Committee 10

Neurologic Urinary and Faecal Incontinence

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ABBREVIATIONS

Most abbreviations used in the text are given here, some in the beginning of the chapter where they are used

Ach: acetylcholine
AchE: acethylcholine esterase
AD: autonomic dysreflexia
ADL: activities of daily living
ALD: Alzheimer's disease
AS: anal sphincter
AUS: artificial urethral sphincter
BCR: bulbocavernosus reflex
BST: bethanechol supersensitivity test
CC: cystometriccapacity
CIC: clean intermittent catheterization
CMG: cystometrogram
CPG: clinical practice guideline
CPT: current perception threshold
CT: computer tomography
CTT: colonic transit time
CUM: continuous urodynamic monitoring
CVA: cerebro vascular accident
CVC: conventional cystometry
DI: double incontinence
DLB: dementia with Lewy bodies
DOA: detrusor over activity
DRS: digital rectal stimulation
DSD: detrusor sphincter dyssynergia
ES: electrical stimulation
EAS: external anal sphincter
EMG: electromyography
EPT: electric perception threshold
FI: faecal incontinence
FTD : fronto temporal dementia
GBS: Guillain Barre Syndrome
ID: indwelling catheter
IC: intermittent catheterization
IVES: intravesical electrical stimulation
IWT: ice water test
LBT: lower bowel tract
LMNL: lower motor neuron lesion
LOE: level of evidence
LS: lumbosacral
LUT: lower urinary tract
LUTD: lower urinary tract dysfunction
LUTS: lower urinary tract symptoms
MPdet: maximum detrusor pressure
MMC: meningomyelocoele
MUP: motor unit potential
MRI: magnetic resonance imaging
MS: multiple sclerosis
MSA: multiple system atrophy
NBo: neurogenic bowel
NBoD: neurogenic bowel dysfunction
NDO: neurogenic detrusor overactivity
NLUTD: neurological lower urinary tract dysfunction
NUI: neurogenic urinary incontinence
NVC: natural fill cystometry
OR: odd ratio
PD: Parkinson's disease
PF: pelvic floor
PFD: pelvic floor dysfunction
PSP: progressive supranuclear palsy
Psym: parasympathetic
PVR: post void residual
QoL: quality of life
RCT: randomised controlled trial
SARS: sacral anterior root stimulation
SCI: spinal cord injury
SCL: spinal cord lesion
SDAF: sacral deafferentation
SIC: sterile intermittent catheterization
SLE : systemic lupus erythematosis
SNS: sacral nerve stimulation
SOM: somatic
SPC: suprapubic catheter
SSEP: somatosensory evoked potentials
SSR: sympathetic skin response
SUI: stress urinary incontinence
Sym: sympathetic
TBI: traumatic brain injury
TRI: transrectal irrigation
TURS: transurethral sphincterotomy
UFM: uroflowmetry
UI: urinary incontinence
UMN: upper motor neuron
US: urethral sphincter
USo: ultrasound
UTI: urinary tract infection
UUT: upper urinary tract
VCUG: voiding cystourethrogram
VSD: vesicosphincteric disorders
VSU: vecicoureteral reflux
WBC: white blood cells

CONTENTS

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A. INTRODUCTION

This chapter deals with all aspects of neurologic urinary and faecal incontinence. To combine this information related to two different structures makes this chapter rather unique though there are sufficient arguments to do so, as presented below.

Its content is written from data found in literature with the keywords “neurologic”, neurogenic”, “bladder”, “bowel”, “lower urinary tract”, “anorectal”, “incontinence“, “continence”, “urinary”, “faecal”, “paralysis”, “dysfunction”, “retention”, “constipation” and the list of the specific neurologic diseases as described in chapter E. Important information from the previous ICI report was used as starting point and some is used as such in this chapter, which is intended to be able to stand alone. For some topics more elaborate information will be found in other chapters as on neurophysiology, diagnostics, urodynamic testing, female, male , frail elderly, faecal incontinence and more. To look up the related information in these chapters will be worthwhile. Also in chapter E not all neurologic diseases will be found as we decided in consensus to look into the most prevalent or consisting of the more challenging in diagnosis and or treatment of incontinence. Other colleagues might have made a different choice.

It is known that the lower urinary tract (LUT) and the lower bowel tract (LBT) are interrelated structures. Embryologically bladder and rectum originate from the same basic structure, the cloaca [1]. Anatomically both viscera lay in close communication and share muscular structures of the pelvic floor.

The innervation of both systems depends on autonomic and somatic nerves (**Figure 1**) that carry fibres of both. In **table 1** a simplified overview is given of the action linked to different peripheral nerves.

Table 1. Overview of function of the abdominal sympathetic (Sym), the pelvic parasympathetic (PSym) and somatic (Som) nerves in the LUT and LBT. US= urethral sphincter, AS= anal sphincter. Exp= only suggested in animal experiments, no clinical evidence.

	Sym Th 10-L 1	PSym S2-S4	Som S3-S5
Bladder	-	+	
Bladder neck	+	-	
Extern US	exp	exp	+
Bowel		+	
Intern AS	+	-	
Extern AS	exp	exp	+
Pelvic floor			+

Central control of both continence and evacuation is similar and is discussed in the chapter on physiology [2].

Very generally LUT and LBT act quite similar, both are autonomic organs regulated to necessary social requirements by a somatic innervation. The voluntary control depends on accurate sensation [3]. Continence relates to contraction of smooth closing structures (bladder neck and internal bowel sphincter) and striated urethral and anal sphincters. An inhibitory effect on detrusor and lower rectum resulting from contraction of the pelvic floor and anal or urethral sphincter has been named a “procontinence” reaction. Micturition and defaecation need a proper relaxation of these latter structures to permit a physiological reflex evacuation of urine or faeces.

Interactions between both functions have been demonstrated. The filling status of the bladder influences sensation in the rectum and vice versa [4]. A vesico-ano-rectal reflex permits voiding without

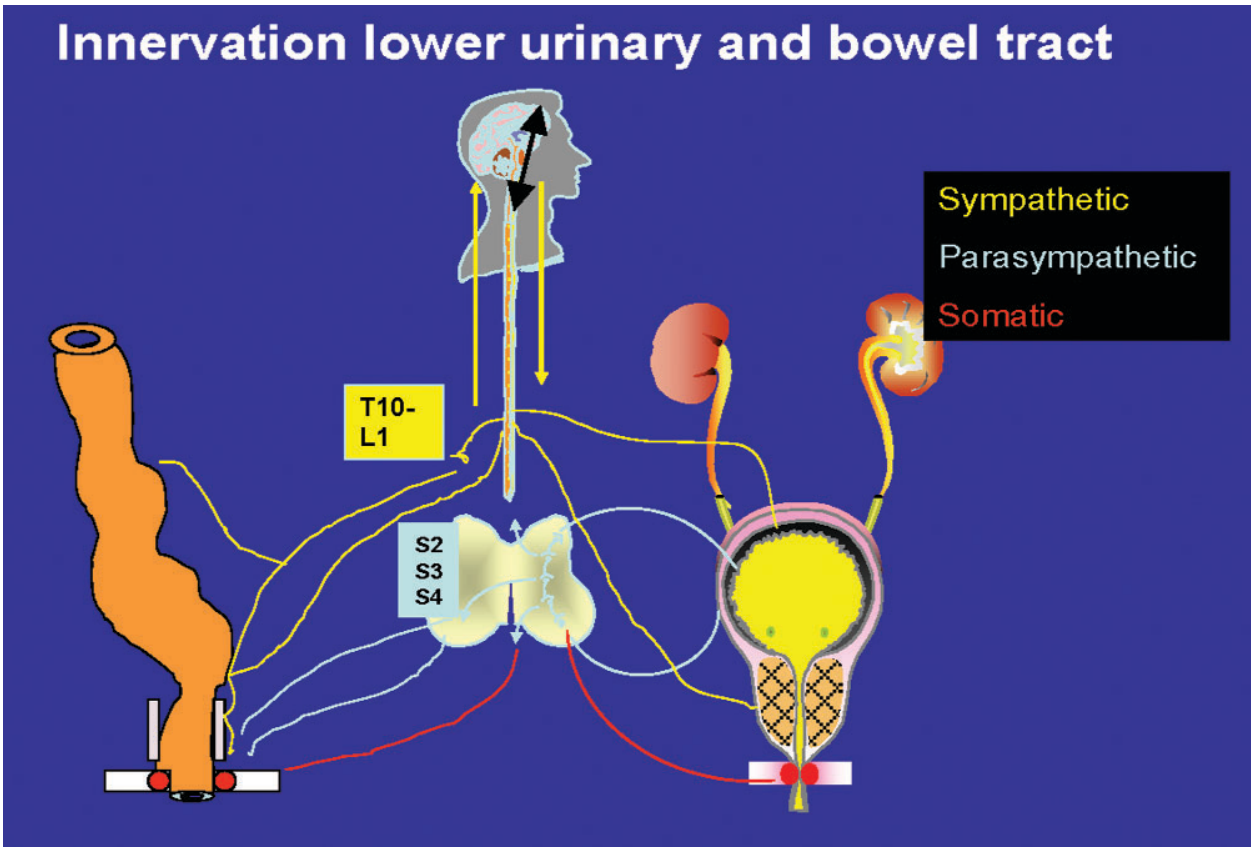

Figure 1: Schematic overview of innervation of LUT and LBT

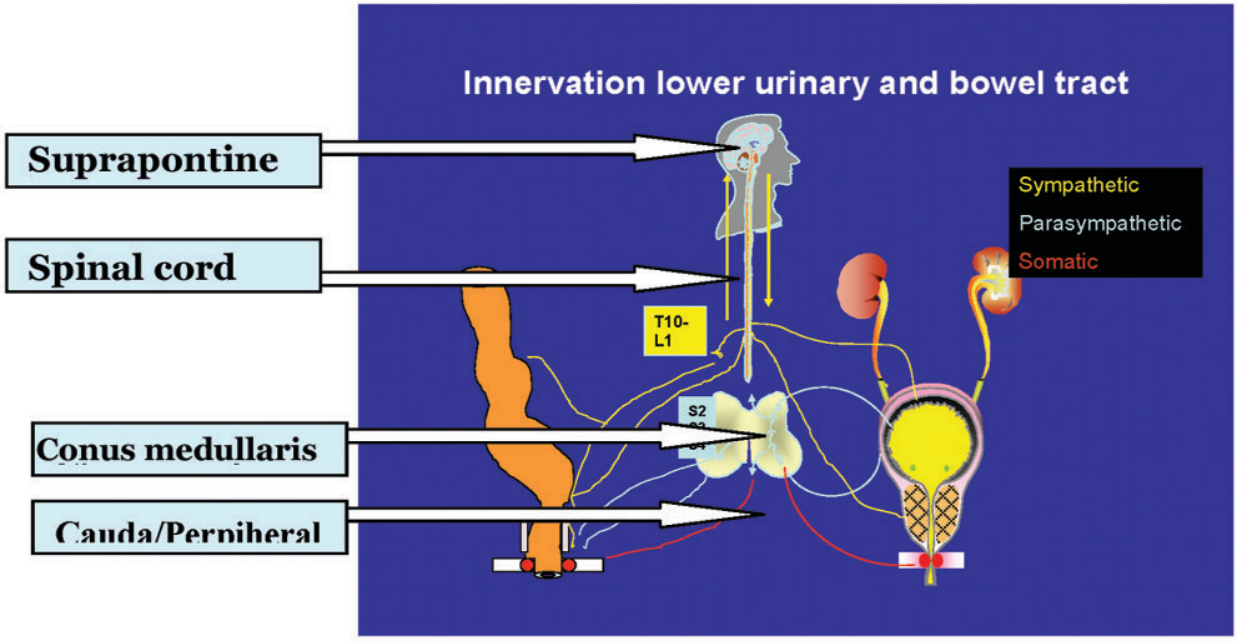

Figure 2 : Frequent sites of neurologic pathology causing neurologic urinary and faecal incontinence.

defaecation [5]. When the bladder is full, sensation of rectal filling is decreased. When healthy people visit the toilet to defaecate, the initiation of micturition often precedes that of defaecation, even if both organs are considered equally full [6]. The prevalence of both urinary and bowel dysfunction is high in many neurological diseases.

There is no study so far on correlation between both functions in patients with neurological pathology.

In this chapter levels of evidence (LOE) and grades of recommendation (A) are used as described in the general introduction of this book.

B. PATHOPHYSIOLOGY

With a neurologic lesion the type of dysfunction that follows in LUT and LBT will depend on the site, the extent and the evolution of the lesion.

Traditionally neurological pathology has been divided in suprapontine, suprasacral spinal cord and subsacral (cauda equina and peripheral nerve) lesions (**Figure 2**).

I. SUPRAPONTINE LESIONS

Patients with lesions above the pons usually continue to have reflex contractions of the detrusor. But the cerebral regulation of voiding and defaecation is often lost. This is the case in lesions as from stroke, head injury, etc, which mostly continue to have a normal coordinated sphincter function. However these patients may purposely increase sphincter activity during an overactive detrusor contraction [7] to prevent urinary incontinence which would otherwise occur. This has been termed “pseudo-dyssynergia” because it is indistinguishable from true dyssynergia on a urodynamic record. Urinary incontinence in suprapontine lesions is due to bladder overactivity [8].

II. SPINAL CORD LESIONS

1. SUPRASACRAL SPINAL CORD LESION

When a lesion is located in the spinal cord below the pons detrusor- urethral sphincter dyssynergia is a common finding. Incontinence may still be caused by detrusor overactivity but the outflow obstruction can also cause retention.

Patients with lesions above the cone usually suffer from an overactive bowel with increased colonic wall activity and anal tone. The central control of the external anal sphincter is disconnected and the sphincter remains tight thereby retaining stool (Dyssynergia). The connections between the spinal cord and the colon remain intact, permitting reflex coordination and stool propulsion. This type of lesion provokes faecal retention at least in part due to the activity of the anal sphincter. Incontinence can be a consequence of faecal impaction and constipation.

2. CONUS LESION

If the nuclei of the pelvic nerves are destroyed, the detrusor becomes areflexic. Retention of urine can provoke stress incontinence (formerly termed overflow incontinence).

III. SUBSACRAL LESIONS (CAUDA EQUINA OR PERIPHERAL NERVES)

The same effect as from lesions of the conus medullaris can result from lesions of the ***subsacral nerves (cauda equina or peripheral nerves***). If the nuclei of the pudendal nerves are harmed, a paralysis of the urethral sphincter and pelvic floor muscles will occur often with loss of outflow resistance and stress incontinence.

A neurological lesion affecting the parasympathetic cell bodies in the conus medullaris will eliminate the pelvic nerve function of the bowel. No spinal-cord mediated peristalsis will occur. It will be the myenteric plexus that coordinates segmental colonic peristalsis. If the pudendal nerve is also destroyed, there is an increased risk for incontinence. Apart from the non contractile external anal sphincter, also the puborectal muscles lack tone, which leads to reduction of the rectal angle. Constipation and incontinence are frequent.

While most traumatic spinal cord lesions give LUT and LBT dysfunctions which can be predicted fairly well from the level and completeness of injury [9], the LUT and LBT function in many other neurologic diseases such as meningomyelocoele are more difficult to categorise [10]. Therefore in this chapter a number of neurologic diseases will be described more in detail.

C. NEUROLOGIC URINARY INCONTINENCE

I. EPIDEMIOLOGY

NLUTD may be caused by various diseases and events affecting the nervous systems controlling the LUT. The resulting lower urinary tract dysfunction (LUTD) depends grossly on the location and the extent of the neurological lesion.

Overall figures on the prevalence of NLUTD in the

general population are lacking, but data are available on the prevalence of the underlying conditions and the relative risk of those for the development of NLUTD. It is important to realise that most of these data show a very wide range of prevalence figures due to low level of evidence in most published data and smaller sample sizes.

Methodology : Pubmed search from 2003 till 2008 with search words- epidemiology, neurologic bladder, neurologic incontinence, neurologic patients, prevalence- gave several references which were added to the list of the previous report 2005. Unfortunately only a very limited number gave data on prevalence and only in specific diseases for which a separate search was done. Data on incontinence are not always present in data on "neurologic voiding dysfunction" or "neurologic cystopathy". No global meta analysis has been found.

In separate searches for specific diseases the prevalence data were also rather limited. Most studies were case series, some retrospective case control studies.

- Several factors can be the cause for this lack of overall data:
- Neurologic problems of the LUT are not always specifically studied
- Some disease are rare or have not been studied in detail
- Series on urologic items deal mostly with urodynamic data, urologic complications or outcome of treatment and include only patients with a known neurologic bladder
- In some neurologic diseases as spinal cord injury no data are to be found on those who did not develop a neurologic bladder.

Results: Following are the data found. While making an interpretation of these data one must realise that incontinence can be a direct consequence of the neurologic dysfunction of bladder, bladder neck or sphincter, but also because of lack of adequate treatment, infection or other anatomical or functional pathology. Literature review does not permit to differentiate between these causes.

1. BRAIN-BRAIN STEM

a) Brain tumours

Brain tumours can cause LUTD in up to 24% of the patients [1]. Mostly case reports-small series have been published more recently [2-3]. In a series of patients with brain tumours voiding difficulty was reported in 46/152 (30 %) of patients with tumours in the fossa posterior, while urinary incontinence occurred only in 3 (1,9 %) [4].

Urinary retention was found in 12/17 children with pontine glioma [5].

b) Dementia

One can not easily distinguish LUT problems caused by age-related changes of the bladder from those due to other concomitant diseases [6]. Therefore the true incidence of incontinence caused by dementia is not known. It has been shown that in geriatric patients with dementia, incontinence is much more frequent than in non dementia patients [7-8].

Alzheimer, Lewy body dementia, Binswanger, Nasu-Hakola and Pick diseases frequently cause non-specific NLUTD [9-13]

The occurrence of incontinence is reported to be between 23% and 48% [14-15] in patients with Alzheimer's disease. The onset of incontinence usually correlates with the disease progression [16].

A male to female ratio of dementia related incontinence was found to be 1:15.

c) Mental retardation

In mental retardation , depending on the grade of the disorder a 12 % -65 % prevalence of LUTD was described [17-18].

d) Cerebral palsy

LUTD in around 30 – 40 % has been reported [19-20]

e) Normal pressure hydrocephalus

Only case reports of LUTD [21-23]

f) Basal ganglia pathology (Parkinson (PD), Huntington, Shy-Drager, etc.)

Parkinson's disease is accompanied by NLUTD in 37.9-70% [24-26]

In the Shy-Drager syndrome almost all patients have NLUTD [27] while incontinence was found in 73 % [28] . Gray et al [29] reported that LUT functional disturbances in PD are not disease specific and only correlated with age. Recent, control-based studies gave a prevalence of LUT symptoms (LUTS) of 27-63.9% using validated questionnaires [30-31], or 53% in men and 63% in women using a non validated questionnaire that included a urinary incontinence category [32]. All these values were significantly higher than in healthy controls. The majority of patients had onset of the bladder dysfunction after appearance of motor disorder.

g) Cerebrovascular (CVA) pathology

CVA causes hemiplegia with remnant incontinence NLUTD in 20-50% of patients [33-34] with decreasing prevalence in the post-insult period [35]. In 1996 Sakakibara et al [36] reported 53 % significant urinary complaints at 3 months. Without proper treatment six

months after the CVA, 20 % - 30 % still suffer from urinary incontinence [37]. The commonest cystometric finding was detrusor overactivity [38-43].

Sakakibara et al [44] reported the urinary symptoms of 39 patients who had brainstem strokes. Almost half the patients had urinary symptoms, nocturia and voiding difficulty in 28 %, urinary retention in 21 % and urinary incontinence in 8 %. A number of case reports describe difficulties with micturition in the presence of various brain stem pathologies [45-46].

2. BRAIN-SPINAL CORD

a) Demyelinization

Multiple sclerosis causes NLUTD in 50-90% of the patients [47-49]. One finds 33 % to 52 % NLUTD in patients sampled consecutively regardless of urinary symptoms, with the incidence being related to the disability status [50]. There is almost a 100 % chance of having LUT dysfunction once these patients experience difficulties with walking. NLUTD is the presenting symptom in 2- 12% of the patients, going to 34 % in some studies [51]. LUT dysfunction appears mostly during the 10 years following the diagnosis [52].

b) Spinal cord lesions

Spinal cord lesions can be traumatic, vascular, medical, or congenital. An incidence of 10.4 to 83 per million inhabitants per year and a prevalence of 223-755 per million inhabitants worldwide. One-third of patients with SCI are reported to be tetraplegic and 50% of patients with SCI have a complete lesion. The patients sustain their injury at mean 33 years old, with a the sex distribution (men/women) of 3.8/1 [53]. Most patients will develop NLUTD [54]. For spina bifida and other congenital nerve tube defects, the prevalence in the UK is 8-9 per 10,000 aged 10-69 years with the greatest prevalence in the age group 25-29 years [55]. In the USA the incidence is 1 per 1000 births [56]. The incidence of urethrovesical dysfunction in myelomeningocele is not absolutely known, but most studies suggest it is very high 90% -97% [57]. About 50% of these children will have detrusor sphincter dyssynergia (DSD) [58-59].

c) Disc disease

Disc disease will cause NLUTD in 28-87% of the patients [60-61]. Cauda equina syndrome due to central lumbar disc prolapse has been reported to be relatively rare, the incidence being from 1 to 5% of all prolapsed lumbar disc [62-70]. Neurogenic dysfunction of LUT without cauda equina syndrome has been described as case reports [71].

d) Spinal stenosis and spine surgery

Spinal stenosis: About 50 % of the patients seeking help for intractable leg pain due to spinal stenosis report symptoms of LUTD such as sense of incomplete bladder emptying, urinary hesitancy, incontinence, nocturia or urinary tract infections [72]. These symptoms may be overlooked or attributed to primary urological disorders. Sixty one-62% would suffer from NLUTD [73-74]. The prevalence of neurologic bladder is more significantly associated with dural sac anteroposterior diameter than with the cross-sectional area of dural sac.

Spine surgery is related to LUTD in 38%-60% [75-76].

3. PERIPHERAL

a) Peripheral neuropathy

1. Diabetes: This common metabolic disorder has a prevalence of about 2.5% in the American population, but the disease may be sub clinical for many years. No specific criteria exist for secondary neuropathy in this condition, but it is generally accepted that 50% of the patients will develop somatic neuropathy and 75-100% of those will develop NLUTD [77-78]. Amongst different types of polyneuropathies in diabetic patients “diabetic cystopathy” occurs in 43% to 87% of insulin-dependent diabetics, with no sex or age differences [79]. It is also described in about 25% of diabetic patients on oral hypoglycemic treatment.[80]

2. Alcohol abuse: Can cause peripheral neuropathy, but its reported prevalence varies widely: 5- 15% to 64% [81]. The NLUTD is probably more present in patients with liver cirrhosis. The parasympathetic system is attacked more than the sympathetic system [82].

Less prevalent neuropathies:

- Porphyria — bladder dilatation in up to 12% of patients [83].
- Sarcoidosis — NLUTD rare [84].
- Lumbosacral zona and genital herpes — Incidence of LUT dysfunction is as high as 28 % if only lumbosacral dermatome-involved patients are considered. The overall incidence is 4 % [85-86]. NLUTD is transient in most patients
- Guillain Barré — The prevalence of micturition disorders varies from 25% to over 80% [87-88] regressive in most [89]. The true incidence is uncertain due to the fact that during the acute phase patients are usually managed by indwelling catheter.

4. OTHER

a) Systemic lupus erythematosis (SLE).

Nervous system involvement occurs in about half of patients. Symptoms of LUT dysfunction can occur; however, data on prevalence are rare and give an incidence of 1% [90-91].

b) HIV

Voiding problems have been described in 12% of HIV-infected patients, mostly in an advanced stage of the disease [92-93].

c) Regional spinal anaesthesia

This may cause NLUTD but no prevalence figures were found [94-95].

d) Iatrogenic

Abdominoperineal resection of rectum has been described to cause NLUTD in up to 50 % [96-97]. It would remain a long-term problem in only 10 per cent [98] though it remains open if this means that the neurological lesion heals or that bladder rehabilitation was successful. Surgical prevention with nerve preservation was shown to be important [99-100].

After simple hysterectomy [101] and after radical hysterectomy or pelvic irradiation for cervical cancer, from 8 to 57% NLUTD was described [102-105]. Surgical prevention is also possible here [106]. After radical prostatectomy neurologic dysfunction of the pelvic floor has been demonstrated [107].

CONCLUSIONS

- **Neurologic dysfunction of the LUT occurs in many patients with neurologic disease but exact figures are seldom available**
- **Meta analysis of prevalence data could give a better idea of how important neurologic bladder is in the patients with neurologic diseases and in the prevalence of incontinence in this population.**

RECOMMENDATIONS

- **Because many diseases or lesions of the innervation can cause pathology of the LUT, patients with known neurologic disease should be evaluated for such dysfunction . (A)**
- **Such evaluation should be made not only when urinary symptoms occur but also as a standard diagnostic approach if prevalence of neurologic bladder is known to be high in a specific disease .(A)**
- **If "idiopathic" LUT dysfunctions occur, the possibility of an unknown neurologic cause should be acknowledged and the diagnostic steps taken to make a proper diagnosis. (A)**

II. SPECIFIC DIAGNOSTICS

- Methods for diagnosis in neurologic LUT dysfunction and in neurologic urinary incontinence are not very different from what is done in non neurologic patients. It consists of clinical assessment including history and voiding diary, urodynamic studies including cystometry (+ EMG), video-urodynamics, uroflowmetry, pressure-flow study, diagnostic imaging with voiding cystourethrography and ultrasonography of the kidneys and LUT. These methods will be dealt with in the relevant chapters of this book(basic assessment, dynamic testing, imaging and other investigations) but we will highlight briefly some data specially related to neurologic patients.

- Some tests developed for the diagnosis of neurologic dysfunction have been evaluated more specifically in this chapter: bethanechol supersensitivity test, ice water test.
- Neurophysiologic studies can be found in the chapter "Clinical Neurophysiological testing" , and only some clinical relevant data on neurologic patients are given here.

Without any doubt before any functional investigation is planned, all "basic" data should be gathered and used for further interpretation of the NLUTD [1-2].

1. HISTORY

The general history aims at gathering information on the neurological and congenital abnormalities, previous urinary complications or treatments. Important are also use of medication with known or possible effects on the LUT, menstrual, sexual and bowel function, and obstetric history. Hereditary or familial risk factors, metabolic diseases and other must be known. Lifestyle factors such as smoking, alcohol, or addictive drug use as well as an evaluation of Quality of life are important.

The signs and symptoms that brings patient to consultation must be documented.

Symptoms related to storage and voiding, continence and /or retention, as well as onset and nature of the NLUTD (acute or insidious) should be determined. If appropriate this information should be compared with the patients' condition before the NLUTD developed.

Very important data are LUTS, urinary incontinence, bladder sensation, mode and type of voiding (catheterization). Warning signs and symptoms that warrant early further investigation are fever, pain, hematuria, catheterization problems, and clinical infections. However, as in non neurologic patients, the "basic tests "also have limitations: individuals with SCI were frequently not accurate at predicting whether they had a UTI based on their symptoms [3]

A urinary diary offers information on the number of voids (frequency and nocturia), the sensation at each void, volumes voided, incontinence, volume and time fluid intake. Voiding diary of 24 hours was shown to be reliable in women with urinary incontinence, but no information is available in patients with neurologic incontinence [4].

2. PHYSICAL EXAMINATION

a) General physical examination

A general impression of patient's physical and mental possibilities from the beginning is important to guide the choice of investigations or to decide from the start to go for least invasive diagnosis and treatment. Severely impaired mobility, extreme spasticity, severe mental disorder, general weakness, presence of severe complications are all important in this respect. Patients with very high neurological lesions may suffer from a significant drop in blood pressure when moved in a sitting or standing position. Patients with spinal cord lesion above D 6 may develop autonomic dysreflexia.

The physical examination will evaluate external genital organs, perineal skin, lower abdomen, lower back. Palpation per vagina or per rectum is done in search of pelvic organ descensus or cervix-uterus/ prostate disease.

b) Neuro-urological examination

As part of a general neurologic examination specific tests are done related to the lumbo-sacral innervation: sensation of touch in the different perineal dermatomes (**Figure 3**), evaluation of bulbocave-rnosus, anal and cremaster reflexes, tone of anal sphincter (**Figure 4**) and possibility to voluntarily contract the anal sphincter/pelvic muscles. A high correlation exists between the clinical neurological findings and the NLUTD in some types of neuropathy such as single level traumatic spinal cord lesions [5-6] but less in other types as in meningomyelocoele or combined traumatic spinal cord lesions [7]. Urinary symptoms and pathological urodynamic findings increase along with the degree of motor function impairment in infantile cerebral palsy [8]

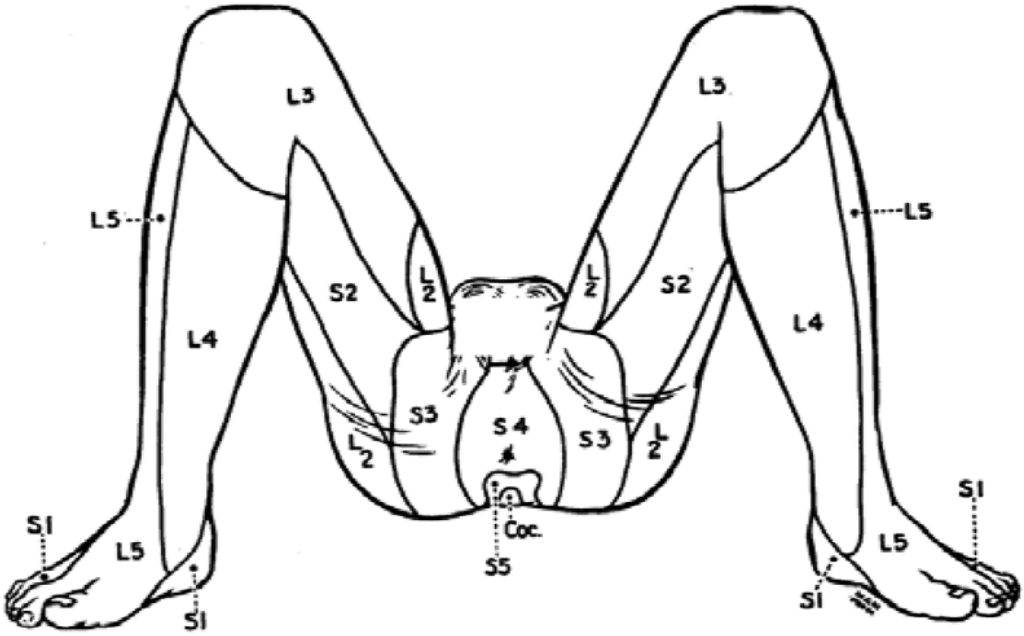

Figure 3 : Dermatomes of spinal cord levels L2-S4

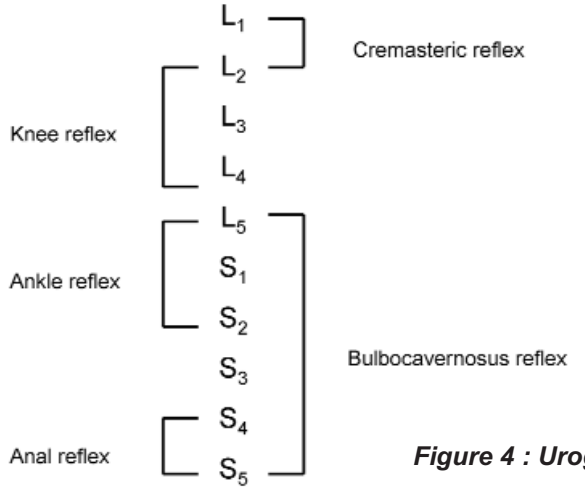

Figure 4 : Urogenital and other reflexes in lower spinal cord

CONCLUSION

- **A combination of data from a clinical neurological examination gives useful information which acceptably corresponds with the LUT function in patients with one level spinal cord injury but not in meningomyelocoele patients**
- **To decide on a detailed individual diagnosis of LUT function in neurologic patients, history and clinical examination prove insufficient.**
- **In elderly male neurologic patients with possible BPH related obstruction, symptoms and clinical examination are not sufficient to differentiate between outflow obstruction and neurologic DOA.**

3. URODYNAMIC TESTS

Classic urodynamic techniques permit us to get multiple functional parameters in patients with neurologic bladder [9].

The recently published International Urodynamic Basic Spinal Cord Injury (SCI) Data Set proposed data to be included in the urodynamic evaluation of patients with spinal cord injury : Variables included bladder sensation during filling cystometry, detrusor function, compliance during filling cystometry, function during voiding, detrusor leak point pressure, maximum detrusor pressure, cystometric bladder capacity and post-void residual [10]

• CMG + EMG has been studied by several authors:

Sundin and Petersen [11] used cystometry-electromyography (EMG) investigation in patients with known or suspected neurologic disorders in whom a defect in bladder emptying, in spite of an active detrusor contraction, was found at cystometry. A voluntary control of the external urethral sphincter relaxation—independent of the degree of bladder filling-was found in most of the healthy volunteers. The cystometry-EMG investigation gave reliable information as to whether a DSD exists. Perkash [12] found rhythmic detrusor contractions on cystomanometry with associated marked increase in EMG activity on attempted voiding to be relevant characteristics of patients with DSD . Rodriquez et al [13] used EMG-gas cystometrogram to select SCI patients for removal of the Foley catheter. Important factors governing success were the amplitude of the detrusor contraction, the presence of detrusor-sphincter synergy and the presence of a flaccid sphincter. Mayo and Kiviat [14] used multichannel urodynamic studies in patients with incomplete bladder emptying secondary to suprasacral SCL. They found that bladder pressure and sphincter EMG measurement during voiding, combined with fluoroscopy, are ideal methods to identify the factors responsible for incomplete emptying in problem cases. Also Perlow and Diokno [15] and Koyanagi et al [16] found CMG-EMG very usefull in SCI patients.

Blaivas et al [17] described on the basis of CMG -EMG 3 types of dyssynergia: type 1 had a crescendo increase in electromyographic activity that reached a maximum at the peak of the detrusor contraction, type 2 had clonic sphincter contractions interspersed throughout the detrusor contraction and type 3 was characterized by a sustained sphincter contraction that coincided with the detrusor contraction. There was no correlation between the clinical neurologic level and the type of dyssynergia.

Simultaneous recording of intravesical pressure, sphincter electromyography and uroflowmetry (CMG.UFM.EMG study) was compared by Aoki et al [18] with cystometry + EMG. They found some influence of the catheter in the urethra. Micturition pressure and opening pressure were larger with CMG+ EMG, incidence of detrusor-sphincter dyssynergia was greater. The authors also found that the Credé manoeuvre exaggerated the DSD. Urodynamics with EMG permitted Kirby [19] to differentiate between patients with pelvic nerve injury, distal autonomic neuropathy, progressive autonomic failure - multiple system atrophy, and idiopathic Parkinson's disease. This influenced the selection of patients for transurethral surgery. Pavlakis et al [20] studied CMG concomitant with perineal floor and rectus abdominis EMG and concluded that the addition of EMG can improve the recognition of intravesical pressure elevation owing to voluntary contraction of the abdominal musculature. EAS motor unit potential (MUP) analysis and EMG cystometry were used to differentiate multiple system atrophy (MSA) from Parkinson's disease in the first five years after disease onset. It showed that involvement of Onuf's nucleus in MSA is time dependent. Before the fifth year of illness, the prevalence of neurogenic change does not seem to be high, so a negative result cannot exclude the diagnosis of MSA.[21]. Rapidi et al used combined urodynamic and electrophysiological study of diabetic cystopathy [22]

The importance of detrusor pressure has been acknowledged for many years. Also recently Bruschini et al [23] evaluated the upper and lower urinary tract in myelomeningocele patients without adequate urological management with clinical, urodynamic and imaging evaluation. The urodynamic.data were correlated with the status of the upper urinary tract (UUT). The cystometry showed detrusor overactivity (DO), poor compliance, increased bladder capacity and normal cystometry in 48, 49, 2 and 1% of the patients, respectively. Detrusor leak point pressure (DLPP) over 40 cm H(2)O was associated with UUT damage. Patients with decrease on functional bladder capacity (FBC) <or= 33% had more renal scars than their counterparts. No difference in cystometric capacity

and intravesical leak point pressure at terminal detrusor overactivity was shown between complete and incomplete spinal cord injury patients in a survey by Moslavac et al [24]. Incomplete SCI patients with neurogenic detrusor overactivity should be tested with cystometry and observed with the same caution as complete SCI patients.

The importance of urodynamic tests for diagnosis and follow up is demonstrated in the study by Abrahamsson et al [25] on cystometrical changes with unthetering in myelomeningocoele children. After untethering 35% of the patients experienced improved bladder function and 5% deteriorated. All of the patients who deteriorated before untethering improved afterward, and 90% of those who were stable preoperatively continued to be stable postoperatively. Regular evaluation of bladder function in children with myelomeningocele is recommended. Also Kang et al [26] used urodynamic tests to determine prognostic factors affecting urological outcome after unthetering surgery for lumbosacral lipoma.

Perkash and Friedland [27] found simultaneous transrectal ultrasonography helpful. They also recommended not to irritate the bladder when introducing the urodynamic catheter and to examine the entire curve of the CMG and not simply the initial rise. [28]

Pressure-flow study can demonstrate an obstructive pattern (high pressure voiding) also in neurologic patients due to urethral relaxation failure [29-30].

Video urodynamics permit a clear image of bladder neck and urethral sphincter activity during filling and voiding [31-32].

Zerin et al [33] found that the urographic position of the bladder neck in relation to the pubic symphysis was correlated with lower motor neuron (LMN) denervation of the urethral sphincter as detected with electromyography in infants and children with myelodysplasia. They concluded that, although not as precise as urodynamic testing, significant descent of the bladder neck is a reliable urographic finding of complete LMN denervation of the external urethral sphincter in infants and children with myelodysplasia.

CMG filling rate seems to be very important especially in neurologic patients: De Gennaro et al [34] performed continuous urodynamic monitoring over 6 hours (CUM) in children and compared this with standard urodynamics. They found CUM feasible and permitting a better diagnosis than standard cystometry in some. Zermann et al [35] investigated the diagnostic value of natural fill cystometry (NFC) in children with neurologic bladder in comparison to conventional videocystometry (CVC). In 45%, NFC detected new findings compared with CVC diagnoses. CVC findings were confirmed in another 45%.

Hess et al [36] studied how closely the intravesical pressures obtained before filling cystometry resembled those obtained during the filling phase of the CMG. Filling pressures during cystometry were significantly higher than the pressures measured at rest. This study also suggests a strong correlation between both. Ko et al [37] determined in SCI patients with neurologic bladder whether cystometry performed by filling using diuretics (FMCG) reveals different findings compared with conventional CMG. Significant differences were found between both in hyperreflexic neurologic bladders with respect to a decrease in MPdet and increase in compliance with FCMG. However, there were no significant differences in MPdet and compliance in hyporeflexic or areflexic neurologic bladders between the two techniques. Natural filling by the production of urine can change the results of cystometry considerably, and should be considered when performing urodynamic investigations and interpreting the results. Because the effects can increase with the time required to conduct the investigation, effort should be made to decrease the total duration of urodynamic investigations.[38]

In men with SCI, cystometric variables and detrusor overactivity remain consistent over sequential studies as shown in a study by Ockrim et al [39].

The amplitude of the first overactive contraction and the maximal detrusor contraction were found to be statistically greater in female patients with multiple sclerosis and neurogenic detrusor overactivity compared to women with idiopathic overactivity. The threshold volume for detrusor overactivity was greater, likely secondary to the elevated post void residual urine volume in the MS patients. In this study using a cut off value of 30 cm H2O for amplitude of the first overactive contraction achieved a positive predictive value of 88% for identifying multiple sclerosis [40].

The determination of CMG filling sensation is important. In 52 SCI patients, 26 % of those with a supposed complete lesion had sensation of bladder filling during cystometry [41]. Also in 41 patients with myelodysplasia the perception of bladder filling proved, rather unexpectedly, to be present in a majority of patients [42].

In a large cohort study it was clearly shown that impaired perception of bladder filling during CMG is a sign of neuropathy [43]. Ersoz and Akyuz [44] investigated bladder-filling sensation in 73 SCI patients with complete lesions above T11 and below T10 and with incomplete lesions Bladder-filling sensation was present to some degree in all incomplete SCI patients, in 82.4% of the patients with complete lesions below T10, and in 38.9% of the patients with complete lesions above T11. Bladder-filling sensation investigations were reproducible in terms of bladder filling sensation category in 36 SCI patients who had a second CMG. The authors concluded that presence of bladder-filling

sensation in many SCI patients reveal the potential for sensation-dependent bladder emptying, especially in the ones with complete lesions below T10 and the ones with incomplete lesions. The safe use of sensation-dependent bladder emptying was shown to be dependent on the urodynamic situation [45].

Complications of cystometry in patients with neurogenic bladder have been documented. Hematuria, due to the urethral catheter, the development of oedema in the urinary bladder wall and the development of urinary bladder spasm as a result of catheter irritation can occur. One case report of twist and knot formation in the double lumen urethral catheter after cystometry of a patient with a hypocompliant bladder has been published [46]. Another case report describes bladder rupture during filling cystometry many years after bladder augmentation in a girl with meningomyelocoele [47]. Symptomatic urinary tract infections after cystometry were found not to be infrequent and antibiotic prophylaxis is advocated [48]. Randomised controlled trials (RCTs) comparing effectiveness of prophylactic antibiotics with placebo or nothing in reducing bacteriologically proven UTI after invasive cystometry not only in patients with neurologic bladder were evaluated by Latthe et al [49]. The use of prophylactic antibiotics in urodynamics reduced the risk of significant bacteriuria.

Though urodynamic tests are recommended in all cases of neurologic bladder dysfunction a recent Japanese study showed that cystometry for the evaluation of vesico urethral function was performed routinely by 52.3% of 333 urologists answering a questionnaire survey to examine current practice patterns of physicians in the urological surveillance and management of spinal cord injury patients in Japan.[50].

CONCLUSIONS

- **Urodynamic tests are very useful in patients with neurologic urinary incontinence though not as generally applied as often thought (LOE 2)**
- **A combination with EMG and /or imaging adds to the diagnostic possibilities (LOE 2)**
- **Filling rate can influence the outcome of several urodynamic parameters (LOE 2)**
- **Pressure development in the bladder is one of the important parameters to be studied and high leak point pressure is dangerous for the kidneys. (LOE 2)**
- **Evaluating sensation of filling during CMG is important for the neurological diagnosis and for treatment options .(LOE 2)**
- **Complications are rare but antibiotic prophylaxis can be advocated (LOE 2)**

4. SPECIAL TESTS

a) Ice water test

The Ice water test was first described as a way to differentiate upper from lower motor neuron lesions. It is based on the principle that mucosal temperature receptors can elicit a spinal reflex contraction of the detrusor, a reflex that is normally inhibited by supraspinal centers. An upper motor neuron lesion interrupts these inhibitory pathways, resulting in manifestation of the reflex, whereas a lower motor neuron lesion does not. A positive test should therefore theoretically occur in patients with upper motor neuron lesions, whereas those with lower motor neuron lesions and neurologically normal patients should have a negative test. Simultaneous measurement of intravesical pressure permits us to rule out false negative tests.

In the more recent literature Geirsson [51] showed in a large cohort study that 97% of patients with complete and 91% of those with incomplete neurologic DOA had a positive or a false negative IWT. About 75% of the patients with multiple sclerosis, Parkinson's disease or previous cerebrovascular accident had a positive IWT. All patients with lower motor neuron lesions or pure stress incontinence had a negative IWT. There was a significant correlation between a positive IWT and an abnormal sensation of bladder filling and inability to inhibit micturition voluntarily, as well as between a negative IWT and the occurrence of phasic detrusor contractions during cystometry. The study shows that the IWT is a sensitive test for differentiating upper from lower motor neuron lesions. It is also a useful parameter for functional subdivision of overactive bladders. In patients with voiding dysfunction in the absence of LUT inflammation, a positive test is an indicator of a silent or overt neurological disorder.

Geirsson and Fall [52] used the ice-water test, in patients suspected of DSD (cystometry and needle EMG). A positive test with a high detrusor pressure indicates detrusor-external sphincter dyssynergia whereas the contrary applies to the negative test. All patients who responded to cold stimulation with detrusor contraction but without fluid leakage (called positive non-leakage IWT), presented DSD according to EMG. The authors conclude that in this situation, the cheap, non-invasive and simple IWT can replace a needle EMG study.

Ishigooka et al [53] evaluated urinary bladder sensation to ice water instillation in patients with diabetes mellitus. There was no apparent relationship between prevalence of peripheral neuropathy and that of negative sensation of ice water test. Impairment of ice water perception was less frequent than that of mechanoreceptor sensation in patients with diabetic cystopathy.

Ronzoni et al [54] studied ice-water test in 148 patients with neurologic bladder dysfunction resulting from a traumatic lesion and in 130 patients with neurologic bladder dysfunction and multiple pathogenic disorders. IWT was positive in 95% of patients affected by complete and in 86% of patients with incomplete medullary lesions. The IWT in patients with lower motor neuron medullary lesions was always negative. The test was used diagnostically in patients with lower motor neuron lesions. In those with upper motor lesions it was used as a rehabilitation method during the medullary-shock phase to accelerate the appearance of the micturition reflex. In 9% of patients it was used to induce micturition during cystography. The authors consider IWT as a useful complement to urodynamic examinations in patients with neurological bladder disease.

Chancellor et al [55] determined the clinical utility of IWT during urodynamic evaluation in spinal cord injured (SCI) patients and found that it did not contribute to their management because of the insensitivity and non specificity. Autonomic hyperreflexia can occur during evaluation. The IWT did not influence clinical management in this group of SCI patients.

Repeating the IWT has been shown to increase its positivity [56]. Combining the IWT and EPT will reinforce the results of both tests and can indicate more clearly the possibility of an unsuspected neurologic pathologic finding in patients with idiopathic DOA. In multiple sclerosis it may have pathophysiological value, indicating a spinal rather than cerebral mechanism of overactive bladder, and diagnostic value, indicating multifocal demyelination. [57]. In vue of these recent data clinical utility should be further assessed.

CONCLUSION

- **The literature results from IWT show value in the diagnosis of neurologic bladder and in the differentiation between reflex and areflex neurologic bladders. It was also shown that the outcome can be improved by repeating the test. (LOE 2)**

RECOMMENDATION

- **The ice water test should be interpreted in the light of all data from the diagnostic evaluation. (B)**

b) Bethanechol supersensitivity test

Bethanechol is a muscarinic agonists known to be able to increase bladder sensitivity correlated with improvement in bladder emptying in some non neurologic patients [58] and can be evaluated by studying the sensation of filling and EPT. The Bethanechol test was developed by Lapides et al in 1962 [59] to try to distinguish between a neurologic and a myogenic etiology in the presence of an acontractile bladder. It is based on the observation that after an organ is deprived of its nerve supply, it develops hypersensitivity to the normal excitatory neurotransmitters for that organ. A neurologically intact bladder should have a pressure increase of less than 15 cm H_2O above the control value, whereas a denervated bladder shows a response greater than 15 cm H_2O. A positive test suggests an interruption in the afferent or efferent peripheral or distal spinal innervation of the bladder. However, the test has been considered not very reliable by some [60].

