the bladder pressure will always be low.[65,66]

2. Detrusorectomy and ileocysto-augmentation plasty will soon, within 10-15 years, probably be obsolete procedures. Bladder mucosa will be cultured on biomatrix (bladder tissue engineering) and will be used as an augmentation plasty in neuropathic bladders.[67,68] This will put an end to all discussions about whatever form of augmentation cystoplasty will be the best.

3. Infections are a continuous threat for spina bifida patients with compromised bladder and kidney function, especially in patients with vesico ureteral reflux.[4,5] However, since bladder and kidney function has improved so much over the last 15 years, our attitude concerning antibacterial chemoprofylaxis perhaps needs adjustment. We need to discriminate risk factors, such as AB0-secretor status and immuno-globuline assessment. Other therapies like Cranberries or intravesical therapy need further attention.[69,70,71] Even simple close surveillance with test strips for leukocytes and nitrite and intermittent antibacterial therapy if needed, may appear to be more effective than continuous antibacterial chemoprofylaxis. At this moment a protocol for this important issue is considered.



4. Although fascial sling graft appeared to be a very effective choice for treatment of bladder neck insufficiency in these patients, we also have to consider other possibilities like the pacemaker operated gracilis muscle graft around the bladder neck. This solution proved to be effective in guinea pigs.[72]

5. As was mentioned the fascial sling procedure did not compromise erectile function in male patients. However, sensitivity of the glans penis is in almost all patients absent. In male patients with a spinal cord lesion under L1, sensitivity of the groin is still present because of the lumbar L1 level of the ileo-inguinal nerve. In a recent pilot study in 3 patients in our institution, an anastomosis of the ileo-inguinal nerve and the dorsal penile nerve was made in order to restore sensitivity of the glans. This operation was successful in all cases.[73]
   This leads us to the final question: how about sex? We simply do not know at this moment. After all these years of focussing on kidney and bladder function, all these urological, neurological and orthopedic operations with still improving results, we know little about sexuality in this group of adolescents with spina bifida. If reinnervation operations will become a standard option, adolescents with spina bifida probably perhaps will be more and more interested in the subject of sexuality.[41]

Much work needs to be done in future years, and this will be possible only if the value of multidisciplinary and holistic approach and treatment is recognised in Paediatric Institutions...

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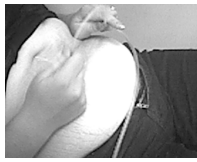

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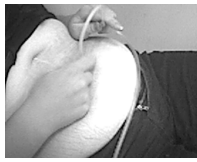

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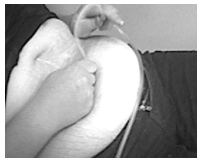

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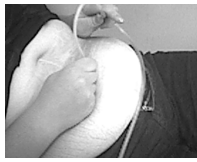
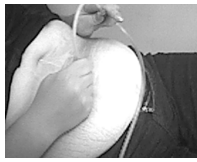


Samenvatting, discussie, conclusies en toekomst-perspectieven

(vertaling in het Nederlands)

II

Samenvatting



Dit proefschrift richt zich op de behandeling van blaassfincter disfunctie. Getracht wordt de blaas- en nierfunctie te behouden en continentie voor urine te bereiken bij kinderen met spina bifida.

Ongeveer 50% van alle patiënten met spina bifida heeft een overactiviteit van het sfinctercomplex, dat bestaat uit blaashals en/of bekkenbodemspier.

Patiënten met een zwak of inactief sfinctercomplex zijn voortdurend incontinent maar lopen een gering risico op beschadiging van de hogere urinewegen. Zelfs bij een overactieve blaas lekt bij hen alle urine weg door de insufficiente sfincter en stroomt het in principe niet terug naar de nieren. Toch kunnen nog wel urineweginfecties voorkomen als gevolg van incomplete blaasontlediging. Op lagereschool leeftijd wordt deze patiënten aangeboden continent te worden door middel van een blaashals-suspensie waarbij een fascie sling onder het blaashals gebied wordt aangebracht. Soms wordt deze ingreep gecombineerd met antireflux chirurgie, detrusorectomie om de detrusor overactitiveit op te heffen en het aanleggen van een continent vesicostoma waardoor intermitterende catheterisatie mogelijk wordt zonder dat een transfer noodzakelijk is. Een vesicostoma verbetert ook de privacy en de onafhankelijkheid van de patiënt, want de onderbroek hoeft niet meer uit voor een catheterisatie.

Patiënten met een overactief sfinctercomplex zijn, indien onbehandeld, eveneens incontinent als gevolg van hoge detrusor drukken. Zij lopen tevens een groter risico op hogere urineweg misvormingen/afwijkingen zoals vesico-ureterale reflux, nierdilatatie en nierfunctieverlies als gevolg van hoge drukken en recidiverende pyelonefritis. Niet alleen infravesicale obstructie leidt tot verdere overactiviteit en hogere blaasdrukken: ook een primair neuropathische oorsprong leidt tot instabiliteit van de blaasspier, de musculus detrusor.
Overactiviteit van de detrusor dient behandeld te worden met anticholinergica zoals Oxybutynin en Tolteridine. Ook chirurgische interventie door middel van detrusorectomie of augmentatie- ileocystoplastiek kan worden uitgevoerd. Deze ingreep kan worden gecombineerd met een antirefuxprocedure, ‘sling’ blaashals elevatie en het aanleggen van een

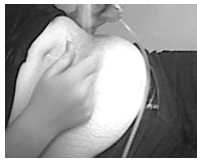
continent vesicostoma. Door de blaasdruk tijdens de vulfase laag te houden, kan de nierfunctie worden behouden. De blaasontlediging vindt meerdere malen per dag door intermitterende catheterisatie plaats.

Recidiverende urineweginfecties dienen behandeld te worden in geval van hoge blaasdruk in combinatie met vesico-ureterale reflux of bij recidiverende pyelonephritis.

Kort na de geboorte kan geen betrouwbaar urodynamisch onderzoek worden uitgevoerd, aangezien het ruggenmerg in een instabiele situatie kan verkeren, zoals 'spinal shock'. Drie à vier maanden na de geboorte wordt een eerste urodynamisch onderzoek uitgevoerd. In de tussentijd wordt de patiënt al intermitterend gecatheteriseerd in combinatie met anticholinergica.
Het onderscheid tussen een kind dat gevaar loopt met een overactief sfinctercomplex en een kind met een inactieve bekkenbodem is op dat moment nog niet genoeg te maken door slechts het beoordelen van residu na een natte luier. Het kind kan immers misschien de blaas met zeer hoge drukken leeggeperst hebben. Daarom worden alle patiënten 4-5 maal per dag gecatheteriseerd en krijgen alle patiënten anticholinergica en antibiotische chemotherapie vanaf de geboorte.