Penders [61] considered the test reliable when the indications are good (large capacity, hypotonic bladder, clinical suspicion of lower neuron lesion) and when the interpretation is based on a right understanding of its mechanism. Pavlakis et al [62] suggest that the bethanechol chloride supersensitivity test is more sensitive and more specific than perineal floor electromyography in corroborating bladder neuropathy. Sidi et al [63] studied patients with neurologic or nonneurologic detrusor areflexia with the bethanechol supersensitivity test, EMG of the urethral rhabdosphincter and bulbocavernosus reflex latency and found the sensitivity of these tests in detecting neurologic areflexia to be 90, 87.5 and 78.1 per cent, respectively, and the specificity 95.6, 76 and 80 per cent, respectively. When all 3 tests were performed together the combined accuracy approached 100 %. They conclude that these combined tests are useful in the diagnosis of patients with equivocal bladder neurologic conditions and in those with subtle neurological lesions. Denervation supersensitivity to bethanechol was demonstrated recently in acute idiopathic autonomic neuropathy [64]

Wheeler et al [65] found the positive BST not diagnostic of neurologic detrusor areflexia because of the many variables that can influence the test. In a later study the same authors [66] suggest that flow rate, surface electromyography, and bethanechol supersensitivity test can not help differentiate neurologic from non-neurologic detrusor failure. Although no one test can accurately differentiate neurologic from nonneurologic female urinary retention, careful neurourologic evaluation will help guide to more appropriate management.

The clinical utility has not been studied in detail recently. This seems an interesting subject for clinical research.

CONCLUSION

The literature on the value of the bethanechol test for the diagnosis of neurologic pathology is contradictory. Several authors state that a positive bethanechol supersensitivity test (BST) usuallyindicates neurologic detrusor areflexia.

Others are more cautious and position the test as one of many in the global evaluation of neurologic LUT dysfunction. (LOE 2)

RECOMMENDATION

The bethanechol supersensitivity test can be used for differentiation between neurologic and non neurologic detrusor areflexia but the test has its limitations. It' s result should be interpreted in the total of diagnostic results. (B)

5. ELECTRODIAGNOSTIC TESTS

There are several tests that explore the innervation of the LUT and can be of interest in the diagnosis.

a) EMG of the urethral sphincter

EMG of the urethral sphincter has been used for decades in the diagnosis of neurologic LUT dysfunction. Its value in practice remains uncertain as well as the best method to use, needle or surface electrodes. Urethral concentric needle electrodes were found to be superior to surface patch electrodes for evaluating relaxation of the muscle during voiding in non neurologic women [67]. Nordling and Meyhoff [68] used cystometry in combination with urethral and anal sphincter EMG in patients with suspected neurologic bladder dysfunction and found anal sphincter EMG to be highly unreliable. Koyanagi et al [69] also found in male patients with SCI, discordant activities between the anal and the external urethral sphincters in 39 %. The degree of bladder dysfunction was related more to the degree of dyssynergia of the urethral than the anal sphincter. But nevertheless Podnar states that although in patients with LUT disorders, external urethral sphincter (EUS) electromyography (EMG) would seem the most appropriate, anal sphincter EMG is the single most useful diagnostic test, particularly for focal sacral lesions, and atypical Parkinsonism [70]. Fowler et al [71] introduced a technique of recording EMG activity of striated muscle in the urethral sphincter by using a concentric needle electrode and an oscilloscope with a delay line and trigger. Individual motor units were isolated and measured. Also Vodusek [72] studied individual motor units. Both conclude that quantitative EMG may be a helpful technique in the investigation of patients with disorders of micturition.

Light et al [73] found in patients with detrusor areflexia and a high spinal cord lesion EMG of the pelvic floor muscles the most predictive neurophysiological test for developing detrusor contractility.

Ziemann and Reimers [74] found the sphincter EMG the most sensitive technique in the diagnosis of chronic pudendal lesions. However, pure afferent lesions cannot be detected by the sphincter EMG. In this case, the BCR, using unilateral stimulation of the dorsal nerves of the penis, provides the opportunity to distinguish between afferent and efferent lesions of the sacral innervation.

Fowler [75] concluded that sphincter electromyography (EMG) has proved to be particularly valuable in identifying patients with parkinsonism who have multiple system atrophy. Tests which examine aspects of nerve conduction velocity have proved to be of lesser value both because such investigations test conduction of nerve fibres rather than levels of innervation, and furthermore examine large myelinated fibre conduction rather than that of the unmyelinated fibres which comprise the autonomic innervation.

De E J et al [76] found a significant disagreement between needle EMG and VCUG for a positive diagnosis of DSD. A combination of EMG and voiding cystourethrogram (VCUG) may identify more cases of DSD than either modality alone and underscores the need for more strict criteria when defining this entity from a urodynamic standpoint.

External urethral sphincter EMG can be used to detect the onset of detrusor contractions in patients with both neurogenic detrusor overactivity (NDO) and detrusor sphincter dyssynergia (DSD) opening a door for the use of triggered devices to inhibit unwanted contractions through continuous electrical stimulation of sensory nerves [77-78].

EMG of the urethral sphincter has been used recently to investigate retention in multiple-system atrophy [79], LUT function in Machado-Joseph disease [80], the impact of pregnancy and delivery on vesico urethral disorders in patients with multiple sclerosis [81], children with cerebral palsy [82], neurourological findings following sacro-coccygeal teratome resection in the newborn period [83].

CONCLUSION

- **EMG can be valuable in the diagnosis of patients with neurologic bladder dysfunction (LOE 2).**
- **EMG of the anal sphincter is considered unreliable by some (LOE 4).**

RECOMMENDATION

EMG of the urethral sphincter can be recommended as diagnostic method in patients with neurologic LUT dysfunction and neurologic urinary incontinence (B B)

b) EMG of Detrusor muscle

Has been very little studied in neurologic patients. La Joie et al [84] recorded simultaneous EMG recordings from the bladder detrusor muscle and the inferior

rectus abdominis muscle in 6 normal subjects, in 4 patients with LMN bladder disease and in 2 patients with an UMN type of bladder lesion. Results of the study demonstrated that the bladder electrodes did not record remote muscle activity from the abdominal muscles so that any increased detrusor electrical activity with abdominal contraction must have some other explanation such as a possible abdominal-detrusor reflex or the production of increased intra-abdominal pressure from abdominal contraction. Also Kaplan and Nanninga [85] analysed of upper motor neuron type neurologic bladders by bladder EMG. Recent data are lacking and therefore we have to consider the technique as not fit for clinical diagnostics today.

c) Dynamic Bulbocavernosus reflex (BCR)

Walter et al [86] studied a dynamic BCR during micturition induced by using periodic dorsal penile nerve stimulation; the evoked reflex response was recorded with an anal sphincter pressure sensing balloon. Results indicate that an enhanced BC reflex is a major factor causing increased urethral resistance during micturition.

Kaiho et al [87] recorded the evoked potential of the BCR (BCR-EP) with a concentric needle electrode at the periurethral striated muscle. They found BCR-EP suppressed during voluntary voiding in normal subjects, but insufficiently suppressed in the patients with neurologic bladder. It was suggested that the measurement of BCR-EP could distinguish involuntary voiding caused by pathological urethral sphincter relaxation from voluntary voiding.

Kaiho et al [88] investigated the change of sacral reflex activity of the striated urethral sphincter in the urine storage phase using evoked potential reaction of the bulbocavernosus reflex (BCR) With BCR-EP in normal male subjects and male patients with neurologic bladder due to suprasacral spinal cord injury. Sacral reflex activity was accelerated by bladder filling in both the normal subjects and SCI patients. And the acceleration in the SCI patients was more remarkable than that in the normal subjects. In addition to the conventional evaluation of the integrity of sacral reflex arc by BCR examination, the observation of changes of BCR affected by bladder filling may provide the information for the continuity of sacral segment and supraspinal micturition center.

CONCLUSION

Very little data on detrusor EMG and BCR-EP in literature and thus these techniques have to be considered as experimental.

d) Motor evoked potentials

MEP has been used to assess neurogenic lesions of the somatomotor efferent nervous pathway to the urethral compressive musculature with and simultaneous recording of evoked pressure curves [89]. MEP recording has been shown to be an accurate and easily applicable test for the diagnosis of lumbosacral spinal cord lesions [90].

Examination by transcranial magnetic stimulation (TMS) was shown to be useful in the diagnosis of cervical spondylotic myelopathy but the possibility of negative central motor conduction time (CMCT) findings upon TMS must be borne in mind.

e) Nerve conduction study

Andersen and Bradley [91] showed in patients with diabetes mellitus decreased conduction velocities in patients with the detrusor reflex as well as in detrusor areflexia. The findings indicated that diabetic vesical dysfunction is principally the result of segmental demyelinization in the peripheral nerve supply to the detrusor muscle and urethra.

Vereecken et al [92] found urethral and anal responses produced by electrical stimulation of penis, bladder neck and anus delayed and the duration reduced.

Carbone et al [93] assessed the effect of urinary bladder filling on the excitability of somatic spinal motor neurones in patients affected by overactive bladder secondary to neurologic and non-neurologic causes with the H-reflex evoked by electrical stimuli applied to the tibial nerve at the

Poplitea fossa and recorded from the Soleus muscle. In healthy subjects, a progressive reduction in the H-reflex amplitude during bladder filling was observed.

In spinal cord-injured patients affected by a neurologic overactive bladder, bladder filling failed to inhibit the H-reflex amplitude; a decrease in the H-reflex amplitude similar to that displayed by normal subjects was observed in patients with a non-neurologic overactive bladder. By contrast, H-reflex behaviour was unmodified in neurologic under active bladder patients and was similar to normal subjects in psychogenic under active patients. H-reflex modulation may be considered a useful tool in the differential diagnosis of voiding dysfunctions.

CONCLUSION

Not many data are found in literature on nerve conduction studies for LUT neurologic problems.

RECOMMENDATION

There are some arguments that the technique can be useful in the further differentiation of the nerve deficits in cases of neurologic pathology of the bladder (C).

f) Somatosensory evoked potentials (SSEP)

Badr et al [94] described techniques of recording evoked potentials in humans in response to stimulation of the urinary bladder.

Galloway et al [95] described a simple method of sacral evoked response to measure the integrity and function of the lower sacral segments of the cord by stimulation at the urethral and anal sphincters.

Mochida et al [96] studied evoked spinal cord potentials (ESCP) in surgical patients with cervical myelopathy. The presence of neurologic bladder was closely correlated with severe limb symptoms and relatively slows ESCP velocity. However, for 47% of the patients with urinary complaints, findings of urodynamic examinations were negative; these patients probably had pathologic or psychosomatic factors other than neurologic bladder due to cervical myelopathy.

Curt et al [97] studied the significance of SSEP recordings in predicting the recovery of bladder function in acute, traumatic spinal cord injury (SCI). They found a good correlation with the recovery of the external urethral sphincter function but not with the urodynamic impairment.

Somatosensory evoked potentials in response to stimulation of the tibial nerve were recently studied in patients with hyperactive urinary bladder to clarify their role in prognosis of tibial neuromodulation efficacy.[98]

RECOMMENDATION

Somatosensory evoked potentials can be of use in the further diagnosis of nervous deficits related to LUT dysfunction (C).

g) Use epidural recording of evoked spinal cord potentials

These showed clinical value in investigating the pathology of cervical spondylotic myelopathy in patients with normal central motor conduction time in upper and lower limbs [99]

h) Afferent nerve recording on sacral roots

Afferent nerve activity from the sacral dermatome, bladder and rectum can be recorded using cuff electrodes placed on the extradural S3 sacral root in humans but improvements in recording quality and sophisticated signal processing methods are needed for chronic application.[100].

CONCLUSION

Epidural recording and direct measurement on sacral nerves is still experimental.

i) Electro sensation in the LUT

Measurement of the sensory threshold of the LUT towards electrical stimulation was performed by Frankl-Hochwart and Zuckerkandl as early as 1899 [101]. After re-introduction of the technique by Markland et al [102] several authors have studied its value in neurologic bladder dysfunction.

Frimodt- Möller [103] described pathological electro sensation in patients with Parkinson's disease, with multiple sclerosis and meningomyelocoele. He also found abnormal electro sensation in half of patients with diabetes and generalized sensory neuropathy but only in 10% of the diabetic patients with a neurologic bladder.

Kieswetter [104] and Powell and Feneley [105] demonstrated abnormal electro sensation in patients with neurologic LUT dysfunction.

Wyndaele [106] determined the threshold of sensitivity to electrical stimulation in several parts of the LUT in 436 consecutive patients. In the groups with different patterns of disturbed sensation a higher incidence of neuropathy was found than in the group with a normal sensation. Further neurological investigation revealed abnormal innervation in 29% of patients who lacked electrosensitivity in one or more parts of the LUT but who had no previous evidence of neuropathy.

Electro sensation proved present in many meningomyelocoele patients with absent skin sensation and absent reflexes and in many patients with suspected complete spinal cord injury on clinical evaluation [41-42].

Standardization is necessary to come to reproducible results [107].

While it is a dream to be able to determine threshold of different fibre types selectively [108] so far no such fibre selectivity has been demonstrated in the bladder [109].

The clinical utility needs to be further studied.

CONCLUSION

To determine the electro sensation in the LUT is valuable to evaluate the afferent innervation in cases of neurologic bladder. Absent electro sensitivity is valuable to decide on further neurologic tests in patients with LUT dysfunction. (LOE 2)

RECOMMENDATION

The determination of electro sensitivity in the LUT is recommended in patients with a known neurologic disease and in patients with idiopathic LUT dysfunction if neurologic pathology is suspected. (B).

j) Sympathetic skin response (SSR)

Schurch et al [110] assessed the degree of sparing of the descending sympathetic spinal tract and correlated these findings with bladder neck function in SCI patients. Evidence is presented that the integrity of the descending sympathetic spinal tract is necessary for a synergic function of the vesicourethral complex and that sympathetic skin responses are of value in the diagnosis of bladder neck dyssynergia. For lesions below the T12 level other investigative methods to exclude bladder neck dyssynergia are necessary.

Rodic et al [111] investigated whether recording the perineal sympathetic skin response, which reflects the sympathetic function of the thoracolumbar spinal cord, represents a reliable and accurate diagnostic tool for assessing bladder neck competence and incompetence. They found that recording the perineal SSR in addition to that of the hand and foot represents a sensitive diagnostic tool for assessing sympathetic nerve function within the thoracolumbar spinal cord. It is of diagnostic value for evaluating neurologic bladder neck incompetence in spinal cord injured patients.

SSR recordings above a spinal lesion level after urethral electrostimulation might provide a useful and technically simple objective diagnostic tool to assess integrity of autonomic (visceral) afferent nerves from the LUT.

Somatosensory deficits are not always paralleled by viscerosensory loss and vice versa. A recent study showed that SSR were superior to visceral sensory evoked potentials which are more difficult to record. The subjective sensations reported by subjects during stimulation could be confirmed in an objective way in 100% of cases by positive/negative SSR findings.[112] The clinical utility needs to be further studied.

CONCLUSION

These publications indicate that sympathetic skin responses are of value to evaluate the integrity of the LUT related sympathetic function and especially for bladder neck competence, incompetence and dyssynergia. (LOE 2)

RECOMMENDATION

Sympathetic skin responses seem promising and the further study of them are recommended for the evaluation of the LUT sympathetic innervation (B)

III. CONSERVATIVE TREATMENT

Therapeutic principles in different patterns of LUT dysfunction depend on the cause of NUI : dysfunction of the detrusor, dysfunction of the sphincter or a combination of both.

Neurogenic detrusor overactivity leads to reflex-incontinence, detrusor areflexia to incontinence with retention (overflow incontinence). An areflexic (incompetent) sphincter causes neurogenic stress-incontinence, a hyperreflexic (spastic) sphincter overflow-incontinence. Quite often detrusor and sphincter are affected simultaneously by the neurogenic lesions with basically four combinations.

In most patients the storage problem, leading to incontinence, is associated with an emptying problem; therefore both aspects have to be considered at the same time.

Therapy of neurogenic incontinence is primarily a conservative one. Timed bladder emptying, by whatever means, controlled fluid-intake and avoidance of urinary tract infections are the prerequisites for successful treatment.

In (a) **SUPRASPINAL LESIONS** neurogenic detrusor overactivity is mostly combined with normal sphincter function, reflex incontinence is the main symptom and antimuscarinic therapy together with behavioural treatment, especially in patients with cognitive impairment, is the method of choice.

(b) **SPINAL LESIONS** mostly cause simultaneous dysfunction of the detrusor and the sphincter.

In suprasacral lesions the combination of a overactive detrusor with a hyperreflexic sphincter is characteristic for the spinal reflex bladder.

Basically spontaneous reflex voiding is possible; however, it is uncontrolled, causing reflex-incontinence and is mostly unbalanced and basically unphysiologic. Detrusor contractions are mostly inadequate, and detrusor striated sphincter dyssynergia is present, both leading to unbalanced voiding.

Triggered reflex voiding is recommended only if it is urodynamically safe and reflex incontinence is manageable. The method of choice nowadays to empty an unbalanced reflex bladder and to manage reflex-incontinence is intermittent (self-) catheterisation. However, to achieve the aims of therapy, - a low pressure LUT situation and continence between catheterisations - additional pharmacotherapy may be necessary.

If bladder relaxing agents fail or are not tolerable, electrotherapy is an alternative in incomplete lesions: ano-genital electrostimulation (penile, clitoral, vaginal and anal) can inhibit neurogenic detrusor overactivity by stimulating pudendal nerve afferents.

If none of the above mentioned treatment modalities is effective to control reflex incontinence and if operative procedures are not indicated or possible, appliances, pads or condom-catheters, are the first choice in males and pads in females. To improve outflow, treatment to lower tone and spasticity of the urethral sphincter can be used.

The indwelling catheter – a suprapubic catheter is preferable to transurethral – remains the last resort for conservative therapy.

For complete conus lesions, also named lower motor neuron lesions, areflexia of the detrusor with areflexia of the sphincter is characteristic. Sphincter incompetence causes neurogenic urinary stress incontinence and may be combined with overflow-incontinence if adequate emptying is not achieved.

Basically, regular bladder emptying achieved by bladder expression, according to the individual bladder capacity, in combination with controlled fluid intake may decrease neurogenic urinary stress incontinence. However, continence is hard to achieve. Bladder expression is potentially dangerous. Pharmacotherapy is not helpful in this situation, appliances and condom catheters are therefore often necessary. Continence can often be achieved only by operative therapy.

Areflexia of the detrusor combined with hyperreflexia of the sphincter may occur in epiconal lesions; however, this pattern may be also due to a decompensation of a neurogenic overactive bladder after chronic urinary retention. With this combination overflow incontinence can be controlled by intermittent catheterization mostly without adjunctive additional pharmacotherapy. If intermittent catheterization is not possible, an indwelling catheter, preferable suprapubic, may be needed.

If overactivity of the detrusor is combined with areflexia of the sphincter, a pattern sometimes found in epiconal lesions, especially in myelomeningoceles, reflex incontinence is combined with neurogenic stress incontinence. Bladder relaxant agents may abolish or diminish neurogenic detrusor overactivity.

In incomplete lesions electrical stimulation of the pelvic floor musculature may improve sphincter function. Thus the combination of pharmacotherapy to treat reflex incontinence with electrotherapy of the pelvic floor muscle may improve continence. However, with this type of neurogenic LUT dysfunction conservative treatment alone is generally unable to restore continence; therefore either appliances or operative treatment must be considered.

(c) **SUBSACRAL (CAUDA EQUINA AND PERIPHERAL NERVES) LESION** are often incomplete lesions. Hypoactivity or areflexia of the detrusor may be combined with a normally functioning external striated sphincter, a combination which can be seen after intrapelvic surgery, when the pudendal nerves remain intact. On the other hand if the pudendal nerve is lesioned and the pelvic plexus remains more or less intact, a combination of a normally functioning detrusor with a hypo- or areflexic external sphincter may be present. For the neurogenic overactive detrusor, again, pharmacotherapy is the first choice. In the hyporeflexic detrusor cholinergics may increase the tone, and the sensation of filling. If the lesions were incomplete, intravesical electrotherapy was reported to increase detrusor contractility. The chances for pharmacotherapy to improve external sphincter weakness as well as to decrease external sphincter spasticity are poor. Injection of botulinum toxin in the striated sphincter has created a new treatment option.

If conservative treatment fails several surgical options are available. They will be discussed in the corresponding part of this chapter.

Since only some conclusions and recommendations are changed and some new references are added to the 2005 chapter, this chapter presents only the new literature, justifying the changes and actual conclusions and recommendations. For previous references as well as for general outlines please refer to the ICI 2005 chapter. Also some recommendation have been compared/changed according to the recent consortium for spinal cord injury [1].

The following text will not deal specifically with the period of spinal shock or cerebral shock in acute neurological lesions when the urologic treatment consists of proper bladder drainage. For the post shock period or for slowly developing dysfunctions several conservative treatments exist:

1. BEHAVIORAL THERAPY

a) Triggered reflex voiding

b) Bladder expression (Crédé and Valsalva maneuver)

c) Toileting assistance

2. CATHETERS

a) Intermittent catheterization

b) Indwelling urethral catheters

c) Condom catheter and external appliances

3. PHARMACOTHERAPY

4. ELECTROSTIMULATION

a) Electrical Neuromodulation

b) Repetitive transcranial magnetic stimulation

c) Deep brain stimulation

d) Electrical stimulation of the pelvic floor musculature

e) Intravesical electrical stimulation (IVES)

1. BEHAVIOURAL THERAPY

a) Triggered reflex voiding (references see ICI 2005 report)

Background

The true automatic or reflex bladder occurs following recovery from spinal shock in spinal cord lesions not involving the conus or cauda equina. If the efferent branches of the pelvic nerve are involved, the reflex emptying is much less complete, and considerable voluntary straining is required to empty the bladder to a satisfactory degree. The stimulation of the sacral and lumbar dermatomes should be used to elicit reflex contractions of the detrusor in cases with upper motor neuron bladders.

The aims of regular triggered reflex voiding are to achieve balanced voiding, to decrease incontinence and/or to achieve continence. Prerequisites for this type of bladder emptying are: the possibility of collecting the urine in a socially acceptable way and an adequate time needed for bladder emptying.The urodynamic function must be safe (low pressure).

Bladder reflex triggering comprises various manoeuvres performed by patients in order to elicit reflex detrusor contractions by exteroceptive stimuli. The most commonly used manoeuvres are: suprapubic tapping, thigh scratching and anal/rectal manipulation.

Frequency of use, intervals and duration has to be specified for each patient. Integrity of sacral reflex is requested for such voiding technique.

Today, learning triggered voiding should not be done without considering bladder outlet obstruction management, continence, appliances, gender, and level and type (complete or incomplete lesions, paraplegic versus quadriplegic patients) of lesion.

Assessment of management by triggered reflex voiding is difficult because of the mostly retrospective nature of the reports and because the management of concomitant bladder outlet obstruction is not specified or incompletely described.

An additional indication could be a quadriplegic patient who is unable to perform self-catheterization but is able to do tapping or triggered voiding. They may choose this option because it gives more independence.

Before considering triggered reflex emptying, one must check if the bladder situation is urodynamically safe (mainly low pressure bladder) and if regular follow-up is guaranteed. The frequency of check-up is not validated, depends on risk factors, but should be between 6 months and 2 years.

To improve emptying and, control autonomic dysreflexia related to bladder filling and contraction as well as to avoid upper tract damage, alpha-blockers or botulinum toxin sphincteric injections (see related part of this chapter) should be tried before sphincterotomy and/or bladder neck incision is performed.

Triggered voiding should not be recommended as first line management of bladder hyperreflexia and neurogenic LUT dysfunction. Intermittent catheterisation has become the gold standard to achieve continence, upper urinary tract protection and improvement of quality of life (see recommendations in the section of intermittent catheterisation).

CONCLUSIONS

- **Reflex voiding is based on an unphysiological sacral reflex. It is potentially dangerous and has a limited role in managing the reflex bladder (LOE3).**
- **The long-term complication rate is not as high as with indwelling catheter, but enough to suggest a trend to avoid this triggered reflex voiding in detrusor overactivity (LOE2).**
- **Costs of appliances and of adjuvant therapies (pharmacotherapy, surgery, urethral prosthesis etc) have to be evaluated (LOE 2).**
- **Treatment of co-existing sphincteric spasticity/ bladder neck obstruction (botulinum toxin, a-adrenolytics) and co-morbidity should be taken into consideration (LOE 1 and 2)**

RECOMMENDATIONS

- **Triggered voiding could be recommended for patients whose situation has proven to be urodynamically safe and stable, and who can manage reflex incontinence. Moreover it is recommended for patients after sphincterotomy and/or bladder neck incision and/or alpha-blockers and or intrasphincteric botulinum toxin injections, in order to improve spontaneous reflex voiding (C).**
- **Reflex voiding can be recommended only if an adequate follow-up is guaranteed (C).**

b) Bladder expression (Crédé and Valsalva) (References see ICI 2005 report)

Background

Bladder expression has been recommended for a long time for patients with a combination of an areflexic detrusor with an areflexic sphincter or with an incompetent urethral closure mechanism of other origin (e.g. after sphincterotomy). Difficulties in emptying the bladder by expression may be due to an

inability to open the bladder neck. However, especially in men, these techniques induce a functional obstruction at the level of the striated external sphincter despite complete paralysis of the musculature of the pelvic floor.

Bladder expression comprises various techniques aimed at increasing intravesical pressure in order to facilitate bladder emptying. The most commonly used are the Valsalva (abdominal straining) and the Crédé (manual compression of the lower abdomen).

With increasing time, using Valsalva and Crédé techniques, more than 50 % of patients could show demonstrable reflux into the prostate and the seminal vesicles and other complications, e.g. epididymo-orchitis. Moreover, the high pressures could cause reflux into the upper urinary tract with all known complications. The stress to the pelvic floor with these techniques several times a day also has a negative influence on the existing minimal storage function of these structures and therefore makes incontinence worse, causes additional genital-rectal prolapse and hemorrhoids.

Adjunctive therapy to decrease outflow assistance includes alpha-blockers, sphincterotomy or botulinum toxin injections. If effective, they usually cause or increase neurogenic urinary stress incontinence. Expression of the bladder for voiding by Crédé and Valsalva can be effective. To empty the bladder, the pressures measured may be high and potentially dangerous for the upper urinary tract. Bladder expression is often not safe. Sphincter-hyperreflexia and detrusor-sphincter dyssynergia are contra-indications for bladder expression.

CONCLUSIONS

- **Bladder expression by Valsalva or Credé is potentially hazardous for the urinary tract due to functional obstruction at the level of the pelvic floor (LOE 3).**
- **It is contraindicated if it creates a high intravesical pressure, or/and if vasal reflux or/and a vesico-uretero-renal reflux are present. In addition, hernias, recto-genital prolapse and hemorrhoids as well as urethral pathology (stricture formation) and recurrent symptomatic UTIs are further contrain-dications (LOE 3).**
- **It may have a negative influence on an existing minimal outflow resistance of a flaccid pelvic floor and therefore incon-tinence may become worse (LOE 3).**
- **Alpha-blockers, sphincterotomy or botulinum toxin may reduce the outflow resistance, but may also induce or increase urinary stress incontinence (LOE 3).**

RECOMMENDATIONS

- **Before recommending bladder expression by Valsalva or Credé, it must be proven that the situation in the LUT is urodynamically safe. Basically the method is dangerous. (B)**
- **Exclude contraindications, such as a vesico-uretero-renal reflux, vasal reflux, genito-rectal prolapse, hernias, urethra pathology and symptomatic UTIs before recommending this type of bladder emptying. (B)**
- **In general, bladder expression should be replaced by CIC in most patients with neurogenic bladder-sphincter dysfunction. (B)**
- **Adjunctive therapy of outflow obstruction can be considered. (B).**
- **Valsalva and Credé guarantee a good quality of life and are cost-effective in the long term only when the indication is proper and when the situation remains stable throughout the years. (B)**

c) Toileting assistance: timed voiding, habit retraining, prompted voiding (references see ICI 2005 report)

For a more complete overview consult the chapters “adult conservative treatment” and “frail elderly”.

1. Background

Adaptation of the drinking and voiding regimen is determined by education and can be implemented by the patient and/or caregivers.

In patients with neurogenic incontinence related to brain diseases, when independent continence cannot be achieved, social and/or dependent continence is sometimes achievable.

The aim of the behavioural process in adults is to re-establish the control of urinary continence. The goals include correcting faulty habit patterns of frequent urination, improving ability to control bladder urgency, prolonging voiding intervals, increasing bladder capacity, reducing incontinent episodes, and building a patient’s confidence in controlling his/her bladder.

Behavioural measures would seem to be beneficial for most neurologic patients in one way or another. Good indications are most common in brain diseases as cerebro vascular disease, Parkinson’s disease, multiple system atrophy, dementia, and cerebral palsy. Other diseases can also be good indications such as multiple sclerosis, incomplete spinal cord injury, transverse myelitis, diabetes mellitus and others. Frail elderly neurologic patients who need assistance can also benefit from these techniques independent of the disease they suffer from.

In dependent patients all these techniques can be proposed and tried, provided that caregivers (physiotherapist, nurse, member of the family…) are aware of them and are motivated to use them.

The following toileting assistance techniques require caregivers/ assistance in many of the patients:

Timed voiding

Prompted voiding

Habit retraining

Bladder retraining

Patterned urge response toileting

2. Timed voiding

Timed voiding is characterized by a fixed interval between toileting. It is a passive toileting assistance program. It is initiated and maintained by caregivers. This technique is considered appropriate for patients who cannot participate in independent toileting. It has been used in patients whose incontinence may be associated with cognitive and/or motor deficits. Its aim is more to avoid incontinence than to restore a normal bladder function.

For neurologic patients it has also been considered as an adjunct therapy to tapping and/or Crédé manoeuvre and/or intermittent catheterisation. Timed voiding is one of the first steps of treating too high bladder volumes, as in diabetes patients with loss of bladder filling sensation.

3. Habit retraining and prompted voiding

Both of these techniques have to be initiated and maintained by caregivers. They are more adapted to patients with brain diseases than to spinal cord diseases and for patients with cognitive and/or motor deficits.

The aim of habit retraining is to help patient to avoid incontinence and/or involuntary bladder contractions by decreasing voiding intervals. Such program has to be adapted to each patient and needs a specific analysis of voiding patterns to select a good individual schedule for voiding. Such a program is very useful for institutionalised patients.

Prompted voiding is used to teach people to initiate their own toileting through requests for help and positive reinforcement from caregiver when they do this. This technique needs an outside individual's participation in the process. There are no specific evaluations on neurologic patients in literature, though the technique may be useful in patients with incomplete neurologic lesions, and in patients with high dependence and good cognitive function.

CONCLUSIONS

- **Behavioural techniques have to be used in conjunction and/or in addition with other therapies (pharmacological treatment, catheterisation) (LOE 2)**
- **There is no consensus, either on the definition of each technique or on the population that can benefit from it. When available, toileting assistance should be used to improve continence of neurologic impaired patients (LOE 3)**
- **There is still some evidence that prompted voiding is able to decrease incontinence episodes. Long-term effect of this therapy is not validated. Moreover there is evidence that patients who should have more benefit of this technique** are **those with less cognitive impairment and higher dependency (LOE** 2/3)

RECOMMENDATIONS

- **Behavioural techniques could be recommended as a part of each individual rehabilitation program. (C)**
- **No guidelines or consensus on correct intervals between bladder emptying has been reported. They should be fixed, but have to be adapted to voiding diary and other related factors as was detailed in the previous report: bladder volume, fluid intake, post-void residual urine volume, urodynamics parameters. (C)**
- **The mental status of a patient must be taken into consideration, and a rehabilitation program realistically tailored to the patient's possibilities. (B/C).**

2. CATHETERS

All technical aspects of incontinence devices can be found in the chapter "Technical aspects of continence devices" of this report. Detailed description of catheter use in neurologic patients can be found in the previous ICI 2005 report under "Conservative management in neurogenic urinary incontinence", page 697 and following. Only literature data published since are summarized here.

a) Intermittent catheterization [IC]

1. Background

Intermittent catheterization (IC) and self-catheterization (ISC) have become properly introduced during the last 40 years. In general, the purpose of catheterization is to empty the bladder and of IC is to resume normal bladder storage and regularly complete urine evacuation. With IC and ISC there is no need to leave the catheter in the LUT all the time, thus avoiding complications of indwelling catheterization (ID).

It is clear that IC can improve incontinence or make patients with neurogenic bladder continent if bladder capacity is sufficient, bladder pressure kept low, urethral resistance high enough, and if care is taken

to balance between fluid intake, residual urine and frequency of catheterization. In young children with SCI, early clean intermittent catheterization and use of anticholinergics appear to prevent upper tract deterioration, improve continence and decrease infections. Serial urodynamics confirm increasing safe capacity with growth in most children. [2,3].

The main aims of IC and ISC are to empty the bladder and to prevent bladder overdistension in order to avoid complications and to improve urological conditions. The optimal post-void residual indicating the need to start bladder catheterization remains to be clarified, though Dromerick et al. [4] (LOE 2) demonstrated in a series of stroke patients that a post-void residual greater that 150ml is an independent risk factor for development of UTI.

2. Technique

There exists neither one best technique nor one best material, as both depend greatly on patients' individual anatomic, social and economic possibilities [5] (LOE 1).

Two main techniques have been adopted, a sterile IC (SIC) and a clean IC (CIC). The sterile non-touch technique involves the use of sterile materials handled with sterile gloves and forceps. In an intensive care unit, some advocate wearing a mask and a sterile gown as well [6].

De Ridder et al.[7] compared the performance of SpeediCath hydrophilic-coated catheters versus uncoated polyvinyl chloride (PVC) catheters, in traumatic spinal cord injured patients presenting with functional neurogenic bladder-sphincter disorders. This 1-year, prospective, open, parallel, comparative, randomised, multi centre study included 123 male patients, > or =16 y and injured within the last 6 months. Primary endpoints were occurrence of symptomatic urinary tract infection (UTI) and hematuria. Secondary endpoints were development of urethral strictures and convenience of use. The results indicate that there is a beneficial effect regarding UTI when using hydrophilic-coated catheters. Bjerklund Johansen et al. evaluated patient openness to changing and satisfaction with catheters used in intermittent catheterisation (IC) for urinary retention from neurogenic bladder dysfunction, They also compared patient response to conventional catheters and a novel packaged hydrophilic catheter: LoFric Primo [8]. 409 neurogenic patients were recruited and 378 (283 males, 95 females; mean age: 43.5 yr) completed a 12-d trial of the novel catheter. Patients evaluated their current catheter at recruitment and the novel catheter after the 2-wk trial by questionnaire. Patient satisfaction was expressed on a Visual Analogue Scale for seven topics covering use and general satisfaction. The main finding was that more than 50% of the patients wished to continue with the novel catheter and reported increased satisfaction regarding introduction of the catheter, handling, time spent, and perception of IC, general satisfaction, and ability to cope with daily life. Kovindah and Madersbacher investigated whether a silicone catheter reused over years for clean intermittent catheterization (CIC) was safe for spinal cord injured (SCI) men [9]. A cross-sectional study was obtained from SCI men who had used CIC with a reusable silicone catheter for more than a year. The clinical outcome, especially with regard to urethral abnormalities with this reusable silicone catheter was as good as with a disposable one. However, to reuse urinary catheters, one should consider the increased risk of infection. Therefore, these authors suggest that for SCI patients in developing countries, CIC with a reusable silicone catheter may be a suitable and safe choice if one cleans and applies it. In the same way, Getliffe performed a systematic Cochrane review summarizing current evidence on the relationship between sterile single-use catheters or clean reused catheters and the incidence of UTI's [10]. 13 trials met the inclusion criteria on intermittent catheterization protocols. There was considerable variation in length of follow-up, definitions of UTI, and numbers of subjects. Attrition was a problem for several studies, and all were underpowered. Several studies were more than 10 years old, and outcome measures were imprecise, making it difficult to draw conclusions on the benefit of one catheterization method over another. They concluded that there are no definitive studies illustrating that incidence of UTI's is affected by sterile single-use or coated catheters compared to clean reused catheters. However the current research base is weak and design issues are significant. Based on the current data, it is not possible to state that one catheter method is better than another and further research on the topic is strongly recommended (LOE1).

Frequency of catheterization: This depends on many factors as bladder volume, fluid intake, postvoid residual, urodynamic parameters (compliance, detrusor pressure). Usually it is recommended to catheterize 4 – 6 times a day during the early stage after spinal cord lesion. Some will need to keep this frequency if IC is the only way of bladder emptying. Others will catheterize 1 – 3 times a day to check and evacuate residual urine after voiding or on a weekly basis during bladder retraining

Adjunctive therapy: To overcome high detrusor pressure antimuscarinic drugs or other bladder relaxants can be indicated. For those who develop a low compliance bladder, upper tract deterioration or severe incontinence, injection of Botulinum toxin in the bladder wall or surgery, such as bladder augmentation, may be necessary.

3. Complications

If catheterization is begun by patients with recurrent

or chronic UTI and urinary retention, the incidence of infection decreases and patients may become totally free of infection. If symptomatic infections occur, improper CIC or misuse often can be found. Chronic infection persists if the cause of the chronicity remains. Treatment of UTI is necessary if the infection becomes symptomatic. Lindehall et al. evaluated the rate of complications associated with catheterization and the risk of urethral lesions in girls with myelomeningocele treated with clean intermittent catheterization for a minimum of 10 years. They found that there were remarkably few problems associated with clean intermittent catheterization despite long treatment periods and use of noncoated polyvinyl chloride catheters. Clean intermittent self-catheterization and large size catheters were associated with few complications [11]. Similarly, they evaluated the risk for urethral lesions and epididymitis in boys with neurogenic bladder dysfunction treated by clean intermittent catheterization (CIC) for a minimum of 10 years and found that the overall rate of complications was low. The incidence of major urethral lesions did not increase during puberty. Self-catheterization and 12C catheter or greater seemed to be protective against major lesions [12] (LOE3). As opposed, Chen et al found that the incidence of urethral strictures increases with a longer follow-up and bladder stone formation was found to be associated with long-term use of CIC in SCI patients [13] (LOE3).

4. Health related quality of life

Oh et al aimed at determining the psychological and social status of patients using clean intermittent catheterization for neurogenic bladder according to health-related quality of life (HRQOL). They conducted a prospective trial involving 132 patients (81 men and 51 women, mean age 41.8 years, range 18 to 80 years) using clean intermittent catheterization because of neurogenic bladder secondary to spinal cord injury [14]. The 150 controls (90 men and 60 women) lived in the same region as the patients and were frequency matched to ensure equal age and sex distributions. HRQOL was measured using the Medical Outcomes Study 36-Item Short-Form General Health Survey (SF-36). Their findings suggest that patients using clean intermittent catheterization because of neurogenic bladder secondary to spinal cord injury generally exhibit a reduced quality of life in all health domains as assessed by the SF-36 (LOE2) [15].

CONCLUSIONS

- **IC is effective and safe to treat the neurogenic bladder in the short term and in the longterm. (LOE 1)**
- **Complications such as UTI are regularly seen and seem to be related to both the catheterization itself and the existing LUT condition (LOE 2)**
- **Urethral and bladder complications seem to increase in the long term (LOE 3)**
- **In order to reduce and prevent complications, appropriate materials and correct techniques should be taught and performed (LOE 3)**
- **Adequate frequency of CIC, a non-traumatizing technique and suitable materials are the key factors for a successful outcome (LOE 2)**
- **Patients using clean intermittent catheterization because of neurogenic bladder secondary to spinal cord injury generally exhibit a reduced quality of life in all health domains as assessed by the SF-36. (LOE1).**

RECOMMENDATIONS

- **It should be recommended to use IC as the first choice of treatment for those with inability to empty the bladder adequately and safely. It is a valuable tool for achieving continence in the neurogenic voiding dysfunction. (A)**
- **Proper education and teaching are necessary to permit a good outcome. (B)**
- **To prevent and reduce complications, a non-traumatizing technique (external lubricant or lubricant coated catheters) with adequate frequency of catheterization and complete emptying should be strictly performed. (B)**
- **Minimal requirements for regular once a year follow-up are history taking, physical examination, imaging, laboratory results and urodynamic tests, in order to early detect risk factors and complications. (B/C)**
- **Based on the current data, it is not possible to state that one catheter method is better than another (Grade D) and further research on the topic is strongly recommended.**

Implications for research

- There is a clear need for robust research in the area of IC, both evaluating clean vs. sterile PVC catheter use and hydrophilic vs PVC use (both sterile and reused). Researchers need to consider the design of the study if comparisons across trials are meaningful. Although cross-over designs mean lower sample size and control for within subjects variation, unless the data at cross-over point is available, these studies cannot entered into a meta-analysis. There it is recommended that journal editors who are publishing cross-over trials request that the authors include first set of data before cross-over (10).

b) Indwelling Urethral Catheters – transurethrally/ suprapubically

1. Transurethral catheterisation (ID)

a. Background

In early 19th century, a urinary catheter with a balloon bag (Foley catheter) was developed. After the World War I, the majority of spinal cord injured (SCI) as well as other neurologic patients were treated with indwelling urethral catheterization (ID) or suprapubic catheterization (SC) due to difficulty in voiding or urinary incontinence. Nowadays, intermittent catheterization (IC) is recommended for neurologic patients. Nevertheless many choose ID as a mean of treating urinary incontinence due to difficulty in performing IC or persistent leakage between catheterizations. In developing countries ID is still the method of choice for those with urinary retention or incontinence.

Studies have shown that ID causes various complications such as urethral trauma and bleeding, urethritis, fistula due to pressure effect caused by improper size of the urethral catheters and improper technique of securing the catheters, bladder and renal stones, cystitis, acute and chronic urinary tract infection (UTI), bladder neck incompetence, meatus and urethral sphincter erosion, and bladder carcinoma. Many of these complications were related to long-term use. Therefore many experts advocate removal of the urethral catheter as soon as possible, and usage of other methods such as IC or SC to decrease urethral complications. However, nowadays the complications of ID seem less, due to better materials, the use of smaller size catheters and a proper technique of securing the catheter. For CIC wet patients contemporary balloon catheter indwelling at night seems to decrease risk of febrile episode due to UTI as compared to CIC alone [16]. The contemporary balloon catheter used consisted of a reusable balloon catheter and a reservoir to inflate the balloon. The patients self-inserted the catheter every night before sleeping, and then removed it the next morning. After use, the catheter is washed with tap water, and stored in a special purpose case filled with disinfectant (LOE3). Transurethral ID needs a lot of meticulous skill and care. Materials used should be sterile and handled properly by a well-trained person. In some centers, a well-trained catheter team has proved to lessen complications related to catheterizations. It is suggested that more frequent catheter change should be performed in patients with recurrent urinary tract infections (once a week or every two weeks) (LOE 4).

The study by Pannek (LOE 3) reported 0.11% incidence of bladder cancer amongst SCI individuals (48 out of 43,561 patients) which is similar to that observed in the general population [17]. However, more than 60% of the patients with SCI initially presented with muscle-infiltrating bladder cancer. The expression of inducible nitric oxide synthase was demonstrated in patients with SC or ID by Wall et al [18] (LOE 3), a finding which may potentially lead to the sustained production of nitric oxide and its oxidative products, the nitrosation of urinary amines and the formation of potentially carcinogenic nitrosamines in the bladder. Hamid et al.[19], however, in their retrospective series, did not find bladder cancer on bladder biopsies in patients with SC I and a mean catheter time of 12.1 years.

A case of osteomyelitis of the pubis was reported by Stern et al.[20] LOE 3).

b. Antibiotic prophylaxis

Routine antibiotic prophylaxis for patients with SC or ID is not recommended. Attempts at eliminating bacteriuria associated with indwelling or intermittent catheters are generally unsuccessful [21] (LOE 4).

For prevention of UTI, general cleanliness and local hygiene should be encouraged. If the patient has a symptomatic UTI, it is important to check for catheter blockade and complications as urinary stones. Symptomatic urinary infections have to be treated with the most specific, narrowest spectrum antibiotics available for the shortest possible time.

Guidelines for selecting antimicrobial agents in SCI patients are similar to guidelines for the treatment of complicated urinary infections in the general population. Characteristics of the quinolones make them well suited for treating UTI in SCI patients [22] (LOE 4).

CONCLUSIONS

- **Transurethral ID is not a safe method for a long-term use in neurologic patients. (LOE 2)**
- **To control urinary incontinence, ID is effective if there is no blockade or urethral/bladder neck erosion (LOE 3)**
- **Catheters size 12-16F with as large a lumen as possible and smaller (5-10 ml) self-retaining balloons are recommended for adults to minimise the pressure effect on the bladder neck and to maximise time to blockage by incrustation. (LOE 4)**
- **Use of less irritating catheters and closed drainage system should be encouraged to minimise complications. (LOE 2)**
- **If available , siliconised catheters may be used with more frequent change. (LOE 3)**
- **Frequency of change largely depends on materials and size of catheter lumen e.g., every 1-2 weeks for siliconised latex catheters, every 2-4 weeks or longer for silicone or hydrogel-coated catheters. (LOE 3)**

- **The indwelling contemporary balloon catheter seems to reduce febrile UTI episodes at long-term use in CIC-wet group. (LOE 3)**
- **Antimuscarinic may be associated with improved bladder compliance, lower bladder leak point pressures, and less hydronephrosis, while infection rate, vesicoureteral reflux, renal scars, stones and serum creatinine levels are not altered. (LOE3)**

RECOMMENDATIONS

- **Whenever a transurethral catheter is applied, full silicone or hydrogel-coated catheters are preferable. (A/B)**
- **Use sterile materials and aseptic technique followed by the routine catheter care to maintain aseptic closed drainage system. (C/D)**
- **Catheters should be changed regularly, if possible, before obstruction or infection occurs. (C/D)**
- **Bladder irrigation and antibiotic prophylaxis are not recommended as a routine infection-control measure. Symptomatic UTI should be treated with narrowest spectrum antibiotic possible. (B)**
- **Patient education on daily cleanliness and hygiene care and a thoroughly urological check-up are mandatory. (C)**
- **A short-term ID during the acute phase is still a safe method for neurologic patients. (B)**
- **Long-term ID may be safe only if a careful check-up of urodynamic, renal function, and upper and lower tract imaging are performed regularly at least yearly. (B)**
- **Bladder screening for bladder cancer is mandatory especially those with ID/SC more than 5-10 years. (C)**
- **Annual cystoscopy and biopsy may be necessary for those after 10 years of ID and those with an episode of gross hematuria, chronic symptomatic UTI refractory to therapy. (C)**
- **Consider the use of antimuscarinic drugs in individuals with suprasacral lesions using chronic indwelling catheters. (C)**

2. Suprapubic catheterisation – special aspects

An alternative to indwelling urethral catheterization is an indwelling catheter placed through the lower abdomen into the dome of the bladder, called a suprapubic catheter (SC).

Overall the benefit and risks of the SC are very similar to the indwelling urethral catheter including the risk for urinary tract infection, stone formation, bladder cancer, and maintenance cost of catheter and bag. However, there are several benefits and one key disadvantage. Its advantages include: minimized risk of urethral trauma in men and women, minimized risk of urethral destruction in neurologically impaired women with even relatively short-term indwelling urethral catheters, and minimized urethral pain. The key disadvantage is that it requires a minor 'surgical' produce to insert the suprapubic catheter with potential to injure structures adjacent to the bladder, especially the large intestine [23]. The preferred insertion technique appears to be quite variable by region and country. There is no evidence that there is one best way to insert the SC.

Long-term management of the neurogenic bladder with the SC is a controversial topic in neurourology. The issue of controversy is that some rehabilitation centers across the world highly favor the suprapubic catheter as a safe and effective long-term management of the neurogenic bladder. On the other hand, a large number of experts have personal experience with suprapubic tube complications during its long-term use.

The literature on suprapubic catheterization is limited, and most of publications are 20 years or older. There are no prospective studies and no RCT's on suprapubic catheterization. The bias of single center case series is the short follow-up with a worrisome large number of patients who are lost for follow-up. It is unclear if these patients may have developed complications and have died or were treated with alternative bladder management at a different hospital.

CONCLUSIONS

- **Suprapubic catheter is a reasonable alternative to indwelling urethral catheter, but both are clearly inferior to intermittent catheterization (LOE 3).**
- **It is a safe and effective short-term management of urinary retention. (LOE 3)**
- **It is not recommended for the routine use for the long-term management of the neurogenic bladder. (LOE 2)**
- **Complications of SC are similar to that of ID, except the unique complication of bowel perforation and no urethral complications. (LOE 3)**

RECOMMENDATIONS

- **Suprapubic catheters are not recommended as a safe method for long term use in neurogenic patients. (B)**

- **Nowadays with less irritating catheter materials, improved closed drainage systems and regular urological check-up, long term complications can be decreased. Nevertheless SC is still the last resort when other methods fail or are not applicable or are not accepted by the patient. (C)**
- **One should consider patient comfort, convenience, sexuality and quality of life before prescribe SC as a long-term management for neurologic patients. (C)**

c) Condom catheter and external appliances

Background

Male patients with neurogenic bladder and chronic urinary incontinence can be candidates for a condom catheter (CC) connected to a urine or leg bag to collect the urine. However some have difficulty in applying CCs, e.g. due to overweight and/or some degree of penile atrophy or retraction.

CONCLUSIONS

- **Condom catheter still has a role in controlling urinary incontinence in neurologic male patients (LOE 3)**
- **Long-term use may cause bacteriuria, but it does not increase the risk of UTI when compared to other methods of bladder management. (LOE 3)**
- **Complications may be less if applied properly with good hygiene care, frequently change of the CC and maintenance of low bladder pressures. (LOE 3)**
- **Special attention should be paid to people with dementia (LOE 3)**

RECOMMENDATIONS
(All grades of recommendation = B/C)

- **To have better control of leakage, a more secure CC should be used, and patients should be educated and cooperative.**
- **To prevent latex allergy, a silicone CC should be used and serological examination of latex-specific IGE is recommended in addition to patient history to better identify patients at risk.**
- **To prevent compressive effects, choose proper size CC with self- adhesive.**
- **To prevent infection, a daily change of the CC could help.**
- **To prevent bladder and upper tract damage, regular bladder emptying with low bladder pressures and low post void residual should be pursued**.

3. PHARMACOTHERAPY

Detailed data on pharmacotherapy are presented in a specific chapter of the Committee on Pahrmacologic treatment. Our chapter deals only with specific issues of pharmacotherapy in neurologic patients. We strongly recommend consulting the Drug Treatment chapter for levels of evidence and recommendations. References can also be found in the ICI 2005 chapter on conservative management of the neurogenic bladder.

The principal causes of urinary incontinence in this subpopulation are neurogenic detrusor overactivity (NDO) and/or incompetence of urethral closing function. To improve urinary incontinence the treatment should aim at decreasing detrusor activity, increasing bladder capacity and/or increasing bladder outlet resistance. This picture is blurred by the occurrence of detrusor/sphincter dyssynergia which can be present concomitantly with NDO.

Pharmacologic therapy has been particularly helpful in patients with relatively mild degrees of neurogenic bladder dysfunction. Patients with more profound neurogenic bladder disturbances may require pharmacologic treatment to improve results of other forms of management such as intermittent catheterization. Although the two most commonly used classes of agents are antimuscarinic and alpha-adrenergic blockers, the drugs used for treating neurogenic bladder/urethral dysfunction should be classified as follows. (Most but not all drugs action was evaluated in neurologic patients).

Drugs for incontinence due to neurogenic detrusor overactivity and/or low compliant detrusor

a) Bladder relaxant drugs

1. Oxybutynin
2. Propiverine
3. Trospium
4. Tolterodine
5. Propantheline
6. Oxyphencyclimine
7. Flavoxate
8.Tricyclic Antidepressants
9. Solifenacin succinate
10. Darifenacin
11. Fesoterodine

b) Intravesical application

1. oxybutynin, lidocaine, nociceptin/orphanin FQ, atropine
2. Vanilloids
a Capsaicin
b Resiniferatoxin
3. Botulinum toxin

Drugs for incontinence due to neurogenic sphincter deficiency

a) Alpha-adrenergic agonists
b) Estrogens
c) Beta-adrenergic agonists
d) Tricyclic antidepressants

Drugs for facilitating bladder emptying

a) Alpha adrenergic blockers

b) botulinum toxin

c) Cholinergics

DRUGS FOR INCONTINENCE DUE TO NEUROGENIRC OAD AND/OR LOW COMPLIANT DETRUSOR

a) Bladder relaxant drugs

Antimuscarinic agents are by far the most useful drugs in the management of the neurogenic bladder: they are used to suppress NDO.

General indications of pharmacological treatment in NDO are to improve or eliminate reflex incontinence, eliminate/ prevent a high intravesical pressure and enhance the efficacy of intermittent catheterization (IC), triggered voiding and indwelling catheters. Neurogenic detrusor overactivity is mostly associated with a functional outflow obstruction due to detrusor-sphincter-dyssynergia (DSD). For the most part, pharmacotherapy is used to suppress reflex NDO completely and facilitate IC. On the other hand bladder relaxant drugs would seem to decrease detrusor-contractility also during voiding. With this situation residual urine may increase and must then be assisted or accomplished by IC. It must be stressed that with the current level of knowledge antimuscarinic therapy is not a causative treatment, but a symptomatic one.

1. Oxybutynin

Oxybutynin hydrochloride is a moderately potent antimuscarinic agent with a pronounced muscle relaxant activity and local anesthetic activity as well. In a prospective, 12-week dose titration trial of controlled release oxybutynin (OXY-XL), Bennett et al. [24] evaluated the efficacy and tolerability of higher dose oxybutynin chloride in patients with neurogenic bladder and multiple sclerosis, spinal cord injury or Parkinson's disease. A 7-day washout period was used before initiation of the starting dose of 10 mg OXY-XL. Doses of OXY-XL were increased by 5 mg at weekly intervals to a maximum dose of 30 mg per day guided by patient perception of efficacy versus side effect. At the end of the study statistically significant decreases in the number of voids in 24 hours, episodes of nocturia and incontinence episodes were observed. Residual urine remained unchanged. No patient experienced serious adverse events (LOE2). In a prospective, open label trial of 3 formulations of oxybutynin (tablets, syrup and extended release tablets), Franco et al [25] evaluated the efficacy and safety of oxybutynin in children with NDO due to neurological conditions. The effect of treatment on average urine volume per catheterization and on secondary urodynamic outcomes was evaluated. Maximal cystometric capacities increased, and mean detrusor and intravesical pressures were significantly decreased at week 24. Improvements in bladder function were consistent across all oxybutynin formulations (LOE 2).

2. Propiverine

In a randomized, double-blind, prospective multicenter clinical study, Stöhrer et al. [26] compared the efficacy and tolerability of propiverine and oxybutynin in patients with neurogenic detrusor overactivity. Propiverine and oxybutynin were equally effective in increasing bladder capacity and lowering bladder pressure. The trend for better tolerability of propiverine compared to oxybutynin achieved significance for dryness of the mouth (LOE1). Propiverine hydrochloride has also been shown to be effective in neurogenic detrusor overactivity in children and adolescents, even in some of those cases unresponsive to other anticholinergics [27,28]. The low incidence rate of adverse events evidenced a favourable risk-benefit profile of propiverine hydrochloride (LOE3).

3. Trospium

Trospium is a quaternary ammonium derivative with mainly antimuscarinic actions, it's effectiveness and safety has confirmed in meta-analysis (see reference ICI 2002). Trospium has been shown to significantly reduced the number of urinations, increased cystometric capacity and mean effective volume of the bladder, and reduced the number of urgent voiding in neurogenic patients [29,30] (LOE1).

4. Tolterodine

Tolterodine is a potent, competitive muscarinergic receptor antagonist specifically developed fro the treatment of overactive bladder. Tolterodine has a high selectivity in vitro and exhibits selectivity for the urinary bladder over the salivary glands in vivo. Several phase II study have demonstrated the efficacy and safety of tolterodine in patients with overactive bladder [32]. Ethans conducted a prospective, randomized, double-blind, crossover trial plus open-label comparative stage, aiming at comparing tolterodine with oxybutynin and placebo in people with neurogenic detrusor overactivity. Tolterodine, when used at at self-selected doses (SSDs) was comparable with oxybutynin at SSDs in enhancing bladder volume and improving continence, but with less dry mouth. Tolterodine at the recommended dosage of 2 mg twice daily improves incontinence and bladder volumes compared with placebo, and without significant dry mouth (LOE1). It seems however that larger doses of tolterodine is needed to achieve best effect on neurogenic bladder [33-34] (LOE3).

5,6,7,8. Propantheline, Oxyphencyclimine, Flavoxate and Tricyclic Antidepressants

are used by many clinicians around the world for bladder relaxation in patients with neurogenic bladder. Local reports claim good clinical effectiveness. In

literature no new data in neurogenic patients on their effect and safety have been reported since ICI 2. Flavoxate does not seem to be effective for treating detrusor overactivity (references in ICI 2005 report.

9. Solifenacin succinate

Solifenacin succinate is a newer anticholinergic drug, used once daily, which has a functional selectivity for the bladder over other organs. Solifenacin has been extensively studied in OAB [35-39] (LOE1). There is up to date no data on the effect of solfenacine in neurogenic detrusor overactivity.

10. Dariferacin

Dariferacin is a chiral diphenylacatamide tertiary amine, marketed as a water hydrobromide salt, and is a selective M3 receptor antagonist. It has been shown to have a higher degree of selectivity for the M3 receptor compared with other anticholinergics. It is extensively metabolized by the liver after oral dosing. Metabolism is mediated by CYP enzymes to its main hydroxylated metabolite. Dariferacin has been extensively studied in OAB [40-43] (LOE1). There is up to date no data on the effect of Dariferacin in neurogenic detrusor overactivity.

11. Fesoterodine

Fesoterodine acts functionally as a prodrug. It is rapidly and extensively hydrolysed by nonspecific esterases to 5-hydroxymethyl tolterodine. The conversion is rapid and virtually complete such that, after oral dosing, only the metabolite, not the parent compound, can be detected in patient plasma. This active metabolite, responsible for the antimuscarinic activity of fesoterodine is also the active metabolite of tolterodine, 5-hydroxymethyl tolterodine (5-HMT). In contrast to tolterodine, the conversion of fesoterodine to 5-HMT bypasses the CYP system, although CYP3A4 and CYP2D6 are involved in subsequent inactivation of the active metabolite. Phase 3 trials have suggested that fesoterodine is an effective and well-tolerated therapy for OAB [44-46] (LOE1). There is up to date no data on the effect of fesoterodine in neurogenic detrusor overactivity.

b) Intravesical application

1. oxybutynin, propantheline, nociceptin/orphanin FQ, atropine

Since the first use of the intravesical application by Brendler et al. [47], there have been over 100 peer review articles reporting successes of intravesical oxybutynin to treat overactive bladder and NDO. The main findings were, at least at short term follow up, an improvement of overactive bladder symptoms, including a decreasing number of incontinence episodes, an increase of maximum bladder capacity and a decrease of the detrusor overactivity in the urodynamic recordings. George et al. compared the therapeutic response of intravesical oxybutynin, propantheline, and capsaicin in the treatment of neurogenic detrusor overactivity [48]. Oxybutynin 5 mg in solution or propantheline 15 mg in solution and capsaicin were instilled intravesically in each patient. Urodynamic studies were done before and after the intravesical instillation of each drug. There was a significant difference in therapeutic response between intravesical oxybutynin, propantheline, and capsaicin in the treatment of detrusor overactivity for leak volume (LV) and leak frequency at 2nd week. When comparing responses of oxybutynin and propantheline, more subjects demonstrated improvement with intravesical propantheline than oxybutynin for reflex volume, detrusor leak point pressure, clean intermittent catheterization volume, and LV (LOE3). Up to now there is however no standard instillation protocol concerning the use of intravesical oxybutynin for overactive bladder. The doses vary between 5-30 mg diluted in 30-40 ml saline [48-49]. Also the instillation frequency is not standardized and varies between 1 to 3 times /d.

Nociceptin/orphanin FQ (N/OFQ), where F and Q represent the first and last amino acid, respectively, phenylalanine (F) and glutamine (Q), is a hepta-decapeptide that exerts several physiologic actions at both the central and the peripheral level by activating a specific G-protein-coupled receptor named nociceptin orphan peptide (NOP) receptor. Among the, animal studies have demonstrated that N/OFQ exerts a robust inhibitory effect on the micturition reflex in the rat [50]. Lazzeri et al. recently studied the feasibility, safety and efficacy of daily intravesical instillation of 1 mg of the endogenous peptide N/OFQ in a selected group of patients who performed clean intermittent catheterization for neurogenic detrusor overactivity (NDO) [51]. A total of 18 patients with NDO and incontinence on clean intermittent catheterization were prospectively randomized to receive 1 mg nociceptin/orphanin FQ in 10 ml saline or placebo (saline) at the first catheterization for 10 days. Mean daily urine leakage episodes significantly decreased from 2.18 at baseline to 0.94 during nociceptin/orphanin FQ treatment, while no significant changes were reported in the placebo group. The total mean voiding diary bladder capacity significantly increased in patient receiving nociceptin/orphanin FQ, while mean voiding diary bladder capacity remained unchanged in patients receiving placebo. The urodynamic parameters recorded during the study showed an increase in cystometric capacity and a decrease in maximum bladder pressure compared to baseline only in patients assigned to the nociceptin/orphanin FQ group. These findings support the use of nociceptin/orphanin FQ peptide receptor agonist as an innovative approach for controlling neurogenic detrusor overactivity incontinence (LOE2).

Fader et al. [52] tested the efficacy and side effect

profiles of intravesical atropine compared to oxybutynin immediate release (IR) when used by individuals with multiple sclerosis. They performed a study to determine the most effective dose of atropine. Eight participants used increasing doses of intravesical atropine (2 to 6 mg in 20 ml NaCl 0,9%) during a 12-day period. Bladder diary data showed that the instillation of 6 mg atropine 4 times daily was most effective for increasing bladder capacity (voided/catheter volumes). Afterwards they performed a randomized, double-blind crossover trial. Participants received 14 days of treatment with oral oxybutynin IR 5 mg twice daily (range 2.5 twice to 5 mg 4 times daily) or with intravesical atropine, followed by 14 days of alternative treatment. Participants recorded a bladder diary and rated side effects and quality of life. The primary outcome variable was bladder capacity. A total of 57 participants with multiple sclerosis completed the study. Average change in bladder capacity was higher in the atropine arm. Changes in incontinence events and voiding frequency were not statistically different between the arms. Changes in total side effect and dry mouth scores were significantly better in the atropine treatment arm. These findings suggest that intravesical atropine is as effective as oxybutynin immediate release for increasing bladder capacity and it is probably better with less antimuscarinic side effects (LOE2)

2. Vanilloids

Have been discussed in the ICI 2005 report, and references before 2002 are to be found there

a. Capsaicin (CAP) (see background and reference ICI 2002)

The use of capsaicin is still largely experimental and limited by the fact of prolonged and painful excitation of the sensory c-fibers. The alcoholic solvent may be a major factor in the poor tolerability of alcoholic CAP instillation, as suggested by the result of one placebo controlled study showing that side effects appeared to be the same after intravesical instillation of CAP diluted in 30% ethanol as after instillation of ethanol alone (LOE2).

b. Resiniferatoxin (see background 2002)

Resiniferatoxin (RTX) acts without the potent neuronal excitatory effect of capsaicin, and therefore elicits less discomfort. Groups comparing RTX in saline or 10% ethanol with CAP in 30% ethanol found better tolerability of RTX (see ICI 2002). The difference in tolerability of the 2 vanilloids (CAP vs. RTX) was usually attributed to the differential pungency of the 2 agents. Nevertheless, because we know the role of the solvent in the irritative effect on bladder mucosa, it is reasonable to assume that differential effects could be related to the use of different vectors. From a technical point of view the choice of the solvent is limited because of the poor hydrosolubility of CAP, imposing the use of an alcoholic, lipidic or glucidic vector. The safety of the lipidic solution could be imperfect because of difficulty of achieving complete elimination of lipidic solution from the bladder. On the contrary, a glucidic solution may represent a safe and valuable alternative to the alcoholic vector. De Seze et al. [53] compared the efficacy and tolerance of intravesical instillations of CAP and RTX using a glucidic solvent for CAP and the 10% ethanol solvent for RTX in a controlled randomized, double blind study in patients with severe urinary incontinence due to spinal cord injury. On day 30, improvement was found clinical and urodynamical respectively in 78% and 83% of patients treated with CAP vs. 80% and 60% treated with RTX. No significant difference between the 2 groups was observed. The benefit remained in two-thirds of the 2 groups on day 90. There were no differences in regard to incidence, nature or duration of side effects in CAP vs. RTX treated patients. These results once more strongly argue for the importance of accounting the role of vanilloid solute when interpreting efficacy and tolerance of vesical vanilloid instillation in detrusor hyperreflexia cases. They suggest that a glucidic solution is a valuable solvent for CAP instillation (LOE2).

RTX seems to have a beneficial effect on NDO (LOE 2). However, good randomized controlled studies are needed to determine its place in the treatment of NDO. Also the optimum doses (concentration) as well as the inter treatment intervals need to be determined

Moreover, the long-term safety of vanilloid agents, particularly concerning mutagenic and carcinogenic effects on the bladder wall is not perfectly known. The use of CAP solved in ethanol seems not to cause morphological changes in the bladder urothelium in patients receiving repeat instillation for as long as 5 years. To our knowledge the long-term safety of RTX remains unproven. Furthermore, RTX belongs to the family of tumor promoting phorbol esters, strengthening the need to ensure the safety of RTX before extending its therapeutic applications.

3. Botulinum toxin A See background ICI 2002

Botulinum neurotoxin (BoNT) decreased neurogenic detrusor overactivity in four full published LOE1 studies [54-56], one LOE2 study [57], and several LOE3 studies. Only 5 complete full publications [54-57] and three abstracts[58-60] were included in this chapter. The majority of the studies involved only participants with neurogenic bladder. Two studies had participants for which as a group, the aetiology of overactive bladder was mixed. In one LOE1 study, 59 patients with spinal cord injury and MS were enrolled in a single treatment, randomized, placebo-controlled, 6-month safety and efficacy study [54]. Patients received either BoNT-A or placebo. Injections were given into the detrusor muscle, leaving out the bladder base and trigone. Injection volume was 30 cc and 30 sites

were injected. A single administration of 200 or 300 units of Botox® into the detrusor muscle was well tolerated and more effective than placebo in reducing the frequency of incontinence episodes, enhancing bladder function, and improving quality of life.

In another LOE1 study, the use of BoNT was studied for refractory neurogenic and non-neurogenic detrusor overactivity [55]. Twenty patients were injected with either placebo (20 ml normal saline) or BoNT-B (Myobloc®, 5000 IU diluted up to 20 ml). After six weeks, treatments were crossed over. The primary outcome was the paired difference in change in average voided volumes. Secondary outcome measures included frequency, incontinence episodes, and paired differences in quality of life, as measured by the King's Health Questionnaire. There were significant paired differences in the change in average voided volume, urinary frequency, and episodes of incontinence between active treatment and placebo. There were also differences in the change in quality of life affecting five domains of the King's Health Questionnaire. This study is limited in that the study population was comprised of a mixed population of patients, with diverse aetiologies of detrusor overactivity (neurogenic and non-neurogenic). This limits the generalizability of the findings. The absence of a sustained washout period before the crossover might have biased the findings, and the low dose of BoNT-B used may have affected the duration of the results.

In another study, BoNT-A injection was compared to resiniferatoxin intravesical instillation) into the bladder in 25 patients with spinal cord lesions and concomitant neurogenic detrusor overactivity [57]. There was a significant decrease in catheterization and incontinence episodes for both treatments at 6, 12, and 18-months of follow-up. However, the BoNT injections provided superior clinical and urodynamic benefits as compared to intravesical resiniferatoxin. There were no significant side effects with either treatment (LOE1).

A recently published study compared a single injection of BoNT-A (500 units Dysport®, diluted in 25 ml saline and injected into 25 injection sites) to placebo in 31 patients with neurogenic detrusor overactivity and urinary incontinence. Time of follow-up was 26 weeks. Patients in the BoNT-A group had a significant change regarding intake of anticholinergic drugs, cystometric bladder capacitiy, maximum detrusor pressure, frequency of urinary leakage and quality of life parameters (LOE1) [61].

There is one study (LOE3) that addressed different injection technique. Karsenty et al. compared to different technique of injections of 300 units of BoNTA (Botox®) [58]. They compared 10 versus 30 injections sites and reported a significant reduction in post-procedure pain only in the group receiving 10 injections. There was no significant difference found in any other measures including incontinence episodes or cystometric capacity. In addition to the study from Schurch et al. two trials (LOE2) assessed the efficacy of different doses of Botox® (100 versus 300 and 200 versus 300) [59,60]. No study reported significant difference between the different dose and the confidence interval were wide.

The safety seems to be quiet acceptable though generalised paraparesis/fatigue has been described especially in patients with high spinal cord lesions. The effect resolves spontaneously after 4-6 weeks.

There are several major reviews coming up in literature that will highlight the actual knowledge of long-term treatment, overall safety and different techniques of application.

DRUGS FOR INCONTINENCE DUE TO NEUROGENIC SPHINCTER DEFICIENCY

Several drugs, including ***alpha-adrenergic agonists, estrogens, beta-adrenergic agonists*** and ***tricyclic antidepressants,*** have been used to increase outlet resistance. No adequately designed controlled studies of any of these drugs for treating neurogenic sphincter deficiency have been published. In certain selected cases of mild to moderate stress incontinence a beneficial effect may be obtained.

DRUGS FOR FACILITATING BLADDER EMPTYING

a) Alpha adrenergic blockers

Alpha-adrenoceptors have been reported to be predominantly present in the bladder base, posterior urethra and prostate. Alpha-blockers have been already reported to be useful in neurogenic bladder by decreasing urethral resistance during voiding (references ICI 2005 report). Only new references are mentioned here.

Tamsulosin has been shown to improve bladder storage and emptying in MS and SCI [62].

Abrams et al. [63] evaluated the efficacy and safety of tamsulosin in patients with neurogenic lower urinary tract dysfunction secondary to suprasacral spinal cord lesions in a 4-week randomized controlled trial (RCT) followed by a 1-year, open label, long-term study. A total of 263 patients were randomized to 4-week double-blind therapy with placebo, or 0.4 or 0.8 mg tamsulosin once daily. The primary efficacy parameter was maximum urethral pressure (MUP). In the long-term study but not in the RCT trial there was a statistically significant mean decrease in MUP from baseline to end point. In the long-term study tamsulosin also decreased maximum urethral closure pressure, improved several cystometry parameters related to bladder storage and emptying, and increased to a statistically significantly degree, from baseline to end point, mean voided volume based on the micturition diary. There was statistically significant improvement for the International Prostate Symptom Score Quality of Life. Both doses were effective and well tolerated. (LOE1)

b) Botulinum toxin

In a LOE1 study, the effects of botulinum toxin versus placebo was studied on DSD in 86 multiple sclerosis (MS) patients[64]. The study employed a single transperineal injection of BoNT-A, 100 units in 4 cc normal saline, or placebo, into the striated sphincter with EMG guidance. The primary endpoint was post void residual volume at 30 days. The secondary endpoints included voiding and urodynamic variables. Results showed that a single injection of BTX did not decrease post-voiding residual volume in this group of MS patients. These findings differ from those in patients with spinal cord injury and may be due to lower detrusor pressures in MS patients.

c) Cholinergics

In general, bethanechol chloride seems to be of limited benefit for detrusor areflexia and for elevated residual urine volume. Elevated residual volume is often due to sphincter dyssynergia. It would be inappropriate to potentially increase detrusor pressure when concurrent DSD exists.

CONCLUSIONS

- **Bladder relaxant drugs, including oxybutynin, propiverine, trospium and tolterodine have a documented suppressive effect on incontinence by controlling overactive bladder, thereby improving storage function (LOE 1).**
- **However, all of these drugs presently available have considerably high incidence of side effects (dry mouth, constipation, urinary retention, etc.), which limits their usage. Tolterodine, propiverine, trospium and controlled-release oxybutynin have significantly less side effects compared to immediate-release oxybutynin (LOE 1).**
- **High doses of OXY-XL seem safe and effective in patients with neurogenic bladder (LOE 3)**
- **Although the oral application is the usual way, intravesical instillation or intrarectal (oxybutynin) may be an alternative (LOE 4).**
- **Intravesical instillation of capsaicin/ resiniferatoxin has been reported to improve spinal reflex incontinence for several months after instillation (presumably blocking sensory input). Resiniferatoxin is preferable (LOE 3).**
- **Botulinum toxin injections into the detrusor muscle was reported to improve incontinence and increase functional bladder capacity in spinal cord injured patients with neurogenic DOA (LOE 1).**
- **Long-term a-adrenergic antagonists are effective and well tolerated in patients with MS and suprasacral spinal cord lesion with neurogenic lower urinary tract dysfunction (LOE1)**
- **Data on the use of botulinum toxin (BonT) for DSD are conflicting. BoNT is probably safe and effective for the treatment of DSD in spinal cord injury patients (LOE2). However, on the basis of one LOE1 study, BonT does not provide significant benefit for the treatment of DSD in MS patients,**
- **There is no adequately designed controlled study of any drug for neurogenic sphincter deficiency.**

RECOMMENDATIONS

- **Bladder relaxant agents should be recommended for the treatment of reflex incontinence evoked by neurogenic detrusor overactivity in patients in whom IC alone is unable to control it (A).**
- **Titration of the dosage of these drugs individually should be done to achieve maximum therapeutic effect and minimal side effect. If one drug is not tolerated, try another drug as it may have less side effects (C/D).**
- **BoNT should be offered as a treatment option for neurogenic detrusor overactivity (A).**
- **Vanilloid intravesical therapy still remains experimental and therefore is not recommended except within clinical trials (C/D)**
- **Further attempts for the treatment of NDO should be undertaken to develop the ideal drug in terms of good efficacy, tolerability and safety (D).**
- **For decreasing outlet resistance in neurogenic bladder a-adrenergic antagonists may be used (B/ C).**
- **BoNT may be considered for DSD in spinal cord injury patients (B)**
- **For neurogenic sphincter deficiency no effective drugs are available up to now; further research is needed (D).**
- **For detrusor areflexia no effective drugs are available up to now (IC remains the gold standard) ; further research is needed**

4. ELECTROSTIMULATION

a) Electrical Neuromodulation

1. Background

In the last decade sacral nerve neuromodulation has been confirmed as a valuable treatment option for patients with symptoms of overactive bladder. The success with sacral neuromodulation has increased the interest in other neuromodulation techniques.

The current techniques of neuromodulation for treating overactive bladder – which includes detrusor overactivity of neurologic origin - are (a) anogenital electrical stimulation, (b) pudendal nerve stimulation, (c) sacral nerve neuromodulation, (d) percutaneous posterior tibial nerve stimulation (Stoller afferent nerve stimulation, SANS), (e) magnetic stimulation and f) deep brain stimulation

It is not really known how neuromodulation works, however, there is strong evidence that neuromodulation works at a spinal and at a supraspinal level [65].For more details about possible mechanism of actions see ICI report 2005

2. Pudendal Nerve Stimulation

It has been shown that electrical stimulation of pudendal nerve afferents can inhibit bladder contractions in patients with SCI, and bladder capacity can be increased by continuous [66] as well as conditional stimulation [67] (LOE3). Implants such as the InterStim® system have made this treatment modality commercially available (see sacral nerve stimulation). Common to these implantable systems is that they use continuous stimulation. Detrusor inhibition is in principal only necessary during an involuntary contraction and, thus, stimulation could be turned off between contractions. Such a stimulation scheme could have a number of advantages. Power consumption may be decreased and, thus, extend battery lifetime. Furthermore, continuous stimulation of a reflex may lead to habituation, which would be minimized or prevented by conditional stimulation. Hansen et al.[68] examined the effect of the automatic, event driven electrical stimulation of pudendal nerve afferents on bladder capacity in patients with SCI. The study included 2 women and 14 men older than 18 years with NDO, bladder capacity below 500 ml and complete or incomplete suprasacral spinal cord injury. Detrusor pressure (Pdet) was recorded during ordinary, natural bladder filling. In a similar subsequent recording Pdet was used to trigger electrical stimulation when pressure exceeded 10 cm H2O. Of the 16 patients enrolled in this study 13 had increased bladder capacity together with a storage pressure decrease as a result of automatic, event driven electrical stimulation. During stimulated filling Pdet never exceeded 55 cm H2O. Thus, storage pressure was sufficiently low to prevent kidney damage. An average bladder capacity increase of 53% was achieved (LOE 3)

3. Chronic pudendal nerve stimulation

Direct pudendal nerve stimulation has beneficial effects on numerous pelvic floor function impairments such as urinary and/or fecal incontinence, retention, and constipation. In preceding literature the implant technique required a fairly complex and invasive surgery, although recent advances with percutaneous placement of the lead through an introducer have made the procedure much less invasive. Spinelli et al.[69] performed staged procedure similar to that of sacral neuromodulation (SNM) to place tined lead near the pudendal nerve, using neurophysiological guidance. They named this approach chronic pudendal nerve stimulation (CPNS).

Fifteen neurogenic patients (eight male, seven female) with symptoms of urge incontinence due to neurogenic overactive bladder underwent CPNS. All patients had complete neurophysiological and urodynamic evaluation at baseline and follow-up and were asked to complete voiding and bowel diary for 7 days. During screening, average number of incontinent episodes per day decreased from 7+/-3.3 to 2.6+/-3.3 ($P<0.02$, paired t-test). Eight patients became continent, two improved by more than 88% (from 9 to 1 daily incontinence episodes) and two patients reduced the number of incontinence episodes by 50%. The implantable pulse generator (IPG) was subsequently implanted in those 12 patients. Three patients without improvement did not continue to second stage. In implanted patients with 6 months follow-up, urodynamic evaluation showed an objective improvement in the maximum cystometric capacity which increased from 153.3+/ -49.9 to 331.4+/-110.7 ml ($P<0.01$, paired t-test). The maximum pressure decreased from 66+/-24.3 to 36.8+/-35.9 cmH2O ($P=0.059$, paired t-test). Eight patients reported significant improvement in bowel function (LOE3).

4. Posteror tibilal nerve stimulation

Posterior tibial nerve stimulation was described 20 years ago as a minimally invasive treatment for urge incontinence due to neurogenic detrusor overactivity (NDO) in spinal cord injury (SCI) patients. Interestingly, the site involves the Sanyijioa (Sp6) point use in Chinese acupuncture for urinary incontinence problems.

Pudendal nerve afferent (S2 to S4) are well know to suppress NDO but it is not intuitively obvious that PTN afferents should have similar effect. However, the PTN is derived from L4 and L5 and S1 to S3 nerve roots and therefore shares common roots with those serving bladder functions. In few reports, SCI and Parkinson patients have been treated with PTN because of NDO and neurogenic incontinence. PTN seems to increase cystometric bladder capacity, enhance bladder volume at which hyperreflexic contraction and associated leakage occurs [70,71] (LOE3).

b) Repetitive transcranial magnetic stimulation

Repetitive transcranial magnetic stimulation (rTMS) of the motor cortex induces a long-lasting modulation of spinal cord excitability [72]. Thus, it represents a potentially useful tool for the treatment of neurogenic urinary disturbances. Centonze et al. [73] investigated the effects of high frequency (5 Hz) excitatory rTMS over the motor cortex on LUT dysfunction in a population of 10 MS patients complaining of urinary symptoms. All but one of the patients reported an improvement of voiding phase LUT symptoms and a significant reduction of post void residual volume. In patients with pure detrusor underactivity, this finding seems to be produced by a better contraction of the detrusor muscle, with consequent increase of Pdet@Qmax and Qmax.

Notably, a similar finding was reported in female Fowler's syndrome patients after sacral neuro-modulation, a procedure that probably shares some central actions with rTMS. In patients with DSD, on the other hand, rTMS produced negligible effects, although the observation of a reduction of Pdet@Qmax seems to suggest a better relaxation of the urethral sphincter (LOE3).

c) Deep brain stimulation

1. Subthalamic nucleus deep brain stimulation (STMN-DBS)

A large proportion of patients suffering from Parkinson's disease presents with urinary dysfunction including urgency, increased frequency or incontinence as predominant symptoms [74]. Deep brain stimulation (DBS) of the subthalamic nucleus (STN) has been established as a surgical treatment of motor symptoms in Parkinson's disease patients [75]. However, data from experimental urodynamic measures in men [76] and animal models [77] have also demonstrated a significant influence of STN-DBS on urinary bladder function. In these studies, the main effect of STN-DBS appeared to be a normalization of urodynamic parameters in the storage phase with a delayed first desire to void and an increased bladder capacity. Herzog et al. aimed at investigating the effect of STN-DBS on the neural mechanisms underlying cerebral bladder control. Using PET to measure changes in regional cerebral blood flow (rCBF), 11 patients with bilateral STN-DBS were studied during urodynamic bladder filling in STN-DBS ON and OFF condition. A filled bladder led to a significant increase of rCBF in the anterior cingulate cortex, which was further enhanced during STN-DBS OFF.

A significant interaction between bladder state and STN-DBS was observed in lateral frontal cortex with increased rCBF when the bladder was filled during STN-DBS OFF [78,79] (LOE3).

2. Thalamic deep brain stimulation

The precise mechanisms underlying cerebral regulation of lower urinary tract function are still poorly understood. Essential tremor (ET) is not known to induce lower urinary tract symptoms (LUTS) or neuropathological changes in the thalamus. Consequently, DBS in patients with ET offers the unique opportunity to investigate the role of the VIM nucleus in lower urinary tract function. Kessler at al. [80] evaluated the effect of thalamic DBS on urodynamic parameters in patients with ET. Seven patients were examined (two females, five males) with ET 15–85 mo after implantation of DBS leads into the ventral intermediate nucleus of the thalamus. They compared urodynamic parameters during thalamic DBS (ON state) and 30 min after turning the stimulator off (OFF state). In the ON compared with the OFF state, there was a significant decrease in bladder volume at first desire to void (median, 218 ml vs. 365 ml, $p = 0.031$), at strong desire to void (median, 305 ml vs. 435 ml, $p = 0.031$), and at maximum cystometric capacity (median, 345 ml vs. 460 ml, $p = 0.016$). No significant differences between the ON and OFF state were detected for changes in detrusor pressure during filling cystometry, bladder compliance, maximum detrusor pressure, detrusor pressure at maximum flow rate, maximum flow rate, voided volume, and postvoid residual (LOE3).

CONCLUSIONS

- **Electrical neuromodulation mostly is not the first line treatment for neurogenic detrusor overactivity. There are some limited reports showing that it may be beneficial (LOE 3).**
- **Automatic, event driven electrical stimulation in the treatment of NDO is feasible (LOE 3).**
- **Chronic pudendal nerve stimulation is feasible. Neurophysiological guidance seems to be mandatory to place the lead near the pudendal nerve either using perineal or posterior approach (LOE3).**
- **Enhancing corticospinal tract excitability by rTMS might be useful to ameliorate detrusor contraction and/or urethral sphincter relaxation in MS patients with bladder dysfunction (LOE3).**
- **Thalamic deep brain stimulation resulted in an earlier desire to void and decreased bladder capacity, suggesting a regulatory role of the thalamus in lower urinary tract function (LOE3).**
- **STN-DBS appeared to be a normalization of urodynamic parameters in the storage phase with a delayed first desire to void and an increased bladder capacity (LOE3).**

RECOMMENDATION

- **If pharmacotherapy fails to relax the hyperreflexic detrusor, electrical neuromodulation may be optional in patients with neurogenic detrusor (C/D)**
- **Although the setup for automatic, event driven electrical stimulation is not suitable in a clinical setting, the treatment modality is promising and it warrants further investigation (D).**
- **Further studies on chronic pudendal nerve stimulation must be carried out to identify the best stimulation parameters and to verify the long term results (D)**
- **The thalamus may be a promising target for the development of new therapies for lower urinary tract dysfunction. Further investigation on this matter is critical before one speculates, that the thalamus will emerge as a target for treatment of lower urinary tract symptoms such as urinary urgency and bladder pain (D).**
- **STN-DBS might ameliorate bladder dysfunction and that this modulation may result from facilitated processing of afferent bladder information (D).**

d) Electrical stimulation of the pelvic floor musculature

1. Background (See ICI 2002 page 740)

The aim of electrical stimulation in patients with neurogenic urinary stress incontinence is to improve the function, which are strength and/or timing of the pelvic floor muscle contraction.

Electrical stimulation is provided nowadays mostly by portable battery powered stimulation. It offers a seemingly infinite combination of wave forms, frequencies, intensities, electrode placements etc.

In patients with incomplete denervation of the pelvic floor muscle and of the striated sphincter, electrical stimulation via anal or vaginal plugs performed over months, may improve pelvic floor function, and may thus improve incontinence. The incompleteness of the lesion should be as such that the patient is able to contract voluntary the pelvic floor, even if such contraction is weak.

CONCLUSIONS

- **Although from the theoretical point of view and based on limited personal clinical experiences electrical stimulation via anal or vaginal plugs could be able to improve the strength of pelvic floor musculature, including that of the striated sphincter muscle, there is no study published which deals with this matter (LOE 4)**

RECOMMENDATION
(Unchanged since ICI 2002)

- **In patients with incomplete denervation of the pelvic floor muscle and the striated sphincter, electrical stimulation via anal or vaginal plugs performed over months, may be an option to improve pelvic floor function, thus improve incontinence. The incompleteness of the lesion should be as such that the patient is able to contract voluntary the pelvic floor even if this is weak (C/D)**

e) Intravesical electrical stimulation (IVES)

Background (read ICI 2002 page 741 and following)

The afferent stimuli induced by IVES travel along afferent pathways from the LUT to the corresponding cerebral structures. This “vegetative afferention” results in sensation of bladder filling/urge to void, with subsequent enhancement of active contractions, and possibly also in voluntary control over the detrusor. Feedback training is mediated by enabling the patient to observe the change of the detrusor pressure on a water manometer, which enables the patient to notice when a detrusor contraction takes place. This also facilitates voluntary control.

The technique involves a catheter with a stimulation electrode, introduced into the bladder and connected to the stimulator. Saline (0,9 %) is used as the current leading medium within the bladder. The neutral electrode is attached to the skin in an area with preserved sensation, usually in the lower upper abdomen.

Intravesical electrical stimulation of the bladder (IVES) is still a controversial therapy for patients with neurogenic detrusor dysfunction.

It is worthwhile to apply intravesical electrostimulation, bearing in mind inclusion and exclusion criteria, especially to verify functional afferent fibers within the bladder and the cortex. Intravesical electrotherapy is able to improve neurogenic bladder dysfunction, primarily by stimulating a-delta mechanoafferents inducing bladder sensation and the urge to void and consequently increasing the efferent output with improvement of micturition and conscious control. Therefore IVES is the only available option to induce/improve bladder sensation and to enhance the micturition reflex in incomplete central or peripheral nerve damage. However, proper indication is crucial and this type of therapy should only be applied in those with afferent fibers between the bladder and the cortex, proved by the evaluation of viscerosensory cortical evoked potentials. If these conditions are respected, IVES can be effective. In ICI 2002 30 studies about IVES have been reviewed. The conclusions for this consultation are not different from what was given in 2002.

Techniques of electrical stimulation involving surgery are to be found in the surgery section.

CONCLUSIONS

- **Basic research during the last decade has proved the underlying working concept of IVES (LOE 3)**
- **The results reported in the literature are controversial, mainly because of different inclusion and exclusion criteria (LOE 3).**
- **In the only sham-controlled study the treatment period is too short and the inclusion and exclusion criteria are not really defined (LOE 3).**
- **The alternative may be either life long intermittent catheterization or bladder augmentation. In this regards IVES is cost-effective (LOE 3)**

RECOMMENDATIONS

- **Intravesical electrotherapy is able to improve neurogenic bladder dysfunction, inducing bladder sensation and the urge to void and consequently increases the efferent output with improvement of micturition and conscious control in patients with incomplete central or peripheral nerve damage. However, proper indication is crucial and this type of therapy should only be applied in those with afferent fibers between the bladder and the cortex, (B/C)**
- **IVES is the only available option to induce/improve bladder sensation and to enhance the micturition reflex in patients with incomplete central or peripheral nerve damage. (B)**
- **Selection of patients is crucial and IVES should be applied only if afferent fibers between the bladder and the cortex are still intact and if the detrusor muscle is still able to contract. If these premises are respected, IVES is effective. (B)**
- **The ideal indication is the neurogenic hyposensitive and hypocontractile detrusor (C)**

IV. SURGICAL TREATMENT

1.SACRAL NEUROMODULATION

Literature survey with the words neurogenic bladder; spinal cord injury; spina bifida; meningomyelocoele; multiple sclerosis, sacral neuromodulation

Two indications for neuromodulation are clearly valid in urology: urinary incontinence (for overactive bladder syndrome) and chronic urinary retention (aside from vesicosphincteric dyssynergia) [1]. We will not discuss in detail the principles of these treatments and their modalities, which are covered in detail in a specific committee report of this ICI. We will focus solely on the possible application of sacral neuromodulation in patients with neurological bladder dysfunction symptoms.

a) Hypotheses on the modes of action of neuro-modulation

The first effects of electricity on the bladder were reported during electro stimulation treatment of pelvic floor muscles (with the aid of electrodes situated in the anus, the vagina, on the penis...) during urinary incontinence reeducation [2-6]. Inhibition of bladder contractions by electrostimulation was seen. Tanagho and Schmidt, the pioneers of neuromodulation, attributed the benefits of neuromodulation in urinary incontinence to a hypertrophy of the pelvic muscles allowing better efficacy and better control [7]. Now, it has long been known that voluntary contractions of the pelvic floor muscles cause a reflex along the somatic afferent branches of the pudendal nerve that leads to relaxation of the bladder. However, such explanation seems simplistic and poorly explains other reported effects of urinary neuromodulation (in the treatment of vesical hypocontractility or pelvic pain). The most widely held hypothesis today is that neuromodulation allows a restoration of normal vesical reflexes [8] [9] [10](LOE4). This hypothesis explains that the stimulation can inhibit the guarding reflex pathway and restore normal urination or turn off supraspinally mediated hyperactive voiding by blocking ascending sensory pathways and therefore decreasing incontinence. The role of cortico-subcortical structures was recently emphasized in studies of incontinent [11, 12] (LOE4) or retentive patients [13](LOE4).

Regardless of the hypothesis authors agree that the somatic afferents are the vectors for neuromodulation signals. Actually, the visceral nerve fibers cannot be activated by the intensities normally used today with this technique [14](LOE4). Despite data obtained in animals [15](LOE4), it seems that neuromodulation cannot be effective in patients with a non functional peripheral nerve circuit.

b) Sacral neuromodulation in the treatment of reflex urinary incontinence in patients with a neurological bladder dysfunction

There is little in the literature concerning sacral neuromodulation (SNM) in this specific indication. Many studies recorded results for incontinence and for retention at the same time, without always separating the results.

Since the technique's first stages, Vodusek [5, 6](LOE4) reported that non-muscular electrical stimulation of the sacral somatic afferents can induce bladder inhibition in patients who present with detrusor overactivity secondary to a medullar lesion, be it due to trauma or to multiple sclerosis (MS).

Two points must be kept in mind when treating patients with neurological bladder:

- the disappearance of wettings between catheterizations can be considered a success by itself in patients who have already used intermittent catheterization (however, in able-bodied patients treating retention with intermittent catheterization is most often considered a failure);
- On the other hand (especially, for example, in comparison with botulinum toxin injections), neuromodulation does not systematically require the use of intermittent catheterization. If this is the case, then stopping the neuromodulation current quickly causes cessation of bladder paralysis; the treatment's reversibility is therefore a strong point that must be considered when devising a therapeutic plan.

The main published series are summarized in **Table 2.** Author definitions for neurological pathology differed widely: some authors considered a history of pelvic surgery as a possible etiology while others included only patients with medullar neurological lesions. Despite this, several points considering the neurological etiology of the bladder dysfunction can be discussed.

A majority of the authors consider that a diagnosis of multiple sclerosis is not a contra-indication for neuromodulation [10, 16, 17](LOE3-4). However, it seems important to propose this treatment only in patients who present with a stabilized form of multiple sclerosis. In addition, patients must be clearly informed that the results of neuromodulation may be altered by the evolution of their underlying illness.

Patients with incomplete medullar lesions, whether of traumatic or other origins, may benefit from neuromodulation [10, 18-23](LOE3-4). On the other hand, all authors agree on excluding patients with complete medullar lesions from neuromodulation's scope of application. This attitude rests upon a cluster of arguments. First, the presumed modalities of neuromodulation's actions, such as this, were given above (LOE4). In addition, the clinical data, especially from the Hohenfellner series [20](LOE3), support among others those reported by Schurch et al in 2003 [24](LOE4). These authors published a study in which they recorded external anal sphincter (EAS) electromyographic activity caused by stimulation of the S3 sacral root during a PNE test in three patients who presented with detrusor hyperactivity and vesicosphincteric dyssynergia at the same time secondary to a complete traumatic medullar lesion. They describe a reflex response with early and late latency in the three patients. They also demonstrated that the EAS contraction observed during the PNE represented an indirect motor response mediated by the afferent nerves towards the spinal cord. Despite the recording of an EAS motor response in the three patients, they did not obtain any urodynamic or clinical effect. This suggests the participation of supraspinal neuronal centers— spino-bulbo spinal pathway—in the SMN mode of action. However, these data are contradicted by an experimental study using bilateral neuromodulation in the cat [15] (LOE4).

The use of chronic neuromodulation of the pudendal nerve, appears promising [23] (NP3). Pudendal nerve stimulation and electrode positioning were carried out under neurophysiological monitoring (using a St. Mark's electrode) in order to guide the electrode in Alcock's Canal as close as possible to the pudendal nerve. Electrode implantation was carried out by a rear approach under local anesthesia according to the method described by the same authors in 2003 [25, 26]. Naturally, these short term results must be confirmed in a larger prospective patient sample. On the other hand, a recent anatomical study [27] demonstrated that the technique for implanting electrodes at the pudendal level can be slightly risky (NP4).

Guys et al [28] determined sacral neuromodulation results to be encouraging. The authors demonstrated significant but limited urodynamic differences between implanted and children without implant (LOE3). However, the clinical translation of these modifications has not been reported. It must be emphasized that, in the absence of electrodes adapted to child sizes, the study was carried out using an implant that was put in use immediately without a test period. Moreover, the utilization of percutaneous electrodes is no longer possible. This necessitates a surgical placement attaching the electrode to the sacral periosteum. Frequent displacements in adults have been seen. A

Table 2. Results of sacral neuromodulation (test and implantation) in neurogenic patients. NP: Not precised, NA: Not applicable; LOE: Level of evidence MS: Multiple sclerosis.

Authors	LOE	Year	n (neurogenic bladder)	Follow-up(months)	Neurological Pathology	Type of trouble	Number of patients tested	Test success Criteria	Number of implantation	Success criteria after the implantation	Number or percentage of success after the implantation at the end of the study
Ruud Bosch et al [17]	4	1996	5(5)	6	MS 5	Incontinence	NA	>50%	5	>50%	4/5
Ruud Bosch et al [18]	4	1998	6(6)	24	MS 5 Incomplete SCI 1	Incontinence	NA	>50%	6	>50%	5/6
Chartier-Kastler et al [10]	4	2000	9(9)	43,6	MS 5 Myelitis 1 Vascular myelitis 1 SCI 2	Incontinence	23	>50%	9/26	>75%	7/9
Spinelli et al [19]	4	2001	196(10)	12	Discal hernia 5 MS 1 Incomplete SCI 2 Cerebral lesion 1	Incontinence Retention	NA	>50%	196(10)	>50%	Retention: 66% Incontinence: 50%
Hohenfellner et al [20]	3	2001	27(27)	54	SCI 9 Myelitis 5 Cerebral lesions 2 Discal hernia 7 Pelvic surgery 4	Incontinence Retention	27	>50%	12	>50%	1/12
Scheepens et al [21]	4	2002	211(24)	NA	Incomplete SCI 9 Caudal syndrome 5 Stroke 3 MS 6 Spina 1	Incontinence	211	>50%	NA	NA	NA
Bross et al [22]	3	2003	24	NA	Pelvic surgery 5 Ependymoma A Cerebral tumours 7 Discal hernia 5 Polyradiculoneuritis 6 Spina bifida 1	Retention	24	>50%	8/24	NP	NP
Guys et al [28]	2	2004	21	12	Spina bifida 13 Partial sacral agenesis 2 SCI 2 Tumour 2 Various 2	Incontinence	NA	NA	21	>50%	NP
Spinelli et al [23]	3	2005	15(15)	6	SCI incomplete 7 Various Medullar lesions 8	Incontinence	15	>50%	12/15	NP	NP
Wallace et al [16]	3	2007	33(33)	12,4	MS 16 Parkinson 6 Spina bifida 2 Stroke 2 Other 6	Incontinence Retention	33	>50%	28/33	>50%	NP (3 neuromodulators removed)

multicenter study on a larger patient population with more severe neurological lesions was done. Essentially, they estimate that the lack of results, especially in the urodynamic study, was due at least in part to the severity of neurological conditions in the population studied.