Het is opmerkelijk dat het zoveel jaren heeft geduurd voordat het concept van intermitterend catheteriseren werd aanvaard om de blaas- en nierfunctie te behouden. Na de Tweede Wereldoorlog overleden veel patiënten met ruggenmergletsel nog aan nierfunctiestoornissen. Pas na oorlogen in Korea en Vietnam werden ruggenmergletsel-patiënten behandeld met intermitterende catheterisatie vanwege urineresidu en recidiverende urineweginfecties. Er bleken minder urineweginfecties voor te komen en de patiënten werden continent. Nierfunctiestoornissen werden nog maar zelden gezien als complicatie bij deze patiënten.

Enkele jaren na publicatie van deze gegevens over de resultaten bij patiënten met ruggenmergletsel werd intermitterend catheteriseren ingesteld door een aantal spina bifida-teams. Tegenwoordig wordt het protocol in vele instellingen over de gehele wereld gebruikt.



In de literatuur wordt echter nu nog steeds gepubliceerd over nierfunctieverlies en terminale nierziekten in de follow-up van patiënten met spinale dysraphie.

Behoud van nier- en blaasfunctie zijn belangrijke doelen bij de behandeling van patiënten met spina bifida. Toch is voor de spina bifida patiënten ook de continentie erg belangrijk. De kwaliteit van leven is immers nog steeds niet erg hoog als een patiënt overleeft met uitstekende nierfuncties, maar incontinent is voor urine en feces.

Tien jaar geleden werd begonnen met colonspoelingen met kraanwater bij deze patiënten. Met behulp van echografisch onderzoek werd vastgesteld dat het rectum geheel vrij was van feces en dat vervolgens gedurende 2 dagen continentie voor feces optrad, zonder bijwerkingen of complicaties.

Bij sommige patiënten was aanvullende chirurgie nodig in verband met urine-incontinentie. Hierbij werd steeds getracht de chirurgische ingrepen te combineren, zoals ureterreïmplantatie, blaasaugmentatie of het aanleggen van een continent vesicostoma.
Wij hebben de 'fasciale sling' techiek gekozen in plaats van de destijds populaire kunstmatige sfincter prothese. Belangrijke redenen voor deze keus waren het feit dat de sfincterprothesen niet toegepast kunnen worden op jonge patiënten[2] en het feit dat het merendeel van de spina bifida patiënten ook nog gecatheteriseerd moeten worden na het aanleggen van een AMS (American Medical Systems) sfincter-prothese. Wij blijken uitstekende resultaten te boeken met de 'sling'procedure, die simpel en goedkoop is.

Hoofdstuk 2

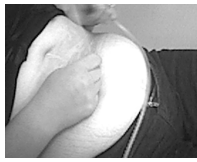
We leerden van de kinderurodynamica dat detrusor-sfincter dissynergie bij 50% van de kinderen met myelomeningocèle functionele blaashals-obstructie veroorzaakt. Deze functionele obstructie brengt nierschade teweeg door hoge intravesicale drukken met secundaire veranderingen in de hogere urinewegen, vergelijkbaar met de veranderingen van de hogere

urinewegen bij congenitale anatomische urethraobstructie.
Ook leerden we van de kinderurodynamica dat bij kinderen met meningomyelocèle de bekkenbodemactiviteit en de detrusoractiveit volledig onafhankelijk van elkaar afwijkend kunnen zijn (hyperactief of inactief). Deze inzichten hebben de behandeling van meningomyelocele veranderd. Kinderen met overactiviteit van de bekkenbodem kunnen op zuigelingenleeftijd worden opgespoord en op 'clean' intermitterende catheterisatie (CIC) gezet worden, om obstructieve uropathie te voorkomen en de nierfunctie te behouden.
Kinderen met detrusor- overactiviteit kunnen eveneens op zeer jonge leeftijd opgespoord en behandeld worden met anticholinergica (=antimuscarine agentia) om onherstelbare schade aan de detrusor te voorkomen en de normale blaascapaciteit en compliance te behouden.

Nu, enige jaren later, weten we dat niet alleen de functionele obstructie hoge blaasdruk veroorzaakt: ook een verstoring van de neuronale innervatie leidt tot neuropathisch blaasgedrag. Dit wordt beschreven in hoofdstuk 3.
Derhalve hebben bijna alle patiënten met instabiele detrusorcontracties behalve intermitterende catheterisatie ook blijvend anticholinergica nodig om hoge blaasdruk en schade aan de nieren te voorkomen.

Hoofdstuk 3

Urodynamische studies zijn uitgevoerd bij 15 spina bifida patiënten vóór en na staken van anticholinergica. De functionele obstructie werd bij deze patiënten langdurig omzeild door de intermitterende catheterisatie en anticholinergica. Na het staken van de anticholinergische medicatie vertoonden 11 patiënten vrijwel onmiddellijk hyperactiviteit van de detrusor en hoog oplopende blaasdruk. Zij kregen nog steeds intermitterende catheterisatie, zodat de hyperactiviteit niet het gevolg kon zijn van obstructie.
Geconcludeerd werd dat detrusor- hyperactiviteit een neuropathische oorzaak moet hebben bij deze 11 patiënten.
Ondanks dat dit een logische conclusie lijkt, werd het in de literatuur altijd aangenomen, maar nooit eerder gepubliceerd. Daarbij wordt in



deze studie waarschijnlijk nog onderschat dat levenslange onderdrukking van de detrusoractiviteit nodig is bij alle patiënten met neuropathische blaas en overactiviteit. Er moeten dus alternatieven gezocht worden voor de behandeling van detrusoroveractiviteit, zeker gezien de de nog vaak ernstige bijwerkingen van de huidige anticholinergische medicatie.

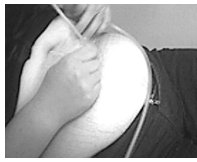
Hoofdstuk 4

Detrusorectomie werd uitgevoerd bij 35 patiënten met spina bifida.
Zij waren incontinent als gevolg van een gering blaasvolume of geringe uitrekbaarheid (compliance) van de blaas, al dan niet in combinatie met een zwakke sfincter en/of bekkenbodem. Bij 19 patiënten werd de operatie uitgevoerd vanwege slechte compliance van de blaas en bij 16 patiënten in een poging antimuscarine te staken.
Van de 51 spina bifida patiënten die blaasaugmentatie nodig hadden, kregen 35 (17 jongens, 18 meisjes) primair een detrusorectomie. Bij 3 patiënten werd later nog een ileocystoplastiek als secundaire procedure uitgevoerd vanwege falen van de detrusorectomie.
Gemiddelde leeftijd van de patiënt bij operatie was 9,9 jaar (range 0,4–17,8), gemiddelde follow-up was 4,9 jaar (1-10,5). Bij 14 patiënten werd een continent catheteriseerbare vesicostomie aangelegd en 8 kregen ureter re-implantatie. 25 patiënten kregen tevens een sling en/of Burch cystoúrethropexie tijdens de detrusorectomie, daarvan zijn er 19 continent en 5 hebben enige lekkage tussen de intermitterende catheterisaties.
Bij 1 meisje was de slingprocedure niet succesvol, zij kreeg vervolgens een blaashalssluiting.
De blaascompliance verbeterde na operatie in 9 gevallen en bleef ongewijzigd in 10 gevallen. Van de 16 patiënten die reeds voor de operatie een acceptabele compliance hadden die niet veranderd was na detrusorectomie konden er 7 stoppen met antimuscarine. Compliance werd slechter in 4 gevallen, 3 daarvan moesten een ileocystoplastiek krijgen.
Het blaasvolume (als percentage van leeftijdsnormaal volume) was na detrusorectomie verhoogd bij 13 patiënten onveranderd bij 11 en verlaagd bij 11. Onder de complicaties werd bij 2 gevallen blaaslekkage gerekend. Bij 1 patiënt moest laparotomie worden uitgevoerd voor urineascites kort na de operatie.

Van de 35 behandelde patiënten verbeterde de compliance bij 16 (46 %), het volume verbeterde bij 13, bij 3 vonden geen veranderingen plaats en 3 hadden een geringe vermindering van volume en compliance. Bij 4 patiënten waren de resultaten slecht. 3 daarvan moesten een secundaire ileocystoplastiek ondergaan. Voorts bleek dat detrusorectomie kon worden gecombineerd met andere procedures zoals ureter re-implantatie, slingplastiek en het aanleggen van een continent vesicostoma. Geconcludeerd kan worden, dat detrusorectomie een veilige en waarschijnlijk zinvolle procedure is om het blaasvolume en de compliance te verbeteren bij patiënten met neurogene blaasdysfunctie en dat de noodzaak voor ileocystoplastiek bij een beperkt aantal patiënten voorkomen kan worden.

In de literatuur worden teleurstellende resultaten van detrusorectomie beschreven. Tijdens wetenschappelijke vergaderingen en ook in de recente literatuur staat het onderwerp nog immer in de belangstelling. Diverse auteurs hebben de blootliggende blaasmucosa getracht te bedekken met van mucosa ontdane gevasculariseerde colonlapjes. Ons relatief hoge slagingspercentage van de detrusorectomie is waarschijnlijk het gevolg van nauwgezet sluiten van de adventitialagen van de blaas over de blaaskoepel in combinatie met onmiddellijk vullen en ontledigen van de blaas na de operatie.
Om onbekende redenen was de operatie in een aantal gevallen niet succesvol. De vraag welke methode van blaasaugmentatie nu het beste is wordt over niet al te lange tijd achterhaald: blaasaugmentatie zal dan waarschijnlijk door middel van het inhechten van een op een matrix gekweekte blaaswand kunnen worden uitgevoerd.

In hoofdstuk 5 en 6 wordt beschreven of bij kinderen met spina bifida het suspenderen van de blaashals door een fasciesling operatie een zinvolle chirurgische procedure zou kunnen zijn. Bij 24 meisjes en 14 jongens met slap verlamde bekkenbodem werd de ‘sling’procedure uitgevoerd.



Hoofdstuk 5

Er bestaan vele chirurgische mogelijkheden om de blaashals sluitingsdruk te verhogen bij vrouwen. De meeste zijn vrij grote ingrepen met een succespercentage tussen 70 en 90.
De slingprocedure, met de sling tussen de anterieure vaginawand en blaashals, houdt een risico in op traumatische laesies van de blaashals (perforatie) en op postoperatieve erosie van de sling in de urethra.
We hebben de resultaten geëvalueerd van de operatieve behandeling van meisjes met spina bifida en slap verlamde bekkenbodem, door de fasciesling suspensie transvaginaal aan te brengen.
Tussen 1991 en 2001 zijn 24 meisjes behandeld met een pubovaginale sling door de vagina. De leeftijd bij operatie was 1 tot 17 jaar (gemiddeld 9 jr). Na identificatie van de blaashals en vaginavoorwand, werden 2 kleine openingen gemaakt in de vagina, links en rechts van de blaashals. De sling werd door deze openingen gebracht en gefixeerd aan het contralaterale os pubis. De sling procedure werd zonodig gecombineerd met ileocystoplastiek, auto-augmentatie, continent catheteriseerbaar stoma en ureterreïmplantatie. 19 van de 24 patiënten waren na de initiële ingreep droog en 3 anderen werden droog na in totaal 4 additionele injecties met een volume-innemende substantie die in de blaashals via een suprapubische naald onder geleide van transurethrale endoscopie werd aangebracht.
Twee patiënten ondergingen een blaashalssluiting: één na ontwikkeling van een vesicovaginale fistel vanuit haar ileumblaas en één andere patiënt koos primair voor blaashalssluiting wegens persisterende incontinentie na de slingprocedure. Er vonden geen infectieuze complicaties plaats in verband met de procedure. Intermitterende catheterisatie was bij alle patiënten mogelijk.
Transvaginale slingsuspensie is veilig, relatief gemakkelijk uit te voeren en kosteneffectief vergeleken met de meeste andere procedures. Het blijkt even succesvol als meer ingewikkelde procedures om urinecontinentie te bereiken bij meisjes met spina bifida.
De in 92% van de patienten behaalde continentie die met deze ingreep kon worden bereikt, is vergelijkbaar met de beste resultaten uit de literatuur. Deze simpele en effectieve procedure is gemakkelijker uit te

voeren dan andere chirurgische mogelijkheden.
Ook bij volwassen patiënten met stress-incontinentie kan deze operatietechniek worden gebruikt, maar de patiënten moeten zich ervan bewust zijn dat er een kans bestaat dat intermitterende catheterisatie moet worden voortgezet.