Despite these encouraging short term results reported by different authors in reflex incontinence secondary to neurological bladder dysfunction, the series published by Hohenfellner et al [20](LOE2) incites some caution. It demonstrates that despite a positive test in about half of the patients tested, long term (54 months) results were poor in almost all patients (1/12 had neuromodulation efficacy).

d) Criteria predicative of successful neuromodulation tests in patients with reflex incontinence secondary to a neurological bladder dysfunction

In 2002 Scheepens et al [21] reported their results of patients tested in their department (six incomplete medullar injuries, five patients with cauda equina syndrome, six with multiple sclerosis, and one with myelomeningocele). They found two prognostic factors for poor response (LOE3): The duration of the symptoms (more than seven months in this study) and the existence of a neurological cause for bladder dysfunction. Neurological patients with a very localized and incomplete nervous condition were the most successful. Patients with herniated disc surgery had a greater chance of good response. Patients with complete medullar lesions were *a priori* poor neuromodulation candidates, as were patients with large sacral lesions.

In general, it is the conviction that urodynamic tests carried out when the electrode is placed are not of value for predicting neuromodulation results. Moreover clinical results of neuromodulation do not necessarily correlate to urodynamic results. Bosch indicated in his series [18] that almost half of the patients considered to have been cured kept a certain degree of bladder overactivity. Essentially, the only publication to find parallelism between urodynamic test data and clinical data was carried out only on injured patients with a neurogenic bladder [10](LOE4). In this particular subgroup of patients, urodynamic monitoring during the acute test may have a benefit. In 2001 Chartier-Kastler [29] et al published the results of a prospective study (NP2) concerning the evolution of urodynamic parameters during the acute phase of the PNE test in 14 patients who presented with a neurogenic detrusor hyperactivity (DH) with UUI (urge urinary incontinence). The authors concluded that the acute phase of PNE was accompanied by a significant change in urodynamic parameters in more than 2/3 of the patients, and that this should be a possible means for selecting patients who present with neurogenic DH who are likely to benefit from the PNE chronic phase. However these promising results are not as yet confirmed.

e) Neuromodulation results in patients with urinary retention in patients with a neurological bladder dysfunction

There are less publications on the urinary retention (especially Fowler's syndrome) than on urinary incontinence [22, 30-33].

The only study which reported specific results for neurogenic bladders is from Hohenfellner et al [20](LOE3), in which a subgroup of 11 patients had bladder retention problems. Of these patients, three were implanted and there were temporarily satisfactory results in only two. Several years previously the same author published an interesting study on the benefit of bilateral pudendal neuromodulation, especially in patients with urinary retention [34](LOE4). The preliminary results did not appear to have been confirmed in the long term.

It seems that neuromodulation has a marginal place in retention patients with neurological bladder. Patients need to be clearly informed of the high risk of failure. It is also necessary to be especially prudent in patients with cauda equina sequel, who may have the illusion of recovering urination by simply making a greater abdominal push to evacuate their bladder. In reflex incontinence, patients with complete spinal cord or cauda equina lesions are poor candidates (LOE4). Before attempting sacral neuromodulation, patients also have to be informed that intermittent self-catheterism remains the best therapeutic option in the case of urinary retention in patients with a neurological bladder dysfunction.

RECOMMENDATIONS

- **Sacral neuromodulation can have an inhibitory effect on neurological detrusor hyperactivity. (C)**
- **While sacral neuromodulation has a place in the care of neurological urinary incontinence or neurological urinary retention, the proportion of patients whose condition is improved is much less than in non-neurological pathologies (B).**
- **The definition of the best indications for sacral neuromodulation (neurological illness) in the care of vesicosphincteric dyssynergia in neurological bladders is still imprecise (D).**
- **Utilization of neuromodulation in neurology presumes a urodynamic evaluation and carrying out a clinical test under sacral electrode (C).**
- **New neuromodulation techniques may allow further improvement of results from the use of neuromodulation in neurology (medial pudendal nerve or pudendal nerve) (D).**

2. SURGERY FOR INCONTINENCE ASSOCIATED WITH POOR BLADDER EMPTYING DUE TO DETRUSOR UNDERACTIVITY

Search for neurogenic bladder; spinal cord injury; spina bifida; myelomeningocele; multiple sclerosis; sphincterotomy; stent

Introduction

In some cases, incontinence in neurological patients can be aggravated by deficient bladder emptying and retention. Two mechanisms can be involved: ***detrusor sphincter dyssynergia*** (DSD) or ***bladder hypo contractility.*** This chapter focuses on alternatives that could be proposed to the patient in this situation, when conservative management fails.

a) Surgical treatment of detrusor external sphincter dyssynergia

Detrusor sphincter dyssynergia (DSD) is a characteristic feature of suprasacral and infrapontine lesions.

The aim of **sphincterotomy** is to produce reflex micturition into a condom catheter, thus protecting the upper urinary tract. For the last thirty years, endoscopic sphincterotomy has been the technique of choice for patients who cannot or do not want to do clean intermittent catheterization. It is invasive, irreversible and the patient has no adaptation period [1, 2](LOE3). This explains the recent development of prosthetic sphincterotomy using a urethral endoprosthesis (or stent).

1. Indications and contra-indications of sphincterotomy

Indication supposes a diagnosis of a neurological cause of DSD that is complicated by hydronephrosis, vesicourethral reflux, autonomous hyperreflexia or repeated urinary infections secondary to poor bladder voiding. Patient should have failed or refused intermittent catheterism.

2. Main contra-indications are [3, 4]:

- Impossibility to retain a condom catheter. **All sphincterotomy techniques, including stenting, are contra-indicated for men who cannot retain a condom catheter (and *a fortiori* for women).** A **s**emi-rigid penile prosthesis can be placed to help retain the condom catheter [5](LOE3). However, patients must be informed that there is a 20% to 30% risk of erosion and infection of the penile prosthesis for those with spinal cord injury, as opposed to only 2.7% in the general population [6, 7] (LOE3).
- Detrusor acontractility or hypocontractility. **Patients with spinal cord injury and no reflex detrusor contraction during urodynamic tests are poor candidates for the various techniques of sphincterotomy.**
- **Patients who wish to father children and are candidates for vibro/electro-ejaculation and an artificial insemination program.**

3. Endoscopic sphincterotomy

Emmett [8] first described endoscopic sphincterotomy in 1948. He performed cervico-prostatic incisions in patients with spinal cord injury, but later realized that the problem lay in the striated sphincter. External sphincterotomy was performed in 1958 by Ross *et al*. [9]. They carried out heavy cold-blade surgery and placed a catheter (CH 22 to 26) for tamponade since nearly all patients required transfusion (one of the ten patients in the series died after surgery).

A few attempts at surgical sphincterotomy via the perineal and subpubic myotomy routes were tried later. The complexity of these interventions, together with frequent and serious complications, explains why they were abandoned [10] [11]. Sphincterotomy with electrocoagulation was finally found to be the best technique.

a. Endoscopic sphincterotomy morbidity

The most frequent morbidity is post-operative hematuria which can be abundant and sometimes difficult to control, requiring transfusion in 2-13% of patients (see **Table 3**, LOE2-3). Twelve o'clock sphincterotomy seems to offer the lowest risk of hemorrhage, with three and nine o' clock sphincterotomies entailing the highest risk [12] (LOE4).

Post-operative impotence is also a common complication. Rates of up to 56% were reported in early series [13-16](LOE3). More recent series (table1, LOE 2-3), most using a median, or slightly deviated incision, have not seen an affected sexual function. However, it should be noted that the population concerned may have many other reasons (neurological, psychological, etc.) for suffering from erectile dysfunction.

When sphincterotomy is accompanied by complete incontinence there are obvious reasons for psychological difficulties during intercourse. This issue must be discussed with the patient before surgery. In our experience, the fear of this sequel sometimes causes the patient to decide against surgery and is a reason why we propose incontinent prosthesis as first-line therapy, to enable the patient to simulate the effects of surgery.

If striated sphincter section fails, the patient must be checked and the possibility of bladder neck sclerosis investigated. Depending on the particular series, this problem is seen in from 2 to 21% of patients .Section of the bladder neck may then improve voiding, but will result in permanent incontinence. Before surgery, the surgeon must make sure that the patient accepts this situation and can use a condom catheter.

Table 3. Results of endoscopic sphincterotomy (LOE: Level of evidence; NK: Not known; PVR: Post-Void Residue)

Authors	Number patients	LOE	Mean Follow-up (months)	Success criteria
Chancellor *et al.* 1999 [40]	26	2	24	- PVR decrease - Hydronephrosis, VR reflux decrease (100%, 100%) - Improved micturition comfort (80%) - Improved autonomous hyperreflexia (100%)
Catz *et al.* 1997 [49]	32	3	NP	- Significant decrease in PVR - Decrease in infections (74%) - Decrease in hydronephrosis, reflux (66%, 40%) - Improved autonomous hyperreflexia (100%)
Perkash *et al.* 1998[42]	37	2	9	NK
Fontaine *et al.* 1996[50]	92	2	20.6	- Decrease in hydronephrosis, reflux (100%, 90%) - Significant decrease in PVR, micturition pressure - Decrease in infections (74%) - Improved micturition comfort (73%) - Improved autonomous hyperreflexia (93%)
Noll *et al.* (1995) [1]	105	3	59	No statistical study, but: - Improved autonomous hyperreflexia (42 to 17%) - Decrease in mean PVR (180 to 70 ml) - Decrease in micturition pressure (from 97 to 37 cm H2O) - Decrease in frequency of symptomatic urinary infections (8.1 to 3.6 per year)
Rivas *et al.* 1995 [41]	22	2	12	- Improved autonomous hyperreflexia (44%) - Significant decrease in PVR, micturition pressure - Decrease in hydronephrosis (40%)
Riccotone *et al.* 1995[19]	11	3	121	- 91% recovery from autonomous hyperreflexia - 82% patients needed at least one repeated sphincterotomy
Juma *et al.* 1995 [2]	63	3	132	- Renal function (creatinine): normal in 97% of patients - on X-ray, 30% of patients showed upper urinary tract impairment. - 2/3 patients had more than one sphincterotomy
Vapnek *et al.* 1994[18]	16	3	39	- 31% required repeated sphincterotomy - 50% failure rate (sub-pubic catheter placed)
Namiki *et al.* 1984[51]	9	4	3	- PVR < 50 (100%)
Ruuru *et al.* 1982[52]	11	4	NS	- Subjective improvement in micturition comfort (56%) - Improved autonomous hyperreflexia (100%)
Carrion *et al.* 1979 [53]	60	3	12	- Reflux disappeared (86%) - Significant decrease in reflux: 75%

b. Results of endoscopic sphincterotomy

Results are summarized in Table 2 (LOE2-3). Any analysis is made difficult by the absence of univocal criteria of success. Some patients are improved by sphincterotomy, even with a 200 ml residue. Most authors use indirect urodynamic criteria to evaluate success (decrease in bladder pressure during micturition, decrease in PVR). The most obvious result is the improvement in autonomic dysreflexia observed in tetraplegic patients. It also appears that the intervention reduces the rate of symptomatic urinary infections. However, the patient must be informed that surgery will not prevent the chronic bacteriuria so often suffered by these patients [17]. The reported results concerning resolution of hydronephroses and vesicorenal reflux differ, and in each series, there are very few patients. Another essential point, well known in practice but rarely reported, is the recurrence of neurogenic DSD in many patients [2, 18, 19] (LOE3). Riccotone *et al* (LOE3) [19] reported 82% recurrence of symptoms after ten years of follow-up. Juma *et al* [2] (LOE3) report similar results after eleven years, with patients undergoing an average of 1.7 sphincterotomies, and about 30% of patient having some impairment of the upper urinary tract. Patients who have undergone this surgery must therefore be regularly monitored to detect any distension of their upper urinary tract.

4. Prosthetic sphincterotomy

In 1990, Shaw *et al*. were the first to propose using a wire mesh stent (Urolume™) to treat patients with spinal injury presenting with DSD [20] (LOE3). Since then, various stents have been used.

Table 4 lists the types of stent used for DSD, according to classification criteria [21, 22].

They can be placed in various sections of the urinary tract: prostatic urethra, through the striated sphincter or more distal in the sub-sphincteric urethra. Our review is limited to placement through the striated sphincter for which there are two solutions: temporary or permanent stents.

a. Temporary prosthetic sphincterotomy

Temporary stents make it possible to carry out a therapeutic test to check the feasibility of condom catheterization, check that placing a foreign body in the urethra does not induce autonomic dysreflexia and ensure the patient accepts the mode of micturition. Moreover, during this trial period, it is possible to study how the bladder empties in the seated position, assess the necessity of a combined treatment for smooth muscle sphincter dyssynergia at the level of the bladder neck. Moreover, as this treatment is simple and reversible, it is possible to propose it very early to the patients, rendering the patient autonomous with regard to carer-assisted catheterization, if this were the prior mode of micturition and leaving the possibility to discuss any fertility and sexual issues, and considering the possibilities of preserving sperm.

Finally, for patients with spinal cord injury, the aims of early temporary stent placement (within six months of trauma) are as mentioned above, but with the

Table 4. Urethral stents used in neurogenic DSD

Temporary stents					
Stent	Expansion method	Size		Material	Maximal duration (months)
		Caliber (F)	Length (mm)		
Not specific to the striated sphincter					
First-generation					
Urospiral™ [54]	Non expandable	21	40-80	Stainless steel	<12
IUC™[55]	Non expandable	16-18	25-80	Polyurethane	<6
Second-generation					
Memokath™ [56]	Heat	22/34	30-70	Nitinol	<36
Specific to the striated sphincter					
Diabolo™ [23]	Self-expansion	18	38	Medical steel	>12

Permanent stents				
Stent	Expansion method	Size		Material
		Caliber (F)	Length (mm)	
Urolume™ Wallstent[57]	Self-expansion	42	20-40	Steel alloy
Titan™ [58]	Balloon	43	19-58	Titanium
Memotherm™ [59]	Heat	42	20-80	Nitinol
Ultraflex™ [60, 61]	Self-expansion	42	20-50	Nitinol

theoretically added advantages of waiting for recovery of upper limb motility to enable self-catheterization, decrease the risk of nosocomial infection during rehabilitation by reducing carer-assisted catheterization, and relieve nursing load during rehabilitation. The last two points, though logical, are yet to be proved by relevant studies. After using a temporary stent, the patient may choose his mode of micturition; i.e., return to his former state, change to an identical stent, depending on the known life span of the temporary stent, replace by a permanent stent or choose surgical sphincterotomy.

By definition, temporary stents should be self-retaining, easy to remove and must not epithelialize. Apart from the temporary stent Diabolo™, which is under assessment [23], no temporary stent is specific for the external urethral sphincter. The results of two types of temporary stenting (test) for incontinence have been published in the same series[24] (LOE3). In a retrospective study of 147 patients, the authors demonstrated a significant effect on incontinence throughout the mean ten month test period, with very low morbidity (15%). The temporary stents were removed easily from all patients without sequellae. After this period, 62.6% of patients chose permanent sphincterotomy, usually by means of a permanent stent. During the study, the authors abandoned the first used stent (Nissenkorn™), preferring a temporary stent currently being developed, Diabolo™.

Memokath™ stent is another device that has been studied in neurological patients[25-29](LOE3-4). Several authors report complications (38-100%) using this stent, which seems to induce a lot of bladder stones and to be quite difficult to remove especially if it is left longer than 18 months.

b. Permanent prosthetic sphincterotomy

Permanent stents are designed to integrate the urethral wall [30]. They resist the striated sphincter and prevent it closing during reflex contraction. They can be removed if necessary, or at the patient's request, with recovery of striated sphincter contraction [31, 32].

Permanent stents are made of biocompatible materials such as nitinol (a nickel and titanium alloy) and titanium. They usually consist of a mesh comprising a single (Urolume™) or several threads (Ultraflex™). None of the stents are specifically adapted for the urethral striated sphincter. Three have been reported for treating neurological patients with DSD: Urolume™, Memotherm™ and Ultraflex™. All can be placed under local anesthesia. **Table 5** summarizes the principal series published on these devices. Only Urolume™ was studied according to strict prospective criteria [17](LOE1-2). Using stringent clinical and statistical methods, they classified the stent as LOE 1 for effectiveness and morbidity in DSD with a 5-year follow-up. 160 patients with spinal cord injury (mean age: 36.3 years; standard deviation = 12.1 years) in 15 North American centres, were treated prospectively with Urolume™ for DSD. Urodynamic parameters for micturition pressure, PVR and functional bladder capacity were measured before treatment and then 1, 2, 3, 4 and 5 years afterwards. Mean micturition pressure, the primary criterion, was significantly lower

Table 5. Results of the main series on sphincterotomy using urethral stents

Authors	Stent	Year	LOE	n	Efficacy (%)	Mean follow-up (Months)	Compli-cations	Migration
Mehta [27]	Memokath	2006	3	29	89	21	23	42
Hamid [25]	Memokath	2003	3	25	89	20	28	48
Vaidyanathan [29]	Memokath	2002	4	10	90	20	10	100
Low [26]	Memokath	1998	3	24	54	16	33	38
Shah [28]	Memokath	1997	3	14	78	24	NA	NA
Game [24]	Nissenkorn/Diabolo	2007	3	147	NR	10	29	30
Denys [61]	Ultraflex	2004	3	47	81	19	22	15
Juan Garcia [62]	Memotherm	1999	3	24	100	15	16	17
Rivas [38]	Urolume/ vs sphincterotomy	1994	2	46	79	16	15	0
Chancellor [17]	Urolume	1999	2	160	84	60	28	20
Chancellor [40]	Urolume/ vs sphincterotomy	1999	1	54	81	24	9	0
Hamid [63]	Urolume	2003	3	12	77	144	NR	16

5 years after stenting. PVR decreased significantly and was maintained after 5 years. Mean bladder capacity remained constant. Hydronephrosis, suffered by 28 patients before surgery, disappeared in 22 (78.6%) and was improved in the others. Autonomous hyperreflexia resolved in 70% of cases. The indwelling catheters of 63 of the 86 (84.9%) patients catheterized before surgery could be removed. The percentage of positive urine cultures remained unchanged after stenting. No case of peri- or post-operative bleeding, soft tissue erosion or bladder lithiasis were observed during the study. One case of prosthetic incrustation occurred during the first year; three during the second year; three during the third year; two during the fourth year and five in the fifth year. Urothelial reaction was reported in 44.4% of cases, but 93.3% of these were mild and none required treatment. No erectile dysfunction was reported. Stents had to be removed from 24 patients (15%), four of whom received new implants. 80% of the patients considered their situation improved by stenting, and 84% of physicians considered the treatment effective. 47 patients required supplementary treatment on the bladder neck (endoscopic section in 20 cases). In the mid-term, prosthetic sphincterotomy using a Urolume™ stent appears to be satisfactory. However, over the long-term, the situation is not so clear. It is not always easy to remove the stent, especially from patients who have not been monitored regularly. Some teams report highly complex surgery for stent removal, especially in the event of associated urethral stenosis [33-36] (LOE3).

5. Should patients be offered prosthetic or endoscopic sphincterotomy?

Endoscopic sphincterotomy is the preferred standard treatment for DSD, where clean intermittent catheterization cannot be performed. The superiority of a new procedure can only be demonstrated by a randomized clinical study with sufficient follow-up. Two prospective studies were carried out in the US in 1994 by Rivas and Chancellor and indicated that prosthetic sphincterotomy was at least as effective as standard sphincterotomy in patients with spinal cord injury, and offered advantages in terms of morbidity, duration of hospitalization and cost [37, 38]. The two studies were not randomized. Follow-up was too short (mean: 15 months), introducing a bias in the case of Chancellor's study. He concluded that external sphincter balloon dilatation was as effective as endoscopic and prosthetic sphincterotomy. After sufficient follow-up, external sphincter balloon dilation was abandoned because it was ineffective in the long-term [39].

A prospective, multicenter, randomized study comparing endoscopic sphincterotomy with prosthetic sphincterotomy was published in 1999 by Chancellor and Rivas, using the Urolume™ stent [40]. Fifty-seven patients in three specialist spinal cord injury centers were included. The study concluded that prosthetic sphincterotomy was as effective as endoscopic sphincterotomy and required shorter hospitalization. As we have already reported, these findings are relevant only for the short and medium-term. The long-term outcome of prosthetic sphincterotomy for incontinence remains unreported. At present, it is vital that stented patients be monitored carefully at least once a year during the years following implant surgery.

6. Other sphincterotomy techniques

As well as prosthesis placement, alternative techniques to surgical sphincterotomy have been reported.

Two authors reported using Nd-YAG lasers for sphincterotomy [41, 42]. Although no randomized study has been conducted, comparison with results from the literature (with very short follow-up), suggests that these techniques are not as good as standard endoscopic sphincterotomy. However, the reported morbidity (particularly hemorrhage) was reduced (LOE2).

External sphincter balloon dilatation was recommended by Chancellor *et al*. [37], with short-term results similar to those of surgical sphincterotomy. However, the technique has been abandoned by its sponsors and the device has not been distributed, probably indicating poor efficacy in the medium and long-term, compared with other mini-invasive methods such as stenting.

RECOMMENDATIONS

- **Where clean intermittent catheterization is not possible, the long-term use of indwelling catheters should be avoided (B).**
- **Whatever type of sphincterotomy is chosen (surgical or prosthetic):**
  - **Patients must think carefully about the different modes of micturition possible for them (A).**
  - **The few studies reporting long-term results of sphincterotomy demonstrate the vital importance of regular patient monitoring for the recurrence of DSD or blockage (B).**
  - **This mode of micturition is contra-indicated in women and men with acontractile bladder and difficulty in maintaining a condom catheter (B).**
  - **Men who wish to have children should be warned of the risk of ejaculatory duct obstruction (B).**
- **For patients who have chosen surgical sphincterotomy:**
  - **The reference technique involves an elective 11, 12 or 1 o'clock incision of the urethral sphincter (B).**

- **Although surgical sphincterotomy is the accepted reference treatment for neurogenic DSD, analysis of the literature highlights the lack of reliable efficacy and reproducibility criteria for the technique (B).**

• **For patients who have chosen prosthetic sphincterotomy:**
  - **Different types of stent are used, depending on whether sphincterotomy is temporary or permanent. Stents are complementary, and different designs can be used for different situations (B).**
  - **Surgical complications depend as much on the surgeon's competence as on the material and may be reduced by experience (C).**
  - **Clinical studies have demonstrated that neurogenic patients prefer prosthetic sphincterotomy because it is reversible, even when permanent stents are placed (C).**
  - **Careful follow-up, using yearly cysto/urethroscopy is mandatory when leaving a permanent urethral stent (B).**

b) Surgery to increase detrusor strength

For some patients, the cause of bladder hypocontractility lies in the bladder wall. In this case, the control circuit functions but the bladder muscle is too weak. At present there is no medical treatment for this situation. The general objective is to reduce peripheral resistances as much as possible and where this fails, to propose intermittent catheterization.

However, over recent years, some teams have suggested placing rolled strips of muscle around the bladder. Some authors have also suggested a strip of *rectus abdominus* muscle. This is easier to perform and may be used essentially for reconstructive surgery, such as bladder extrophy [43-45] (LOE4). The only team to have published results on bladder hypocontractility in man is that of Ninkovic *et al*. [46] (LOE2). They recently reported interesting results from twenty patients suffering from bladder hypocontractility of neurological origin and requiring self-catheterization. They reported a technique that they had designed in animal experiments [47, 48](LOE4) and which consisted of transferring a free strip of great dorsal muscle, which was anastomosed to the epigastric vessels and the lowest branch of the intercostal nerve. Out of twenty patients, with a mean follow-up of 44 months, 60% no longer required self-catheterization, with PVR below 100 ml. After complementary surgery on the bladder neck, there was a 90% success rate that was stable over time. The authors reported no heavy morbidity, particularly with regard to the donor site. Other teams need to confirm these results, but it appears to be a very promising approach. Future development could use tissue-engineering techniques to construct vascularized and contractile strips implanted around the bladder with the same procedure.

RECOMMENDATIONS

The use of a free strip of great dorsal muscle on the bladder is a promising technique that needs to be validated further (D).

3. DENERVATION PROCEDURES FOR TREATING REFLEX URINARY INCONTINENCE DUE TO DETRUSOR OVER ACTIVITY

a) Introduction

Neurosurgery has a particular role in the management of neurogenic detrusor overactivity [1]. Many different procedures have been described: open surgery for complete or partial rhizotomies (radicotomies) (ventral or dorsal), selective or otherwise. Direct injection of various neurolytic substances has also been suggested. In this part, we consider the main series reported in the literature and will briefly describe the various possible options together with their functional effects and long-term results.

b) Peripheral bladder denervation

The most popular technique today is the injection of botulinum toxin which is dealt with also elsewhere in this report. Various techniques of peripheral bladder denervation, such as prolonged hydrodistension or bladder transsection, are no longer used. Some authors have reported transient improvement in certain patients after prolonged hydrodistension, but unfortunately detrusor overactivity recurs rapidly and the procedure is not quite so simple. Moreover, there are no reports for patients presenting specifically with neurogenic detrusor overactivity [2]. Bladder transsection was briefly popular at the end of the 70s [3-5]. It involved complete section of the bladder wall from one urinary meatus to the other. The technique was indicated essentially for urge incontinence and pollakiuria, and rarely in the context of detrusor overactivity. However, a lack of anatomical and physiological information to support the mechanisms of efficacy of the procedure, and a lack of reproducible results from the initial series, explains why it is no longer used.

Another bladder denervation technique was developed by Ingelman-Sundberg [6, 7] (resection of the inferior hypogastric plexus in contact with the bladder). The procedure is technically simple and can be performed under local anesthetic. The surgeon makes an inverted U-shaped vaginal incision in contact with the trigone and dissects the bladder both laterally and posteriorly,

and as widely as possible. After dissection, the vaginal mucosa is simply closed in one plane by separate sutures. In the most recent paper [6], the authors report up to 54% recovery over a mean follow-up of about three years. However, it should be noted that each published series is from the same group, is always retrospective, the sample size was small (LOE4). Moreover, the technique is said indicated more often for urge incontinence and pollakiuria than for neurogenic detrusor overactivity. However, we mention it here because of its simplicity and the few reported complications.

c) Sacral root surgery

1. Isolated rhizotomy of ventral and/or dorsal sacral roots

Historically, attempts at sacral root surgery first focused on destroying the motor (ventral) sacral roots. Despite various technical artefacts, it was soon clear that this method failed within three to six months.

With a slightly different objective, Brindley [8] developed a technique involving stimulation of ventral sacral roots to obtain controlled and complete bladder voiding in cases of spinal cord injury. He quickly realised that patients only acquired continence if the stimuli causing reflex bladder contraction could be destroyed [9]. Early techniques consisted in selective destruction of the dorsal sacral roots that produce peri-operative detrusor contractions. These selective rhizotomies did not, however, give the best results. Only after complete de-afferentation of the sacral micturition centre by intradural rhizotomy were better results obtained [10-13] (LOE2-3).

Sacral root surgery may be envisaged for patients who cannot undergo electrostimulation of the anterior sacral roots (evolutive diseases such as MS, patients who cannot mount toilets, etc.).

The technique of “selective” dorsal sacral rhizotomy has been studied more extensively. It involves, as described above for Brindley’s technique, making an extra-dural approach to the sacral roots (S2 to S5), isolating and stimulating the dorsal (sensitive) contingent whilst monitoring any changes in urodynamic pressure within the bladder in order to section only those fibres responsible for hyperactivity. To retain reflex erection, S2 must be preserved, at least on one side. This treatment may be proposed for patients with neurogenic detrusor overactivity, and also those with urge incontinence/pollakiuria (this is important since results are more difficult to evaluate in these patients). The literature records only case series without control groups. Preliminary results were promising but were based on a small number of cases with short follow-up times [14-16] (LOE4). The outcome seemed to deteriorate over time. Opsomer *et al*. [17] reported deterioration after one year for all their eight patients (LOE4). Torrens, one of the first to use the technique, was led to re-evaluate his long-term results [18]. The most recent article by Lucas *et al. [19]* concerning 22 patients (LOE3), also reported a significant, but less marked, deterioration at four years. At this mean follow-up interval, 39% of patients retained a urodynamically stable bladder with satisfactory clinical response. The authors ascribe these improved results to a more extensive rhizotomy. However, it should be noted that there was a marked heterogeneity of patients in this series, three out of the eight, considered to be “successes”, were patients with leakage due to detrusor overactivity with an indwelling catheter.

A recent original approach to ablative mini-invasive surgery to treat neurogenic reflex urinary incontinence due to detrusor overactivity was reported by Mertens *et al*. [20]. It consisted in applying a technique used for limb spasticity, microsurgical DREZotomy. The aim is to destroy the dorsal root entry zone (DREZ). This zone, first defined in 1972 by Sindou [21], is a functional anatomical entity that groups together the proximal portion of the dorsal root, the medial portion of the dorso-lateral tract and the superficial layers of the dorsal horn. The technique involves making a micro-surgical lesion (by micro-coagulation) on the ventro-lateral portion of the entry zone, near the apex of the dorsal zone. The effect of DREZotomy is to selectively block nociceptive afferents, and their relays, and myotatic afferents. The procedure blocks the afferents of the mono and polysynaptic reflexes. The benefit of the limited lesion is to avoid complete abolition of tactile and proprioceptive sensitivity and to prevent the development of deafferentation phenomena. To treat neurogenic detrusor overactivity, the lesion must be made on both sides from S2 to S3 or even S4, according to the case. The results from the first series concerned 38 patients treated for incapacitating lower limb spasticity, treated by extended DREZotomy from L2 to S1. It should be noted that 58% of these patients were permanently catheterized. At six months, detrusor overactivity had disappeared in 82% of these patients, with 63% having significantly improved bladder capacity. At 18 months post-surgery, leakage had disappeared in 89% of cases.

Hohenfellner [22], following Brindley’s experience, proposed “neurogenic bladder augmentation” in certain cases. This involved completely destroying the ventral and dorsal sacral roots, possibly followed by continent cystotomy and simplified urinary catheterization. The author reported his experience with eight patients retrospectively (LOE3). After surgery in all patients, bladder capacity increased from about 177 ml to 670 ml, with complete disappearance of detrusor overactivity. Interestingly, continent vesicostomy was proposed to four patients. If these outcomes persist for the long-term, and if no serious (particularly trophic) complication occurs, this therapeutic option could be an alternative to augmentation enterocystoplasty.

2. Percutaneous sacral root block

Sacral root block is an old technique, since Dogliotti [23] proposed it as early as 1931 to relieve vertebral cancer pain by chemically sectioning several dorsal

roots. An injection of alcohol causes denervation due to the fragmentation of myelin in the endoneurium. In the 1950s, Bors [24] applied the technique to the bladder, standardized the procedure and described preliminary results. Later authors reported on a few series (LOE3) [25, 26], but always with the same result; the benefit disappeared after a few months; an example of neurological plasticity. Phenol, considered to be "selective" for C fibers was then tried but the results were no better [27-29].

Chemical destruction of the sacral nerve roots has proved ineffective and is accompanied by a high rate of minor complications (pain), requiring prolonged hospitalization and significant discomfort (LOE3)[25, 26].

Recently, Mulcahy *et al*. [30] proposed sacral rhizotomy by percutaneous radiofrequency for neurogenic bladder (LOE4). The initial results are interesting but no medium and long-term results have been published.

3. Rhizotomy of posterior sacral roots and stimulation of the anterior sacral roots

Electrostimulation to improve micturition in patients with spinal cord injury has been extensively researched since 1954. Direct stimulation of the detrusor, the spinal cone, the splanchnic and sacral nerves have not produced reliable results. Since 1969, G.S. Brindley has developed a set of electrodes for stimulating the spinal roots in the *cauda equina*. The technique, first tested in baboons, led to the development of an implanted stimulator to induce micturition in paraplegic patients. Sacral rhizotomy performed during implant surgery makes it possible to control bladder hyperactivity and ensure continence.

The equipment comprises two elements. The energy source and the microprocessor for adjusting the stimulation parameters are not implanted. The transmitter transforms the electric current from the energy source into electromagnetic waves, which are picked up by the implanted receptor and re-transformed into an electric current that circulates to the electrodes in contact with the nerve. Depending on the surgeon's decision, the implant is placed within the membranes of the dura mater or outside them, so as to stimulate the sacral roots from S2 to S4. At the same time, it is essential to perform posterior rhizotomy from S2 to S4 to remove any detrusor overactivity.

Micturition is not continuous: the detrusor cannot be stimulated without also stimulating the sphincter. The parasympathetic fibers and the fibers destined for striated muscles are stimulated together. The response of detrusor smooth muscle fibers causes a gradual increase in pressure, which continues after stimulation has ceased. The "on-off" response to stimulation of striated muscle fibers is different. When stimulation stops, the striated sphincter immediately relaxes, whilst the detrusor continues to contract. A new wave of stimulation increases and maintains sufficient detrusor pressure to cause micturition after stimulation stops. The careful selection of stimulation and stopping times results in a discontinuous, but satisfactory, micturition. Neurotomy of the somatic fibers destined for the striated sphincter is difficult to perform [31](LOE4). Sphincter fatigue due to electrical stimulations, blocking of pudendal nerve motor fibers [32](LOE4) or use of specific detrusor stimulation by performing an anodal block [33] (LOE 4) have been reported, together with poor efficacy.

Stimulation can help defecation and erection, but it should be remembered that the principal object of sacral nerve stimulation combined with posterior rhizotomy is to achieve urine continence and bladder voiding. Erection is a secondary benefit but not an indication for the procedure.

Not all patients may benefit from this surgery. It can only be performed in those with spinal damage who are para- or tetraplegic. The sacral reflex arc must be preserved. Without going into further detail concerning indications for surgery, alternative less aggressive treatments should be preferred. As previously stated, men about to undergo this surgery should be warned that they would lose reflex erection after posterior rhizotomy (although this could be compensated by erection obtained with another set of parameters using sacral anterior root stimulation).

The results of the intervention are summarized in **Table 6.** Briefly, the outcome with regard to continence and bladder voiding are good (LOE 2-3). Failures result from incomplete rhizotomy, where bladder hyperactivity persists, or from sphincter insufficiency which may be treated by complementary surgical placement of an artificial sphincter [12, 13](LOE3). Incomplete rhizotomy can be surgically repaired [12, 13, 34] (LOE 2-3). In all reported series, mean bladder capacity increased significantly (LOE 2-3). Micturition was obtained by electrostimulation with a post-voiding residue (PVR) of ≤ 50 ml in 69 to 100% of patients. All series reported decreased incidence of urinary infection, but the defining criteria were too varied to allow conclusions to be drawn. Within the limits of a relatively short mean follow-up, it appears that this surgery preserves the upper urinary tract. Posterior sacral rhizotomy probably protects the upper urinary tract from detrusor overactivity. It can solve the problem of pre-operative reflux [34, 35](LOE4). However, posterior sacral rhizotomy should be complete. Indeed, in a series of 500 patients, Brindley [34] (LOE3) reported twelve cases of impaired upper urinary tract, ranging from grade I reflux to upper urinary tract dilation. Amongst these twelve patients, ten had undergone partial or sacral rhizotomy.

The results of the sacral anterior root stimulation on autonomous hyperreflexia (AHR) may be debated. The authors of many studies report a decreased AHR. Schurch [36] focused on the specific problem of AHR and recorded its persistence during stimulation in all patients who had suffered prior to surgery, but with marked improvement in symptoms.

Table 6. Results of series on Sacral anterior root stimulation technique + Sacral deafferentation (AHR: autonomous hyperreflexia)

Authors	Patient numbers	Sex ratio (M/F)	LOE	Mean follow-up *(extremes)*	Pre-op. continence (%)	Post-op. continence (%)	Pre-op. bladder capacity (ml)	Post-op. bladder capacity (ml)	% complete micturition *(PVR < 50 ml)*	Pre-op AHR . (%)	Post-op. AHR (%)	Pre-op. urinary infections (%)	Post-op. urinary infections (%)
Brindley *et al.* *(*1994)[34]	500	271/229	3	4 years	-	-	-	-	82	-	-	-	
Barat *et al. (*1992)[37]	40	26/14	3	2 _ years	2,5	90	210 (50-500)	463 (200-600)	82	-	-	100	30
Van Kerrebroeck *et al.* (1996)[38]	52	29/23	3	3.5 years		81	285	592	87	14	4	4.2/year	1.4/year
Schurch *et al.* *(*1997)[36]	10	3/7	3	3.4 years	0	80	160	> 500 ml	100	60	60	80	30
Egon *et al. (*1998)[12]	96	68/28	3	5.5 years (0.5-14)	1	88	200 (40-600)	565 (300-600)	89	22	0	100	32
Van der Aa *et al.* *(*1999)[35]	37	33/4	3	(0.4-12)	-	84	75% < 400 ml	95% > 400 ml	91	-	-	-	-
Creasey *et al.* *(*2001)[39]	23	16/7	3	> 1 year	65	87	243 (30-450)	> 400 ml	69	35	7	82	78
Bauchet *et al.* *(*2001)[11]	20	6/14	3	4.5 years (1-8.5)	0	90	190 (40-600)	460 (350-800)	90	15	0	100	-
Vignes *et al. (*2001)[40]	32	-	3	8 years (4-11)	0	90	220 (50-600)	550 (350-600)	80	18	2	100	30
Ktuzenberger (2005)[13]	464	244/220	2	6.6 (6-17)	-	83	173	470	81	-	-	6.3/yr	1.2/yr

CONCLUSION

It is interesting to know the various techniques used for bladder denervation, in order to be able to offer patients the whole range of therapeutic options, should medical treatments fail. Currently, bladder denervation is mainly reserved for those suffering complete spinal cord injuries, but increased selectivity may one day make it possible to perform this type of surgery in patients with less neurological damage.

RECOMMENDATIONS

- **No peripheral bladder denervation technique has passed the test of time. The only technique used nowadays (the Ingelman-Sundberg technique) is not sufficiently effective to be used to treat neurogenic bladder hyperactivity (D)**
- **Injections of neurolytic products to treat detrusor overactivity should be abandoned, since they are ineffective in the medium and long term and expose patients to morbidity (A)**
- **Sacral dorsal rhizotomies need to be quite extensive to treat successfully neurogenic bladder hyperactivity. So they may be performed only in patients with lower limb neurological impairment (B)**
- **In certain situations, dorsal rhizotomies can be associated with ventral root stimulators (Brindley's technique) or even with continent cystostomy (B)**
- **Electrostimulation of the anterior sacral roots is a validated option for managing neurogenic bladder in patients with spinal lesion, with long-term follow-up (B)**
- **It must be combined with destruction of all or part of the posterior sacral nerves, and cannot therefore be performed in patients with conserved lower limb motility(B)**
- **The reflex arc must be intact(B)**
- **Posterior rhizotomy exposes men to a loss of reflex erection and women to a loss in reflex vaginal lubrication(B)**
- **It is vital to assess the patient carefully before implantation so as to determine whether he/she will be able to mount a toilet or grasp a urinal handrail (B)**

4. SURGERY FOR STRESS UI DUE TO SPHINCTERIC INCOMPETENCE

• Keywords used for the medline research

neurogenic bladder; spinal cord injury; spina bifida; myéloméningocèle; multiple sclerosis; stress incontinence; artificial urinary sphincter; sling; bulking agent; dextranomer; polydimethylsiloxane; Polytetre-fluoroethylen; collagen

• Introduction

Patients with bladder dysfunction secondary to a neurological cause may have a certain degree of sphincter dysfunction. In certain cases, this is secondary to a neurological impairment (for example in *cauda equina* syndrome). In other cases, it could be the consequence of previous surgery (for example sphincterotomy). In women, stress urinary incontinence may be related to simple cervico-urethral hypermobility [1].

It is of course very important to confirm that the bladder reservoir is well-balanced and filling under low pressure; where this is not the case, a treatment addressing the bladder condition would need to be added to that for increasing sphincter resistance.

The context of the neurological disease, and the presence of any concomitant treatment for detrusor hyperactivity of neurological origin, will require stringent, pre-operative investigation. Indeed, the risk of chronic urinary retention is particularly high in such patients (in certain situations, for example patients already using intermittent catheterization , it could even be the goal of surgery). Patients must be informed therefore of the potential need for intermittent catheterization (IC), and they should be capable to perform intermittent catheterization (IC). A patient who has never used this technique should be trained in order to meet any possible future problem. Two situations can be identified: patients not already using IC, patients already using IC.

a) Patients not using IC

1. Suburethral tapes

In this case, a pre-operative assessment to look for prognostic factors must be carried out. This point is already treated in a specific chapter. In patients with a neurological disease, clinical examination should be conducted as in non-neurological patients. The clinical examination may include the Bonney test and tetsing of continence during a TVT procedure [2]. In the event of peripheral neurological disease with perineal floor denervation, it is especially important to check for any associated urogenital prolapse, a condition often exacerbated by the effort involved in micturition and defecation.

The urodynamic investigation must evaluate the quality of sphincter function, since several studies have suggested that suburethral tape techniques gave poorer results in the event of low urethral closure pressure (LOE 4) [3]. Furthermore, recent research based on prospective comparative studies suggests that in the event of low closure pressure, techniques using tapes placed retropubically give better results than transobturator techniques (LOE 2) [4 , 5-7].

To our knowledge, only one study has specifically assessed the efficacy of suburethral tension-free tape in adult women with neurogenic bladders (the use of suburethral slings will be discussed later). It was a retrospective series with 12 women treated by TVT [8] (LOE3). The study revealed that, for those patients who did not self-catheterize (3/12), the treatment was effective and intermittent catheterization was not required. The authors did not report any particular complication.

For adult male patients, the use of synthetic tapes is increasing since the description of bone anchored tape for post prostatectomy incontinence [9](LOE2). To our knowledge, no specific study on patients with a neurological cause to their incontinence has been reported. We could only suppose that the risk for urinary retention is higher than in the general population and therefore prepare the patient to accept IC before consenting to this type of surgery. The different therapeutic options are presented in the following chapter.

2. Bulking agents

The use of various types of bulking agent has been reported in three main indications: stress urinary incontinence in women, post-prostatectomy incontinence and children incontinence. Various agents have been used. Polytetrafluoroethylen (TEFLON®) was one of the first[10, 11]. It was once very popular for treating vesico-ureteral reflux, but it has been progressively abandoned after several authors reported a possible migration and granulomatous reaction of this product [12, 13](LOE2). Collagen has also been used in this indication [11, 14-21]. More recently, several authors shifted to synthetic products like polymethylsiloxane (MACROPLASTIQUE®) or Dextranomer Hyaluronic Acid copolymer (ZUIDEX®), because they found these type of products easier to use without the risk of allergic reaction or previous contamination which may occur with other biological products [10, 22-28]. Henly et al [29] demonstrated that distant migration of particulate silicone was observed in animals after periurethral injection with polymethylsiloxane (LOE4). This was not demonstrated with dextranomer acid copolymer injections [30] (LOE4).

Bulking agent results in female stress incontinence and post-prostatectomy incontinence will be discussed elsewhere. We will focus our review on patients with a neurological problem (**Table 7**) [10, 11, 14-28, 31-39].

It is important to underline that although a high proportion of the patients in these studies use intermittent catheterisation, some patients have a good result without using it.

One of the main advantages of this technique is that it is easy to perform, usually as an outpatient procedure. Most of the studies are on children. Usually the authors inject the product in the bladder neck, by a retrograde endoscopic approach, in two to four points. The bulking agent is injected until full lumen closure is noted. Dean et al [28] recently suggested performing an antegrade way for injections, using a percutaneous access to the bladder.

The results of the procedure of injection with all the recent bulking agents used are summarized in **Table 7.** It is very difficult to compare the results because of the various definitions for the surgical results that are used by the authors. We report what many authors call an improvement, or “social continence”**.** Many authors do not accept this definition. Therefore, it seems reasonable to consider only the more reliable results, namely the rate of “dry patients” (even if some authors add to this result a notion of “dryness for some hours” between voiding or catheterization). Using this definition, 0 to 36% of the patients are considered as cured using bulking agents (LOE2-3). Moreover, these results are observed after a mean follow up that rarely exceeds 2 years (LOE2-3), although one author has reported long-term lasting effect up to 7 years after the last injection [23].

Two other points have to be underlined in the studies published. The first is that the studies in children mix frequently patients with two types of problems: urological malformations (epispadias, bladder extrophy) or neurogenic bladder (mainly myelomeningocoele). This is important to know, because it seems that in children, bulking agents work slightly better in patients with malformations than in patients with a neurological bladder dysfunction [10, 17, 23, 25]. The global results of the series are therefore probably more optimistic than the results that could be specifically observed in neurological patients. The second point is that these children have frequently already had a various amount of surgical procedures, which could modify the results of the injection procedure.

Although the authors have reported no severe complication, there is a controversy regarding a possible greater difficulty to perform a bladder neck surgery after repeated bulking agents injection [10, 23, 25]. Some authors [40] advocate that the number of unsuccessful procedure could be considered as a complication. Most of the authors [23, 25] agree that

Table 7. Results of the bulking agent injection procedures in patients with a neurological bladder dysfunction. DHAC (Dextranomer Hyaluronic Acid Copolymer) PDS (polydimethylsiloxane), PTFE (Polytetra-fluoroethylene),NP (Not Precised), LOE (Level of evidence)

Authors	n	LOE	Neurogenic bladder/total n patients	Bulking agent	Mean or Median age (years)	Male /female	Follow up (years)	Dry (%)	Improved (%)
Leonard et al [19]	18	3	10/18	Collagen	10.5	12/6	1.3	36	28
Perez et al [18]	32	3	25/32	Collagen	9	23/9	0.9	20	28
Bomalaski et al [17]	40	2	25/40	Collagen	12.1	28/12	2.1	22	54
Caione et al [26]	16	2	3/16	DHAC	10.1	9/7	1	18.7	56.3
Sundaram et al [15]	20	3	12/20	Collagen	9.5	12/8	1.3	5	25
Kassouf et al [21]	20	3	20/20	Collagen	13.3	15/5	4.2	5	15
Chernoff et al [20]	11	3	8/11	Collagen	10.6	6/5	1.2	36	18
Block et al[16]	25	3	25/25	Collagen	11.7-21.9	15/10	2.9-4.7	4	44
Hamid et al [24]	14	3	14/14	PDS	41	14/0	2.9	36	21
Godbole et al [Godbole, 2004 #	15	3	14/15	PTFE, collagen, PDS	10.2	10/5	2.33	20	53
Halachmi et al [22]	28	3	10/28	PDS	12.5	22/6	1	0	42
Misseri et al[27]	16	3	12/16	DHAC	4 to 18	6/10	0.8	19	31
Lottmann et al [23]	61	2	27/61	DHAC	10.3	41/20	3	26	26
Guys et al [25]	49	3	49/49	PDS	14	21/28	6.1	33	14
Dean et al [28]	34	3	28/34	DHAC	11.7	18/16	0.3	NP	71
Dyer et al [10]	34	3	12/34	PTFE, DHAC	2.7 (PTFE)/14 (DHAC)	NP	NP	6	12

there is no need to attempt more than two injections if the patient's incontinence is not improved or cured on a long-term basis. Gender, previous bladder/ sphincter surgery don't seem to be reliable prognostic factor regarding the success of the injections.

Future studies using autologous myoblasts and fibroblasts are currently under way in patients without neurological impairment [41] and may bring a renewed interest in the field of bladder neck or peri-urethral injections in the next years.