Hoofdstuk 6

In dit hoofdstuk worden de resultaten geëvalueerd van slingprocedures in combinatie met intermitterende catheterisatie bij patiënten met spina bifida, waarvan eenderde incontinent is als gevolg van bekkenbodemparalyse.
Tussen maart 1992 en april 1997 ondergingen 14 mannelijke patiënten (gemiddelde leeftijd 11,7 jaar, spreiding 6,5-15,2) met spina bifida en neurogene sfincter-incontinentie, een puboprostatische sling suspensie als primaire behandeling.
De ingreep, via een abdominoperineale benadering, bestaat uit suspensie van de blaashals door een eenvoudige, U-vormige rectus abdominus fascial sling.
De perineale benadering wordt toegepast om het vlak tussen het rectum en de fascia van Denonvillier te ontwikkelen en de doorgang te maken voor de sling langs de prostaat.
Tegelijk met de slingprocedure kregen 8 van de 14 patiënten een auto-augmentatie van de blaas en twee een ileocystoplastiek. Alle patiënten gebruikten dagelijks CIC. De erectiele functie werd geëvalueerd middels verslag van de patiënten en hun ouders. De continentie werd middels verslag en urodynamische studies geëvalueerd.
Van de 14 patiënten bereikten er 13 continentie zonder aanvullende procedures. In één geval was nog submucosale injectie met siliconen-partikels in povidone jodium (Macroplastique®) ter hoogte van de suspensie noodzakelijk om continent te worden. Twee patiënten rapporteerden lichte lekkage 's nachts.
Voor de operatie, rapporteerden op één na alle patiënten spontane of mechanisch veroorzaakte erecties, geen enkele patiënt had erectie door psychologische stimulatie. Na operatie was de erectiele functie behouden bij 13 van de 14 patiënten. In één geval was er een probleem bij het vaststellen van het juiste dissectievlak tussen rectum en prostaat, maar

spontane erectie kwam een jaar na operatie weer terug.
Bij mannen blijkt de abdominoperineale puboprostatische sling suspensie dmv rectus abdominus fascie een succesvolle behandeling te zijn bij sfincter incontinentie van patiënten met spina bifida met behoud van de erectiele functie.
Met het oog op het dissectievlak bij deze ingreep, is het opmerkelijk dat de erectiele zenuwen gespaard bleven bij de slingoperatie bij mannen.
In de urologie bij volwassenen is dit precies het gebied bij radicale prostatectomie operaties waarbij zo dicht mogelijk bij de prostaat geprepareerd wordt om de zenuwen te sparen die noodzakelijk zijn voor behoud van erectiele functie.
Sexualiteit bij patiënten met spina bifida was, toen we met deze ingreep begonnen, nog niet eerder aan de orde geweest. Sinds patiënten langer leven, met een redelijke quality of life en uitstekende nierfuncties, werd sexualiteit een interessant gegeven, te meer toen bleek dat jongens normale erecties hebben na de slingprocedure. Bij de procedure wordt de sling onderlangs de blaashals gelegd op een veilige afstand van de erectiele zenuwvezels. We weten van andere observaties dat wonderbaarlijk genoeg, de sling meegroeit als het kind groter wordt en dat later, in de adolescentie, de zenuwen niet bekneld raken. Tegenwoordig wordt meer aandacht besteed aan sexualiteit als routine bij de continue follow-up van spina bifida patiënten.

Hoofdstuk 7

Welke resultaten werden geboekt met de vesicostomieën? Een retrospectieve studie werd uitgevoerd bij 36 patiënten, bij wie een catheteriseerbaar vesicostoma werd aangelegd. Deze ingreep werd uitgevoerd bij 3 patiënten met blaasexstrofie, 27 met neurogene blaas, 2 patiënten met encephalopathie en 4 met overrekte blaas als gevolg van urethrakleppen.
Het bleek dat een hoog percentage van onze patiënten met zogenaamde continente vesicostomie problemen hadden met stenose en lekkage van de vesicostomie.
De vesicostomie werd bij 18 patiënten geconstrueerd uit appendix (Mitrofanoff procedure), urachus bij 1, een buis uit een ileumlapje (Monti procedure) bij 3, een blaaswand buis (Boari flap) bij 11 patiënten.

Drie ureters werden als continent stoma gebruikt. Gemiddelde follow-up was 38,5 maand. Van de 36 patiënten moesten 21 een secundaire ingreep ondergaan. 10 incontinente stoma's werden behandeld met submuceuze injectie van Macroplastique®, wat bij 5 van hen leidde tot continentie. Bij één patiënt was de Monti tube stoma te wijd. De buis werd vernauwd om het resultaat te verbeteren. 9 stenoses resulteerden bij 8 patiënten in een doorgankelijk vesicostomie na gemiddeld 1,2 secundaire ingrepen. Bij één patiënt ging het stoma verloren aan recidiverende stenose en een andere patiënt kreeg een volledig nieuwe vesicostomie (Monti-tube). Tijdens de evaluatie hebben 6 patiënten (16%) nog last van enige lekkage of stenose.
Bij de voorbereiding op een continent catheteriseerbaar blaasstoma moeten we de patiënt waarschuwen voor de 58% kans op complicaties na de ingreep. Na diverse interventies heeft 16 % nog steeds last van lekkage of stenose.
We concluderen ook dat stomastenose verminderd kan worden door de stomacatheter langer in situ te laten: minstens 3 weken. In sommige instellingen wordt 6 weken bepleit. De circulaire wand heeft een betere kans op genezing, zodat stenose kan worden voorkomen.
Ondertussen hebben we bemerkt dat de injectie van Macroplastique® in de wand van een lekkend stoma, niet veel blijvend resultaat levert. Kennelijk wordt het materiaal weggeduwd door de herhaaldelijke catheterisaties. Lekkende stoma's kunnen beter hersteld worden door verlenging van de submucosale tunnels in de blaas, dan door een endoscopische procedure. Na een soms frustrerende periode van lekkage of stenose, zijn patiënten en ouders uiteindelijk zeer tevreden met de mogelijkheid van een catheteriseerbaar vesicostoma.

Hoofdstuk 8

Verbetert de nierfunctie bij verlaging van de blaasdruk? Nierverlittekening en nierfalen blijven in veel centra een groot probleem bij kinderen met spina bifida, zonder inclusie van overlijden gedurende het eerste jaar in meer dan 20% van de gevallen.
Onze gegevens tonen aan dat met optimale behandeling van de neurogene blaas vanaf de geboorte bij de meeste spina bifida patiënten de