3. Artificial urinary sphincter

The last theoretical option is the use of an artificial urinary sphincter. However, the rate of urinary retention following this procedure is very high in patients with a neurological bladder dysfunction. Therefore, as previously stated for the other treatments, this procedure should be used only after the patient has accepted and is ready to use IC.

b) Patients using IC or prepared to use IC:

A large majority of the series published in this chapter are about children. One of the main questions is whether it is necessary or not it is necessary to perform systematically a bladder augmentation in complement to the treatment of the sphincteric deficiency. A majority of the authors report the necessity to proceed to bladder augmentation in at least a third of their patients. Even with a thorough urodynamic and radiologic preoperative evaluation, some patients will have late bladder compliance deterioration [42-59]. To illustrate that, two retrospective studies were recently published specifically on this topic and gave two opposite conclusions. Snodgrass et al [60] (LOE3) published the retrospective analysis of 30 children (mean age: 8,6 years) who had a bladder neck sling procedure and appendico-vesicostomy without augmentation. At 22 month of mean follow-up, only one patient had to undergo a bladder augmentation procedure. In a subset of the patients (16) who had urodynamics at 24 months, 13/16 had an increase of their maximum bladder capacity at 24 months. However, 67% of the patients have to use anticholinergic therapy. Although this series is interesting, the follow-up is relatively short. On the opposite of this study, Dave et al [61] (LOE3) strongly advocate the case for systematic bladder augmentation. Hence, the authors report a series of 15 children followed at least 5 years after an isolated bladder outlet procedure (5 Pippi-Salle, 5 slings and 5 artificial urinary sphincter). At a mean follow-up of 11.25 years, all the patients underwent a bladder increase procedure, either for recurrence of the incontinence or for upper urinary tract deterioration.

At present, no definitive conclusions can be drawn. The majority of the authors recommend performing a concomitant bladder augmentation when performing a bladder outlet procedures [40] (LOE4). The advent of the botulinum toxin injection in children will perhaps allow having new design for studies that could help to answer to this question.

1. Surgery of the bladder neck

Three main procedures have been described. Historically, the technique of Young[62], later modified by Dees[63] and Leadbetter[64] has been the first used, essentially for reconstruction in cases of extrophy and epispadias. The principle was to dissect extensively the trigone (after ureteral reimplantation) allowing excising most of the tissue from the bladder neck to constrict the trigone around a small catheter. Although some authors[65, 66] described its use in neurogenic patients, it is almost abandoned in this indication. Tanagho [67](LOE3) described a variation of this technique which could be used in difficult situations in incontinent adult patients, when the implantation of an artificial urinary sphincter is not possible [68].

The Kropp's procedure [69] consists in tubularizing a flap of the anterior bladder wall, pediculized on the bladder neck. This tube is then fixed on the posterior bladder wall between ureteral orifices. In the initial technique, the tube was tunnelled submucosally, but this manoeuvre was supposed to augment the risk of tube stenosis [70, 71](LOE3).

The last technique described is the Pippi-Salle technique[72]. It is considered as a variant of the Kropp procedure (also called Kropp-onlay), with an anterior bladder wall flap that is not tubularized. At the beginning, the authors reimplanted systematically the ureters. This was abandoned in the last patients in the absence of reflux [73, 74] (LOE3). In a systematic review, Kryger et al [40] (LOE4) stated that only data on 83 patients for the Kropp technique and 25 with the Pippi sale procedure have been published. Since then, we didn't found any added study with these techniques. The continence results are good (50-69% for the Pippi Salle procedure, 78-81% for the Kropp procedure) [70, 71] [73, 74] [40]. However, several problems exist with the two techniques. First, the technique doesn't allow easy endoscopic access to the bladder. This is a major problem, because it prevents or limits future endoscopic procedures (especially ureteroscopy, botulinum toxin injections). Second, a high percentage of patients (especially male) report catheterisation difficulties in the Kropp technique : 28 to 45% of cases. In Pippi Salle procedure, the continence rate is lower than in the Kopp procedure, but few cases of catheterisation difficulties have been reported [40]. However, a new procedure is necessary in 12 to 17% of cases for uretrovesical fistula [73, 74] (LOE3). Moreover, this procedure has rarely been tried in male patients.

2. Complete bladder neck closure

This can sometimes be proposed as a complement to continent cystostomy. It is always a difficult

procedure, despite all the technical artefacts presented in the literature (interposition of muscle or omentum), and re-permeation is both frequent and problematic [76]. Moreover, patients with a bladder dysfunction secondary to neurological illness are at high risk of lithiasis of the bladder reservoir or the upper urinary tract, so it does not seem logical to prevent potential endoscopic treatment by closing the ureter (LOE4). Finally, preserving the natural urethra may constitute a safety measure if high pressure persists (dysfunction of the augmentation graft, hyperactive or hypo-compliant residual bladder) or in the event of any complication on the abdominal continent tube [2, 77] (stenosis, transient impossibility to self-catheterize, etc.) (LOE4).

3. Aponeurotic or prosthetic bladder neck slings:

For women, suburethral tape can easily be placed during bladder augmentation surgery in order to reinforce stress continence and prevent stress leakage. Results of the main recent series are summarized in **Table 8**. Complete continence is observed in 83 to 89% of the patients [44, 60, 78, 79] (LOE3). Bladder neck slings appear to provide good results for male children, although the results seem to be less satisfactory than with female patients [60, 79, 80] (LOE3). Studies in adult men need to be awaited.

All the authors report a low morbidity rate of this procedure. The risk of urethral erosion is very low with the fascial slings. When the intention of surgery is to induce urinary retention with subsequent post-operative IC, an aponeuvrotic sling rather than a synthetic sling seems to be more suitable because of the risk of secondary urethral erosion when the sling must be tight [81-84](LOE3). Although these findings have not been confirmed by comparative studies, some authors report up to 80% erosion with bladder neck slings [81] (LOE3). The risk of erosion with synthetic tapes exists also in suburethral tapes, and excessive tension is often evocated [84](LOE4). It is interesting to notice that the only case of male sling erosion to date was described in a patient with a cauda equine syndrome [85](LOE4). New refinements in the technique for male patients involve a higher tension on the tape, and already one case of urethral erosion has been published [82](LOE4). The use of this type of device in patients with underlying neurological illness should therefore be very cautious(LOE4). High bladder pressure when slings are placed is also supposed to be a risk factor for urethral erosion [84] (LOE3).

At present, there are no specific reports concerning the new perineal slings for men (bone-anchored or

Table 8. Results of the bladder neck sling procedure in patients with a neurological bladder dysfunction (LOE: level of evidence, NP not précised)

	n	LOE	Neurogenic bladder/total n patients	Mean or Median age (years)	Male /female	Bladder augment. surgery (%)	Follow up (years)	Continence rate (%)
Snodgrass et al, 2007 [60]	30	3	30/30	8,6		0	1.9	57
Karsenty et al, 2007 [78]	11	3	11/11	42	0/11	100	3.6	72
Albouy et al, 2007 [80]	14	2	14/14	14	7/7	100	5	79
Castellan et al, 2005 [79]	58	3	58/58	11.4	15/43	100	4.2	88
Austin et al, 2001 [42]	18	3	18/18	14	8/10	33	1.8	87
Barthold et al, 1999 [43]	27	3	26/27	NP	7/20	81	2,1/3,6	28(sling)/ 50(wrap)
Gosalbez et al, 1998 [44]	30	3	28/30	10	6/24	97	3,1	93
Kakizaki et al, 1995 [45]	13	3	11/13	13	10/3	69	3	76
Gormley et al, 1994 [98]	15	3	15/15	NP	0/15	13	NK(0,5 -8,5)	85
Elder et al, 1990 [99]	14	3	14/14	12,6	4/10	7	1	86

transobturator route) in patients with a neurologic disease. The use of new minimally invasive devices such as ACT and pro-ACT balloons (Uromedica) [86, 87] for patients with a neurological bladder dysfunction has not yet been published.

4. Artificial urinary sphincter (AUS)

Since it was introduce in clinical practice [88], the artificial urinary sphincter is recognized as one of the most effective treatments for urinary incontinence. The benefit lies in the fact that it mimics bladder function as closely as possible to physiologically normal, with low-pressure micturition. Its effectiveness in regard to stress incontinence ranges from 75 to 87%. The satisfaction rate ranges from 85 to 95%. These rates, given for mixed populations of patients mostly suffering stress incontinence after radical prostatectomy, are probably similar to those of neurogenic patients when the bladder reservoir is stable (LOE4) [89].

Before using AUS in neurogenic patients, several factors must be considered. The risk of infection related to bacteriuria is probably higher, even though little information is available to support this statement. For neurological patients, we recommend pre-operative assessment of bacteriuria and urine decontamination before surgery [90] (LOE4). Theoretically, patients must be strong enough to activate the pump of the AUS, either to open the cuff to urinate or during IC [89]. They must also accept the need for IC should the bladder reservoir be hypocontractile. Recent studies seem to indicate that the cycling activation of the pump could be avoided in patients performing IC (LOE3)[47, 91]. Finally, it is necessary to know the ejaculatory status of males in order to discuss where to implant the cuff.

The cuff implantation site in adult patients with a neurological bladder dysfunction is debated. Partisans of bladder neck implantation argue that perineal incisions may cause cicatrisation problems for patients in wheelchairs. Moreover, traumatic catheterization is a well-known risk factor of urethral erosion in the non-neurological population undergoing an AUS [54] (1 to 5.5% in contemporary series). Even if it is recognized that IC is possible in AUS implanted patients [92], the risk of traumatic catheterization could be higher on the bulbar urethral site than on the bladder neck. Finally, the bladder neck implantation retains the possibility for patients to recover antegrade ejaculation [93, 94] (LOE4).

On the other hand, inserting an AUS cuff around the bladder neck is more difficult in adults in comparison with peri-bulbar implantation (LOE4), and the rate of erosion in the published series is higher than in the post-prostatectomy incontinent population [46-59, 95](which is always implanted around the bulbar urethra).

As previously stated, a thorough urodynamic evaluation of the bladder is mandatory to evaluate the possible degradation of bladder reservoir compliance following AUS implantation, which has been reported in several retrospective series (LOE3) [46-59, 95]. The reasons for this change in bladder behaviour are not known, and it has been observed particularly in populations of patients with myelomeningocoele [51, 55, 56, 58, 96]. In the event of any doubt on the quality of the bladder reservoir, bladder augmentation should be performed. This may change in the future, with the development of intra-detrusor injection of botulinum toxin, to control incontinence in certain patients [97].

The main results of the recently published series are summarized in **table 9**. The continence rate is high, especially when a bladder augmentation has been performed (59 to 100% of the patients) [46-59, 95]. The older series comprise patients with the previous version of the AMS 800 (AMS 792). Therefore, long-term results could be even better as AMS 800 is considered as a better device than AMS 792. The bladder neck or urethral erosion is the main risk with AUS and appears to be higher in these series than it is in the general population (approximately 5 to 15%). These erosions seem to happen more frequently in the first two years after the procedure. However long-term erosions are still possible [50] (LOE3). The average “survival” for AUS exceeds rarely ten years. This particular point has to be explained to the patient, especially when they are very young. However, the majority of the authors consider AUS to be the “gold standard procedure to treat sphincter deficiency, even in patients with a neurological bladder dysfunction [41].

RECOMMENDATIONS

- **Suspected neurological bladder requires careful investigation before implanting suburethral tape. Tests must include: a micturion diary, a detailed interview using validated questionnaires, and urodynamic tests to provide the patient with optimum information on post-operative risk of complications and failure (C).**
- **The clinical assessment must also evaluate the degree of patient handicap to determine whether they may perform self-catheterization. Sub-urethral tape can be used in patients with a neurological bladder. However, it is contraindicated where patients cannot perform self-catheterization (D).**
- **Autologous slings can be proposed to patients with a neurological bladder dysfunction after careful assessment of their general handicap and if the patient accepts**

Table 9. Results of the artificial urinary sphincter in patients with a neurological bladder dysfunction.

	n	LOE	Neurogenic bladder/ total n patients	Mean or Med age (years)	Male /female	Bladder augment. surgery (%)	Follow up (years)	Continence rate (%)	Cuff Implantation Site	Complication/revision rate (%)
Bersh et al 2008*[47]	51	3	51/51	38.7	37/14	19.6 (sacral root surgery)	8	70.6% (total) /90.2% (social continence)	Bladder neck	7.8/35.3
Lai et al [54]	218	3	11/218	46.3	215/3	NP	2.4	69	Peri-bulbar	18.2/36.4
Lopez Pereira et al [56]	35	3	35/35	14.4	22/13	20/35	5.5	91.4	Bladder neck	11.4/20
Patki et al [57]	9	4	9/9	38.2	9/0	NP	5,9	77	Peri-bulbar	22/43
Murphy et al [100]	30	3	13/30	54	29/1	NP	NP	23	Peri-bulbar	33/70
Herndon et al [52]	134	3	107/134	10	94/41	85/134	7.5	86%	Bladder neck (122), peri-bulbar (12)	16/41
Castera et al [48]	49	3	38/49	14	39/10	9/49	7.5	67	Bladder neck (37), peri-bulbar (12)	20/12
Shankar et al [95]	45	4	NP	11	45/0	NP	7	89	Bladder neck	4.4/6.7
Kryger et al [53]**	32	3	28/32	6.7/14.5	25/7	9/32	15.4	100/	Bladderneck	41/95
Elliott et al [49]	323	3	10/323	Global: 60.4	313/10	NP	5.7	NP	Bladder neck/peri bulbar	Global: 26.2/28.6
Fulford et al [50]	61	3	34/61	26	43/18	7/34	10 to 15	88	Bladder neck (female)/peri-bulbar (male)	29.4/91.2
Levesque et al [55]	54	3	49/54	10/12	34/20	23/54	NP (>10)	59.3	Bladder neck	24/67
Singh et al [59]	90	3	90/90	26	75/15		4	92	Bladder neck/ peri-bulbar	16.7/28
Simeoni et al [58]	107	3	107/107	13.7	74/33	22/107	5	76.6	Bladder neck(98)/ peri-bulbar(9)	22.3/19.6
Gonzales et al [51]	19	3	19/19	8.4	19/0	7/19	8	84.2	Bladder neck	5/100
Belloli et al [46]	37	3	37/37	13-19	35/2	2/37	4.5	59	Bladder neck(33)/peri-bulbar(4)	10.8/38

**** AUS modified**AUS modified and two groups of patients depending of their age at AUS implantation***

or is able to perform intermittent catheterization (B). In this indication, it seems better to use an aponevrotic tape (C).

- **AUS can be proposed to patients with a neurological bladder dysfunction after careful assessment of their general handicap and a detailed discussion regarding the sphincter cuff implantation site (A). Even if one third of the patients would be able to urinate, it is preferable to be sure that the patient accepts or is able to perform intermittent catheterization (B).**
- **Bulking agents can be used in patients with a neurological bladder dysfunction demanding a minimally invasive treatment (D). It is probably better to verify that the patient accepts or is able to perform intermittent catheterization (D).**
- **When a continent cystostomy has been performed, and if no other treatment is possible, bladder neck closure can be proposed to patients with a neurological bladder dysfunction (D).**
- **Bladder neck surgery should be proposed, in patients with a neurological bladder dysfunction only if no other treatment option is available (D).**

5. SURGICAL ALTERNATIVES EXCLUDING DENERVATION PROCEDURES TO TREAT REFLEX INCONTINENCE DUE TO NEUROGENIC DETRUSOR OVERACTIVITY

• Keywords

neurogenic bladder; spinal cord injury; spina bifida; myéloméningocèle; multiple sclerosis; bladder augmentation; enterocystoplasty; gastrocystoplasty; sigmoidocystoplasty; colocystoplasty; ureterocystoplasty ; autoaugmentation; detrusorectomy

a) Bladder augmentation using intestinal segments

The aim of bladder augmentation is to provide long-term protection to the upper urinary tract by reducing the risk of impairment due to high bladder pressure, as well as to improve micturition comfort [1].

First performed in man in 1889 by Von Mickulicz [2] who used a segment of small intestine, the technique has regained popularity since the 1970s after the introduction of intermittent catheterization [3].

Unlike complete bladder replacement, enterocystoplasty preserves the integrity of the trigone of the bladder with the urethra and ureters and reimplantation is not necessary. A segment of the gastrointestinal tract is then removed and sutured onto the bladder. Various augmentation techniques using different segments of the gastrointestinal tract (caecum, colon, and ileum) have been described.

1. Indications

Bladder augmentation is indicated wherever bladder capacity and compliance is reduced, or in the event of detrusor overactivity, when all conservative treatments (medical treatments, detrusor injections of botulinum toxin and/or neuromodulation of the posterior sacral roots) have failed [1, 4].

Before performing bladder augmentation, it is essential to ensure that:

- There is no malignant disease or lithiasis in the bladder.
- Renal function is normal and the upper urinary tract is unimpaired (screen particularly for lithiasis).
- There is no gastrointestinal tract disease (Crohn's disease, hemorrhagic rectocolitis, short gut syndrome, etc.).
- The patient is capable of, and willing to, perform self-catheterization. This can be combined with continent cystostomy, a topic to be dealt with in a separate chapter.

2. Technical principles

There are two stages to the surgical procedure: first bladder preparation and then augmentation. Usually open surgery is performed, but recently laparoscopy has been reported [5, 6](LOE3). At present, except for technical articles on laparoscopy, there are no publications comparing this technique with open surgery.

The bladder can be prepared either by clam cystoplasty or by supratrigonal cystectomy. The preferred preparation depends on the quality of the detrusor, and more particularly on whether the bladder has retained its visco-elastic properties. Where the detrusor is very fibrous and thick, supratrigonal cystectomy should be envisaged, since exclusion of the ileal patch may occur. Nowadays, supratrigonal cystectomy is often performed because compliance disorders in a bladder that has retained its visco-elastic properties can be treated effectively by detrusor injections of botulinium toxin [7].

a. Bladder preparation

• Clam cystoplasty

Clam cystoplasty involves freeing the anterior/posterior surfaces and dome of the bladder and then sectioning from front to back in the sagittal plane. The bladder can be opened either in the transverse plane or sagittal plane, the incision starting and ending about 2 cm above the bladder neck. The lateral surfaces are not freed. The umbilical arteries are preserved to maintain vascularization of the bladder dome.

• Supratrigonal cystectomy

Supratrigonal cystectomy involves resection of the bladder tegument and sparing the trigone. The bladder is freed under the peritoneum and the right and left umbilical arteries ligated and sectioned. The bladder tegument is completely freed and the bladder pedicles ligated and sectioned laterally up to the trigone, which is preserved. During the bladder dissection, care must be taken to spare the ureteral vascularization. Supratrigonal cystectomy is performed by making a circular incision with an electric scalpel into the tegument 1 to 2 cm above the trigone.

• Ureteral reimplantation

Ureteral reimplantation must be carefully discussed in the event of vesicorenal reflux. Several authors have reported that improved bladder compliance precludes the need for vesicoureteral reimplantation (LOE 3) [8-11]. They have reported a resolution rate of about 85% for vesicorenal reflux, classified below grade IV. For grade V reflux, improvement was observed in 2/3 of patients. It is important to point out that, except for the work of Simforoosh [8], these consistent results were obtained in small heterogeneous series of children (neurogenic bladders and congenital anomalies). The results were published after relatively short mean follow-up times (1 to 5 years).

Recently, Hayashi et al. [12] reported on 22 patients treated by ureteral reimplantation during bladder augmentation (LOE 3). Their work was original in that it gave detailed account of renal function after long-term follow-up (mean: 12 years). In the hands of this experienced team, ureteral reimplantation during bladder augmentation did not result in greater morbidity and 97% of patients recovered. Renal function was preserved and satisfactory.

It is therefore too early to rule out the need for ureteral reimplantation during bladder augmentation, especially for cases of grade V reflux. However, it is clear that improved compliance will reduce some vesicorenal reflux.

b. Intestinal segments

• Standard technique

The choice of intestinal segment depends on patient's history and the local conditions. All segments of the gastrointestinal tract may be used, except the jejunum because of the risk of water-electrolyte disorders. The most frequently used segment in adults is the ileum because it is easy to remove, is close to the bladder and may be shaped easily into a reservoir. Colon segments are used more often in children.

The removed intestinal segment must always be detubularized to reduce peristalsis to a minimum and to obtain a reservoir with low pressure. The segment is then placed and sutured onto the bladder in the form of a patch. For supratrigonal cystectomy, the intestinal segment needs to be longer and fashioned into a neo bladder [4].

• Technical variations

The main objective is to reduce mucus secretion and prevent the reabsorption of urine by the intestinal mucosa that leads to metabolic acidosis. Two variant techniques have been proposed but not developed extensively, probably because they involve relatively major surgery for the benefits they bring.

The first is seromuscular colocystoplasty lined with urothelium. This involves removing the detrusor, leaving the bladder mucosa intact, and then covering it with a demucosalized sigmoid patch [13].

The second technique is seromuscular entero-cystoplasty. After preparing the bladder, a segment of the ileum or the sigmoid is removed and detubularized. The mucosal membrane of the intestinal segment is surgically removed, or destroyed by argon beam [14] and the segment is then placed on the prepared bladder [15].

c. Results of enterocystoplasty

The main published series for patients undergoing surgery for neurogenic bladder are summarized in **Table 10**.

• Early morbidity and mortality

Peri-operative mortality is estimated between 0 and 3.2% (LOE 2-3). The most frequently reported early morbidity (LOE 2-3) is prolonged post-operative ileus. It occurs in up to 11.7% of cases [16-18]. However, it should be noted that systematic and prolonged use of a nasogastric catheter is no more justified in neurological patients than in the general population (LOE3)[19]. Other common complications include episodes of febrile urinary infection (4.8 to 9%), urinary fistula (0.4 to 4%) that usually resolve and thrombo-embolic complications (1 to 3%). When the pelvis has been irradiated, the patient must be warned of the increased risk of entero- or colovesicular fistula.

• Late morbidity

Chronic bacteriuria always occurs with intermittent catheterization and should not be considered a complication [20](LOE4).

The risk of calculus in the enlarged reservoir ranges from 10 to 50% [21-24] (LOE 2-3). It would appear that there is a higher risk of developing upper urinary tract lithiasis than in the general population [25-27] (LOE3).

After bladder augmentation, intestinal transit disorders are frequent and probably underestimated (0 to 30% of cases [17, 28-30]). Several explanations have been proposed (ileocecal valve not preserved, biliary salt malabsorption, etc.). Somani et al. recently conducted

Table 10. Main series concerning gastro-intestinal bladder augmentation in neurological patients with bladder dysfunction (Max BC:Maximal Bladder capacity, DP: Detrusor pressure at the maximal bladder capacity)

Authors	LOE	Total number of patients (neurological patients)	Type of bladder augmentation	Max BC pre-op	Max BC post-op	DP pre-op	DP post-op	Mean Follow-up (months)	Increased compliance (% patients)	Post-op continence status	Results for quality of life
Blaivas (2005) [45]	3	76 (41)	Ileum, cecum	166	572	53	14	108	NP	Cured 70%/ Improved: 18%	NP
Mor (2004) [44]	3	11(11)	Ileum	NP	NP	NP	NP	115	NP	Cured/improved: 82%	NP
Quek (2003) [72]	3	26(26)	Ileum	201	615	81	20	96	92	Cured: 69%/Improved: 27%	NP
De Foor (2003) [38]	3	105 (47)	Stomach, ileum, colon	NP	NP	NP	NP	88,8	NP	Cured/improved: 92%	NP
Medel (2002) [73]	3	26(26)	Stomach, ileum, colon	NA	NA	NA	NA	45.6	100	Cured: 84.6% Improved: 5.4%	NP
Nomura 2002 [74]	3	21(21)	Ileum	149	396	>60	NP	66	100	Cured/improved: 95%	NP
Shekarriz (2000) [16]	3	133(100)	Ileum, sigmoid, autoaugmentation	NP	NP	NP	NP	64	NP	Cured/improved: 95%	NP
Arikan 2000[75]	3	18(18)	Sigmoid	86	370	NP	NP	40	NP	Cured/improved: 95%	NP
Chartier-Kastler (2000) [17]	2	17	Ileum	174.1	508	65.5	18.3	75.6	100	Cured/improved: 88.5%	NP
Venn (1998) [76]	3	267 (152)	Ileum	NP	NP	NP	NP	36	NP	Cured/improved: 86.6%	NP
Herschorn (1998) [43]	2	59(59)	Ileum, cecum, sigmoid	220	531	48.9	15.8	72.6	100	Cured: 67% Improved: 28.8%	Excellent : 69.5% Good: 20.3%
Flood (1995) [40]	2	122 (59)	Ileum, sigmoid	NP	NP	NP	NP	37	95	Cured: 75% Improved: 20%	NP

Table 10. (Ctd) Main series concerning gastro-intestinal bladder augmentation in neurological patients with bladder dysfunction (Max BC:Maximal Bladder capacity, DP: Detrusor pressure at the maximal bladder capacity)

Authors	LOE	Total number of patients (neurological patients)	Type of bladder augmentation	Max BC pre-op	Max BC post-op	DP pre-op	DP post-op	Mean Follow-up (months)	Increased compliance (% patients)	Post-op continence status	Results for quality of life
Hasan (1995) [18]	2	48 (13)	Ileum	307	588	NP	NP	38	69	Cured/improved: 92%	Good: 83% Moderate: 15%
Mast (1995) [77]	3	28(24)	Ileum	235	511	72	46	30	95	Cured/improved: 95%	NP
Mc Inerney[42]	3	100(50)	Ileum	196	867	NP	NP	24	92	NA	NP
Singh (1995) [41]	3	78	Ileum, cecum, sigmoid	NP	NP	NP	NP	100	NP	Cured/improved: 93.6%	NP
Khoury (1992) [78]	3	100	Ileum, cecum, sigmoid	NP	NP	NP	NP	37	NP	Cured/improved: 91.7%	NP
Luangkhot (1991) [79]	3	21(21)	Ileum, cecum	185	595	53	16	37	100	Cured/improved: 95%	NP
Nasrallah (1991) [11]	3	14(14)	Sigmoid	101	383	61	NP	25	NP	Cured/improved: 86%	NP
Robertson[80]	3	25(19)	Ileum, cecum	122	659	23	7	14		Cured/improved: 40%	NP
Hendren (1990) [81]	3	129	Ileum, stomach, sigmoid	NP	NP	NP	NP	NP	NP	Cured/improved: 94%	NP
Sidi[82]	3	12(12)	Cecum, sigmoid	134	562	NP	<30	1.3	NP	Cured/improved: 100%	NP
Lockhart[83]	3	15(15)	Ileum, cecum, sigmoid	<150	330-480	>40	18-38	NP	NP	Cured/improved: 86%	NP

a cohort study (LOE2) focusing on this particular problem [31]. They report a high rate of intestinal transit disorders, affecting almost 50% of patients treated for neurogenic bladder. These complications distressed patients and nearly 10% regretted having undergone surgery. Although transit disorders cannot be imputed to surgery alone (patients with neurogenic bladder may have intestinal transit disorders unrelated to surgery), patients should be informed of this risk.

Since the gastrointestinal tract mucosa resorbs urine, water-electrolyte disorders may occur. Hyperchloremic acidosis is reported in up to 15% of cases (LOE 2-3). These water-electrolyte disorders may be accompanied by anomalies of calcium metabolism that do not appear to have any significant long-term effect, particularly on child growth, but the subject is still under debate (LOE 3) [32-35]. However, care must be taken when treating patients with a marked decrease in creatinine clearance, since metabolic acidosis is no longer compensated [4](LOE4).

In theory, diversions performed using the ileocaecal junction and the end segment of the ileum would expose patients to a risk of vitamin B12 deficiency (with possible onset of megaloblastic anemia). The fact that the intestinal segments measure less than 50 cm would explain why very few patients suffer vitamin B12 deficiency.

The risk of cancer development of the newly formed reservoir is particularly feared since neuro-urological surgery is often indicated in patients with long life expectancy, many being children. The general consensus today is that patients with a bladder reservoir are at higher risk of developing a tumour than is the general population, but this risk has not as yet been clearly defined. The figures usually given for the risk of tumour development range from 1 to 3% [36, 37]. (LOE 4). Most of the published cases concern adenocarcinoma at the junction of the intestinal mucosa with the urothelium. These usually developed long after the initial surgery (over 10 years in most cases). Some patients developed urothelial tumours with the typical risk factors. Two facts should be emphasised with regard to neurogenic bladder (augmented or not):

- The sensitivity and specificity of the routine bladder tumour diagnostic and monitoring tools (urinary cytology, BTA test, simple cystoscopy, etc.) are reduced. Patient monitoring can only be envisaged by regular cystoscopy with biopsy of suspect areas.
- Monitoring is essential, since many patients develop tumours without symptoms and may be not be diagnosed until late.
- The most serious and possibly life-threatening complication is cystoplasty perforation (LOE3). This can happen whichever gastrointestinal segment is used, but occurs more often after ileocystoplasty [38](LOE3). It is estimated to occur in 5 to 13% of cases [16](LOE3). Perforation usually occurs on the graft or at the junction of the bladder with the enterocystoplasty and often results from high pressure within the enterocystoplasty, or more rarely from traumatic catheterization or urodynamic investigations [39](LOE4).

• Functional outcome

The functional outcome of bladder augmentation by enterocystoplasty is given in **Table 10-Table 10 ctd**. Only series of patients undergoing bladder augmentation for neurogenic bladder were retained in our analysis. Given the wide range of indications, surgical techniques and enteric segments used, it is difficult to draw any clear conclusions from these studies. Furthermore, most were retrospective studies; however certain points should be noted.

All authors reported an improvement in bladder capacity and compliance (LOE2-3) [17, 18, 40-42]. Improved vesicorenal reflux has already been mentioned. More than 90% of patients achieved nocturnal continence, and between 91 and 100% achieved diurnal continence [17, 18, 40-42] (LOE2-3).

Two quality-of-life studies (LOE2) reported improvement rates exceeding 90% [18, 43]. However, we would draw attention to one potential bias due to the heterogeneous population in these studies. Some patients underwent augmentation for detrusor overactivity of neurological origin, and others for idiopathic overactive bladder. We may conclude that these results can be applied to the sub-population of neurogenic patients, since they have already accepted intermittent catheterization before surgery.

If the bladder compliance defect persists, exclusion or ischemia of the intestinal patch must be investigated [37, 42]. Sometimes urinary leakage is related to sphincter deficiency and may be treated by an artificial urinary sphincter [44] or other means of urethral pressure reinforcement [37, 45]. However most authors consider that this type of adjunctive treatment should not be performed routinely since most patients have a good functional outcome after bladder augmentation, and only those with marked sphincter deficiency prior to surgery require these measures.

b) Possible alternatives to enterocystoplasty

1. Gastrocystoplasty and ureterocystoplasty

The use of a pediculated segment of stomach (gastrocystoplasty) or ureter (ureterocystoplasty) as an alternative to enterocystoplasty has been reported mainly for children with a neurogenic bladder. In theory, its advantage lies in the absence of metabolic acidosis, but in adults this is very theoretical. Moreover, both these intestinal segments secrete less mucus than the small and large intestines [46-50]. Abdel-Azim *et al*.

[48] recently published the only recent study of the gastrocystoplasty technique in adults (LOE3). In the light of their experience with children, they decided to use this technique in a set of young adults (mean age: 23 years, range: 4-32 years). Their paper records that the short-term results (3 years mean follow-up) of gastrocystoplasty were satisfactory, with increased functional bladder capacity and no impairment of the upper urinary tract (LOE3). However, two disadvantages are reported. First, a hematuria-dysuria syndrome requiring occasional use of antacids sometimes accompanied gastrocystoplasty. Second, the maximum bladder capacity was slightly lower than that observed in patients having undergone enterocystoplasty. This may have a benefit for easier bladder voiding but a negative effect due to the fear that in the long-term, the bladder may lose its capacity and further surgery will be required. The outcome in the very long-term for patients who have undergone this procedure remains unknown.

2. Autoaugmentation by detrusor myotomy

Bladder autoaugmentation without any associated gastrointestinal tract surgery as an alternative to enterocystoplasty was proposed as early as 1972 by Mahony and Laferte [51] who performed detrusorotomies (detrusor incision without resection) to increase bladder capacity and reduce incontinence. With Cartwright and Snow [52], the technique then evolved to detrusorectomy. This involves excising a thick segment of muscle from the dome of the bladder, leaving only the mucosal membrane in place. Bladder pressure gradually dilates the “demuscularized” area resulting in bladder augmentation.

The intervention, initially described by extra peritoneal laparotomy, can be performed by simple video-assisted surgery [53, 54] (intra or extra peritoneal celioscopy) or by robot-assisted surgery [55](LOE4). The detrusor can be dissected by laser [56](LOE3). The area around the detrusorectomy can be protected using the omentum [57] or a striated muscle [58] (rectus abdominus muscle) to prevent perforation and retraction(LOE4).

Techniques using free-graft or pediculated de-epithelialized gastric patches [59, 60] require gastrointestinal tract surgery and were therefore not included in the present work. Furthermore, most of the previously published studies concerned children. All the studies are retrospective and with few patients. For children, most authors [57, 61-65] report poor results after surgery, both symptomatic and urodynamic, together with a risk of upper urinary tract impairment(LOE4). Two authors recently reported better results with certain technical artefacts, namely an extensive detrusorectomy [66](LOE4) and rectus muscle hitch and backing [58](LOE4). The last technique supposes a large dissection of the rectus muscle. Urothelium is the sutured to this muscle in the theoretical objective to prevent its retraction and shrinkage.

Only three series are available for adults and all are retrospective studies. The first, published by Stöhrer et al in 1997 [67] (LOE3), reports interesting results for efficacy, with increased functional bladder capacity. However, the authors did not report mean follow-up and described a mixed population with 39 patients with neurogenic bladder and 11 patients without. The two other published series concerning adults [61, 62] did not confirm these findings but did confirm the marked superiority of enterocystoplasty with respect to both urinary symptoms and upper urinary tract impairment (LOE3). An analysis of the paper by Kumar [61] shows that the results of enterocystoplasty may differ according to the type of detrusor overactivity (DO). He reported good results for patients presenting idiopathic DO. Conversely, with a mean follow-up of 79 months, nearly all patients (5 of 6) with neurogenic detrusor overactivity were not improved (LOE3).

There is little information on specific complications, but detrusorectomy is simpler and seems to present less risk than enterocystoplasty. A comparative retrospective study (LOE4) reported 20% complications for enterocystoplasty (infectious digestive and parietal complications) against only 3% for detrusorectomy [62]. The rate of secondary rupture and/or perforation is poorly documented. An experimental animal study concluded that the bladder rupture pressure was slightly lower after detrusorectomy than after enterocystoplasty, thus exposing the patient to an increased risk of rupture [68] (LOE4).

3. Bladder augmentation using biomaterials

It is not yet possible to use artificial bladders. However, bladder augmentation using porcine intestinal submucosa (SIS, Cook®) [69](LOE4) or an acellular matrix of porcine dermal collagen and elastin fibres (Pelvicol, Bard®) [70](LOE4) have been described. These biomaterials can only be used after performing clam cystotomy since the area to be colonized should not be too large. It also appears that the use of biomaterials is associated with higher incidence of bladder lithiasis. To date, the number of reported cases remains limited. Larger trials are necessary to evaluate routine use of biomaterials. The use of autologous tissue may also be envisaged. In 2006, Atala [71] has published promising preliminary results on a small prospective study of 7 young patient with a neurogenic bladder (LOE 2). In this article he describes his technique, which consists in seeding patient’s urothelial and muscle cells on a biodegradable scaffold. After 7 weeks, this engineered artificial bladder could be implanted in patients. Although the small number of patients doesn’t allow definitive conclusion, a trend to a better bladder capacity and compliance was observed. Future studies will have to confirm these very exciting results.

RECOMMENDATIONS

- **Any segment of the gastrointestinal tract may be used for bladder augmentation, but the ileum seems to give the best results in terms of ease of use, risk of complications and efficacy (B). Few data are available concerning gastrocystoplasty and urete-rocystoplasty in adults (D)**
- **When the bladder suffers a significant compliance defect, supratrigonal cystectomy is preferable to clam cystoplasty (B).**
- **Bladder augmentation may solve low-grade vesicorenal reflux. In the event of grade IV or V reflux, ureteral reimplantation may be necessary (C).**
- **Patient should be informed that the most frequent and serious complications are bladder calculi and perforation at the bladder/bowel junction, usually caused by over-pressure (B).**
- **Bladder augmentation may have sequelae such as intestinal transit disorder, and patients should be informed of this before surgery (C).**
- **The body of evidence concerning detrusor myomectomy in neurological patients is controversial. Therefore, detrusor myo-mectomy should not be recommended in these patients with impaired bladder function (D)**
- **Bladder augmentation using biomaterials or tissue engineering is promising, but the preliminary results need to be confirmed by larger studies (D)**
- **Due to risk of complications regular follow up is needed (B)**

6. CUTANEOUS CONTINENT URINARY DIVERSION

- **Keywords used for the medline research**

Continent urinary diversion; vesicostomy; cystostomy; neurogenic bladder; spinal cord injury; spina bifida; myelomeningocele; multiple sclerosis

a) Introduction

For certain patients, urethral catheterization can be or become, unacceptable or even impossible. The following list is not exhaustive, but describes the more frequent reasons:

- Functional limitations of the upper limbs (Tetraplegia [1] unilateral or bilateral plexus problems, musculoskeletal trauma problems)
- Cognitive disorders (forgetfulness, lack of comprehension, refusal)
- Difficulties in terms of mobility and/or undressing (spasticity, upper spinal cord injury resulting in difficulty in maintaining the equilibrium of the trunk and or limited control of the upper limbs, obesity).
- Failure to reach the urethra independently (more common in women, compounded by the tilted pelvis and all other factors that cause mobility difficulties.)
- Urethral injuries (stenosis, fistulas, hyperesthesia), urethral pain.

In these situations, the realization of a continent cystostomy may be an option. The general principle is to permit the emptying of a full bladder, independently and easily, by intermittent catheterization through an efferent tube attached to the wall of the lower half of the abdomen. The absence of any leakage from the cystostomy is controlled by its own watertight system associated with the return process of a capacitive and compliant reservoir.

This will require careful selection of patient candidates especially when there is any function impairment of the upper limbs (trauma to the spinal cord) [2-4](LOE3).

A pre-operative assessment is indispensable and must include the motivation of the patient, capabilities for dressing and undressing, capability of catheterization in the planned stomal area, tolerance for the time and potential discomfort involved.

In the case of cognitive difficulties that are too significant, if a severe upper limb dysfunction exists [1] or if compliance of the patient remains an impossible obstacle, continent diversion is not indicated. Contraindication can also be a deteriorated renal function [5]).

In neuro-urology, techniques for heterotopic continent neo-reservoir (derivation supra-bladder such as Koch pocket, Benchekroun, Mainz, Miami…) are seldom used initially. They can be offered to patients with vesico-renal reflux, with incontinence through the native urethra despite bladder enlargement or when closure of the bladder neck will be needed (e.g. uretro-vaginal fistula).

b) Results of the different types of cystostomy:

The series are in the vast majority, retrospective (LOE 3) and frequently combine several techniques. This makes the analysis of the results difficult, but some major facts can be gleaned from them.

The catheterizable tube must be able to penetrate the intact or enlarged bladder and it must be able to reach the abdominal wall through a direct pathway with easy access for the patient that has already been predetermined by pre-operative research. The pathway

of the tube must be direct in order to facilitate self-catheterization. Two major families of techniques can be used: simple tubes implanted with an anti-reflux system and intestinal loop invaginations.

1. Simple tubes:

a. Technique:

Virtually any anatomical structure that is tubular or that can be tubularized and that is vascularized can be used to make a continent catheterizable tube [4](LOE4).

The two structures that are the simplest to use are:

The appendix: Transappendicular cystostomy according to Mitrofanoff's procedure [6] has long been the most used technique(LOE3). Different modifications have been proposed, especially to gain more length by removing a cecal cuff.

A short, remodeled intestinal segment (small intestine, less frequently the sigmoid or right colon). Yang and Monti simple [7] (LOE3) or double technique and the Yang-Monti technique modified according to Casale in order to gain length by avoiding a double tube [8] (LOE3).

Other structures have been used in a more anecdotal manner, primarily in children: cecum and appendix monobloc [9] (LOE4), bladder [10](LOE4), stomach [11] (LOE4), distal ureter [12](LOE4), tube, Meckel's diverticulum [2, 13](LOE4), or the preputial or clitoral skin [14] (LOE4).

For most authors, continence of the tube was guaranteed by implantation in the native bladder or in the augmentation via a submucosal path similar to that used in ureteral reimplantation for vesicorenal reflux. (LOE4). The submucosal path length must be at least 2cm, and is adapted to the bore of the tube (two to three times the diameter) [4] (LOE4). A posterior or posterolateral bladder flap (kept in case of a supratrigonal cystectomy) should allow a more solid implantation of the tube in the bladder [15](LOE2). Direct implantation into the digestive plasty has also been reported.

The stoma's cutaneous anastomosis is made in the lower half of the abdomen, at the umbilicus, most frequently by principle, or in the right or left iliac fossa. Most authors recommend the interposition of a skin flap in the distal end of the tube in order to avoid frequent stenosis on the circular orifice scars. Several techniques have been proposed: flap in V, VQZ [16] (LOE3), and VR [17](LOE3). However, at present, the results published do not confirm that the risk of stenosis is avoided by any of the techniques.

It seems essential that the site of the stoma would be determined preoperatively in patients with functional limitations of the upper limbs. The site is chosen based on the patient's capabilities and the position during self-catheterization (seated in a chair, supine, other). The surgical technique used in this particular case must allow access to any point on the lower half of the abdominal wall [3, 18, 19].

b. Results:

Table 11 summarizes the results in terms of stoma continence, utilization of the DUCC (carrying out ASPI across the DUCC), and complications. We retained only points specifically related to the continent stoma in the articles. The necessity of reservoir augmentation (80% of published cases) and techniques allowing reinforcement of ureteral continence are addressed in another chapter. Similarly, complications of the upper apparatus were not detailed. They are in essence found in the oldest series, in which bladder augmentation was seldom proposed, and/or during a ureteral reimplantation procedures (reflux treatment).

In adults as in children, techniques especially of Mitrofanoff (or variations using the appendix) and of Yang-Monti allow functional, continent stomas to be obtained in 75 to 100% of cases (LOE3).

Seven studies indicate significant improvement in quality of life after the procedure related to improved autonomy in bladder evacuation, to continence, and to improved sex life [3, 15, 19-23] (LOE2-3).

The rate of stoma complications (16 to 60%) is dominated by the risk of stenosis, which is most often treatable by a simple dilation [24] (LOE3). Many authors emphasize the fact that this complication occurs most often in the year following surgery. However, Liard's [25 16] results (LOE3), which reported an elevated (65%) intervention rate at 20 years of monitoring, must be emphasized. For most authors the rate of complications related to the tube continent was lower when the segment used was the appendix or intestines remodeled according to Yang-Monti (LOE3). However, these two plasties seem to have equivalent complication rates. Only Narayanaswamy et al [26] (LOE3) reported higher rates for catheterization difficulty and reintervention with the Yang-Monti tube in comparison to the appendix. The Monti tubes in this study were double tubes in 68% (17/25) of cases, and the majority of the complications were related to the junction area for the two hemi-tubes and not to stoma stenosis. Therefore it seems that this lengthening method should be used with caution. If there is a problem with tube length, the method proposed by Casale [8] (LOE4) has the theoretical advantage of avoiding an anastomosis on the tube or a bent pathway at the junction of the two tubes.

The umbilical anastomosis site for the stoma may be related to an increased frequency of stoma stenosis [10, 27] (LOE3). The poorer vascularization of the umbilicus has been proposed as an explanation [27]. However, results on this point are contradictory with more recent studies [15].

Table 11. Primary neurological bladder results from the DUCC series. (DUCC on remodeled or intact native bladder)

Team	Year	LOE	n (neurogenic bladder)	Mean follow-up (months)	Technique	Functional continent cystostomy (%)	Stoma complication (%)	New procedure on the stoma
Mhiri [35]	2007	3	20(28)	53	Mitrofanoff	100	13	3
Karsenty [15]	2007	2	13(13)	44	Mitrofanoff 7 Yang-Monti 6	100	0	0
Touma [23]	2007	3	12(12)	33	Casale	100	17	0
Franc-Guimond [17]	2006	3	12(12)	18	Mitrofanoff	100	8	8
Thomas [24]	2006	3	78 (62)	28,4	Mitrofanoff:33 Yang-Monti: 30 Bladder: 16	98	23	8
Castellan [13]	2005	3	135 (100)	38	Mitrofanoff 74 Yang-Monti 45 Gastric tube 8 Bladder tube 2 Meckel tube 1	NP	23,5	8
Blaivas [31]	2005	3	98(15)	108	NP	87	42	16
Chulamorkodt [36]	2004	3	54 (48)	30	Mitrofanoff 47 Yang-Monti 7	95	16	NP
Barqawi [37]	2004	3	109 (60)	46	Mitrofanoff 114 Yang-Monti ileac 21 Ureter 11 Others 5	92	36	NP
Lemelle [38]	2004	3	46(32)	64	Mitrofanoff 23 Yang-Monti 18	96	46	NP
Walsh [19]	2004	4	6(6)	44	Mitrofanoff 3 Hemi Kock 2	NP		NP
Zommick [3]	2003	3	21(21)	59	Mitrofanoff 7 Hemi Kock 2 Kock 6 Indiana 2	70	11	NP
De Ganck [27]	2002	3	53(45)	32	Mitrofanoff 45 Yang-Monti 8	90	36	NP
Cain [10]	2002	3	31 (15)	41	Bladder	100	45	NP
Tekant [21]	2001	4	46(11)	28	Mitrofanoff 38 Yang Monti 6	86	19,5	NP
Kochakarn [39]	2001	4	12(12)	12	Mitrofanoff 10 Yang Monti 2	100	NP	NP
Narayanaswamy [26]	2001	4	92 (21)	30	Mitrofanoff 69 Yang Monti 25 (17 double, 8 simple)	NP	Appendix 26 Yang Monti 60	NP
Liard [25]	2001	4	23(22)	240	Mitrofanoff 20 Bladder flap 2 Ureter 1	75	39	65
Harris [40]	2000	4	31/50	51	Mitrofanoff	96	16	16
Cain [41]	1999	4	69/100	48	Mitrofanoff 57 Yang Monti 22 Bladder tube 21	98	20	Appendix 21 Yang Monti 10 Bladder tube 29
Mollard [2]	1997	4	56(46)	120	Mitrofanoff 48 Distal ureter 8	92	16	NP
Sylora [18]	1997	4	7(7)	NP	Mitrofanoff 5 Yang-Monti Ileac 2	86	14	NP

c. Other types of continent urinary stoma:

Techniques are extremely varied and are better described in the series on bladder cancer. Two technical approaches can be broadly outlined here:

Invaginated valves (Koch pocket, Benchekroun, Mainz) in which the continence mechanism is tied to the flattening of the invaginated valve by urine accumulated in the neo-reservoir;

Ileal-caecal reservoirs in which a portion of the ileum and the ileal-caecal valve are used as a continence mechanism (Indiana pouch, Charleston pouch, Miami pouch).

Data in the literature do not allow a determination to be made as to the superiority of one type of stoma over the others. However, the catheterization difficulties seem to be lower with stomas that use the appendix; the risk of lithiasis seems to be higher with the stomas which require the use of metal staples [28] (LOE4). Several authors have also specifically reported results in neurological patients [20 , 29-34] (LOE3).

Continence rates for the stoma vary between 63 and 100%. Complication rates for the stoma are between 10 and 23%. The need to proceed systematically to ureteral reimplantation is aggravated to a certain degree by short term stenosis (0 to 18%), but, as in “simple” tube techniques, few long term follow ups of patients are available.