nierfunctie kan worden behouden.
Tussen januari 1988 en juni 2001 werd een groep van 146 spina bifida-patiënten vanaf kort na de geboorte behandeld met blaasdrukverlaging door anticholinergica en reguliere blaaslediging doormiddel van intermitterende catheterisatie. Beloop/ontwikkeling van de nierfunctie werd onderzocht: echografie van de nieren, DMSA scan en serum kreatinine en kreatinineklaring (Schwartz formule). De blaasfunctie werd onderzocht met behulp van urodynamische studies. Ook werd geinventariseerd welke chirurgische behandelingen werden toegepast. Gegevens over 144 van 176 kinderen konden worden geëvalueerd aan het eind van de studie; 109 patiënten met spina bifida aperta en 35 met occulte spinale dysraphie. Van de overige 32 patiënten overleden 25 kort na de geboorte. 3 hadden nierafwijkingen: 1 had nierdilatatie en bij 2 patiënten ontbrak de linkernier. 7 patiënten vielen uit deze studie als gevolg van verhuizing naar een andere plaats of ziekenhuis.
Van de 109 patiënten met aperta, hadden er 60 een overactieve sfincter. Twaalf daarvan hadden reflux en 3 hadden nierlittekens. Van de 35 patiënten met spina bifida occulta hadden slechts 2 een overactieve blaas. Van 26 patiënten met inactieve sfincter hadden 7 vesico-ureterale reflux en 3 nierlittekens. Geen van de patiënten ontwikkelt momenteel een eindstadium nierlijden. Alle 3 de patiënten met nierlittekens in de occulta-groep begonnen met intermitterende catheterisatie en antimuscarine pas na hun eerste verjaardag. In de apertagroep onderging slechts één van de patiënten met nierlittekens een 'late onset therapie'. Kinderen met aangeboren meningomyelocèle kunnen waarschijnlijk levenslang doen met hun eigen nieren, mits zij urologisch adekwaat worden behandeld. Om de hogere urinewegen te beschermen is lage intravesicale druk noodzakelijk. Vroeg aanvangen met intermitterend catheteriseren is de voorkeursbehandeling en toediening van anticholinergica om de detrusor instabiliteit en hoge blaasdruk tegen te gaan, is in de meeste gevallen onmisbaar.

Aanvullende opmerkingen

Recent heeft een nieuwe evaluatie plaatsgevonden met betrekking tot de schade aan de nieren. Een DMSA scan werd uitgevoerd bij 38 patiënten

in verband met verdenking op nierverslechtering of bij patiënten met ernstige scoliose of positie afwijkingen van de nier met onbetrouwbare echoresultaten. Bij in totaal 10 patiënten werden nierlittekens aangetroffen. Bij 3 patiënten werden preëxistente deformiteiten bevestigd. Eén meisje, met reflux in de kleine linker nier met 7% functie, heeft tevens een preëxistente dysplasie van de rechter nier.
Hoe langer deze moeilijke groep patiënten wordt gevolgd, hoe meer mogelijke problemen gevonden zullen worden. Over 10 jaar zullen opnieuw followup gegevens worden gerapporteerd.

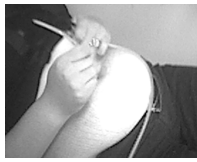
Bij een onderzoek van 132 patiënten met spina bifida tussen 1974- 1986 in ons ziekenhuis, werd aangetoond dat de verdeling van risicofactoren bij urodynamisch onderzoek als volgt lag:

Bij het huidige onderzoek van 144 spina bifida patiënten tussen 1988 en 2001 wordt de verdeling van risicofactoren samengevat in de volgende tabellen: Vergeleken met oudere gegevens die beschreven staan in het proefschrift van Prof Dr Jan D. van Gool van de spina bifida patiëntengroep uit 1974 - 1986, is de apertagroep niet verbeterd. Maar in de occultagroep worden volledig andere percentages gevonden. 24 van de 35 occulta patiënten zijn continent. Dit is overigens opmerkelijk aangezien 20 van de continente patiënten niet een overactieve bekkenbodem lijkt te hebben met urodynamisch onderzoek. Detrusoroveractiviteit of andere factoren

Tabel 1. De verdeling van het patroon van activiteit en inactiviteit van sfincter en detrusor bij 132 patiënten met spina bifida aperta van 1974 tot 1986.

132 patiënten spina bifida aperta 1974-1986

		DETRUSOR	
		Niet overactief	Overactief
SFINCTER	Niet overactief	**35** (26%)	**42** (32%)
	Overactief	**13** (10%)	**42** (32%)



Tabel 2. De verdeling van het patroon van activiteit en inactiviteit van sfincter en detrusor bij 109 patiënten met spina bifida aperta van 198 tot 2001.

109 patiënten spina bifida aperta 1988-2001

		DETRUSOR	
		Niet overactief	Overactief
SFINCTER	Niet overactief	**33** (30%)	**16** (15%)
	Overactief	**22** (20%)	**38** (35%)

Tabel 3. De verdeling van het patroon van activiteit en inactiviteit van sfincter en detrusor bij 35 patiënten met spina bifida occulta van 1988 tot 2001.

35 patiënten spina bifida aperta 1988-2001

		DETRUSOR	
		Niet overactief	Overactief
SFINCTER	Niet overactief	**21** (60%)	**5** (15%)
	Overactief	**7** (20%)	**2** (5%)

zoals houding en mobiliteit lijken bij patiënten met spina bifida occulta een grotere rol te spelen ten aanzien van het ontwikkelen van continentie en min of meer normale mictie.

Hoofdstuk 9

Geschiedenis van intermitterend catheteriseren. Teneinde de huidige ontwikkeling en toekomstige aanpassingen van urologische therapieën voor patiënten met neuropathische blaas te begrijpen, is het nodig om de

geschiedenis te kennen: pas na de 2e wereldoorlog en de oorlog in Korea werden dwarslesie- en ruggenmergletsel-patiënten met neurologische retentieblaas op grote schaal met intermitterende catheterisatie behandeld. Daarna duurde het nog jaren voordat Dr Jack Lapides in de jaren 70 de intermitterende catheterisatie propageerde voor vrouwen met recidiverende urineweginfecties en weer later ook voor paraplegie patiënten. In de tachtiger jaren werd dit idee voor het eerst toegepast bij spina bifida patiënten in een klein aantal instellingen, maar heden ter dage wordt het op grote schaal toegepast.

Conclusies

Spina Bifida is een van de meest voorkomende en meest invaliderende aangeboren afwijkingen. Patiënten kunnen tegenwoordig overleven na initiële sluiting van het ruggemerg en zonodig tot stand brengen van lage intracraniële druk door plaatsing van ventriculaire peritoneale drains. Scoliose operatie en pees- reallocaties kunnen volgen om de patiënten overeind te houden. Urologische ingrepen kunnen volgen om nierfunctie te behouden en continentie te bewerkstelligen. Zelfs na meerdere operaties kunnen nog vele problemen blijven bestaan die nadere oplossing behoeven. Kwaliteit van leven wordt steeds belangrijker. Het eenvoudige concept van vroeg starten met intermitterende catheterisatie in combinatie met anticholinergica en antibacteriële chemotherapie levert een grotere verbetering van het behoud van nierfunctie dan andere behandelwijzen. Het eenvoudige concept van ‘fasciale sling’ blaashalssuspensie blijkt zeer effectief voor het bereiken van continentie bij kinderen met neurogene blaas. Belangrijk voordeel van deze procedure boven kunststof sfincterprothese is het feit dat die uitgevoerd kan worden bij elke lichaamsafmeting en kan blijven functioneren bij toenemende lichaamslengte. Het is goedkoper dan de meeste vergelijkbare procedures. En bij jongens heeft het geen nadelige gevolgen voor de functie van de erectiele zenuwen vlakbij de blaashals.
De procedure die gebruikt wordt voor de blaasaugmentatieplastiek door een groot deel van de detrusor te verwijderen, blijkt in 50% van de gevallen effectief te zijn. In geval van falen, kan altijd nog een standaard darm’patch’ cystoplastiek worden uitgevoerd. De aanwezigheid van

darmweefsel in de blaas kan echter complicaties veroorzaken zoals slijmretentie, steenvorming, recidiverende infecties, electrolyt- en pH-verstoringen en mogelijk maligne ontaarding op latere leeftijd. Het is daarom gerechtvaardigd om andere opties, zoals detrusorectomie, eerst te proberen. Patiënten dienen nauwkeurig urodynamisch vervolgd te worden met betrekking tot blaasdruk en blaascompliance.

Toekomst perspectieven:

1. Alternatieven voor anticholinergica moeten gevonden worden vanwege de vele bijeffecten die deze middelen kunnen veroorzaken. Droge mond kan cariës tot gevolg hebben. Droge huid kan aanleiding zijn voor oververhitting van patiënten in een warme omgeving. Vele patiënten lijden aan psychologische bijverschijnselen als concentratiezwakte of angstdromen. Minder bijeffecten worden gerapporteerd indien de anticholinergica direct in de blaas worden aangebracht. Ook andere stoffen, zoals Capsaceïne, kunnen intravesicaal worden toegediend. Hoopvolle resultaten worden gemeld over locale injecties van Botox (botuline toxine) in de M. Detrusor. Wij hebben inmiddels een beperkt aantal spina bifida patiënten behandeld met Botox en zagen uitstekende resultaten, gedurende meer dan 9 maanden. Een mogelijkheid voor definitieve denervatie van de detrusor zou ventrale wortel rhizotomie van S2-3 kunnen zijn tijdens de primaire sluiting van de spina bifida. Hierdoor verdwijnt de noodzaak voor toediening van anticholinergica en dergelijke middelen, aangezien de blaasdruk definitief wordt verlaagd.

2. Detrusorectomie en ileocysto-augmentatieplastiek zullen binnen 10-15jaar obsolete procedures zijn. Blaasmucosa zal op biomatrix gekweekt worden en gebruikt kunnen worden voor augmentatieplastiek van de neuropathische blaas. Hiermee wordt elke discussie over de beste soort augmentatiecystoplastiek beeindigd.

3. Infecties zijn een voortdurende bedreiging voor patiënten met blaas- en nier problematiek. Aangezien de blaas- en nierfunctie de afgelopen 15 jaar aanzienlijk verbeterd zijn, dient onze houding ten opzichte van antibacteriële chemoprofylaxe ook enigszins te worden bijgesteld. We

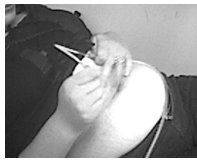
moeten rekening houden met risicofactoren zoals AB0-secretor status en immunoglobuline status. Andere therapieën, zoals drank of capsules van Cranberries of intravesicale toediening van medicatie, verdienen nadere aandacht. Zelfs eenvoudige controle met teststrips, op leukocyten en nitriet en zonodig intermitterende antibiotische chemotherapie, kan effectiever blijken dan onderhoudsdoseringen antibacteriële chemoprofylaxe. Een protocol voor deze belangwekkende materie gaat binnenkort van start!

4. Hoewel de 'fasciale sling' graft een zeer effectieve keus bleek voor de behandeling van blaashalsinsufficientie bij deze patiënten, moeten we toch ook andere mogelijkheden niet uit het oog verliezen, zoals de pacemakergestuurde musculus gracilis graft onder de blaashals. Deze oplossing is bij cavias effectief gebleken.

5. Zoals eerder vermeld, wordt de erectiele functie bij mannelijke patiënten bij de fasciale sling procedure niet aangetast. Het gevoel in de glans penis is bij vrijwel alle patiënten echter afwezig. Bij patiënten met een ruggenmerglesie onder L3 is de sensitiviteit van de lies nog wel aanwezig, door de oorsprong van de nervus ileo-inguinalis. Bij een pilotstudie van 3 patiënten hebben wij een anastomose aangelegd tussen de nervus ileo-inguinalis en nervus dorsalis penis om de gevoeligheid van de glans te herstellen. Deze operatie bleek succesvol in alle gevallen. Dit leidt tot de volgende vraag: hoe zit het met sex? Op dit moment weten we dat nog niet. Na jaren lang gefixeerd te zijn geweest op nier-en blaasfunctie, urologische-, neurologische- en orthopedische operaties met steeds betere resultaten, weten we nog weinig over de sexualiteit bij de spina bifida adolescenten. Adolescenten vermijden het onderwerp sex meestal nog zoveel mogelijk, maar als volwassene wordt sexualiteit belangrijker voor ze en beginnen zij in toenemende mate vragen te krijgen daaromtrent. Wanneer re-innervatie-operaties meer gemeengoed worden, zullen adolescenten met spina bifida waarschijnlijk meer geïnteresseerd raken in het onderwerp sexualiteit.

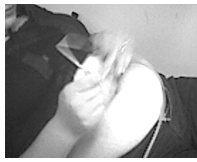
Er zal de komende jaren nog veel onderzoek verricht moeten worden….