RECOMMENDATIONS

- **Indication for cystostomy presumes a multidisciplinary evaluation involving the urologist and a neurologist or a reeducation doctor, as well as stomatherapy nurses or occupational therapists for estimating patient catheterization capabilities (A)**
- **Use of the appendix to carry out continent cystostomy is the standard method today, but few long term data are available in adults (C)**
- **If the patient has undergone an appendicectomy the use of a segment of the small intestine can be proposed, with slightly poorer short term results (C)**
- **Long term follow up of the patients having had a continent cystostomy is needed to have a better idea of the long term results of the various procedures (C).**

7. NON-CONTINENT CUTANEOUS URINARY DIVERSION IN NEUROUROLOGY

- **Keywords for Pubmed search**

neurogenic bladder; spinal cord injury; spina bifida; myéloméningocèle; multiple sclerosis; urinary diversion; ileovesicostomy; Bricker; ureterostomy; vesicostomy; ileal conduit

a) Introduction

Non-continent cutaneous diversion refers to all methods used to divert urine, and where incontinence remains or where a system of extra-physiological continence is created, i.e. urine flow is continuous and requires a means of collecting urine attached to the skin.

In the context of neurogenic bladder, these diversions make it possible to obtain low bladder pressure and to preserve the upper urinary tract.

This type of surgery is a last resort for the many complications related to neurogenic bladder (and congenital anomalies of the lower urinary tract), in patients for whom other therapies have failed to help.

Four techniques are described for non-continent urinary diversions for patients with neurological vesico-sphincter disorders. In order of frequency these are: ileal conduit urinary diversion, ileovesicostomy, cystostomy and cutaneous ureterostomy.

b) Ileal conduit urinary diversion

Ileal conduit urinary diversion is the type of diversion most frequently performed on neurological patients with bladder dysfunction. It differs only slightly from the cystectomy performed for bladder cancer [1]. Pre-operative location of the intended stoma site is crucial and must be adapted to the patient's main position (wheelchair or bed); the stoma site must be easy to access for management. The ileal segment must be as short as possible to prevent stasis [2](LOE3). There is a variant to this technique whereby a segment of jejunal loop is removed and a stoma made on the left hemi-abdomen. This technique can be proposed after irradiation of the pelvis minor, if the ileum has been impaired and a short loop must be used (about 10 cm) to avoid metabolic disorder (jejunal conduit syndrome: hyperkaliemia, hyponatremia, hypochloremia, acidosis) [3](LOE3).

In neurological patients, ileal conduit urinary diversion by laparoscopy and by robot-assisted laparoscopy have been described [4-7](LOE4). Patients seem to benefit from the procedure, though this remains to be confirmed in the medium and long-term [8] (LOE 2).

1. Results in neurological patients with bladder dysfunction

Some series of neurological patients were evaluated to determine the onset of early and late complications [8-14](LOE2-3). Early series of children can be evaluated to determine the morphology of the upper urinary tract and renal function after urinary diversion over a long period (up to 20 years) [15-20](LOE3).

2. Early complications

Mortality is estimated between 0 and 3.4% (LOE2-3) [8-14].

The commonest early complication is intestinal occlusion (4 to 12.6%), usually reversible after prolonged intestinal drainage [8-14](LOE2-3). The risk of gastrointestinal fistula should also be taken into account (0 to 3.3%). As for enterocystoplasty, the current trend is to try to reduce nasogastric tube drainage time to a few hours [21](LOE3).

The most frequent medical complications encountered (3 to 8%) are febrile urinary infections and thrombo-embolism (2 to 3%)[8-14](LOE2-3).

Other major complications include: urinary fistula in 0.3 to 3.4% of patients which may be prevented by placing a ureteral catheter for about ten days [8-14](LOE3). This complication could be a risk factor for later uretero-ileal anastomosis (LOE4).

3. Late complications

a. Gastrointestinal risk

The risk of long-term intestinal occlusion is difficult to evaluate. It ranges between 5 and 7% (LOE3) [9-14]. Even when a short intestinal segment is used, some patients can experiment transient constipation or diarrhoea, which could adversely affect their quality of life[22](LOE2).

b. Complications affecting the bladder left in situ

For the particular indication of neurological patients with bladder dysfunction, several authors have proposed not carrying out cystectomy so as to avoid potentially morbid surgery. At present, this is debatable for several reasons:

- First, there is a risk of pyocyst formation in the unused bladder (21-50%) [9, 10, 14, 23] (LOE3). Even where conservative treatments have been attempted (combining vesicular irrigation with antibiotherapy)[24] (LOE3), secondary cystectomy is then necessary in 50 to 100% of cases [10, 15, 17]. For women, a surgical alternative is vaginovesicostomy, which appears to be effective [11, 17](LOE4).
- Furthermore, the unused bladder is frequently infected and may become an "irritative thorn", especially in patients with spinal injury or multiple sclerosis (LOE 4) [10, 25].
- A final argument in favour of cystectomy is that the risk of bladder neoplasia is higher in neurogenic patients, the principal risk factors being long-term indwelling catheterization (more than 8 years), bladder calculi and smoking [26-28](LOE3). Moreover, screening by cystoscopy-biopsy is not effective [29, 30] (LOE3).
- Finally, improvement of the cystectomy technique (noticeably laparoscopic cystectomy) has considerably reduced related morbidity [8] [31](LOE2-3). Supratrigonal cystectomy can be performed in men, preserving the prostate and preventing any genital and sexual sequellae.

c. Upper urinary tract complications

Stenosis of the uretero-ileal anastomosis may occur in the medium and long term. This is very damaging to the upper urinary tract and requires regular monitoring of the morphology. In contemporary series of neurological patients with bladder dysfunction, it occurs in 2 to 7.8% of cases within 10 years [9-14] (LOE3). For cases followed for more than 10 years, the finding of 16.5 to 50% stenosis is essentially that of early paediatric series [15-20](LOE3). Impairment of the upper urinary tract and renal function seems to be correlated mainly with stenosis of the uretero-ileal anastomosis, but also with a long ileal graft and stomal stenosis leading to poor voiding and pyelonephritis [16](LOE4). In the event of poor functioning of the uretero-ileal anastomosis, some authors suggest endoscopic dilation before further surgical repair of the anastomosis (LOE3)[13, 32-34]. Surgery however remains the reference treatment [32](LOE3).

The risk of upper urinary tract lithiasis (3 to 31%) is always present in these patients (even without stenosis of the uretero-ileal anastomosis) [9, 10, 13, 14](LOE3). Patient monitoring should include regular screening of the upper urinary tract to detect any lithiasis and to implement timely treatment (LOE 4).

Chronic bacteriuria is frequent but should not be treated if asymptomatic. Both patients and attending physicians must be informed so as to avoid the administration of unnecessary antibiotics. However, the risk of febrile infection persists over the long term and is logically favoured by uretero-ileal stenosis (12 to 34%) [9, 10, 13, 14].

d. Stoma complications

These are relatively frequent (18.6 to 30%) and varied [10, 13, 14]. The risk of peristomal eventration is the most frequently reported (between 7.7 and 10%). Stomal stenosis may also occur. Stoma complications appear to occur more often in obese patients (LOE3) [35].

Finally, it should be noted that some patient could ask for undiversion. These mainly concern adults who underwent surgery as children and who later wished to recover a continent system, or who have had complications with their non-continent urinary diversion [36-40](LOE3-4).

c) Ileovesicostomy [41-50]

This technique was first described by Cordonnier in 1957 for treatment of three children suffering from myelomeningocele [48](LOE4). Its theoretical advantages are relative simplicity, the absence of dissection and suture of the ureter, thus preventing ureteral complications and the potential of "*restitutio ad integrum*" of the bladder (only one case described) [47](LOE4).

The surgery consists in removing a 10 cm ileal segment from about 15 to 20 cm above the ileocecal valve. One side of the segmnt is anastomosed to the dome of the bladder and the other to the skin halfway between the ileac spine and the umbilicus. A partial cystectomy is performed to reduce reservoir volume and possible urine stagnation. Surgical variants have been described with simple partial detubularization of the ileum before vesico-ileal suture [50], or the creation of a modified Boari flap on the bladder associated with partial detubularization of the ileum [42, 45-47, 49](LOE3). These improve drainage by reducing the ileal segment. Laparoscopic ileovesicostomy seems to be feasible [41, 44] (LOE4).

One of the problems with this type of surgery, particularly in women, is the need for further surgery to prevent residual urinary leakage. All authors agree that this significantly prolongs surgery time. This further surgery may consist in closing the bladder neck or placing a suburethral tape [47, 49, 51, 52] (LOE3). Some authors propose performing this surgery later, where necessary [50](LOE3).

1. Early complications

Early complications are related to the underlying condition of these patients, which is often poor. No case

of post-operative mortality has been reported in the published series [42, 43, 45-47, 49, 50, 52](LOE3). In some cases of poor drainage through the stoma, the drainage was prolonged to six weeks (instead of the usual three). Other early complications were related to poor results of the surgery performed to render patients continent (**Table 12**). Patients with this type of problem are the most likely to resort to cystectomy with ileal diversion (3 to 6%) [47, 51](LOE3).

2. Late complications

These are summarized in Table 10. No reported series to date has more than five years of follow-up. The most frequent problems appear to be poor voiding related to stenosis of the stoma or the ileovesical anastomosis. Only one report specifically mentions problems related to stoma equipment that occur in about 28% of patients [51](LOE3). The incidence of renal or vesicular lithiasis appears to be low, and several authors report that affected patients had history of lithiasis.

Renal function appears to be preserved with this procedure at least with a mean follow-up of five years (LOE 3) [16, 42, 43, 45-47, 49-51, 53]. No case of impaired renal function, or even post-operative uretero-hydronephrosis was reported.

Finally, it should be underline that two patients in the series with the longest follow-up who developed a bladder tumor [45](LOE4).

d) Vesicostomy

Vesicostomy was described by Blocksom in 1957 [54] and detailed more recently by Lapides [55, 56].

The technique consists in constructing a bladder tube anastomosed to the skin by making a transverse suprapubic incision to reach the space of Retzius. The stoma is located half way between the umbilicus and the incision.

The principal benefits of vesicostomy are its simplicity and reversibility, particularly in children [57-63], making it possible to envisage temporary surgery to treat an acute urological problem. In pediatric series, an improvement in the symptoms of infection was reported, with 6 to 20% of patients suffering bladder calculi and 6 to 18% stomal stenosis. Hydronephroses improved or stabilized in most cases. The rate of end-stage renal failure varied between 6 and 18% for mean follow-ups of 6-7 years.

Nowadays, it is rare to conserve a vesicostomy long term. The results of Lapides are therefore all the more interesting: after two years of follow-up, no urinary infection, 16% poor drainage and 12% calculi [56] (LOE3). Renal function was preserved. At 10 years of age, however, 9.6% of deaths due to end-stage renal failure, mainly due to calculi and repeated infection of the upper urinary tract, were reported [56] [64](LOE3). At 20 years, the rate of chronic renal failure is around 16.6%[54-65](LOE3).

e) Cutaneous ureterostomy

During this procedure, the ureters are placed in direct contact with the skin without using the gastrointestinal tract. There is no gastrointestinal resection/ anastomosis which is a marked source of morbidity and mortality. Surgery via the retroperitoneal route is quick and simple.

The main inconveniences are: cutaneous stenosis if the stoma is left without catheter, upper urinary tract infections and calcification around catheters if stoma is equipped. Moreover, it is frequently necessary to construct a double stoma.

It is used in adults, usually in the context of palliative urinary diversion for those with obstructive pelvic cancer (bladder, uterus, rectum), and rarely in neurological patients [66-71].

Surgery is simple: in the absence of cystectomy, two short lateral incisions are made in the iliac fossa, at approximately 3-4 cm from the anterosuperior iliac

Table 12. Results for contemporary series of ileovesicostomy

	LOE	n	Mean follow-up (months)	Re operation following primary surgery (%)	Stomal problems (%)	Kidney lithiasis	Bladder lithiasis	Continent (%)	Post-op hydrone-phrosis (%)	Symptomatic urinary infection (%)
Tan, 2007 [51]	3	50	26,3	54	38	2	6	72	0	10
Gauthier, 2003 [43]	4	7	37,4	NP	1/7	1/7	0/7	NP	0/7	1/7
Atan, 1999 [42]	3	15	23,2	NP	16	33	20	67	0	20
Gudziak, 1999	3	13	23	23	8	8	0	92	0	8
Leng, 1999	3	38	52	NP	13	10	5	NP	3	3
Mutchnik, 1997	4	6	12	1/6	1/6	0	0	6/6	0/6	0
Rivas, 1995	3	11	24	NP	NP	NP	NP	100	0	0
Schwartz, 1994	3	23	45	NP	21	0	0	NP	0	NP

spine. Direct retroperitoneal access is made and the two ureters located on the internal border of the psoas muscle or above the iliac vessels.

It is important that the peri-ureteral region be spared and the ureter sectioned as low as possible. The ureter is then catheterized and raised to the skin. The stoma is formed by attaching the ureter to the skin, or by spatulating the sutured ureter on a V-shaped cutaneous incision (separate sutures with fine resorbable thread).

Variants are described so as to obtain only one stoma: Y-transuretero-ureterostomy, implantation of both ureters in a single stoma, implantation of a single ureter (ureter ligated to the least functional kidney, or even nephrectomy). The use of cutaneous plasties may remove the need for ureteral catheterization [72].

Cutaneous ureterostomy was first performed in the 1960s, to treat children with spina bifida and severe upper urinary tract impairment [68, 71]. The technique was also developed to treat malformative uropathies (extrophy of the bladder and the posterior urethral valves) [66, 68-70].

Long-term results with a mean follow-up of 8 years are given hereafter: rates of stenosis between 8.7 to 11%, infections from 6.6 to 10% and calculi from 10 to 15.5%) [67, 70](LOE3).

Renal function was preserved for short follow-up times, but fatal end-stage renal failure occurred in up to 26.6% of children during long-term follow-up [69](LOE3).

This technique is almost never used for neurological patients with bladder dysfunction anymore because conservative treatments (intermittent catheterization, urological endoscopy) have improved and the number of children suffering from spina bifida or presenting with complex malformation of the lower urinary tract has gradually lowered. Moreover, new urinary diversion techniques have been developed.

RECOMMENDATIONS

- **Non-continent urinary diversion is the last resort for patients with neurogenic bladder (A).**
- **Bladder should be removed during the procedure because of the risk of later complications at this site (B)**
- **It may be indicated for urological dysfunction or in the event of a motor handicap that prevents other modes of micturition (C).**
- **Ileal conduit urinary diversion has the best long-term results for non-continent diversion, if the following pre- and peri-operative precautions are taken (B):**
  - **Pre-operative location of the stoma, with wheelchair test, if necessary.**
  - **Utilization of a short intestinal segment (10 cm maximum).**
  - **Minimal dissection of the ureters.**
- **There are several reports of good results for ileovesicostomy, but the medium-term results need to be confirmed in the long term. Quality-of-life studies should also be performed (C).**
- **Vesicostomy may be a useful transient solution, particularly for children (D)**
- **Cutaneous ureterostomy shouldn't be used for non continent urinary diversion in adult patients because of the rate of long term complications (B).**

D. NEUROLOGICAL FAECAL INCONTINENCE

I. EPIDEMIOLOGY

• Summary from the previous edition [1]

There have been limited numbers of references giving data on prevalence of faecal incontinence (FI) following neurological diseases. Searching from Pubmed from 1964 to 2004, 36 papers were included and the prevalence and incidence of FI varied due to different definitions, severity and also causes/diseases.

The incidence of FI among spinal cord injury (SCI) patients after discharge from rehabilitation was reported between 11% and 75%; the prevalence of constipation and/or FI among multiple sclerosis (MS) ranged from 20% to 73%; and 30% to 50% of Parkinson's disease (PD) patients reported bowel incontinent.

Regarding stroke patients, during acute admission 32% to 79% of the patients reported FI; the prevalence dropped to 25% to 28% at discharge and 12% to 19% at 6 months. New-onset FI in stroke survivors was transient. Modified risk factors for FI at 3 month after stroke onset were anticholinergic drug use and difficulty with toilet access. It was recommended that bowel dysfunction should be evaluated jointly with bladder dysfunction.

• Search strategy

To add new information to the previous edition, we searched from Pubmed from 2004 to 2008 with search words neurogenic bowel, faecal incontinence, prevalence, incidence, epidemiology, stroke, SCI, MS, PD. Relevant papers from Pubmed, non-Pubmed,

and also other relevant papers that were not cited in the previous edition were recruited and summarized as follows:

1. SPINAL CORD INJURY

During rehabilitation phase, Aya? et al (2006)[2] studied 24 traumatic SCI patients before applying abdominal massage and found that 45.8% had abdominal distention, 41.7% had FI and 25% had difficult intestinal evacuation. New PW (2007) [3] retrospectively reviewed 70 non-traumatic SCI consecutively admitted for initial rehabilitation, 5% of the patients (excluded who died) reported having FI, incontinent at least once per week before discharge.

According to the survey of the impact of secondary conditions after SCI reported in 2007 [4], 13.8% of 65 chronic SCI persons (mean current age 43.8 years, mean years since injury 13.7) rated bowel dysfunction (FI, constipation, diarrhea) as significant or chronic problem, equal to bladder dysfunction and circulatory problem.

Regarding chronic SCI, Tongprasert and Kovindha (2006) [5] studied 100 chronic traumatic SCI patients (duration from onset > 6 months, average 6 years) in Chiang Mai, Thailand and compared with 55 normal persons; 86% of the SCI patients reported constipation, 35% reported FI and 16% had hemorrhoids. The prevalence of constipation and FI were significantly different (P<0.0013) from the normal population (constipation 5%, FI 1.8%). However, prevalence of hemorrhoid between SCI and normal persons was not different (16% vs. 20%, p = 0.338). According to the study of Ng et al (2005)[6] done in 110 established traumatic SCI persons (> 12 months after injury, median 17 years) in Sydney, Australia, the prevalence, based on the Rome II Integrative Questionnaire, was as follows: 41% of FI, 22% abdominal bloating, and 46% constipation (including laxative use). Another prospective, multicentre follow-up observational study was reported in 2007 by the Italian Group for the Epidemiological Study of SCI [7], only 2.7% of 403 traumatic SCI persons (mean duration from discharge to follow-up 3.0+/-0.68 years) reported no bowel continence (= FI), 20.1% had partial, 77.2% had full bowel 'continence' (absence of unplanned bowel evacuations) and 70.5% had bowel autonomy (patient's ability to perform bowel management without assistance). According to the survey in Canada reported in 2004 by Liem et al [8], the most common complication among 352 SCI volunteers for more than 20 years was bowel problems: 47.9% constipation and 41.8% diarrhea/bowel accidents.

FI was found to associate with higher level of anxiety (odd ratio, OR = 2.4, p =0.05) [6] and severity of injury [5] but not with the level of injury [5,6]. According to the study of Vallès et al (2006)[9], they found that in 54 patients with motor complete SCI (mean duration from onset 6 years), 67% presented with constipation (according to Rome II criteria) and 85% some degree of FI. They also found associations between bowel abnormalities i.e., constipation and FI and different neuropathophysiologic patterns. Those with SCI above T7 had frequent constipation (86%) and not severe FI; those with SCI below T7 with preserved sacral reflexes had not so frequent constipation (50%) and not severe FI; and those with SCI below T7 with no sacral reflexes had not very frequent constipation (56%) and greater severity of FI. When compared with those with spinal sacral reflexes, those with no such reflexes had significantly more severe FI (p < 0.005)[9].

According to Krog et al (2006)[10] who did a study in 424 SCI patients to develop and validate a symptom-based score for NBoD, those with daily FI had 10 times more impact on QOL than those with no FI (OR 10.0, p <0.05). Moreover, studies showed that NBoD had significant impact on QOL of chronic SCI patients [10] and they had significantly lower Gastrointestinal QOL score as compared with the normal persons (92.51 +/- 16.21 vs 118.33 +/- 14.17, p <0.001)[5]. From the Italian study [7], loss of bowel/bladder autonomy was correlated significantly with complications (OR 2.202; 1.357-3.574; p <0.001), re-admission (OR 2.097; 1.306-3.366; p < 0.002) and death (OR 5.457; 2.350-12.670; p <0.0001).

Regarding constipation, its association with level of injury was supported by many studies [5,6,9] i.e., upper motor neuron NBoD vs lower motor neuron NBoD (p =0.0013)[5]; cervical injury had more than 5 times more frequent constipation than lumbar injury (OR =5.6, p =0.02)[6]; lesion above T7 had more constipation than lesion below T7 (p <0.05)[9]. In addition, constipation was also associated with severity of injury [4] and taking bladder relaxants [5]. Moreover, it was associated with a 97% increase in the likelihood of needing more help with activities of daily living (ADL) [8].

2. STROKE

In 2006, Brittain et al [11] reported prevalence of isolate UI, FI and double incontinence (DI) in stroke survivors living in community of Leicestershire, United Kingdom. Those living in institutional care were excluded. Of 1,483 stroke survivors, the prevalence was as follows: 6.9% any FI, 4.7% major FI, 2.2% minor FI, 4.3% FI and UI (or DI) and 0.8% isolated FI. Major FI (soiling of underwear or more on a monthly basis) was 4.5 times as prevalent in stroke survivors as in the non-stroke population. DI (major FI and monthly urine leakage) was more than 4 times as high in stroke survivors than in the non-stroke population (4.3% vas 0.9%, P < 0.001). Isolated FI as well as isolated UI was also significantly higher in the stroke population. According to the epidemiologic multi-centre study of the Thai Stroke Rehabilitation Registry [12], on admission to rehabilitation, 31.5% of 327 stroke patients (median 24 days; about 5%

admitted one year after onset) reported of bladder and bowel problems: 24.5% UI, 8.6% urinary difficulty and 11.9% FI.

Regarding factors related to FI in stroke, urinary incontinence (adjusted OR 8.1; 95% CI 6.62-9.69) and functional limitation (adjusted OR 4.02; 95% CI 3.27-4.95) were significantly related to major FI in stroke living in community [11].

3. MYELOMENINGOCELE

According to the Dutch study on the prevalence of incontinence in young adult spina bifida reported in 2007[13], of 179 participants (142 with spina bifida aperta and 37 with spina bifida occulta), 60.9% had UI and 34.1% had FI (defined as having accident once a month or more); 109 were diagnosed as having myelomeningocele, 13 as having meninogocele and 119 suffered from hydrocephalus. When classified by type of lesions, 40.8% of spina bifida aperta and 8.1% of spina bifida occulta; 46.2% of those with hydrocephalus and 10% of those with no hydrocephalus; and 39.7% of those having lesion at L5 or above and 13.2% of those having lesion below L5 reported FI ($P < 0.05$). Moreover, about 2/3 of those with spina bifida aperta, hydrocephalus and lesion at L5 or above had UI as well; and most of them perceived FI and UI as problem.

4. PARKINSON'S DISEASE

Recently Krogh et al (2008) [14] did a study to compare bowel symptoms in PD with normal control subjects. Most of the cases had minor constipation-related symptom. However 7% of 416 PD but 0% of normal controls reported severe constipation; 27% and 23% with PD had bowel movements less than every second day and incomplete emptying every week, respectively. The severity of PD was associated with assisted defecation ($p < 0.001$) and unsuccessful attempts at defecation ($p < 0.001$). Regarding incontinence, 6% of PD patients reported incontinence to solid stool at least one per month, 6% to liquid stool at least one per month; 32% of PD patients had flatus incontinence at least one per week; these were no statistically significant difference to normal control group. They believed that the increase in obstructed defecation symptom but the less prevalence of FI are due to dystonia of the external anal sphincter but intact internal anal sphincter with normal anorectal sensibility.

5. TRAUMATIC BRAIN INJURY (TBI)

According to the report from the Traumatic Brain Injury Model Systems national database [15], the incidence of FI among TBI patients was 68% at admission to inpatient rehabilitation, 12.4% at rehabilitation discharge and 5.2% at 1-year follow-up; and FI was significantly associated with admission Glasgow Coma Scale score, length of coma and post-traumatic amnesia (PTA), length of stay (LOS), frontal contusion, functional independence measure (FIM) scores and urinary tract infection.

6. MULTIPLE SYSTEM ATROPHY (MSA)

Wenning et al (1994) [16] described the clinical features and natural history of 100 patients diagnosed as probable MSA. The most frequent autonomic symptom in men was impotence, and in women was UI. Moreover, Parkinsonism was the initial feature in 46%, but had subsequently developed in 91% of subjects at latest follow-up. According to the North American Multiple System Atrophy Study Group (2005) [17], UI occurred commonly. According to Sakakibara et al. (2004) [18], 93% of MSA patients showed neurogenic motor unit potentials in anal sphincter EMG and concluded that FI resulted from weak anal sphincter due to denervation.

CONCLUSIONS

- **Faecal incontinence is prevalent among neurological patients, but less prevalent than urinary incontinence. (LOE 3)**
- **In spinal cord injured patients, constipation is more frequent than faecal incontinence; faecal incontinence is more severe in those without external anal sphincter responses/ reflexes; and constipation is more frequent in those with higher level of injury. (LOE 3)**
- **The prevalence of faecal incontinence in stroke and traumatic brain injury survivors in community was lower than in hospital-based patients; and urinary incontinence, anticholinergic drug use and functional limitations were associated with faecal incontinence. (LOE 3)**
- **Faecal incontinence is commoner in spinal cord injured than in stroke patients. (LOE 3)**
- **Faecal incontinence is a significant problem of chronic neurological patients but not of multiple system atrophy patients. (LOE 3)**

RECOMMENDATIONS

- **Variation of definition of faecal incontinence as well as constipation should be minimized.**
- **More epidemiologic study on neurogenic bowel dysfunctions and its consequences in other neurologic diseases.**

II. SPECIAL DIAGNOSIS OF FAECAL INCONTINENCE IN NEUROPATHIC PATIENTS

1. SEARCH STRATEGY

To add new information to the previous edition, we searched from Pubmed from 2004 to 2007 with search words of neurogenic bowel and faecal incontinence. There have been only 9 relevant papers and they are summarized as follows:

2. GENERAL PRINCIPLES

According to the previous section D2 in the chapter 17 of the 3rd ICI on Neurologic Urinary and Faecal incontinence [1], 22 papers published from 1996 to 2004 were reviewed. Specific diagnostic tests for faecal incontinence (FI) are tests to assess anal sphincter including levator ani complex functions and structures, anal sensation, rectal sensation and rectal accommodation/compliance.

For neuropathic patients, comprehensive neuro-physiologic or electrodiagnostic tests – rectal mucosal electrical sensory threshold, thermal sensation, pudendal nerve latency, and needle EMG of the anal sphincter or puborectalis muscle, may be helpful to distinguish non-neurogenic from neurogenic causes of FI especially in those with lower motor neuron lesions (LMNL) including conus medallaris, cauda equina and peripheral nerve damage. For those with suprasacral or upper motor neuron lesions, electromyography (EMG) during straining and balloon expulsion test may show dyssynergic pattern. In addition, saline enema test has been suggested as patients with tethered cord lesion showed hyperactive rectum, diminished rectal saline retention ability and diminished maximal flow.

In spinal cord injured (SCI) patients, FI was not a common problem like constipation. However one should be reminded that constipation is one of the main causes of FI in SCI patients; and anal manometer and colonic transit time (CTT) were frequently selected to assess constipation. In addition endoanal ultrasound (US) or magnetic resonance imaging (MRI), and puborectalis and pelvic floor motion, assessed by dynamic MRI may be helpful to determine myopathic damage that may coexist in neuropathic patients. Moreover as FI has a strong impact on quality of life, QOL. Therefore QOL as well as patients' environment, physical disabilities and co-morbidity should be assessed in order to plan a comprehensive and appropriate management.

3. CLINICAL ASSESSMENT

Vallès et al. (2006)[2] studied and identified a comprehensive neurogenic bowel (NBo) pattern in 54 patients with motor complete SCI based on clinical assessment, total and segmental CTT quantification, anorectal function evaluation by manometry, intrarectal balloon distension, and surface EMG. They revealed 3 patterns: Pattern A, present in above T7 injuries, characterized by very frequent constipation (86%) with significant defecatory difficulty and not very severe incontinence (mean Wexner score 4.5); it was related to moderate delay in CTT (mainly in the left colon and recto-sigma), incapacity to increase the intra-abdominal pressure, and the absence of anal relaxation during the defecatory maneuvre; Pattern B, present in below T7 injuries with preserved sacral reflexes, characterized by not so frequent constipation (50%) but very significant defecatory difficulty and not very severe incontinence (Wexner 4.8); the pathophysiological counterpart was a moderate delay in CTT, capacity to increase intra-abdominal pressure, increased anal resistance during the defecatory maneuver, and presence of external anal sphincter (EAS) contraction when intra-abdominal pressure increased and during rectal distension; Pattern C, present in below T7 injuries without sacral reflexes, characterized by not very frequent constipation (56%) with less defecation difficulty and greater severity of incontinence (Wexner 7.2); this was associated with severe delay in CTT (mainly in the left colon), capacity to increase intra-abdominal pressure, absence of anal resistance during the defecation maneuver, and absence of EAS contraction when intra-abdominal pressure increased and during rectal distension.

Krogh et al. (2005)[3] did a cross-sectional questionnaire study to develop and validate a symptom-based score for neurogenic bowel dysfunction (NBoD). It included 39 questions about background parameters, FI, constipation, obstructed defecation, and impact on quality of life (QOL – no, little, some and major). Based on odds ratios for associations between items and impact on QOL, each item was given a corresponding number of points in the NBoD score; and 10 items met the criteria: frequency of bowel movements (0-6 points), headache, perspiration or discomfort before or during defecation (0-2 points), tablets and drops against constipation (0-2 points each), time used for each defecation (0-7 points), frequency of digital stimulation or evacuation (0-6 points), frequency of FI (0-13 points), medication against FI (0-4 points), flatus incontinence (0-2 points) and perianal skin problems (0-3 points); and if the score is >/= 14, NBoD is severe; if the score is 10-13, NBoD is moderate; if the score is 7-9, NBoD is minor and if the score is 0-6, NBoD is very minor.

4. ANORECTAL MANOMETRY

According to the study of Ito et al. (2006)[4], (**Table 13**) normal physiology of the lower urinary tract (LUT) and the caudal part of the lower gastrointestinal tract (LGIT) in 15 normal healthy volunteers by using the same videomanometry method revealing fluoroscopic images, subtracted bladder/rectal pressures, urethral/

anal sphincter pressures, sphincter electromyography, and urinary/fecal flow. Spontaneous phasic rectal contractions (SPRC) and abdominal strain are features of the LGIT, whereas micturition bladder contraction is a feature of the LUT. These features can aid in understanding the possible rectal 'artifacts' of videourodynamics and neurogenic pelvic organ dysfunction .

Li and Xiao (2006)[5] investigated the anorectal status by anorectal manometry in 26 patients with lumbosacral (LS) cord injury (2 AIS: A and 24 AIS: B-D; median age 43.7 years; median time since injury 59.1 months) with mixed symptoms of constipation and/or FI and 13 normal volunteers. The maximum anal resting pressure in the patients group was slightly lower than that in the control group (P=0.939). During defecation maneuvers, 23 of 26 (88.5%) patients and 1 of 13 (7.7%) normal volunteers showed pelvic floor dysfunction (PFD) (P<0.0001). Rectoanal inhibitory reflex was identified in both patients and the controls. The rectal volume for sustained relaxation of the anal sphincter tone in the patient group was significantly higher than that in the control group (P<0.0001). The mean rectal volume to generate the first sensation was 92.7 ml+/-57.1 ml in the patient group, and 41.5 ml+/-13.4 ml in the control group (P<0.0001).

According to the study of Sakakibara et al. (2004)[6], at the resting state, patients with multiple system atrophy (MSA) had a lower anal squeeze pressure (external sphincter weakness) and a smaller increase in abdominal pressure on coughing; during rectal filling, they showed smaller amplitude in phasic rectal contraction, which was accompanied by an increase in anal pressure that normally decreased, together with leaking in 3 patients; during defecation, most of them could not defecate completely and had larger post defecation residuals due to weak abdominal strain, smaller rectal contraction on defecation, and larger anal contraction on defecation (paradoxical sphincter contraction on defecation). They concluded that the responsible sites for these dysfunctions (constipation and FI) seem to be both central and peripheral nervous systems that regulate the lower gastrointestinal tract [6].

5. PELVIC FLOOR IMAGING

Adding fluoroscopy, Ito et al. (2006)[4] used the same videomanometry to reveal fluoroscopic images of the caudal part of the LGIT to help understand the possible rectal 'artifacts' of videourodynamics and neurogenic pelvic organ dysfunction in normal volunteers. During the last three years, there was no such study in neuropathic patients.

6. ELECTRODIAGNOSTIC TESTS

In 2006, there were two review articles. One was the study of Craggs et al. [7] who reviewed details of the interactions of somatic and autonomic lumbosacral pathways responsible for coordinating the bladder and sphincters, the nature of their aberration post-injury and those aspects of neural control of the pelvic organs that are amenable to neurophysiological examination in man; and the other was the study of Lefaucheur [8] who reviewed the neurophysiological techniques (**Table 14**) currently available to evaluate anorectal disorders.

To determine risk factors for development of FI, Dubravica and Demarin (2004)[9] examined the anal sphincters in 110 women with SCI and 91 women with spinal cord lesion (SCL) by means of standardized

Table 13. Shows normal values from manometry of the lower urinary tract (LUT) and the caudal part of the lower gastrointestinal tract (LGIT) derived from the study of Ito et al. (2006) [4] with 15 normal healthy persons

	LUT	LGIT
Resting phase		
- Sphincter pressure (cmH20)	70	68
Storage phase		
- Volume at first sensation (mL)	170	129
- Maximum capacity (mL)	405	320
- Compliance (ml/cmH20)	99	65
- Spontneous phasic contactions	not present	present
- Leakage	none	none
Emptying phase		
- Contraction pressure (cmH20)	42	14
- Abdominal pressure (cmH2O)	14	70
Urethral sphincter pressure		
- during defecation (cmH_2O)	13	
- during micturition (cmH_2O)	-52	

Table 14. Shows electrodiagnostic tests that may help in diagnosis of FI suggested by Lefaucheur (2006)[8]

Tests	Diagnoses
(Concentric) needle EMG	External anal sphincter (EAS) denervation
Terminal motor latency (TML)	Anal motor nerve lesion, if latency is prolonged
Motor evoked potentials (MEPs)	Spinal or supraspinal lesion, if peripheral conduction is normal
Sacral anal reflexes (SARs)	Sacral cord or nerve lesion, if abnormal or absent
Somatosensory evoked potentials (SEPs)	Sensory neuropathy
Quantification of electrical/thermal thresholds (QSTs)	Sensory neuropathy
Sympathetic skin responses (SSR)	Autonomic neuropathy

EMG technique with concentric needle electrode. The results demonstrated predominantly neurogenic lesion of the anal sphincters in SCL women and predominantly normal findings in SCI women. Sakakibara et al. (2004) [6] also studied anal sphincter EMG and showed neurogenic motor unit potentials in none of control subjects but in 93% of multiple system atrophy (MSA) patients; and FI resulted from weak anal sphincter due to denervation.

7. COLONIC TRANSIT TIME (CTT)

According to Sakakibara et al. (2004)[6], MSA patients had significantly prolonged CTT in the rectosigmoid segment and total colon. Constipation in MSA most probably results from slow colonic transit, decreased phasic rectal contraction, and weak abdominal strain.

8. QUALITY OF LIFE ASSESSMENT

According to the study of Krogh et al. (2005)[3], differences in NBoD score representing very minor, minor, moderate and severe NBoD groups of SCI patients reporting no, little, some or major impact on QOL were statistically significant (all $P<0.001$). In addition, frequency of FI, medication against FI and flatus incontinence were significantly associated with impact on QOL (OR 13.1, $p < 0.0001$; OR 3.6, $p <0.01$; OR 1.8, $p < 0.05$, repectively).

9. COMPREHENSIVE ASSESSMENTS

Bharucha (2006)[10] reviewed and summarized the indications, methods, strengths, and limitations of anorectal testing in clinical practice (**Table 15**). In patients with FI, diagnostic testing complements the clinical assessment for evaluating the pathophysiology and guiding management. When neurogenic sphincter weakness is suspected, anal sphincter EMG is recommended as the measurement of pudendal nerve latencies has several limitations [6,9,10].

CONCLUSIONS

- **Greater severity of faecal incontinence was found in SCI individuals with no sacral reflexes due to absence of external anal sphincter contraction when intra-abdominal pressure increased and during rectal distension. (LOE 3)**
- **Anorectal manometry could show pelvic floor dysfunction during defecatory manoeuvres, impaired rectal sensation functions and abnormal cough reflex in those with lumbosacral cord injury. (LOE 3)**
- **Electrodiagnostic tests are complementary to other methods of investigation to establish the diagnosis and guide therapeutic management of neurogenic anorectal disorders. (LOE 3)**
- **Faecal incontinence in SCI individuals shows correlation to impact on QOL. (LOE 3)**

RECOMMENDATIONS

- **Perform electrodiagnostic tests, especially external anal sphincter needle EMG, in addition to anorectal manometry, to identify or confirm neurogenic cause of faecal incontinence. (C)**

Table 15. Shows diagnostic tests recommended for assessing faecal incontinence according to Bharucha's review (2006) [10]

Tests	To measure	For identifying
Manometry	Resting pressure	Internal anal sphincter function
	Squeeze pressure	External anal sphincter function
	Recto-anal pressure gradient during straining	Defecation function
Rectal balloon expulsion test		Defecation function - constipation
Endoanal ultrasound		Anal sphincter pathology, esp. internal sphincter
Magnetic resonance imaging (MRI)		External sphincter atrophy
Dynamic MRI		Excessive pelvic floor mobility
Barium defecography		Rectal evacuation and puborectalis contraction; excessive perineal descent or a rectocele.
Anal sphincter electromyography		Neurogenic sphincter weakness

III. CONSERVATIVE TREATMENT

1. SUMMARY FROM THE PREVIOUS EDITION[1]

Bowel care is a procedure devised to initiate defecation and accomplish faecal evacuation. This can be achieved by bowel training with scheduled and stimulated defecation program consisting of cleansing the colon, normalizing of stool consistency with adequate fluid and fiber intake, and stimulating evacuation of stool on a regularly scheduled basis. Timing a bowel movement to take advantage of the gastro-colic reflex may be useful to achieve complete evacuation with the rectum free of stool, thus decrease the chance of faecal incontinence (FI).

Reflex-triggered bowel evacuation with mechanical stimulation – digital rectal stimulation and/or chemical stimulation – suppositories, enemas, can be helpful. In addition, Valsalva or manually-generated external pressure, oral medications – stool softeners, stimulant laxatives and prokinetic agents; diet modification; biofeedback; electrical stimulation and functional magnetic stimulations may be useful. However successful bowel care needs intensive patient education and training. If conservative bowel management fails, surgical management may be necessary.

2. SEARCH STRATEGY

Search from Pubmed 2004-2008 by using key words of faecal incontinence, neurogenic, neuropathic, neurologic, neurogenic bowel, bowel care, conservative treatment, and practice guideline. From such searches, there are 17 relevant papers of various levels of evidence as follows:

3. BOWEL PROGRAMME /BOWEL CARE

In 1998, the Consortium for Spinal Cord Medicine [2] published the "Neurogenic Bowel (NBo) Management in Adults with Spinal Cord Injury (SCI)" Clinical Practice Guideline (CPG). Later in 2005, to improve an adherence to the CPG recommendations through a targeted implementation strategy, Goetz et al [3] did a multi-site clinical trial study at 6 Veterans Affairs SCI centers. The CPG adherence was determined from medical record review for 3 time periods: before guideline publication (T1), after guideline publication but before CPG implementation (T2), and after targeted CPG implementation (T3). In focus groups before the intervention, the barriers were identified by SCI providers and then, two specific implementation strategies were chosen to address: the development and dissemination of a standardized documentation template and the development of a patient-mediated intervention to enhance guideline adherence. Because of the effective chart-based reminders, there was significant increase in overall adherence to recommendations related to NBo between T2 and T3 ($P < 0.001$) for 3 of 6 guideline recommendations: patient history, physical examination and documentation but the overall adherence of documentation was still low (40%). Moreover, it was found that other 3 recommendations i.e., functional assessment, education and competency, had high-rate of adherence in all 3 phases.

a) Mechanical stimulations for bowel movements

1. Digital rectal stimulation

Digital rectal stimulation (DRS), a gentle and slow rotation or circular movement of finger, is recom-

mended for reflex bowel as an adjunctive to facilitate bowel evacuation [2]. It dilates an anal canal and relaxes puborectalis muscle, thus decreases the ano-rectal angle and reduces outflow resistance to the passage of stool. Korsten et al (2007) [4] applied DRS, with a gloved finger fully inserted into the anal canal and distal rectum and contacted with the anal mucosa; each lasted for 1 minute with a 2-minute interval between successive DRS, to measure colonic motility by using a manometric catheter affixed endoscopically to the spleen flexure. In addition, evacuation of barium oatmeal paste was assessed simultaneously using fluoroscopic techniques. In 6 SCI patients, the results showed that the mean number (+/- SEM) of peristaltic waves per minute increased from 0 at baseline to 1.9 (+/- 0.5/min) during DRS and 1.5 (+/- 0.3/min) during the period immediately after cessation of DRS ($P < 0.05$). The frequency of contractions, as well as amplitude of contractions, during or immediately after DRS was not significantly different; peristaltic contractions disappeared 5 minutes after the cessation of DRS; and the manometric changes in response to DRS were accompanied by expulsion of barium oatmeal paste in every subject by the fifth DRS. This proved that DRS contributes to bowel evacuation in individuals with SCI in part by increasing left-side colonic motility.

However, mechanical stimulation may cause local trauma and induce autonomic dysreflexia (AD) in SCI individuals. Furusawa et al (2007)[5] studied the relationship between bowel manoeuvres and AD in cervical SCI patients and demonstrated that insertion of rectal medication induced a significant increase in systolic BP, which persisted during additional DRS; furthermore, the manual removal of stool induced AD, with maximal increases of systolic BP. However, after the end of stool flow the insertion of a finger into the anus did not cause a further increase in systolic BP which recovered to pre-program values within 5 min after defecation. The combined effects of rectal and/or anal sphincter distension and uninhibited rectal contraction in response to the manual removal of stool are assumed to induce AD. According to the CPG [6], if the elevated systolic blood pressure is less than 150 mmHg, gently instill a topical anaesthetic agent into the rectum, wait for 2 minutes, gently remove the stool; if AD becomes worse, stop manual evacuation, instill additional topic anesthetic and recheck the rectum for the presence of the stool after 20 minutes

b) Chemical stimulants

According to the meta-analysis review done by Coggrave et al (2006)[7] to determine the effects of management strategies for faecal incontinence (FI) and constipation in people with neurological diseases affecting the central nervous system. Most of the ten trials were identified were small and of poor quality. Oral medications for constipation were the subject of four trials. Cisapride does not seem to have clinically useful effects in people with SCI (three trials). Psyllium was associated with increased stool frequency in people with Parkinson's disease but did not alter colonic transit time (CTT) (one trial). Prucalopride, an enterokinetic did not demonstrate obvious benefits in this patient group (one study). Some rectal preparations to initiate defaecation produced faster results than others (one trial). Different time schedules for administration of rectal medication may produce different bowel responses (one trial). Mechanical evacuation may be more effective than oral or rectal medication (one trial). The clinical significance of any of these results is difficult to interpret.

During the last 3 years there has been no research study on the effectiveness of such medications in patients with neurogenic bowel dysfunction (NBoD).

c) Assistive techniques for defecation

1. Abdominal massage

Another assistive technique usually applied to enhance bowel movement is abdominal massage in a clockwise motion up the ascending colon, across the transverse colon, and down the descending colon [2]. To investigate its effect on clinical aspects of NBoD and CTT, Aya? et al (2006)[8] did an uncontrolled clinical trial in 24 SCI patients whom were placed on a standard bowel program (phase I), after which abdominal massage was added to the regimen (phase II). In phase I, 45.8% had abdominal distention and 41.7% had FI; corresponding results for phase II were 12.5% and 16.7% ($P = 0.008$ and 0.031, respectively) and no significant differences between the proportions of patients with difficult intestinal evacuation or abdominal pain or in mean time required for bowel evacuation in phase I vs. phase II. The mean frequencies of defecation in phases I and II were 3.79 +/- 2.15 (2.75-4.55) and 4.61 +/- 2.17 (3.67-5.54) bowel movements per week, respectively ($P = 0.006$). Mean total CTT decreased from 90.60 +/- 32.67 (75.87-110.47) hrs in phase I to 72 +/- 34.10 (58.49-94.40) hrs in phase II ($P = 0.035$). According to this study, abdominal massage is an effective technique in enhancing bowel movement and defecation and thus reducing bowel accident, FI in SCI persons.

2. Anal stimulation with water streams (LOE 3)

In 2007, Uchikawa et al (2007)[9] reported the effectiveness of a newly modified washing toilet seat equipped with a CCD camera monitor and an electronic bidet to facilitate precise hitting of the anal area with water streams to stimulate bowel movement in patients SCI who were at least 5 months post acute injury, and could change their position on the toilet seat while watching the monitor. The stimulation was provided for a maximum of 30 minutes. Bowel movement was successfully induced in 15 of the 20 patients (75%) and success was not related

significantly to injury level, ASIA impairment scale, or ability to voluntarily squeeze. Moreover, no complications were observed and time needed for successful bowel movement was shortened in 11 of 13 patients as they usually spent more than 30 minutes before stimulation.

3. Transanal / Transrectal irrigation

Christensen et al (2006)[10] did a prospective, multi-center, randomized controlled trial (RCT) involving 5 specialized European SCI centers, and 87 SCI patients with NBoD were randomly assigned to either transanal irrigation (TAI) using the Peristeen Anal Irrigation system with 750-1,500 ml of tepid water in 42 patients and conservative bowel management, scheduled bowel care at least every 2 days, at the same time of the day and after ingestion of food and liquid, diet modification, adequate fluid, regular physical activity; and laxatives or constipating medicine when necessary as recommended in the American CPG (2) in 45 patients for a 10-week trial period. Results showed that the TAI improved constipation, FI, and symptom-related QOL much better than conservative bowel management. In addition, urinary tract infection (UTI) was less in the TAI group than in the conservative group (5.9% versus 15.5%, P = .0052); AD tended to be less in the TAI group because the underlying faecal impaction was tested; and wheelchair users and those confined to be seem to have the highest benefit of the TAI. However, half from the TAI group discontinued due to failure of the TAI.

Later in 2008, Del Popolo et al (2008) [11] did a multi-center study in Italy to evaluate the effect of the Peristeen Anal Irrigation[10]. Twenty-four of 36 SCI patients with NBoD became less dependent on their caregiver; 28.6% of 32 who completed the study reduced or eliminated their use of pharmaceuticals; 68% and 63% of the patients reported successful outcome with FI and constipation respectively. Moreover, there was a significant increase in patients' opinion of their intestinal functionality, QoL score and satisfaction.

To evaluate the outcome of transrectal irrigation (TRI) using 200-600 ml of lukewarm tap water without salt, Mattsson and Gladh (2006)[12] did a clinical trial in 40 myelomenigocele (MMC) children with NBoD (21 boys, 19 girls; aged 10 months to 11 years). The TRI was given by the Stoma Cone Irrigation set or Colotip daily or every second day. A questionnaire on the effects on FI, constipation and self-management was completed by the parents, 4 months-8 years (median 1.5 years) after start. Effects on rectal volume, anal sphincter pressure and plasma sodium were evaluated before and after the start of irrigation. At follow-up, 35 children remained on TRI, four had received appendicostomy, while one defecated normally; 85% of all, the TRI worked satisfactorily, but a majority found it very time consuming and only one child was able to perform it independently. All children were free of constipation; most (35/40) were also anal continent. Rectal volume and anal sphincter pressure improved, while plasma sodium values remained within the normal range. They concluded that TRI with tap water was a safe method to resolve constipation and FI in children with MMC and NBoD, but it did not help children to independence at the toilet.

4. APPLIANCE/ASSISTIVE TECHNIQUES FOR FAECAL INCONTINENCE

a) Anal plug (LOE 2)

Previous studies of an anal plug have yielded conflicting results. Bond et al (2007)[13] did a multi-centre RCT to evaluate the Conveen anal plug (Coloplast Limited) for the management of FI in congenital, acquired and neurogenic children and adults. It was used for 12 months. The main outcome measure was a condition-specific score on a 0 to 100 scale. Thirty-one intervention and 17 control patients were recruited. At baseline, patients managed their condition preemptively or protectively. Intervention patients used the plug as a complete management substitute or as an adjunct to existing management and majority retained the plug most of the time. Compared with control group, there was greater improvement from baseline in mean condition-specific score in intervention group but this difference was not statistically significant (t test p=0.053). Complete data analysis using analysis of covariance showed the mean difference between the intervention groups in condition-specific score of 9.9 (95% confidence interval-1.4, 21.1). Intention to treat analyses using imputation showed similar results.

b) Neuromodulation

According to Fowler's review (2004)[14] on treatment related research in faecal and urinary incontinence, afferent innervation is important in sensing the degree of bladder fullness and in forming the input limb to involuntary detrusor contractions in neurogenic detrusor overactivity (NDO). It is likely that homologous mechanisms are involved in control of the bowel. Experimental evidence suggests that the "procontinence" reaction consists of an inhibitory effect on the detrusor and presumably the lower rectum resulting from contraction of the pelvic floor and the anal or urethral sphincter. Development of methods of enhancing the inhibitory reflex effect could lead to improved voluntary control of micturition and defecation for patients with SCL.

1. Intravesical electrical stimulation (IVES)

Han et al (2004)[15] retrospectively reviewed the effect of IVES on NBoD – controlling FI, in 9 boys and 15 girls (mean age 8.1 years) who completed a mean of 30.3 daily sessions of IVES. After IVES, the mean number of overall FI episodes decreased

significantly from 7.36 to 4.8 a week ($p < 0.05$). Greater than 50% decrease in the episodes of FI was observed in 75% of the children but there was no significant change in the number of daily bowel movements before (1.8 daily) and after (1.55 daily) IVES.

5. QUALITY OF LIFE (LOE 3)

In 2005, there was one study of Luther et al [16] that compared patient outcomes and QOL for people with NBoD using either a standard bowel care program or colostomy. This study was part of a larger study that evaluated CPG implementation in SCI. The sample included 1,503 SCI veterans with the response rate of 58.4%. For comparison, a total of 74 veterans with SCI and colostomies were matched with 296 controls, using propensity scores. Seven items were designed to elicit information about the respondent's satisfaction with their bowel care program, whereas 7 other items were designed to measure bowel-related QOL. No statistically significant differences in satisfaction or QOL were found between the responses from those with colostomies and those with traditional bowel care programs. Both groups had received training for their bowel care program, experienced relatively few complications, such as falls as a result of their bowel care program, and that their QOL related to bowel care was generally good. However, 55.7% of respondents with colostomies and 41.7% of those without colostomies reported that they were very unsatisfied with their bowel care program.

Zickler and Richardson (2004)[17] did a review on MMC and other neural tube defects children with NBoD and NBD, who had a physical inability to attain continence. However, they can attain continence when the appropriate modifications to the traditional routines are made. Enabling the child to attain continence would improve parental relationships and self-concept.

CONCLUSIONS

- **Apart from relaxing the external anal sphincter, digital rectal stimulation increases peristaltic contractions by facilitating excitory anorectal (ano-colonic) reflex and enhances bowel movement and evacuation in reflex bowel. (LOE 3)**
- **Abdominal massage has positive effects on some clinical aspects of neurogenic bowel dysfunction including defecation function and faecal incontinence. (LOE 3)**
- **Transanal irrigation seems to be a safe method to improve constipation and faecal incontinence in individuals with neurogenic bowel dysfunction. (LOE 3)**
- **An anal plug seems to benefit in controlling faecal incontinence in neurological patients but not better than control (without anal plug). (LOE 2)**
- **To increase adherence rate with bowel care programme/clinical practice guideline, implementation strategies should be addressed to care providers. (LOE 3)**

RECOMMENDATIONS

- **Apply appropriate mechanical stimulation - digital rectal stimulation, and/or assitive techniques – abdominal massage, transanal/ transrectal irrigation to improve defecation and reduce faecal incontinence in neurological patients with neurogenic bowel dysfunction. (B)**
- **Be aware of autonomic dysreflexia when using mechanical stimulation and assistive techniques with neurologic patients with a high cord lesion. (B/C)**
- **Provide appropriate modifications to the bowel care program to improve bowel functions including defecation and continence. (B/C)**

RECOMMENDATIONS FOR RESEARCH

- **Further study to prove the existence of the excitatory ano-colonic reflex in response to digital rectal stimulation in individuals with lower motor neuron lesions.**
- **Further study to confirm that the newly anal stimulation with water stream is an appropriate method to facilitate bowel movements without complications.**
- **Well-designed controlled trials with adequate numbers and clinically relevant outcome measures of bowel management are needed.**
- **Larger and good quality randomized crossover trials are needed to confirm the effects of neuromodulation for controlling faecal incontinence and reducing constipation in neuropathic people.**

IV. SURGICAL TREATMENT

• Methods

Using MEDLINE we identified English-language journal articles and reviews published from 2000 to April 2008, looking for the keywords neurogenic constipation and faecal incontinence, surgery, sacral nerve stimulation, ante grade, continent enema procedure, dynamic graciloplasty, artificial anal sphincter and colostomy.

- **Surgery should be normally reserved for patients who have failed conservative therapy.**

Surgical treatment of faecal incontinence in the general population is overviewed in the Chapter on the Surgery for Faecal Incontinence. Therefore, this section focuses on specific aspects in neurogenic patients. Although traumatic lesion of external sphincter is treated by reconstruction of the external sphincter, functional impairment of anal sphincter without mechanical defect of the sphincter in neurogenic patients can not be treated by this simple surgical repair, and thus options for surgical treatment of neurogenic bowel dysfunction are limited. However, they consist of 1) sacral nerve stimulation, 2) ante grade continent enema procedure, 3) dynamic graciloplasty, 4) artificial anal sphincter, and 5) elective colostomy.

1. SACRAL NERVE STIMULATION (SNS)

Electrical stimulation of sacral nerve roots has been reported to restore continence in patients with intact muscle structure. The procedure is divided in three steps: acute percutaneous testing, temporary percutaneous nerve evaluation and permanent electro stimulation phase with an implantable neurostimulation device. An electrode inserted into the S3 sacral foramen provides low grade stimulation. Only when patients respond to acute and temporary percutaneous sacral nerve stimulation tested for 2 to 3 weeks, permanent stimulation via a chronic stimulator implanted under the anterior abdominal wall is applied or subcutaneously in the gluteal region. The first case report with this technique was published by Matzel et al al [1] in 1995 who described a successful outcome in three patients with faecal incontinence. Since then, ten articles have been published [2-11] (**Table 16**).

Recently, Matzel et al [2] reported a multi centre, prospective trial with chronic sacral nerve stimulation in a series of 34 patients at a median follow-up of 23.9 months. At least 83 % of patients had a 50 % or greater improvement in total number of incontinent episodes per week and at least 71 % of patients a 50 % or greater improvement in total number of days per week with continence during the course of follow-up. Continence was fully restored in at least 12 (37%) patients. Quality of life improved in all four ASCRS (American Society of Colon and Rectal Surgeons) scales ($p<0.0001$) and in seven of eight SF-36 scales, though only social functioning was significantly improved ($p=0.0002$).

Although 12 patients had 19 device-related adverse events including pain (ten episodes in 9 patients), lead breakage in one patient, recurrent infection needing device removal in one patient and deterioration of bowel symptoms in three patients, resolution rate was 63.2 % and 100 % for all and severe complications, respectively. However, this study excluded patients with neurological diseases.

Similar success rates (73-100 %) with this technique have been reported from other centres [3-5, 7-11]. Among these reports, only one case-series by Rosen et al [12] targeted mainly on faecal incontinence in patients with neurological lesions. In that study, 20 patients (15 neurogenic, 5 idiopathic) with severe faecal incontinence were initially treated by temporary external stimulation over a period of 10-14 days. Sixteen patients (11 patients with neurogenic causes including 5 spinal cord injuries, 4 post spinal cord surgeries, 1 myelomeningocele, 1 multiple sclerosis, and 1 Friedreich ataxia, and 5 idiopathic patients) who had shown a positive response to the temporary stimulation subsequently underwent permanent implantation. The median follow-up was 15 months (range, 3-26 months). All patients who had received a permanent implant revealed a marked reduction in their incontinent episodes as well as an increase in retention time. In the neurogenic subpopulation, the median numbers of incontinence episodes decreased significantly ($p<0.01$) from 7 (4-15) to 2 (0-5), and a median retention time significantly ($p< 0.01$) increased from 2 minutes (0-5) to 7 minutes (2-15) after chronic stimulation. Assessment of QOL scales using ASCS questionnaire after 6 months treatment showed significant improvement on all scales. Three patients (2 neurogenic and 1 idiopathic) had severe infections needing explantation of devices and wound drainage 0-3 months after implantation. Another one patient had dislocation of the permanent electrode.

No complications were observed I n the remaining 12 patients (60 % of total series). All of those patients with functioning systems have showed improved incontinence during the follow-up period. Although the mechanism of SNS to improve faecal incontinence is uncertain, rises in anal resting and squeezing pressures and changes in rectal sensitivity and motility have been proposed. Particularly in neurogenic patients, neuromodulation of sacral reflexes and regulation of rectal sensitivity appear to be the major reasons for the functional improvement [7].

Alternatively, the diagnostic stage can be performed as a staged implant, with a quadripolar foramen electrode (tined lead, Medtronic model 3886). This technique improves the results of the test period in the urological literature from a 50 % success rate with the wire electrodes up to 80 % using already the quadripolar foramen electrodes in the test phase Kessler et al., 2005 [13]. The tined lead has four active electrodes (compared with a single electrode used in PNE) and has self-retaining flanges, which prevent lead migration. Usage of the tined lead has the benefit of minimizing false-negative results. Recently, Jarrett et al (2005) [14] reported on their experience with sacral nerve stimulation for faecal incontinence in patients with previous partial spinal injury including disc prolapse: the spinal insults were disc prolapse (six), trauma (four), spinal stenosis (one) or occurred during neurosurgery (two).

Table 16. Reported data on sacral nerve stimulation for fecal incontinence

Authors reference no., year	Level of evidence	No. of patients (neurogenic patients) with chronic stimulation	No. of patients underwent test stimulation	Median follow up (months) (range)	Success rate (fully continent rate)	Complications
Matzel et al [2], 2004	Level 3	34 (0)	37	23.9	83% (37%)	
Ripetti et al [3], 2002	Level 4	4 (0)	21	15(6-24)	100%	
Ramussen et al [4], 2002	Level 4	10	14	4.5	90%	
Kenefick et al [5], 2002	Level 4	14 (0)	ND	24Åi3-60)	100% (73%)	
Matzel et al [6], 2001	Level 4	6 (1)	ND	36(5-66)	100%	removal 2 for pain
Rosen et al [7], 2001	Level 4	16 (11)	20	15(3-26)	75%	
Ganio et al [8], 2001	Level 4	16 (2)	ND	15.5(3-45)	100%	
Leroi et al [9], 2001	Level 4	6 (0)	9	6	50%	
Ganio et al [10], 2001	Level 4	5	23	19.2(5-37)	100%	
Malouf et al [11], 2000	Level 4	5	ND	16	100%	

Temporary SNS was performed in thirteen patients (median age 58,5, range 39-73 years). Twelve patients had successful temporary stimulation and proceeded to permanent implantation. The median follow-up time was 12 (range 6-24) months, the mean number of episodes of incontinence decreased from 9.33 (7.64 per week at baseline 2.39 (3.39) at last follow-up (p= 0.012). The number of days per week with incontinence and staining decreased significantly (p = < 0.001). The ability to defer defecation improved from a median of not being able to defer (range 0-1 min.) to being able to defer 5-15 (range 0->15) mean (p = 0.022). The authors conclude that SNS can benefit patients with faecal incontinence following partial spinal cord injury. Holzer et al (2007) [15] report on 36 patients included in a trial of SNS, 29 subsequently had a permanent implant. After a medium follow-up of 35 (range 3-71) months, 28 patients showed a marked improvement: Incontinence to solid or liquid stool decreased from a median of 7 (range 4-15) to 2 (range 0-5) episodes in 21 days (p = 0.002).

Saline retention time increased from a median of 2 (range 0-5) to 7 (range 2-15) min. (p = 0.002). The quality of life on all scales among patients who received the permanent implant increased at 12 and 24 months after operation, also Also Holzer et al stated that SNS is of value in selected patients with neurogenic faecal incontinence.

CONCLUSIONS

- **Although there are no controlled studies comparing SNS with artificial anal sphincter or dynamic graciloplasty, unlike the two other operations this is a minimally invasive procedure, and seems to be an option applied to faecal incontinence due to functional deficit of anal sphincter without structural defect (LoE 4).**

RECOMMENDATIONS

- **However, studies on larges series with long term follow-up are needed to determine its role in the treatment of faecal incontinence associated with neurological lesions (D).**

2. ANTEGRADE CONTINENCE ENEMA (MACE)

The original procedure was developed by Malone et al [1]. The principles of antegrade colonic washout and the Mitrofanoff non-refluxing catheterisable channel were combined to produce a continent catheterisable colonic stoma. The intention was that ante grade washouts delivered by this route would produce complete colonic emptying and thereby prevent soiling. Malone et al reported successful results in five children with intractable faecal incontinence. This procedure

has been applied mainly to paediatric population with neuropathic bowel dysfunction and anorectal anomaly, and successful outcome was achieved in 70-100 % [2-22] (**Table 17**). Overall, stoma stenosis is the most common complication, affecting 10-41 %. In a study of 62 children with median follow-up of 5.4 (3.25 to 8.25) years, 84 percent were completely continent or had soiling less than once a month [4]. There was a significant correlation between the level of continence and satisfaction with the procedure [4] Improvement of self-esteem and psychosocial function after the ACE procedure in children with myelomeningocele has been reported [6]. Several modifications have been reported including laparoscopic technique, left colonic continence stoma, etc [7-9, 11-13]. This procedure was also applied to adult neurogenic patients with faecal incontinence [3,12,14], and similar success rates (83-100 %) were reported. Casale et al (2006) [23] compared total continence reconstruction to staged-reconstruction of neuropathic bowel and bladder: In this retrospective chart review of all patients with Myelomeningocele who underwent reconstruction with a cutaneous catheterisable urinary channel or Malone ante grade continence enema. The authors were unable to find any differences in the continence rate or stoma complications between total continence reconstruction or/and staged recons-truction. However, because of shared pathology the authors believe that most patients benefit from intervention in the gastrointestinal and the genitourinary tract. Therefore, a major advantage of total continence reconstruction is avoidance of the morbidity of a second major surgical procedure (LOE 3).Recently, Herndon et al 2004 [24] reported on in situ Malone ante grade continence enema in 127 patients reflecting a 6-year experience: ACE in situ technique was performed in 76 females and 51 males, average patient age at the time of surgery was 9,6 years, diagnosis included myelomeningocele in 116 cases, lipomeningocele in 6, spinal cord injury in 2, posterior urethra walls in 1, sacral agenesis in 1 and functional constipation in 1.The mean follow-up was 26,9 months. Faecal continence was reported by 91 % of the patients, 13 stoma revisions (stenosis 10, prolapse 2 and leakage 1) were required in 11 patients. Major complications included a caecal volvulus requiring a right hemico-lectomy in one patient, small bowel obstruction in two and a shunt infection and or malfunction in two. The authors conclude that the in situ MACE procedure has reliable long-term results for treating faecal incontinence associated with neuropathic bowel.

CONCLUSIONS AND RECOMMENDATIONS

- **This procedure is effective for controlling faecal incontinence and constipation associated with neurogenic bowel dysfunction especially in neuropathic children (LoE 3; Grade B). Patients should be properly selected to determine appropriate motivation.**

3. DYNAMIC GRACILOPLASTY

This procedure consists of transposition of the gracilis muscle around the anal canal and subsequent implantation of a pulse generator to stimulate the gracilis muscle. Before continuous stimulation is applied, the muscle is trained for 4 to 8 weeks according to a protocol. During a stimulation program the fatigable type 2 skeletal fibres are replaced by slow type 1 fibres, which are able to sustain a long lasting contraction. Satisfactory continence has been reported in 56% to 81% of patients [1–13] (**Table 18**). Recently, a prospective study of 200 consecutive patients with a follow-up of at least two years showed a 72% overall success rate [6]. Complication rate is rather high (42%-92%), especially infectious complications which occur in about one fourth of the patients. Impaired rectal emptying has occurred in 16% to 29%. A prospective controlled comparative study of single stage with the conventional two-stage procedure showed no significant difference in infection rates, continence rates, morbidity or quality of life between the two groups after a mean 521-day follow up [11]. A prospective controlled study comparing dynamic graciloplasty with artificial anal sphincter in 16 patients (8 in each group) showed that both of the two procedures had a high incidence of technical failures and complication requiring re operation [12]. Chapman et al [13] reported a systematic review article of this procedure, where they searched articles published until November 1999, and found 40 articles met the inclusion criteria. Mortality rates were around 2% for both graciloplasty and colostomy. However, morbidity rates reported for graciloplasty appear to be higher than those for colostomy.

Rongen et al [11] reported an 80% success rate with this procedure in 16 patients with neurogenic faecal incontinence. However, all studies presently available expect this report include quite small number of neurogenic patients, and there is no information on the outcome in neurogenic subgroup of patients.

CONCLUSIONS AND RECOMMENDATIONS

- **Since dynamic graciloplasty seems to be associated with high complication rates, and outcome appears to correlate to surgeon's experience, this procedure should only be carried out in specialist centres with a reasonably large number of patients, and should be reserved only for carefully selected patients with intractable faecal incontinence where other methods have failed (C).**
- **Further studies are needed to determine its role in the neurogenic subpopulation.**

Table 17. Summary of reported data on antegrade continent enema for faecal incontinence

Authors reference no., year	Level of evidence	No. of patients	Mean age (range)	Median follow up (range)	Success rate	Overall complication rate	Stomal stenosis
Malone et al [1], 1990	Level 4	5	(8-18)	(2-8 mos.)	100%	40%	
Teichman et al [2], 2003	Level 4	7	34	4,5 yrs. (all>4 yrs.)	83%	67%	
Dey et al [3], 2003	Level 4	62	11,5 (3,8-17,6)	5,4 yrs. (3,25-8,25)	84%	66%	42%
Liard et al [4], 2002	Level 4	24	15	3,7 yrs.	100%		
Aksnes et al [5], 2002	Level 4	20	10,9 (6,8-17)	16 (9,5-23)mos.	80%	30%	20%
Liloku et al [6], 2002	Level 4	7	8-21	(1,5-18 mos.)	71%	29%	14%
Tackett et al [7], 2002	Level 4	45	10,5 (3,8-25,8)	25,3 (4-65) mos.	87%	22%	18%
Perez et al [8], 2001	Level 4	12	14 (7-20)	15 mos.	92%		58%
Kajbafzadeh et al [9], 2001	Level 4	40	9,5 (4-22)	22 (8-48) mos.	100%	2,5%	
Van Savage et al [10], 2000	Level 4	16	12 (4-21)	1,5 yrs	100%	50%	6,3%
Bruce et al [11], 1999	Level 4	7	33,6 (23-54)	22,4 (3-34) mos.	100%		14%
Robertson et al [12], 1999	Level 4	30	9,5 (5-16)	>1yr. (3mos.-3,5yrs.)	90%	33%	27%
Teichmann et al [13], 1998	Level 4	7	32	11 mos.	100%	57%	28%
Meier et al [14 1998	Level 4	20	10 (4-18)	24 (9-45) mos.	90%	10%	5%
Driver et al [15], 1998	Level 4	29	10 (5-16)	28 (7-71) mos.	79%		38%
Hensle et al [16], 1998	Level 4	27	16 (10-31)	(9-30 mos.)	70%	37%	18,5%
Levitt et al [17],1997	Level 4	20	(3-27)	(1-29 mos.)	95%	25%	10%
Goepel et al [18], 1997	Level 4	10	13,2 (6-26)	18,5 (8,5-36) mos.	100%	20%	
Dick et al [19], 1996	Level 4	13	8 (6-14)	32 (24-60) mos.	85%	46%	38%
Ellsworth et al [20],1996	Level 4	18	12 (5-31)	6,6 (2-24) mos.	96%	22%	17%
Koyle et al [21], 1995	Level 4	22	13 (5-26)	>4 mos.	77%	36%	9%
Squire et al [22], 1993	Level 4	25	(3-18)	13 (2-61) mos.	88%	24%	20%

Table 18. Summary of reported data on graciloplasty for neurologic faecal incontinence

Authors reference no., year	Level of patients	No. of patients	No. of neurogenic patients	Median follow up (range)	Success rate (success rate in neurogenic pts.)	Complication rate	Infection rate	Explantation rate	Emptying problem
Rongen et al [1], 2003	Level 3	200	16	>2 yrs.	72% (80%)	69%	12%	12%	16%
Wexner et al [2], 2002	Level 3	129		2 yrs.	56%				
Bresler et al [3], 2002	Level 4	24			79%	92%	25%		
Matzel et al [4], 2001	Level 3	121	0	1.5 yrs.		77%	37%		27%
Baeten et al [5], 2000	Level 3	123	0	1 yr.(1-52 mos.)	74%	74%			
Madoff et al [6], 1999	Level 3	128		2 yrs.	66%		11%		
Sielenzneff et al [7], 1999	Level 4	16	1	20 (6-37) mos.	81%	50%	44%		31%
Christiansen et al [8], 1998	Level 4	13	0	(7-27mos.)	77%		8%		23%
Geerdes et al [9], 1996	Level 4	67	0	2.7 yrs.(14wks.-8.7yrs.)	78%	79%	16%		
Baeten et al [10], 1995	Level 3	52	2	2.1yrs.(12wks.-7.4yrs.)	73% (50%)		13%		

4. ARTIFICIAL ANAL SPHINCTER

Implantation of an artificial anal sphincter was first reported in 1987 [1] . The sphincter used was originally designed for treatment of urinary incontinence, but subsequently the device has been modified. The system consists of an inflatable cuff placed around the upper anal canal, a pressure-regulating balloon to maintain closure of the cuff placed in the subperitoneal space lateral to the bladder and a control pump accessible to the patient to empty the cuff for defaecation placed in the scrotum or labium. The system is left deactivated for 4 to 6 weeks. A multi centre prospective, non-randomized trial in 112 patients with one year follow-up showed 73 revision operations were required in 51 (46 %), and the infection rate necessitation surgical revision was 25 %. Forty-one patients (37 %) have had their devices completely explanted [4]. The reported success rates obtaining acceptable continence range were 41 % to 90 % [4-14] (**Table 19**). Explantation rates in the reported series were 20-40 %. One series with long-term follow-up (more than 5 years) showed that 7 of 17 patients had the system removed due to infection, malfunction or obstructed defaecation [13]. Technical complications like rupture of the cuff, which occurred frequently with the earlier modification of the device, are now rare. Emptying problems, without anatomical stenosis, as described for dynamic graciloplasty, have also occurred frequently (13 % to 45 %) in most series and have in some patients required explantation. Other complications leading to explantation have been erosion of the cuff through the skin or into the anal canal.

As shown in the Table, most studies have a small number of neurogenic patients or do not indicate the number of neurogenic patients included. In the study reported by Christiansen et al [10], 10 (59 %) out of 17 patients had neurological disorders, and the overall success rate was 47 %, which seems to be lower than the others. The authors mentioned that the result in neurogenic subgroup was clearly poorer than that in non-neurogenic subgroup.

In a prospective, randomized controlled clinical trial of placement of the artificial bowel sphincter for the control of faecal incontinence O'Brian et al (2004) [8] compared its effects to a program of supportive care and patients were followed for six months from operation or entry into the study.

The principal outcome measure was the level of continence, measured with the Cleveland Continence Score, representing perfect control through a total incontinence. Secondary outcome measures were peri-operative and late complications in the artificial bowel sphincter group and the changes in quality of life in both groups. In the control group (N = 7) the Cleveland Continence Score was not significantly altered. The artificial bowel sphincter group (N = 7)

Table 19. Summary of reported data on artificial anal sphincter for faecal incontinence

Authors reference no., year	Level of evidence	No. of patients (neurogenic)	Mean age (range)	Median follow up (month) (range)	Success rate (in neurogenic)	Explantation	Complication rates		Emptying problem
							Infection rate	Revison rate	
Parker et al [2], 2003	Level 4	45(2)	44(15-72)		51% (50%)	40%	34%	21/13pts	11%
Michot et al [3], 2003	Level 4	37(16)	51(22-73)		79%	30%			37%
Devesa et al [4], 2002	Level 4	53(9)	46(16-76)	26,5(7-55)	65%	19%	13%	26%	22%
Wong et al [5], 2002	Level 3	112(ND)	49(18-81)		53%	37%	25%	46%	
Ortiz et al [6], 2002	Level 4	22(ND)	47(17-72)	26(6-48)	63%	44%			9%
Altomare et al [7], 2001	Level 4	28(4)	58(35-79)	19(7-41)	75%	32%	11%		57%
O´Brien et al [8], 2000	Level 4	13(1)	44(16-71)		77%	23%			
Lehur et al [9], 2000	Level 4	24(4)	44(14-80)	20(6-35)	75%	29%	12%	17%	45%
Christiansen et al [10], 1999	Level 4	17(10)	46(32-65)	7(5-10)years	47%	41%	18%	63%	13%
Vaizey et al [11],1998	Level 4	6		10(5-13)	83%	16%			
Lehur et al [12], 1998	Level 4	13		30(5-76)	85%				
Lehur et al [13], 1996	Level 4	13(2)		20(4-60)	90% (69%)	23%	15%	15%	
Wong et al [14], 1996	Level 4	12(3)		58	50% (75%)	33%	25%	42%	
Christiansen et al [1], 1987	Level 4	1		3	100%				

showed a highly significant improvement. One patient in the artificial bowel sphincter group had failure of healing and implantation of the device. There were major improvements in the quality of life for all measures in the artificial bowel sphincter group. The authors conclude that the placement of an artificial bowel sphincter is safe and effective when compared with supportive care alone. Peri-operative and late problems are likely to continue to occur and between 15 % and 30 % of patients may require permanent explantation. For the authors the device is easy and discrete to use, highly effective in achieving continence and able to generate a major improvement in the quality of life (LoE 3).

CONCLUSIONS AND RECOMMENDATIONS

- **Implantation of the artificial anal sphincter may be done for the same indications as for dynamic graciloplasty except in patients with previous perianal infections or with a thin and scarred perineum where a muscle transplant is preferable. It should be emphasized that due to the relatively high risk of treatment failure and of complications requiring re-operation patient selection for both procedures should be very strict (C).**

5. COLOSTOMY

Spinal cord injury (SCI) has a significant effect on bowel dysfunction, in terms of faecal incontinence, urgency, and toileting methods.

This results in a marked impact on quality of life [1-2]. Several retrospective studies on the effect of colostomy formation on bowel care and QOL in SCI patients showed a significant decrease in the average time spent on bowel care per week and improvement on QOL [3-13].

The early and long-term complication rates reported are 6 to 15 %, and 15 to 37, 5 %, respectively. The commonest long-term complication is mucus discharge per rectum. It should be noted that one of the frequent, persistent, problematic complic-ation is diversion colitis [9-10]. Symptoms include hemorrhagic purulent rectal discharge, abdominal pain and tenesmus. This condition is thought to result from a deficiency of luminal short-chain fatty acids [11]. Steroid enemas, 5-aminosalicylic acid enemas or suppositories, or short-chain fatty acid enemas have been reported to be helpful [12].

CONCLUSIONS AND RECOMMENDATIONS

- **Elective colostomy may be an option for some SCI patients with severe uncontrolled faecal incontinence (C).**

E. SPECIFIC NEUROLOGIC DISEASES

I. DEMENTIA

1. DEMENTIA AND *URINARY INCONTINENCE*

• Methods

Using MEDLINE we identified English-language journal articles and reviews published from 2000 to April 2008, looking for the keywords Alzheimer's disease, vascular dementia, Lewy bodies dementia, fronto-temporal dementia, urinaray incontinence, bladder dysfunction, management.

The dementias can be categorized according to clinical presentation, neuropathology and/or etiology into four major dementia groupings, (I) Alzheimer's dementia; (II) the vascular group (including large and small vessel disease); (III) the Parkinson's group (including Lewy Body disease, dementia of Parkinson's and Alzheimer's dementia with Parkinson's); (IV) the frontotemporal group (including Pick's disease and Semantic dementia) [13]

a) Alzheimer's disease

1. EPIDEMIOLOGY AND PREVALENCE

Alzheimer's disease (ALD) is the most common type of dementia in clinical and autopsy surveys. AD affects mostly elderly people. The symptoms include worsening of the memory, impairment of language and other cognitive functions (analytical thinking, abstract reasoning). Ultimately, there is loss of self-hygiene, eating, dressing and ambulatory abilities and incontinence and motor dysfunction. The onset of incontinence usually correlates with the disease progression (LOE 3) [1]. The prevalence of incontinence is reported to be between 23 % and 48 % (LOE 3) [2-3].

2. PATHOLOGY AND DISEASE SPECIFIC LUT PROBLEMS

ALD at the outset was identified by its unique pathology, the plaques and tangles that Alzheimer referred to as "a clotting of fibrils…. in addition an extraordinary number of peculiar patches disseminated throughout the entire cortex."

The clinical hallmark of Alzheimer's disease is memory impairment. A sense of memory failure, detected by the patient or a close relative, is usually the presenting symptom. Motor and sensory symptoms are absent until late in the course of the disease. However, other cognitive domains, such as language, praxis and recognition skills, are affected even early in the presentation.

ALD has a gradual and progressive course, typically 10 years from diagnosis to death. The advent of cholinesterase inhibitors has had some effect on the course of disease for individual subjects, though population trends have been harder to demonstrate (10, 11).

In a study by Del Ser et al (LOE 3) urinary incontinence was associated with severe cognitive decline in pure Alzheimer's disease but usually preceded severe mental failure in patient with dementia due to diffuse Lewy body disease [4]. Nobili et al (LOE 3) performed quantitative EEG in Alzheimer's patients, finding that incontinence was predicted by alpha power in the right side [5]. In another study by Nobili et al (LOE 3) the value of regional cerebral blood flow from a posterior temporal-inferior parietal area in each hemisphere predicted development of incontinence [6]. Brain computer tomography study done by Sugiyama et al (LOE 3) in Alzheimer's disease patients showed that the degree of brain atrophy was more severe in those with detrusor overactivity than those without it [9].

Detrusor overactivity was found in 61 % of their patients. Haddad et al (LOE 3) described two patients with vesicoureteral reflux, one of them showing buccosalivary, gastroesophageal, vesicoureteral, urethroprostatic and urethrovesicular reflux as a consequence of the neurologic dysfunction [8].

There is no systematic review of type and grade of LUT dysfunctions in Alzheimer's disease, nor a study about progression of those dysfunctions as the disease progresses.

3. Disease specific diagnosis and treatment

EEG and regional cerebral blood flow might predict when and if incontinence will occur during the course of the disease [5,6]. Franssen et al (LOE 2) examined the occurrence of following developmental reflexes: the tactile suck reflex, the palmar and plantar grasp reflexes, and the plantar extensor reflex in healthy elderly, cognitively and functionally mildly impaired patients, and patients with Alzheimer's disease [9].

Prevalence of all five reflexes was more than 6 times higher for those categories that comprised only permanently doubly incontinent patients as compared to those categories that comprised only continent individuals. It is interesting that the frequency of developmental reflexes rose sharply with the onset of progressive incontinence, suggesting its cortical origin. As demonstrated above, the development of incontinence in Alzheimer's disease patients is associated with cognitive impairment and brain degeneration, suggesting its central nervous system origin. Therefore behavioural therapy, toilet training and prompted voiding would be most useful treatment modalities for this type of incontinence.

Hutchinson et al (LOE 3) suggested that caregivers of patients with Alzheimer's disease should study the toileting behaviours. This would permit them to provide physical and cognitive assistance while attempting to avoid accidents and catastrophic events [10]. Tariot (LOE 4) stressed the necessity for taking into account different factors (like mobility, cognitive functions, general medical conditions), when planning treatment (also for incontinence) in Alzheimer disease patients [11].

Again the general guidelines should apply for choosing the best management of incontinence in Alzheimer's disease patients. The treatment should be however tailored to individual patient needs and disease status.

There is still some controversy that the central Acethylcholinesterase (AcHE)- inhibitors given by the neurologist might exacerbate urinary incontinence in those patients (18). Donepezil hydrochloride is a selective central acetylcholinesterase (AchE) inhibitor, which decreases degradation of acetylcholine in the brain, then increasing the concentration of acetyl-choline in the synaptic cleft [21]. This drug is widely used to ameliorate cognitive decline in patients with Alzheimer's disease [15; 20] which is thought to be due to a decrease in cholinergic innervation of the cerebral cortex and the basal forebrain [14]. Since the bladder is innervated by the parasympathetic cholinergic nerves [16] neurogenic lower urinary tract (LUT) dysfunction occurs in a subset of patients with AD [19; 22].

Although donepezil may facilitate cholinergic neurotransmission mostly in the central nervous system, common adverse effects of donepezil, such as nausea and abdominal discomfort, have been attributed to the peripheral nervous system (PNS) [15; 21]. Therefore, the increased bladder contraction is reasonably attributed to the PNS effects as seen with other cholinergic drugs. However, according to Sakakibara et al (2005) [12] the patients with AD showed a slight increase in the bladder capacity, which can not be explained by the PNS effects alone. Although it is unknown to what extent central cholinergic circuit may participate in the regulation of micturition, recent experimental studies showed that lesions in the nucleus basalis Mynert in the basal forebrain (central cholinergic nucleus projecting fibres to the frontoparietal cortex) give rise to decreased bladder capacity [19]. In addition, improved cognitive status and alertness may well lead to proper initiative to hold urine in the patients. Central AchE inhibitors including donepezil hydrochloride, therefore, may have complex effects on the LUT function. Although the number of the patients was small, it seems possible that donepezil could ameliorate cognitive function without serious adverse effects on the LUT function in patients with AD. This should be true also for other selective central AchE inhibitors.

4. Guidelines for further research

There is still no cure for Alzheimer's disease, which is progressive and a type of dementia associated disease. We are still lacking studies evaluating LUT disorders in Alzheimer's disease. No systematic review has been performed regarding the possibilities of medical management (both pharmalogical and behavioural) of incontinence.

An open issue also remains the question of aggressive surgery for LUT problems in these patients. Should we offer a surgical therapy for incontinence in female patients with stress incontinence and progressive Alzheimer's disease? This is a question so far unanswered.

CONCLUSIONS

- **Detrusor overactivity seems to be the most common cause of incontinence in Alzheimer's disease patients (LOE 3).**
- **The degree of incontinence is associated with cognitive impairment and brain degeneration (LOE 3).**
- **EEG studies, occurrence of developmental reflexes and regional blood flow studies can predict the development of incontinence in Alzheimer's disease patients (LOE 3).**
- **Selective AchE inhibitors ameliorate a cognitive function without serious adverse effects on LUT functions in patients with ALD (LOE 3).**

RECOMMENDATIONS

- **The extensive and aggressive therapy of incontinence in Alzheimer's disease patients should be reserved for those with good general status and ambulation (C).**
- **In case of ambulatory patients, prompted voiding, behavioural therapy and oral anticholinergics seem to be the treatment of choice (C).**

b) Vascular dementia

1. Epidemiology and prevalence

Vascular dementia is the second most commonform of dementia after Alzheimer's disease among the elderly. Pooled prevalence from eight European countries was 1.6% for vascular dementia in subjects older than 65, compared to a prevalence of 4.4% for ALD (LOE 3) [13].

A meta-analysis of the European studies on the incidence of dementia showed vascular dementia constituted 17.6% of all incident dementia (LOE 3) [1].

2. Diagnosis

Vascular dementia may be the result of a single strategic infarct, multiple cortical or lacunar infarcts, or a microvascular insult in which neither clinical symptoms of stroke nor infarcts by imaging are evident. There is an elevated risk for subsequent dementia in patients who have had a stroke in comparison to controls without any evidence of a stroke (LOE 2)[2]. Diabetes and hypertension are stronger risk factors for vascular dementia than for Alzheimer's disease (LOE 3)[3]. The apolipoprotein e4 genotype is a risk factor for vascular dementia as well as AD (LOE 3) [4].

3. Pathology and disease specific LUT problems

Sakakibara et al (LOE 2) found that mainly the medial frontal lobe is responsible for urinary dysfunction in patients after stroke [5] . Griffiths (LOE 2) in his PET studies, shows that cognitive function was slightly more impaired in patients with genuine urge incontinence. But the strongest and most specific association was with impaired temporal orientation [6]. Genuine urge incontinence with reduced bladder filling sensation was associated with global under-perfusion of the cerebral cortex and more specifically, with underperfusion of the frontal areas of the brain, especially on the right. Jirovec et al (LOE 3) found that cognitive ability and mobility differ significantly between continent and incontinent patients [7]. When the variables were examined together, mobility emerged as the best predictor of the patient's urine control, followed by cognitive impairment.

In a study by Resnick et al (LOE 2) performed in institutionalized elderly, detailed urodynamic studies in 94 of the 245 incontinent patients showed that detrusor overactivity was the predominant cause in 61 percent, with concomitant impaired detrusor contraction present in half these patients. Other causes among women were stress incontinence (21 %), underactive detrusor (8 %), and outlet obstruction (4 %) [11]. Among the relatively few men in this sample, outlet obstruction accounted for 29 % of the cases. Yoshimura et al (LOE 3) found a 47 % prevalence of detrusor overactivity which correlated with the prevalence of dementia [9].

4. Disease specific diagnosis and treatment

No specific diagnostic tests to evaluate dementia related incontinence were described. Since patients with dementia and incontinence usually have one or more concomitant diseases, the evaluation of the LUT functions should follow the general rules, bearing in mind that this is the population of frail elderly.

The treatment should start with modification of patient's behaviours and general rehabilitation targeted at making patient more ambulatory, as it was demonstrated that movement limitations are strongly

related with incontinence. No other specific treatment in dementia have been described, however certain issues like prompted voiding, anticholinergic drugs and intermittent catheterization have been studied.

In his review of trials where prompted voiding was implemented Eustice et al (LOE 1) found that prompted voiding increased self-initiated voiding and decreased incontinence episodes in the short-term [10]. A single small trial suggested that adding oxybutinin, reduced the number of incontinent episodes in the short-term. In a study by Suzuki et al (LOE 3) the best results were obtained with ambulatory patients with the use of a portable chamber pot and induced urination, while no improvement was seen in bedridden patients treated with anticholinergics [11]. Sugiyama et al (LOE 3) studied the effects of anticholinergics therapy in patients aged 65 years or older with and without dementia. The patients received anticholinergic agents for more than two weeks [12]. Urodynamic studies demonstrated significant increase of maximum bladder capacity in the dementia group and the non-dementia group. There was no significant difference in rate of objective improvement between both groups. On the other hand, rate of subjective improvement was significantly higher in the non-dementia group (40 %) than in the dementia group (15 %). Improvement of functional bladder parameters was not associated however with improvement of subjective symptoms in the demented patients. In case of emptying failure, like in other bladder diseases intermittent catheterization is a treatment of choice. Lieu et al (LOE 3) found that carer-assisted clean intermittent urethral catheterization is an effective and safe treatment option for persistent urinary retention in elderly female patients with cognitive impairment and other disabilities [13].With this method of treatment, 54 % of the patients were able to void spontaneously and were continent after a median period of 6 weeks with a range of 1 to 40 weeks. Twenty-seven per cent had significant improvement in the symptoms of urinary incontinence and the residual urine volumes became progressively smaller. However, 19 % failed this treatment modality. The recovery of spontaneous voiding was found to be significantly influenced by the age of the patient, the carer performing the intermittent catheterization and the development of catheter-related urinary tract infection. Twenty-five per cent of the study patients developed symptomatic urinary tract infection which was associated with a delay in the recovery of spontaneous voiding. Its development was also found to be significantly associated with the presence of pre-existing diabetes mellitus, the person doing the catheterization, the presence of dementia and with more predisposing common medical conditions.

Another interesting issue is the surgical treatment in patients with dementia. Two major groups of surgical procedures could be identified: prostate surgery and incontinence surgery. Yonou et al (LOE 3) studied a group of 13 patients with dementia who underwent TURP procedure [14]. Six patients reported good urination, 3 reported some improvement in urination after surgery, although requiring intermittent catheterization and 1 developed mild incontinence. No specific study addressing the issue of incontinence surgery in woman with dementia was performed; however it seems that the incontinence surgery in patients with dementia should be reserved only for the cases with good ambulation and without concomitant functional disorders of micturition (overactive bladder, hypocontractile detrusor).

5. Guidelines for further research

Since dementia is not a homogeneous disease a population study targeted at specific disorder of micturition is urgently needed. Also, a study evaluating different treatment modalities in patients with dementia (especially anticholinergic treatment for overactive bladder and surgical treatment for stress incontinence) is lacking.

CONCLUSIONS

- **Dementia associated incontinence occurs in 30-100 % of patients with dementia (LOE 3).**
- **The degree of incontinence is strongly associated with patient's general status and ambulation (LOE 3)**
- **There is no one major cause for incontinence in these patients; however overactive bladder is responsible for a significant portion of incontinence (LOE 3)**
- **LUT surgery is not contraindicated in this group of patients (LOE 3-4)**

RECOMMENDATIONS

- **The extensive and aggressive therapy of incontinence in dementia patients should be reserved for patients with good general status and ambulation (C)**
- **In case of ambulatory patients, prompted voiding, rehabilitation and oral anticholinergics seems to be treatment of choice (C).**
- **In case of significant post-void residual, intermittent catheterization is the treatment of choice (B); however in elderly non-ambulatory patients the recovery of LUT functions is not so good (C/D).**

c) Dementia with lewy bodies

1. Epidemiology and prevalence

Dementia with Lewy bodies is thought to be the third most common type of dementia in the elderly,

accounting for 10 – 15% of cases at autopsy. In population-based studies of subjects aged 65 and older, the prevalence of dementia with Lewy bodies was found to be 0.7%, which is consistent with its rate of 10 – 15% of hospital-based cases at autopsy [3]. The epidemiology of dementia with Lewy bodies is sparse; age and gender distribution and potential risk factors have yet to be defined.

2. Pathology and disease specific LUT problems

Dementia with Lewy bodies primarily affects the basal ganglia. Lewy bodies and Lewy neuritis are pathologic aggregations of alpha-synuclein, a ubiquitously expressed synaptic protein that has been implicated in vesicle production [1]. Lewy bodies also contain chaperone proteins and elements of the ubiquitin-proteasome system.Immunohistochemical staining for alpha-synuclein has been shown to be the most sensitive and specific method for detecting Lewy bodies and can be used in a semiquantitative grading of severity of Lewy related pathology [2].

In dementia with Lewy bodies (DLB), autonomic dysfunctions can occur and is actually included as a supportive feature for clinical diagnosis [8].

The essential feature for a diagnosis of possible or probable dementia with Lewy bodies is progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational function. Fluctuations (waxing and waning of cognition, functional abilities and arousal from almost normal to markedly confused or hypersomnolent) are a core feature of dementia with Lewy bodies.

Horimoto et al (LOE 3) found 97 % incidence of urinary incontinence amongst patients with Levy body dementia.

Many patients with dementia with Lewy bodies also have Alzheimer's disease pathology, which alters the clinical presentation. Dementia with Lewy bodies' patients who also have many neurofibrillary tangles display more core clinical features of AD [4]. Conversely, Lewy bodies also occur in more than half of all patients with sporadic and early-onset AD [5].

3. Lower urinary tract symptoms in dementia with Lewy bodies, Parkinson and Alzheimer's disease – a comparison

From the urological point of view patients with dementia with Lewy bodies (DLB) tend to develop urgency and urge incontinence more often than do patients with Parkinson (PD) or Alzheimer disease (ALD). Similar bladder capacity, detrusor pressure at maximum voiding, maximum urine flow, mean voided volume and post-void residual volume were found in these diseases, however detrusor overactivity, the major cause of urgency and urge incontinence, was more prevalent in DLB than in PD and in ALD [7]:

Urinary symptoms were recorded in 35 % of patients with DLB, compared to 70 % in MSA and 25 % in PD patients. Detrusor overactivity, the major cause of urge and urge incontinence was more prevelant in DLB and AD. No detrusor-sphincter-dyssynergia was observed. DLB patients with detrusor overactivity had significantly higher Hoehn and Yahr scores than did those without detrusor overactivity. Since the prevelance of frequency, urgency, urge incontinence and detrusor overactivity is markedly lower in AD than in Lewy Body disease, LUT'S may contribute to the differential diagnosis of these two entities.

4. Disease specific diagnosis and treatment

Since patients with Lewy Body disease and incontinence usually have one or more concomitant diseases, the evaluation of the LUT functions should follow the general rules, bearing in mind that this is most often the population of frail elderly (LOE3).

5. Guidelines for further research

Since dementia is not a homogeneous disease and can be classified in four main categories, further studies should aim whether there is a difference in LUT symptoms between these four groups and if yes, whether they could influence the urological treatment strategy.

RECOMMENDATIONS

- **They do not differ from those in ALD and are very much dependent on the general condition of the patient (C).**

d) Frontotemporal dementia

1. Epidemiology and prevalence

Prevalence studies of FTD are inconsistent (LOE 3), giving ranges of 3,6-15,0 per 100,000 [1]. There is a high familial occurrence of FTD [2].

The distribution of FTD is equal between men and women. The mean duration of illness from onset to death is 4-6 years, with a range of 2-20 years. Progression to death in FTD is much more rapid than in ALD (average of 4,2 years and 6,0 years, respectively).

2. Pathology and disease specific LUT problems

Frontotemporal dementia (FTD), also known as Pick's disease, encompasses a diverse group of clinical and pathological disorders. There are several distinct clinical presentations, most commonly behavioral changes, but a language disorder, usually in form of a progressive non-fluent aphasia, can be the main presenting sign. The most common clinical presentation of FTD is characterized by profound changes in personality and social conduct, including a decline in manners and social skills that are incongruent with the patient's premorbid behaviour. Affected patients lack emotional warmth, empathy and sympathy and are indifferent to others.

At autopsy markedly gross atrophy of the frontal and temporal lobes is seen in FTD. On histologic examination the salient features include neuronal loss, micro-vacuolization and astrocytic gliosis centered on cortical layer II.

MRI of patients with FTD often shows atrophy in the frontal and temporal lobes (LOE 2), wich may be asymmetric [3].

There a no data on LUTS in patients with fronto-temporal dementia, however it is obvious that due to the cognitive state these patients have incontinence, either because they forget to take down clothes when they go into the toilet, or they have difficulty finding the toilet, they may urinate in inappropriate places and pass urine more often than usual. Moreover, they may be effected by constipation, diarrhoea or faecal incontinence.

3. Disease specific diagnosis and treatment

No specific diagnostic tests to evaluate dementia related incontinence were described. There are no studies which show the significance of LUTS in fronto-temporal dementia.

4. Guidelines for further research

As there are no studies which show the significance of LUTS in fronto-temporal dementia, such studies would be of value.

CONCLUSIONS

- **There are no studies available which show the significance of LUTS in patients with fronto-temporal dementia.**
- **However, from the underlying pathology – gross atrophy of frontal and temporal lobes - autonomic dysfunction including LUTS should be present, but needs further investigation.**

RECOMMENDATIONS

- **The recommendations do not differ from those with other types of dementia**

2. DEMENTIA, CONSTIPATION AND FECAL INCONTINENCE

• Methods

Using MEDLINE we identified English-language journal articles and reviews published from 1990 to April 2008. The key words included constipation, faecal incontinence and dementia. Special attention was given also to data regarding persons aged > 65 years.

a) Prevalence

MEDLINE research detected only **one** paper related to the influence of dementia on the prevalence of urinary and faecal incontinence in an age group of 85-year-old men and women[1]. This is surprising, because patients with faecal incontinence experience anxiety, embarrassment, and social isolation.[2]

Hellström et al.[1] investigated the influence of dementia on the prevalence of urinary and faecal incontinence in 85 year-old men and women in the random sample n= 485 of the total population of 85-year-olds from the city of Gothenburg, Sweden.