Dankwoord



Marga, lieve vrouw van mij, zonder jouw immer aanwezige steun was het allemaal niets geworden. Jij zorgt altijd voor een thuisfront dat een oase van rust is na een hectische dag op het werk. Ook in de afrondingsfase van dit proefschrift, kort voor onze vakantie in onze “hut in Frankrijk” zorgde jij voor de letterlijke en figuurlijke steun in de rug. Dank voor je vertalingen en typewerk, correcties van mijn spel - en stijlfouten en aanvullende bezigheden. En ook onze kinderen, Emilie en Maarten hartelijk dank voor het begrip en geduld dat jullie voor mij toonden. De voorplaat van dit boekje is door jullie bedacht en getekend. Goed hoor!
Dit proefschrift beschouw ik niet als een produkt van mijzelf alleen. Juist doordat iedereen in ons team een zeer aanzienelijke bijdrage aan zorg en onderzoek heeft geleverd zijn uiteindelijk de artikelen verschenen die in dit boekje verzameld zijn. Met dit proefschrift wordt dan ook een van de hoofdlijnen van de afdeling kinderurologie aan de buitenwereld getoond als produkt van ons denken en doen.
De afdeling kinderurologie heeft altijd gestreefd naar multidisciplinaire behandeling van onze patiënten. Zo ontstond het kinderniercentrum bijna achtien jaar geleden door samenwerking met de kindernefrologen. De aanpak van problemen bij kinderen met spina bifida geschiedt ook al sinds vele jaren door middel van een holistische en multidisciplinaire visie. In tijden van bezuinigingen en telkens vernieuwend management stond het spina bifida team vaak op de nominatie om weggecijferd te worden. Toch is men er steeds in geslaagd dit naderend onheil op diplomatieke wijze af te wenden. Het heeft jaren geduurd totdat de wijze waarop het spina team functioneert een welverdiende erkende plek in onze ziekenhuis organisatie kreeg.
Prof. Dr Jan van Gool (kinderarts nefroloog), jou beschouw ik als een van mijn grote "oude" leermeesters. In discussies kom je meestal opeens met chirurgische precisie tot de kern van het vraagstuk. Jouw bijdragen aan de urologische en nefrologische inzichten zijn van onschatbare waarde gebleken. Jij bent een van de eerste wetenschappers geweest die nefrologische ziekten en urologische afwijkingen met elkaar in verband bracht en daardoor uitblonk in het “orgaansysteem-denken”.
Dr(s) Marc Lilien (kinderarts nefroloog), ik dank je voor de stimulerende werking die van je uitging in het promotietraject waarin wij beiden dit jaar terechtkwamen (jij promoveert enkele dagen na mij). Ik kreeg helemaal

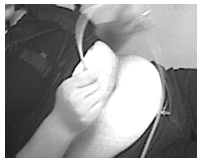
het heilige vuur toen jij mij jouw kant en klare manuscript liet zien toen ik nog zeker twee hoofdstukken moest voltooien.
Dr(s) Aart Klein (kinderuroloog), jij promoveert het komende jaar op een prachtig onderwerp. Aan meerdere artikelen in mijn boekje heb jij een bijdrage geleverd. Dank je voor je scherpzinnige visie op zoveel aspecten in ons vak en in onze samenwerking.
Dr Laetitia de Kort (fellow-kinderuroloog), door jouw komst in onze kinderurologische groep is eindelijk de werkdruk voor ons wat afgenomen, waardoor ook een beetje tijd vrijkwam om dit proefschrift eens te voltooien. Wij vormen in Utrecht thans een grote kinderurologische afdeling. Mede dank zij jouw recente proefschrift en gepubliceerde artikelen staan we ook internationaal met ons vakgebied in de aandacht. Ik heb bewondering voor je efficiënte tijdsindeling en zakelijke zienswijze. Persoonlijk denk ik dat jou nog een grote toekomst in ons vak te wachten staat.
Dr Tom de Jong (kinderuroloog), leermeester en co-promotor. Over je grote operatieve vaardigheden blijf ik mij, na al die jaren, nog immer verbazen. Wat dat betreft denk ik vaak aan het Latijnse gezegde: "quod licet Iovi, non licet bovi". Jij hebt al zo vaak getoond visionaire ideeën te hebben. Ik heb zelfs gemerkt dat er mensen zijn die het echt hinderlijk vinden dat je zo vaak gelijk blijkt te hebben. Ook dit proefschrift is gestart met een mening die 15 jaar geleden helemaal niet door alle andere kinderurologen gedeeld werd. Na vele jaren tegen de stroom van gevestigde ideeën opboksen komt de nationale en internationale erkenning voor jouw onzegbare weten ("tacid knowing"). Er is helaas een groot verschil tussen gelijk hebben en gelijk krijgen, zoals je weet. Maar van mij krijg je groot gelijk.
Cuno Uiterwaal zorgt op onze afdeling steeds op voortreffelijke wijze van de statistische onderbouwing. Wat zou het UMC Utrecht moeten zonder het Julius Centrum? Onze afdeling is dankbaar voor de goede samenwerking.
Het gehele spina bifida team ben ik veel dank verschuldigd. We zijn - samen met de ouders van de patiënten - teamspelers in de begeleiding van onze patiënten, zo voel ik dat althans. Wij weten dat nog steeds veel valt te verbeteren, maar we weten ook dat veel goed gaat.
Dr Rob Gooskens (kinderneuroloog): Dank voor je visie en al je onderricht. Jij vervult naar mijn gevoel in Nederland een voortrekkersrol op het



gebied van spina bifida problematiek.
Dr Teau de Jong - de Vos van Steenwijk (kinderarts): Dank voor je kritische blik en constructieve meedenken aan de artikelen waaraan je een bijdrage leverde. Er is nog veel werk dat je hopelijk samen met de afdeling kinderurologie zult verrichten. Ik denk daarbij onder andere aan het onderzoek over urineweginfecties dat binnenkort van start gaat.
Dr Marja Schoenmakers (fysiotherapeute), jij hebt mij veel geleerd over de aspecten van welbevinden bij kinderen met spina bifida, die je recent hebt beschreven in je prachtige proefschrift.
Drs Marja van Tol (revalidatie arts), wanneer wij kinderen met spina bifida kort na de geboorte onderzoeken en in het spina team met elkaar beoordelen hecht ik enorm aan je oordeel over het latere functioneren. Als revalidatie arts ben jij in staat de problematiek op lange termijn goed te overzien en ik vind jou een holist bij uitstek!
Dr Pruijs (kinderorthopaedisch chirurg), wij doen samen zo nu en dan

Het multidisciplinaire spina bifida team van het Wilhelmina Kinderziekenhuis in 2004.

bijzondere waarnemingen. Zo viel het ons bijvoorbeeld op dat spina bifida patiënten, die bij urodynamisch onderzoek een beperkte blaascapaciteit hadden en eigenlijk een blaasaugmentatie nodig zouden hebben, na de operatie, waarbij jij de rug rechtzette en de ernstige lordose en scoliose verbeterde, opeens een verbeterde blaascapaciteit vertoonden. Jammer genoeg was het aantal patiënten nog te klein om dit als artikel of hoofdstuk in dit proefschrift op te nemen.
Dr Patrick Hanlo (kinderneurochirurg). Dank voor je klinische en praktische visie binnen ons team. Onze samenwerking heeft er toe geleid dat wij een keer samen een neurochirurgische operatie deden: dat was een bijzondere ervaring voor een kinderuroloog!
Madelon Kleingeld (maatschappelijk werk): In de loop van de jaren hebben we heel wat zorgenkindjes en ouders samen besproken. Jouw achtergrond-informatie, waarmee je overigens zeer discreet bent, heeft mij dikwijls goed geholpen ook bij de afweging voor het stellen van operatieindicaties.
Henny Huttinga, dank voor het telkens weer opzoeken van patiëntengegevens en het mij steeds weer helpen herinneren aan allerlei kleine details. Jammer dat je het spina team nu verlaat, maar je hebt op een andere afdeling een nieuwe uitdaging gevonden. Irma Borgers zal het van je overnemen.
Marijke Steijn, onze kersverse en enthousiaste stoma verpleegkundige heeft de taak overgenomen van Carla Nesselaar, die vele jaren de kinderen met spina bifida liefdevol heeft bijgestaan. Goede begeleiding voor faecale continentie is een absolute noodzaak! Ik verheug mij telkens weer over de goede samenwerking.
Wendy Stolker en Talitha van Manen, dank jullie zeer voor de secretariële ondersteuning bij de totstandkoming van dit werkstukje: denk daarbij aan het typewerk, vermenigvuldigen van het manuscript, verzending van het proefschrift etc.etc.
De Medische Assistentes Admistratieve Zorg (MAAZ) Clasien de Jong, Nicolette Vink, Joke Drieënhuizen en Trudie Vlastuin, dank je voor al het begrip dat jullie steeds weer voor mij weten op te brengen. Vooral als jullie weer eens een status moesten zoeken, die ik voor dit proefschrift nodig had en voor details op mijn kamer hield.
Laurence Hermsen en Ellen de Bruijn. Dankzij de altijd geduldige wijze waarop jullie praktisch zelfstandig de urodynamica bij onze patienten



uitvoeren, beschikken wij over zeer betrouwbare en reproduceerbare gegevens. Dank voor het uiterst professionele werk dat jullie leveren.
Onze incontinentie therapeutes zorgen altijd voor een goed klankbord als het gaat over diagnostiek en behandeling van incontinentie problematiek. Niet zelden zijn zij erin geslaagd een aantal patiënten, die in dit proefschrift beschreven staan, te helpen bij nog resterende incontinentie- en catheterisatieproblemen. Dank voor jullie inspirerende inbreng, Florentine Sikkel, Annie Wingens, Leontine Berntssen, Maaike van Schaijk en niet op de laatste plaats Marianne Vijverberg.
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Drs Carl Weiburg, destijds aangetreden als een soort super-co met bijzondere belangstelling voor de urologie. Goed dat je nu in opleiding bent. Dank voor je bijdrage aan een van hoofdstukken van dit boekje.
Drs Liesbeth AB, jij bent eerste auteur van een mooi artikel over het mechanisme van detrusoroveractiviteit. Je bent een zeer betrouwbare en betrokken onderzoekster. Het liefst hadden wij gezien dat je in opleiding zou zijn gekomen om kinderarts te worden. Dank je wel voor je inzet en enthousiasme!
Dr George Tsachouridis: In het jaar 2000 ben je als junior-fellow bij ons op de afdeling geweest. In korte tijd heb je Nederlands leren verstaan, spreken en schrijven. Dank voor je bijdrage aan het artikel over detrusorectomie. Nu ben je werkzaam als kinderuroloog en urodynamicus in Athene, waar je de ideeën die je in Utrecht geleerd hebt ook in de praktijk kunt brengen. Met belangstelling zal ik je verrichtingen blijven volgen. Onze gezamenlijke grote vriend Athanasios Fidas hebben wij helaas verloren. Ook hij interesseerde zich in het bijzonder voor neurogene blaasfunctiestoornissen. Ik gedenk hem met grote genegenheid.
Ik dank mijn opleiders Dr A.P. Brinkhorst, Prof.Dr F.H. Schröder, Dr S. Miranda, Prof Dr R.J Scholtmeijer en hun naaste medewerkers voor de tijd en moeite die zij aan mij hebben willen besteden en het vertrouwen dat zij mij gegund hebben.
Prof. Dr T.A. Boon: Ik kijk terug op vele jaren van goede samenwerking. Eerst, toen ik nog assistent in Rotterdam was, bij de oprichting van de

"Urograaf". Ik wilde daar wel graag cartoons in tekenen en jij zag altijd zo perfect het beeld voor je, dat ik daarna moest tekenen. Ons gevoel voor humor kan vaak dicht bij elkaar liggen. Later, toen ik in het militair hospitaal werkte en academisch mocht aanleunen tegen jouw afdeling in het AZU, hebben we een enorm leuke tijd gehad, ook samen met Joop Noordzij. Het CMH bleek een goede kweekvijver voor aanstormende talentvolle assistenten die een opleiding wilden en ik geloof dat iedereen zonder uitzondering goed is weggekomen. Bij moeilijke operaties zorgde jij altijd voor optimale begeleiding en "back-up" en we hebben zelfs ook samen met Bart Schrier en Tycho Lock nog leuk wetenschappelijk werk kunnen doen. Ik heb het enorm gewaardeerd hoe jij mij altijd, ook in moeilijke tijden, gesteund hebt. Ik ben erg blij dat jij mijn promotor hebt willen zijn. Ik beschouw het als een mooie afronding van onze samenwerking. Ik zal niet licht vergeten hoe we in de zonnige tuin van je kasteel aan de Vecht de laatste details van het manuscript zaten door te nemen.
Drs Jan Dirk Westbroek (chirurg) en Dr Bert Smit (kinderarts, neonatoloog): Onze vriendschap gaat al zo ver terug. Ik hoef hier natuurlijk niet precies uit te leggen hoeveel het voor mij betekent dat jullie mijn paranymfen willen zijn!
Een flinke bijdrage in de drukkosten is gedaan door de Nierstichting en door de Stichting Kindernierziekten. Ook door de firma Astra Tech is een grote bijdrage geleverd. Astra Tech maakte het eveneens mogelijk dat een groot aantal spina bifida patiënten naar aanleiding van het tot stand komen van dit proefschrift een fantastische geheel verzorgde dag in het Dolfinarium te Harderwijk kreeg aangeboden. Dat is denk ik echt uniek.
Tot slot van dit dankwoord wil ik mijn ouders danken voor alle liefde en vertrouwen die zij mij in mijn leven geschonken hebben en voor alle mogelijkheden die zij mij geboden hebben. Het is jammer dat mijn vader inmiddels overleden is, weliswaar op zeer hoge leeftijd. Zo'n promotie had hij echt leuk gevonden om mee te maken. Maar ik ben erg blij dat mijn moeder er wel getuige van mag zijn. We zijn er allebei uiteindelijk een veelvoud van 7 jaar voor geworden. Je hebt altijd veel geduld gehad, mams.