The prevalence of urinary and faecal incontinence and dementia were 38%, 17% and 29% respectively. Demented men (50%) and women (60%) were more often incontinent than non-demented men (18%) and women (36%). Also faecal incontinence was more prevalent in demented (34,8%) than non-demented subjects (6,7%): both urinary and faecal incontinence were more prevalent in demented women (43% and 20% respectively) than in men (27% and 11% respectively). The prevalence of urinary and faecal incontinence and dementia were higher in residents of a nursing home or hospital (74%, 51% and 92% respectively) than in subjects living at home (32%, 9% and 18% respectively): of the demented residents in an institution 78% were incontinent compared with 37% living at home.

b) Management of faecal incontinence in demented people

No specific paper was found on the management of faecal incontinence in demented people; however it should not be too different from the management in frail elderly. Faecal incontinence in demented people can be negatively influenced by stool impaction, medications and neuro-muscular dysfunction.

Demented patients may benefit especially from a bowel habit training programme, which also includes management of constipation with non-pharmacologic (such as exercise and fibre) and pharmacologic measures.[3]

CONCLUSIONS

- **Although the prevalence of faecal incontinence (as well as of urinary incontinence) in demented people is prevalent, no paper was found dealing with the disease specific management of faecal incontinence (LOE3).**
- **However this management should not be too different from that in frail elderly, focusing on bowel habit training programmes including management of constipation. (LOE 3)**

RECOMMENDATIONS

- **Studies on the prevalence of faecal incontinence in dementia are needed**
- **Studies should be undertaken to find out, which management is preferable for constipation and faecal incontinence in demented people.**

II. MULTIPLE SYSTEM ATROPHY

• Methods

Using MEDLINE we identified English-language journal articles and reviews published from 2000 to April 2008, looking for the keywords Multiple System Atrophy, Urinary Incontinence, Bladder Dysfunction, Bowel problems, Constipation, Faecal Incontinence, Management.

1. URINARY INCONTINENCE

a) Epidemiology and prevalence

Multiple system atrophy (MSA) is a rare, adult-onset degenerative disease of the nervous system of unknown origin. Autonomic failure (postural hypotension and urinary dysfunction) is fundamental to the diagnosis of MSA: it is diagnosed when the criteria of either postural hypotension (systolic blood pressure fall > 30 mmHg or diastolic > 15 mmHg) or urinary dysfunction (persistent, urinary incontinence/ incomplete bladder emptying) or both are fulfilled, along with poorly levodopa-responsive parkinsonism or cerebellar dysfunction.[1] Based on the major motor deficits MSA can be classified as MSA-P (parkinsonism - predominant) or MSA-C (cerebellar-predominant). [1] The discovery in 1989 of glial cytoplasmic inclusions in the brains of patients with MSA [2] provided a pathological marker for the disorder (akin to Lewy bodies in idiopathic Parkinson's disease), which combined three disorders previously called striatonigral degeneration, sporadic livopontocerebellar atrophy, and Shy-Drager syndrome.

Urinary symptoms of incontinence are caused by neurologic detrusor overactivity and external sphincter weakness [3] (LOE 2). Sphincter electromyography (EMG) abnormalities were found in 91% of the patients with MSA [3] (LOE 2). Approximately 60% of patients with MSA develop urinary symptoms either prior to or at the time of presentation with the motor disorder [4] (LOE2). This indicates that many of these patients seek urological advice early in the course of their disease. Although postural hypotension was thought to be a marker for autonomic failure in MSA, Wenning et al [5] (LOE2) noted urinary incontinence in 71%, urinary retention in 27%; postural faintness in 53%, and syncope in 15% of 100 patients with MSA. Sakakibara et al [4] (LOE2) found that urinary symptoms (96%) were more common than orthostatic symptoms (43%) ($p < 0.01$) among 121 patients with MSA. Kirchhof et al [6] (LOE2), found that bladder symptoms preceeded symptoms of orthostatic hypotension in 76% of their 71 male patients. Sakakibara et al [4] (LOE2) also found that among 53 patients with both urinary and orthostatic symptoms, those who had urinary symptoms first (48%) were more common than those who had orthostatic symptoms first (29%), and some patients developed both symptoms simultaneously (23%).

b) Pathology and disease specific lut problems

Urinary dysfunction is divided to that of storage and voiding, respectively. Sakakibara et al [7] (LOE2) performed an extensive study of the urological symptoms in MSA patients. They found the following prevalence of different symptoms: difficulty of voiding in 79%, nocturia in 74%, sensation of urgency (recently called an overactive bladder) in 63%, urge incontinence in63%, diurnal urinary frequency in 45%, enuresis in 19% and urinary retention in 8% of the patients. All of MSA patients presented with some kind of LUT symptoms. In addition, many of them had storage and voiding urinary symptoms together; suggesting altered storage and micturition functions in this disorder.

Among 245 urodynamic cases of MSA, Ito et al [8] (LOE2), found that average volume of post-void residuals as a marker of voiding dysfunction was 71ml at the first year, which increased significantly to 170ml at the 5th year ($p<0.01$) after onset of the disease. Patients were not always aware of their post-void residuals. The frequency of weak detrusor by a pressure-flow analysis was 20% at the first year, which increased to 53% at the 5th year ($p<0.05$). The frequency of detrusor-external sphincter dyssynergia was 12% at the first year, which increased to 39% at the 5th year ($p<0.05$). Therefore, detrusor underactivity seemed to contribute to voiding dysfunction in MSA more than detrusor-external sphincter dyssynergia did. The responsible sites of lesion (micturition-facilitating area) for voiding difficulty and retention in MSA seem to be the locus coeruleus (pontine micturition center). The work of Bennaroch demonstrated, that in MSA there is severe depletion of catecholaminergic neurons of the CI and AI areas in the ventrolateral medulla, and this may contribute to orthostatic hypotension and endocrine disturbances in this disorder, respectively. Additionally loss of corticotrophin-releasing factor (CRF) neurons in the pontine micturition area may contribute to neurologic bladder dysfunction [9] (LOE 2). In addition, the sacral intermediolateral cell columns, where preganglionic neurons innervating the bladder are located, are affected in post-mortem MSA cases.

Regarding the storage abnormalities, the frequency of detrusor overactivity was 61% at the first year,

which increased to 75% at the 5th year ($p<0.05$) [8] (LOE2). The frequency of neurogenic pattern in the sphincter EMG was 52% at the first year, which increas ed to 83% at the 5th year ($p<0.05$) [10] (LOE2). Abnormalities in the videourodynamic study included open bladder neck at the start of filling in 53% of MSA patients, suggestive of bladder neck denervation [11] (LOE2). Similar results were reported by others [12]. The responsible sites of lesion (storage-facilitating area) for urinary urgency and incontinence in MSA seem to be the basal ganglia, cerebellum [13], lumbar intermediolateral cell columns where preganglionic neurons innervating the bladder neck are located, and sacral Onuf's nucleus innervating the external sphincter, all of which are affected in post-mortem MSA cases, causing urinary stress incontinence.

Repeated urodynamic studies in MSA patients showed that the cystometrogram changed from detrusor overactivity to low-compliance or acontractile detrusor, and from negative to positive bethanechol super-sensitivity [4] (LOE2). In fact, as the disease pro-gresses, symptoms may change from urinary urgency and frequency to those due to incomplete bladder emptying. These findings suggest that the responsible sites of the bladder cholinergic disorder may change from the center to the periphery. Whereas in the midst of disease, the cystometrogram of patients with MSA often show neurogenic detrusor overactivity with impaired contractile function (DHIC), mostly accounting for urinary urgency / frequency and large post-void residuals, respectively. This condition presumably reflects lesions in both storage and voiding-facilitating areas in this disorder. [15]

Beside bladder disorders, patients with MSA may have nocturnal polyuria, which results in nocturia and morning hypotension. In normal children over 7 years and adults, the circadian release of arginine vasopressin from the posterior pituitary gland into plasma peaks at night. This leads to a nocturnal decrease in urine formation. The ratio of nighttime to daytime urine production is usually <1:2, which can be estimated by a bladder diary. A postmortem study of the brains of patients with MSA revealed the degeneration of arginine vasopressin neurons in the suprachiasmatic nucleus [16] (LOE 2), leading to impairment of the circadian rhythm of the plasma arginine vasopressin concentration in MSA [17] (LOE 2).

c) Disease specific diagnosis and treatment

Since LUT functional disturbances precede very often orthostatic hypotension and other autonomic nervous system symptoms in MSA patients, the diagnosis of lower urinary tract (LUT) symptoms is of paramount importance. Further discussion of the differentiation between MSA and Parkinson's Disease is to be fould in the section on PD.

Amongst different tests external sphincter EMG is the most sensitive one. Sphincter motor unit potential analysis showed neurologic motor unit potentials in 93% of those with MSA, suggestive of external sphincter denervation. Palace et al [18] (LOE 2) demonstrated abnormal sphincter EMG in 93% of MSA patients, which can differentiate this disorder from idiopathic Parkinson's disease. Oertel et al[19] (LOE2) suggested that reduced genital sensation in females could be pathognomonic for MSA (with equal importance as erectile dysfunction in males). A total of 47% of the MSA patients and 4% of the control group had reduced genital sensation. Moreover, the appearance of reduced genital sensitivity in female MSA patients showed a close temporal relation to the onset of the disease. Hahn and Ebersbach[25] (LOE 2) investigated the value of sonography of the bladder to evaluate post-void residual urine (PVR) for the differential diagnosis between idiopathic Parkinson's disease and Multiple System Atrophy. The positive predictive value of increased residual urine for MSA was 91.6 % in the study, the negative predictive value was only 67,8 %. They state, that bladder sonography is an objective, simple and safe tool that allows one to screen for urinary retention which is highly suggestive, but incompletely sensitive for MSA. Because sonography is easily accessible and rapidly performed, it is feasible for routine assessment of atypical Parkinson syndromes. Also Takashi et al 2006 (LOE 2) commented that urinary retention can be a major cause of morbidity in Multiple System Atrophy. The grand average volume of PVR was 140 cc in their patients, the average PVR volume increased from the first year from 71 cc to 129 cc in the second year and 270 cc in the 5^{th} year.

When treatment of the voiding disorders in MSA is concerned, again the general principles of urodynamic based therapy should be used. However It is important to observe that aggressive surgical therapy is not recommended in MSA patients. Chandiramani et al [20] (LOE2) found that all MSA patients who underwent transurethral resection of the prostate (TURP) due to voiding problems were incontinent postoperatively, most probably due to pre-existing sphincter weakness. The same observations were done by Beck et al [3] (LOE2), who evaluated the results of TURP and stress incontinen ce surgery in MSA patients. They concluded that the results of surgery were unfavorable. Patients benefited from clean, intermittent catheterization (CIC), anticholinergic medication and desmopressin spray [21] (LOE 3), which improved continence in 82%.

A nearly half of the MSA patients suffer from voiding difficulties, its management by other means than CIC would be very attractive. Sakakibara et al [22] (LOE 3) compared different non-selective and alpha I A selective alpha blocking agents (prazosin and moxisylite) in the treatment of LUT dysfunctions in MSA patients. The respective means for reductions in residual urine volume for the prazosin and moxisylite groups were 38.1% and 35.2% and there was lessening of urinary symptoms. Side effects due to

orthostatic hypotension were seen in 23.8% of the prazosin group but in only l0.7% of the moxisylite group. A more recent study showed that the effects of alpha blocking agents, as well as those of TUR-bladder neck, for lessening post-void residuals lasted for up to 2 years in MSA, although during that period patients benefited from the therapies [8] (LOE2). On the contrary, administration of amezinium, an adrenergic drug for ameliorating postural hypotension, may increase the risk of retention and post-void residual volume compared to that before treatment [23] (LOE2). Amezinium most probably stimulates the alpha receptors, both in the vascular wall (alpha$_{1B}$ receptors) and the proximal urethra (alpha$_{1A/D}$-adrenergic receptors).

Both postural hypotension and bladder dysfunction are common clinical features in MSA. Pyridostigmine, an acetylcholinesterase inhibitor, can be effective in lessening post-void residual volumes, since it stimulates muscarinic acetylcholine receptors on the bladder (M2/3-muscarinic receptors) that are innervated by parasympathetic cholinergic neurons. Pyridostigmine also lessens postural hypotension, presumably by enhancing nicotinic acetylcholine receptor transmission in the sympathetic ganglia[24] (LOE3).

d) Guidelines for further research

MSA is a slowly progressive disease without any cure. More research is needed to evaluate the effects of long term LUT treatment and to evaluate the effects of different drug treatment modalities.

CONCLUSIONS

- **LUT symptoms often precede the clinical manifestation of multiple system atrophy (LOE2).**
- **The most common LIJT disturbances are detrusor overactivity, detrusor-external sphincter dyssynergia, sphincter and detrusor weakness (LOE2).**
- **Significant post void residual is observed in about half of the multiple system atrophy patients (LOE2).**

RECOMMENDATIONS

- **The most sensitive test to detect multiple system atrophy associated LUT abnormalities is sphincter EMG (A),and post-voiding residual volume , especially when differencing from Idiopathic Parkinson's disease.**
- **Due to progressive nature of the disease aggressive treatment and LUT surgery (e.g. TURP) are not recommended (A).**
- **Treatment of choice in case of increased post void residual are alpha blocking agents and IC (B).**

2. FECAL INCONTINENCE

a) Epidemiology and prevalence

Lower gastrointestinal tract (LGIT) dysfunction is also common in patients with multiple system atrophy (MSA) . Sakakibara et al [1] (LOE2) performed a bowel questionnaire in 15 patients with MSA and in 10 age-matched healthy control subjects. MSA group showed decreased bowel frequency (< 3 times a week) in 9, difficulty in expulsion in 11, and faecal incontinence in 3; whereas control group showed decreased bowel frequency in only 2, mild difficulty in expulsion in 2, fecal incontinence in none. Therefore, constipation is the major bowel dysfunction in this disorder; although in advanced stages faecal incontinence is not uncommon.

b) Pathology and disease specific lut problems

Previous studies on the mechanism of bowel problems in this disorder are scarce. Stocchi et al [2] (LOE2) performed anorectal manometry in 16 patients with MSA; and 13 patients showed paradoxical anal sphincter contraction on fictive straining. Bardoux et al [3] (LOE3-4) reported a case of fecal incontinent patient due to MSA, who showed inability of anal squeezing. More recently, Sakakibara et al [1] (LOE2) performed colonic transit time, sphincter electromyography (EMG) and rectoanal video-manometry in 15 patients with MSA and 10 age-matched healthy control subjects. Compared with the control subjects, MSA patients had significantly prolonged colonic transit time in the rectosigmoid segment ($p<0.05$) and total colon ($p<0.05$). Sphincter EMG showed neurogenic motor unit potentials in none of control subjects but in 93% of MSA ($p<0.01$). At the resting state, MSA patients showed a lower anal squeeze pressure (external sphincter weakness) ($p<0.01$) and a smaller increase in abdominal pressure on coughing ($p<0.01$). During rectal filling, MSA patients showed smaller amplitude in phasic rectal contraction ($p<0.01$), which was accompanied by an increase in anal pressure that normally decreased, together with leaking in 3 patients. During defecation, most MSA patients could not defecate completely with larger post-defecation residuals ($p<0.05$). MSA patients had weak abdominal straining, smaller rectal contraction on defecation and larger anal contraction on defecation (paradoxical sphincter contraction on defecation, or anismus), though these differences were not statistically significant.

Therefore, constipation in MSA most probably results from slow colonic transit, decreased phasic rectal contraction and weak abdominal straining, whereas fecal incontinence results from weak anal sphincter due to denervation. The responsible sites for these dysfunction are still not entirely clear. However, as described in idiopathic Parkinson's disease, they most probably reflect lesions of both central and peripheral nervous systems that regulate the LGIT.

c) Disease specific diagnosis and treatment

LGIT functional disturbance is often preceded by LUT dysfunction in MSA patients. Abnormalities in colonic transit time and rectoanal videomanometry in MSA were mostly similar to those in idiopathic Parkinson's disease, except for the sphincter denervation and resultant fecal incontinence in MSA.

When treatment of the bowel disorder in MSA is concerned, use of objective parameters is recommended in order to clarify the action of drugs. A few such studies are available: Eichhorn and Oertel [4] (LOE3) gave polyethylene glycol 3350, an osmotic agent with high water binding capacity, in 2 patients with MSA, and found an improvement in stool frequency and difficult defecation in both patients. Similarly, Sakakibara et al [5] (LOE2) measured colonic transit time in 4 patients with MSA.

After administration of calcium polycarbophil, an osmotic and highly bulking agent, colonic transit time of total and the right segment shortened significantly. Liu et al [6] (LOE2) performed colonic transit time and rectoanal videomanometry in 7 patients with MSA. After administration of mosapride citrate, a novel selective 5-HT4 receptor agonist, the patients showed a shortened total and rectosigmoid segment colonic transit time; lessened first sensation and an augmented amplitude in phasic rectal contraction.

During defecation, mosapride augmented the amplitude in rectal contraction and lessened the volume of post-defecation residuals significantly. Similar results were obtained in a study by Sakakibara et a l[7] (LOE2), in which dietary herb extract Dai-Kenchu-To, one active component of which is hydroxy-beta-sanshool (5-HT3 receptor agonistic action), was prescribed.

d) Guidelines for further research

MSA is a slowly progressive disease without any cure. More research is needed to evaluate the pathophysiology of LGIT dysfunction, and to evaluate the effects of different drug treatment modalities.

CONCLUSIONS

- **Patients with multiple system atrophy have often abnormal bowel function (LOE2) .**
- **The most common bowel disturbances are slow colonic transit, decreased phasic rectal contraction and weak abdominal straining, and faecal incontinence results from weak anal sphincter due to denervation (LOE2).**
- **Bowel dysfunction such as constipation is common and has significant impact on quality of life of patients with multiple system atrophy (LOE3).**

RECOMMENDATIONS

- **More studies on neurologic bowel dysfunction and management in patients with multiple system atrophy are needed before giving any recommendation**.

III. PARKINSONS DISEASE

1. URINARY INCONTINENCE

a) Epidemiology and prevalence

Parkinson's disease (PD) is a movement disorder due to degeneration of dopaminergic neurons in the substantia nigra and a loss of dopamine-containing nerve terminals in the basal ganglia. Degeneration of the nigrostriatal pathway is accompanied by decreases in corresponding biochemical markers, including dopamine, tyrosine hydroxylase, dopamine metabolites, and dopamine transporter. These central nervous system changes have also influence on autonomic functions, including voiding in affected patients. The most common are gastrointestinal (constipation), perspiratory (hypohidrosis) and urinary systems.[1]

Lower urinary tract (LUT) dysfunction in PD was estimated to occur in 37-71% in uncontrolled studies. Among these, in a study of Hattori et al [2] (LOE3) 60% of PD patients had urinary symptoms, which could be divided in the following categories: irritative in 28%, obstructive in 11%, and both symptoms in 21%. The frequency of urinary symptoms statistically correlated with severity of the disease, but not with the duration of illness. Gray et al [3] (LOE3) reported that LUT functional disturbances in PD are not disease specific and only correlated with age. In the more recent, control-based studies [4,5,6,7] (LOE2) the prevalence of LUT symptoms (LUTS) was found to be 27-63.9% using validated questionnaires [4,5,6], or 53% in men and 63% in women using a nonvalidated questionnaire that includes a urinary incontinence category [7], with all of these values being significantly higher than healthy controls. The majority of patients had onset of the bladder dysfunction after appearance of motor disorder. In one study, urinary incontinence in PD frequently occurred in conjunction with fecal incontinence, whereas no significant relation was observed between bladder and sexual dysfunction [7]. Also, it is of particular importance to note that that bladder dysfunction substantially affects the quality of life in patients with PD [7] (LOE2). There has been shown a correlation between bladder dysfunction in patients with PD and neurological disability [4] (LOE2), and a correlation to stage of disease [7] (LOE2), both suggesting a relationship between dopaminergic degeneration and LUTS. LUTS was more common in a group of PD patients with older age than that with

younger age, as it is seen in healthy populations [7]. Among LUTS, nocturia (nighttime urinary frequency) is the most prevalent symptom reported by patients with PD (>60%) [4,5,6,7] (LOE2). Patients also complain of urinary urgency (33-54%), daytime frequency (16-36%), and urinary incontinence in 26% of their male and 28% of their female patients with PD [7].

Although less common than storage symptoms, PD patients also show voiding symptoms. In the study by Sakakibara et al [7] (LOE2), the PD patients had significantly higher rates of retardation in initiating urination (44% of men only), prolongation/poor stream (70% of men only), and straining (28% of women only) compared with the control group. However, despite the voiding symptoms, PD patients have low post-void residuals.

b) Pathology and disease specific lut problems

The net effect of the basal ganglia on micturition is thought to be inhibitory [8], whereas in PD, in which the basal ganglia is affected, the bladder becomes hyperactive. Functional neuroimaging during bladder filling resulted in activation in the globus pallidus of normal volunteers [9] (LOE2) and in the putamen in PD patients with detrusor overactivity[10] (LOE2). In contrast, dopamine transporter imaging (indicating brain dopamine neurons) was decreased in PD patients with urinary dysfunction than in those without it [11,12] (LOE2). The micturition reflex is under the influences of nigrostriatal dopamine[13] (both inhibitory in D1 and facilitatory in D2) and GABA (inhibitory). Deep brain stimulation in the subthalamic nucleus results in amelioration of motor disorder as well as increased bladder capacity and decreased post-void residuals [14] (LOE2). Therefore, urinary dysfunction in PD could reflect degeneration of the nigrostriatal dopaminergic cells associated with specific motor disorders. In addition to the nigrostriatal dopaminergic projection, the ventral tegmental area (VTA, the A10 cell group)-limbic cortex and the hypothalamic (the A11 cell group)-spinal cord dopaminergic projections are presumably involved in urinary dysfunction in PD.

In a study of PD and multiple system atrophy (MSA) patients, Sakakibara et al [15] (LOE2) found urinary symptoms in 72% of PD patients. They were mostly attributed to detrusor overactivity (81%) and external sphincter relaxation problems (33%). During micturition PD patients did not demonstrated detrusor-sphincter dyssynergia, however detrusor-hypocontractility was observed in 66% of women and 40% of men. In addition, patients with PD had mild outlet obstruction, e.g., mean Abrams-Griffiths number (outflow obstruction > 40) was 40 in women and 43 in men, respectively. Nevertheless, average volume of post-void residuals in PD was only 18 ml. Similar observations were done by Defreitas et al [16] (LOE2). The urge incontinence prevalence was around 54%, however no statistically significant correlation between the duration or severity of PD and urodynamic parameters was found.

c) Disease specific diagnosis and treatment

In voiding dysfunctions associated with presumed PD it is important to differentiate between PD and MSA. Chandiramani et al [17] (LOE2), suggested several criteria for distinguishing LUT symptoms caused by MSA from these caused by PD. Presence of the following features: urinary symptoms preceding or presenting with parkinsonism; urinary incontinence; a significant post-void residual urine volume; erectile failure preceding or presenting with parkinsonism, is strongly suggestive of MSA rather than PD. External urethral sphincter EMG is also helpful to distinguish between these two entities, since detrusor- external sphincter dyssynergia was not seen in patients with PD but was present in 47% of those with MSA [15] (LOE2). This is also confirmed by studies of palace et al [18] (LOE2) who demonstrated abnormal sphincter EMG in 82% of MSA patients.

It is possible that levodopa and other antiparkinson medication may affect bladder function in PD. Aranda et al [19] (LOE3) studied the effects of apomorphine in 2 *de novo* PD patients (patients who have not had antiparkinsonian medication previously), and found that the bladder capacity increased. They gave oral levodopa to one of the patients, and the bladder capacity increased. In another study, after 3 months of treatment with levodopa, the storage urodynamic parameters were improved in *de novo* PD [20] (LOE3).

In contrast, in non-*de novo* patients, studies concerning the effect of dopaminergic drugs on micturition have produced conflicting results. Some reports have shown *storage-facilitating effects* of dopaminergic drugs as follows. A questionnaire study has shown that in non-*de novo* patients, voiding symptoms (intermittency and sensation of residual urine) were more common in those taking levodopa and bromocriptine (D2-selective agonist) than in those taking levodopa alone [7] (LOE2). In contrast, Kuno et al [21] (LOE3) showed that change of bromocriptine to pergolide (D1<2 agonist) brought lessening of nocturia, and Yamamoto [22] (LOE3) described improvement of detrusor overactivity by pergolide. Others have shown *voiding-facilitating effects* as follows. Christmas et al [23] (LOE3) have studied the effects of apomorphine in 10 parkinsonian patients, and found that acontractile bladder became normal in 2, and post-void residuals was ameliorated in 6 of these patients. More recent studies have shown that in early PD [24] (LOE2) and advanced PD with the on-off phenomenon [25] (LOE2), a single-dose of levodopa exacerbates detrusor overactivity in the filling phase, but also improves bladder emptying through increased detrusor contractility. We still do not know the exact reasons for the discrepancy.

There are several factors underlying the complex bladder behavior in non-*de novo* PD patients. Post-synaptic dopamine D1 (excitatory) and D2 (inhibitory) receptors have a millimolar affinity to dopamine, whereas dendritic D2 (inhibitory) autoreceptors have a picomolar affinity to dopamine [26]. Therefore, when levodopa is administered externally, it may first stimulate dendritic D2 autoreceptors, which might suppress the nigral cells and facilitate the micturition reflex. In cases of PD under long-term treatment with levodopa, dopamine receptors are down-regulated and potential hypersensitivity might occur [27]. Bladder overactivity might also involve an activation of D2 receptors in the spinal cord [28].

Detrusor overactivity should be treated according to the general knowledge of anticholinergic drugs. There are no specific studies on systematic anticholinergic drugs to treat neurologic detrusor overactivity in PD patients; however since anticholinergics were the first drugs available for the symptomatic treatment of PD and since they are still widely used today there is no reason to believe that they will produce any specific adverse events in these patients. A systematic review of anticholinergic use (centrally acting) to treat PD was recently done by Katzenschlager et al [29] (LOE I).

For emptying failure the treatment of choice remains clean, intermittent catheterization (CIC); however PD patients rarely have post-void residual volume > 100ml [15] (LOE2). An interesting treatment option was suggested by Finazzi-Agro et al [30] (LOE3), who implanted subthalamic nucleus electrodes in patients with PD. They observed that during chronic subthalamic nucleus stimulation bladder capacity and reflex volume were increased for and the amplitude of overactive detrusor contractions was decreased (non significantly) in comparison with the studies performed when the stimulator was switched off.

As in MSA a very important issue in PD affected patients is the indication for pelvic surgery. Myers et al [31] (LOE2) found that women with PD and LUT complaints have a lower maximum cystometric capacity and a higher rate of detrusor overactivity at lower bladder volumes in comparison with non-neurologic control. Therefore surgery for stress incontinence in women with PD should be performed only when no significant detrusor overactivity is present, since it is well known that this type of surgery can evoke or aggravate detrusor overactivity and subsequent urge incontinence.

The issue of selecting the right patient for prostate surgery was described above. Staskin et al (LOE3) described the results of TURP in MSA rather than in PD patients. Since external urethral sphincter acontractility is extremely rare in true PD, prostate surgery should not be contraindicated in this group of patients.

d) Guidelines for further research

Despite there is no definite cure for PD, with the current knowledge we can slow down the disease process and bring patients to an almost normal live. Therefore it would be of extreme importance to introduce a validated scheme for LUT dysfunction therapy.

CONCLUSIONS

- **LUT symptoms are associated in PD with degeneration of dopaminergic neurotransmission (LOE2).**
- **The most common LUT disturbances are detrusor overactivity, and detrusor hypocontractility (LOE2).**
- **The effect of levodopa on LIJT in PD patients remains to be elucidated (LOE3).**

RECOMMENDATIONS

- **Treatment of choice for detrusor overactivity in PD patients is antimuscarinics (B).**
- **For voiding failure in case of significant post void residual the treatment of choice remains intermittent catheterization (B).**
- **LUT surgery for patients with Parkinson's symptoms is an option as long as MSA is excluded. However stress incontinence surgery should not be offered to patients with significant detrusor overactivity (C).**

2. FAECAL INCONTINENCE

a) Epidemiology and prevalence

Lower gastrointestinal tract (LGIT) dysfunction is common in Parkinson's disease (PD). It occurs in more than half of PD patients in uncontrolled studies.

In the more recent, control-based studies [1,2,3] (LOE2), the incidence rate of decreased stool frequency (< 3 times a week) in PD patients ranges from 20% to 81%, that of difficulty in stool expulsion in 57-67%, and that of diarrhea in 21%. All of these values are significantly higher than in the normal population (range, decreased stool frequency, 0-33%; difficulty in stool expulsion, 26-28%; diarrhea, 10%). Fecal incontinence has been reported to be 10-24% in PD [2,4] (LOE2). Therefore, constipation is the most prominent LGIT symptoms in patients with PD. Indeed, PD is a risk factor for elderly nursing home residents to have constipation. Of particular importance is that bowel dysfunction affects the quality of life in patients with PD. Among three pelvic autonomic dysfunctions, the rate of dissatisfaction for bowel dysfunction (59%) is significantly higher than those for urinary (28%) or sexual dysfunction (29%) in PD, although the prevalence rate of all three dysfunctions

is almost the same (more than 60%). The rate of dissatisfaction for the bowel dysfunction in PD is also significantly higher than in healthy controls (16%) [2] (LOE2).

Difficulty in expulsion, and diarrhea are more common in the higher grade of Hoehn and Yahr staging [2,5] (LOE2), suggesting a relationship between dopaminergic degeneration and LGIT symptoms. Fecal incontinence in PD occurs commonly with urinary incontinence, whereas no significant relation has been seen between bowel and sexual dysfunction [2] (LOE2). Constipation in PD occurs commonly with a low coefficient of variation in electrocardiographic R to R intervals [6] (LOE3. The findings indicate that parasympathetic dysfunction might underlie these abnormalities.

A recent epidemiological study revealed an association between the frequency of bowel movements and the future risk of developing PD [7] (LOE1). This observation is in line with the pathological staging of PD by Braak et al [8] (LOE1), in which disease process in the central nervous system starts earlier in the dorsal motor vagal nucleus than in the substantia nigra in PD. From a clinical perspective, it is of particular importance that patients with PD see gastroenterologists or physicians first because of their bowel dysfunction, before they see neurologists and a correct diagnosis of PD is made. Therefore, constipation as the initial presentation of PD is akin to urinary dysfunction as the initial presentation of multiple system atrophy.

b) Pathology and disease specific lut problems

The enteric nervous system contains a program in order to generate the peristaltic reflex that promotes bowel transport within the LGIT [9]. The peristaltic reflex consists of two components: ascending contraction oral to, and descending relaxation caudal to the site of stimulus. Cholinergic receptors have a major role in the ascending contraction reflex. The strength of cholinergic transmission is regulated by opposing receptors; serotonin 5-HT4 receptor-mediating excitation and dopamine D2 receptor-mediating inhibition [10,11]. Postmortem studies of bowel in PD have shown decrease in dopaminergic myenteric neurons and the appearance of Lewy bodies along the proximal-distal axis, e.g., they were most frequent in the lower esophagus, but scarce in the rectum[12,13,14] (LOE2). These findings clearly showed that PD affects not only central, but also peripheral (enteric) nervous system.

LGIT function primarily consists of (1) colonic transport of the bowel content to the anorectum, (2) transient anorectum reservoir, and (3) defecation from the anorectum with the aid of strain. In PD, constipation results primarily from decreased transport and/or disturbed anorectal evacuation. Fecal incontinence may result from disturbed anorectal reservoir, or overflow secondary to constipation. Previous reports have shown that total colonic transit time (CTT) is increased beyond the normal threshold in 80% of PD patients, which translates into an increased average CTT ranging from 44 hours to 130 hours in PD[4,15,16] (LOE2), and in 89 hours in *de novo* PD patients [15] (LOE2), all of which are significantly longer than those of controls (range, 20-39 hours). Prolonged CTT has also been documented in PD patients without subjective constipation [17] (LOE2). Slow colonic transit is the major cause of decreased stool frequency. The slow colonic transit is likely to reflect a decrease in slow waves and spike activities of the colon [9].

In the resting anal manometry, the anal pressure of PD patients is low or normal [16,18] (LOE2). The resting anal pressure may reflect sympathetic innervation in the internal anal sphincter, since lesions or anaesthetic blocks at T12-L3 (where the sympathetic preganglionic neurons are located) substantially lessen the anal pressure [19]. Similarly, most PD patients have normal anal pressure increase on squeezing. This finding corresponds to a lack of neurogenic changes in the external sphincter EMG in this disorder. Nevertheless, the latent anal sphincter dysfunction may explain the fecal incontinence that occurs in most advanced cases.

In the slow-filling rectoanal videomanometry, PD patients had the same rectal volume at first sensation and a maximum desire to defecate, and the same rectal compliance as control subjects [16,18] (LOE2). In contrast to the bladder, the normal rectum shows spontaneous phasic contraction [20]. However, the amplitude of the spontaneous phasic rectal contraction in the PD patients is significantly less than that in control subjects [16,20] (LOE2). The decreased spontaneous phasic rectal contraction may share the same aetiology with the decrease in CTT.

During defecation, the healthy subjects utilized the final wave of spontaneous phasic rectal contractions for defecation [20] (LOE2). However, rectal contraction on defecation in PD patients is smaller than that in controls [16] (LOE2). In addition, in PD patients the abdominal straining is smaller [20] (LOE2). In PD patients paradoxical sphincter contraction on defecation (PSCD), or anismus, is observed in studies using sphincter EMG, radiography, and anal pressure measurement [16,18,21] (LOE2). The mechanism of the impaired straining in PD may include rigidity and reduced contractility of the axial muscles, and a failure of coordinated glottis closure [22] (LOE2). However, neuronal degeneration in the brain of PD patients relevant to straining is yet to be clarified. Mathers et al [21] consider PSCD a focal dystonia. PSCD also occurs in spinal cord-injured patients [23], suggesting that dysfunction in the suprasacral descending pathway to the external sphincter is a contributing factor. Apomorphine is shown to lessen PSCD [21] (LOE2). This effect was not antagonized by

domperidone, which did not penetrate the BBB, suggesting that the central nervous system pathology may produce PSCD.

c) Disease specific diagnosis and treatment

Insoluble dietary fibers produced an improvement in stool consistency and an increase in stool frequency in PD, which paralleled an improvement in levodopa absorption [24] (LOE3). More recently, dietary fibers such as psyllium [25] (LOE2) and polyethylene glycol 3350 [26] (LOE2), or bulking and highly hydrophilic agent polycarbophil [27] (LOE2), improve constipation in neurodegenerative disorders, including PD. Although psyllium does not alter CTT or anorectal parameters in PD patients, polycarbophil shortens the total CTT, particularly in the proximal bowel segments [27] (LOE2).

It is possible that levodopa and other antiparkinson medication may affect bowel function in PD. Endogenous dopamine is thought to inhibit intestinal motility via D2 receptors. However, no reports are available to see whether levodopa might change gut function in *de novo* PD patients.

Since levodopa is absorbed from the small intestine, bowel dysfunction in PD may interfere with levodopa absorption, worsen the motor disorder, or even lead to malignant syndrome [28] (LOE3/4). Domperidone, a peripheral D2 receptor antagonist that does not cross the blood-brain barrier, causes a mean 12% increase in peak plasma levodopa concentrations that occurs a mean of 10 min earlier than when levodopa is given alone [29].

After cisapride has been withdrawn in many countries due to cardiotoxicity, mosapride, a novel selective 5-HT 4 receptor agonist, appeared in clinical use; it shortened total CTT (particularly the caudal segment), and augmented the amplitude in rectal contraction during defecation in patients with PD [30] (LOE2).

It is of particular importance that improvement of parkinsonism is more significant with pergolide-mosapride than with pergolide-domperidone,[31] presumably reflecting better levodopa absorption (LOE3). Similar results were obtained in PD by dietary herb extract Dai-Kenchu-To, one active component of which is hydroxy-beta-sanshool (5-HT3 receptor agonistic action)[32] (LOE2).

d) Guidelines for further research

Despite there is no definite cure for PD, with tile current knowledge we can slow down the disease process and bring patients to an almost normal live. Therefore it would be of extreme importance to introduce a validated scheme for LGIT dysfunction therapy.

CONCLUSIONS

- **Patients with PD have often abnormal anorectal function (LOE2).**
- **The most common bowel disturbances in PD are slow colonic transit, decreased phasic rectal contraction and weak abdominal strain, and paradoxical sphincter contraction on defecation (or anismus) (LOE2).**
- **Bowel dysfunction such as constipation is common and has significant impact on quality of life of PD patients (LOE2).**

RECOMMENDATIONS

- **It seems possible that constipation in PD is treated by drugs acting on dopamine D2 receptors or 5-HT4 receptors in the bowel. (C)**
- **However, more studies on management of neurologic bowel dysfunction in PD are needed before giving any recommendation.**

IV. CEREBRAL LESIONS AND CEREBRO-VASCULAR ACCIDENTS

Listing of terminology used for the

searches: cerebrovascular accident, cerebral lesions, bladder dysfunction, urinary incontinence, faecal incontinence

1. URINARY INCONTINENCE

a) Epidemiology and Prevalence

Cerebro-vascular accidents are the third most frequent cause of death in industrialised countries after myocardial infarction and malignancies. Based on age-dependence of cerebro-vascular accidents (CVA) and the increase of the elderly in our population the importance of this disease enhances: currently one out of 200 inhabitants will suffer from a CVA, 80 to 90% of them above the age of 65. The 5-year-survival rate is 56 % in men and 64 % in women.

At the time of maximal impairment 41.1% of 4499 stroke patients (46.0% of females and 37.3% of males studied) had urinary incontinence [1]. An analysis of the symptoms of 532 patients seen within 7 days of their stroke found that the presence of urinary incontinence appeared to be a more powerful prognostic indicator for poor survival and eventual

functional dependence than a depressed level of consciousness in this period [2, 3]. It was suggested either incontinence was the result of a severe general rather than specific loss of function or that those who were incontinent were less motivated to recover from both continence and more general function. Outcome was so much better in those who remained or became dry that it seems possible that recovery of continence may promote moral and self-esteem which can actually hasten overall recovery. Urinary incontinence with impaired awareness of bladder sensation seem to be associated with poorer outcome than urge urinary incontinence with preserved bladder perception [4]. In Nayhama paper 20 % - 30 % of the patients still suffer from urinary incontinence six months after the CVA if no proper treatment has been instored [5]. Recently, it was shown that six months after stroke 16% of stroke patients experience urine loss, and that urinary loss was perceived as urinary incontinence when it occurred at least monthly [6].

b) Pathology and disease specific LUT problems

1. Cerebral lesions

Prior to the findings of PET-scan studies [7] all that was known about the cortical control of the bladder was based on clinical studies of patients with brain lesions. The most influential study was that by Andrew and Nathan, 1964 [8]. The typical clinical picture of frontal lobe incontinence they described was of a patient with severe urgency and frequency of micturition and urge incontinence, without dementia, the patient being socially aware and embarrassed by the incontinence. Micturition was normally co-ordinated, indicating that the disturbance was in the higher control of these processes. Nathan concludes his translation notes to the paper with a comment “this paper was written because people did not believe that there was such a thing as cerebral disturbance of the bladder“.

There have been a number of urodynamic studies of groups of patients who have had CVA’s and subsequently developed urinary symptoms. The conclusions drawn from these groups of patients with disparate cortical lesions are that, in general, voiding is normally co-ordinated as no patients showed evidence of detrusor sphincter dyssynergia, and that the commonest cystometric finding is detrusor overactivity[[9-11]

In 1996 Sakakibara et al. [12] reported on the bladder symptoms of 72 patients who had been admitted with an acute hemispheric stroke. When assessed at 3 months, 53 % were found to have significant urinary complaints. The commonest clinical problem was nocturia which occurred in 36 %, while urge incontinence affected 29 % and difficulty in voiding 25%. Urinary retention was seen in the acute phase of illness in 6 %. A significant positive correlation was found between the occurrence of a urinary disturbance and hemiparesis. Brain imaging techniques confirmed a more anterior location of brain lesions in these groups. Urodynamic studies on 22 symptomatic patients showed detrusor overactivity in 68 %, detrusor-sphincter dyssynergia in 14 % and uninhibited sphincter relaxation in 36 %. If this was really a detrusor-sphincter-dyssynergia, which should not occur in suprapontine lesions, or a hold-on manoeuvre to prevent urinary leakage, can not be clarified from the paper. There was some indication that lesion size was related to the occurrence of urinary symptoms. In contrast to the findings of Maurice-Williams [13] and Kuroiwa et al. [11]who found a correlation of urinary incontinence with lesions of the right brain hemisphere, Sakakibara et al. [12] could not find a preponderance of right sided lesions for incontinence. Their findings suggest that the damage to the antero-medial frontal lobe, its descending pathway and to the basal ganglia is mainly responsible for micturition dysfunction in stroke patients.

Urinary incontinence in stroke patients is usually interpreted as the loss of central inhibition, however also the loss of bladder perception as concomitant factor came recently into the focus of attention. Deficit of bladder sensation seems to be associated with poorer general outcome. Interestingly, those patients had more parietal lobe but less frontal lobe impairment than patients with urge urinary incontinence and preserved bladder sensation [12]. Another paper by Mochizuki and Saito [14], looking at patients with frontal lobe lesions (tumours) concluded the damage to the right superior bifrontal region was associated with temporary incontinence, whereas permanent incontinence was associated with bilateral damage.

Urinary retention has also been described in patients with brain lesions: Three case histories of elderly females with various forms of right frontal lobe pathology were described as urinary retention. In two, one with an abscess and the other with a haematoma, successful treatment brought recovery of bladder function [15, 16]

An experimental model for studying the effect of forebrain lesions and voiding dysfunction was recently developed in the rat by occluding the middle cerebral artery under pentobarbital or halothane anaesthesia. At thirty minutes after recovery from anaesthesia bladder capacity in animals with cerebral infarct was markedly decreased indicating an overactive bladder. The decreasing bladder capacity continued as long as four months after artery occlusion. Based on the effects of two different types of receptor antagonists on OAB induced by left middle cerebral artery occlusion, the authors Yokoyama et al. [17]conclude that the NMDA receptor (N-methyl-D-aspartate) has an essential role in the development of OAB after CVA. Therefore, a glutamate receptor antagonist can

be expected to be beneficial for treating overactivity caused by cerebrovascular disease, as the induced potentiation of bladder reflexes seems to depend on NMDA glutamate transmission (LOE 4).

2. Brainstem lesions

Already in 1926 Holman[[18]noted that voiding difficulty could be a sign of tumours in the posterior fossa. In a series of patients with brain tumours Ueki et al [19]reported voiding difficulty to occur in 46/152 (30 %) of patients with tumours in the posterior fossa, while urinary incontinence occurred only in 3 (1.9 %).

Renier and Gabreels [20]found urinary retention in 12/17 children with pontine glioma. There are a number of case histories published presenting difficulties with micturition in the presence of various brain stem pathologies .[21-24]

Sakakibara et al. [23] reported the urinary symptoms of 39 patients who had brainstem strokes. Almost half the patients had urinary symptoms, nocturia and voiding difficulty in 28 %, urinary retention in 21 % and urinary incontinence in 8 %. The problems were more common following haemorrhage, probably because the damage was usually bilateral. Urinary symptoms did not occur in those with lesions of the midbrain, but they did in 35 % of those with pontine lesions and in 18 % of those with medullar stroke. Urodynamic studies in 11 symptomatic patients showed detrusor overactivity in 8/11, low compliance in 1/11 and detrusor acontractility in 3/11 three months, six months and 3 years after the occurrence respectively. A non-relaxing sphincter on voiding was found in 5/11 and uninhibited sphincter relaxation in 3/11 (LOE 3).

c) Disease specific diagnosis

Basic diagnosis comprises a targeted history and clinical investigation, urine analysis, postvoid residual urine and a bladder diary. In patients with significant residual urine of over 100 cc or more than 50 % of bladder capacity an urodynamic investigation is recommended to differentiate between detrusor weakness and functional or morphological outflow obstruction.

d) Disease specific treatment

Immediately after the stroke accident in the Stroke Unit, an indwelling transurethral or suprapubic catheter allows control of the urinary output. Diuresis should be monitored. Once the stroke situation is stabilised and diuresis is normalised the catheter should be removed and the patient put on intermittent catheterisation if voiding is unbalanced. In the early stage after the stroke, urinary incontinence can be managed by a condom catheter or by pads. Further treatment comprises, as the two main stays of management, behavioural therapy, initially toileting, later on micturition training and anticholinergic therapy, if the voided volumes are below 250 cc. The patient's ability to squeeze voluntarily the anal sphincter is a good prognostic sign to achieve continence further on. In the early phase, especially during catheter drainage, special care must be taken to avoid urinary tract infections with secondary complications. In diabetic patients low dose infection prophylaxis is recommended [LOE 4).

A recent systematic review on treatment of urinary incontinence after stroke in adults assessed the available knowledge on behavioural interventions (timed voiding and pelvic floor muscle training), specialised professional input interventions (e.g. continence nursing), compliment therapy and pharmacological/hormonal intervention (e.g. oxybutynin). It was concluded that data from the available trials are insufficient to guide continence care of adults after stroke and that better quality evidence is required concerning interventions for continence care after stroke .[25] (LOE C).

e) Guidelines for further research

There is a need for further epidemiologic studies of the true incidence of LUT symptoms incl. incontinence after cerebro-vascular accidents in long term. There is a considerable lack of evidence concerning efficacy and safety of currently used therapeutic interventions. Controlled studies comparing behavioural therapy and anticholinergic medication alone and in combination should show which treatment regime is best.

CONCLUSIONS

- **Incontinence after CVA is not only a distressing symptom but also a powerful prognostic indicator for survival and eventually functional dependence. (LOE 2)**
- **The commonest urological problems after stroke are nocturia (36 %), urge incontinence (29 %) and difficulty in voiding (25 %). (LOE 2/3)**
- **There is a positive correlation between the occurence of urinary dysfunction and hemiparesis. (LOE 2/3)**
- **Urodynamic studies revealed detrusor overactivity in 68 %, sphincter relaxation problems in 36 % (LOE 4).**
- **Damage to the antero-medial frontal lobe and its descending pathway and the basal ganglia are mainly responsible for voiding dysfunction in stroke patients. With brainstem pathology symptoms of impaired voiding (urinary retention) predominate. (LOE 3)**

RECOMMENDATIONS

- **As the urological symptoms, especially incontinence are very distressing, urological care is mandatory for these patients (B)**
- **Prevention of early urinary tract infection, especially when during the acute phase an indwelling (Foley-) catheter is used. Thereafter, management with toileting, later micturition training, combined with anticholinergic therapy are the main stays (C)**
- **Rarely intermittent catheterisation is necessary due to unbalanced voiding mostly in men with pre-existing infravesical obstruction till general recovery allows surgical measures to relieve obstruction, if alpha-blockers and 5-alpha reductase inhibitors are not effective (C).**

2. FAECAL INCONTINENCE

a) Epidemiology – (LOE 3)

Brocklehurst et al. [26] observed that 14% of stroke patients with faecal incontinence became so beyond 8 weeks after the acute event, leading to speculation that constipation, immobility and dependence may be primary underlying causes. The incidence of incontinence was 51% [urine) and 23% (faeces) within one year. Faecal incontinence at onset is associated with measures of severity of stroke and of immobility.

In the Copenhagen Stroke Study, Nakayama et al. [5] did a survey of urinary and faecal incontinence using subscores of the Barthel Index during the hospital stay and at 6-month follow-up in 935 acute stroke patients. In the acute state, almost half of an unselected stroke population had urinary and/or faecal incontinence (40%). The proportion declined to one fifth for urinary incontinence and one tenth (9%) for faecal incontinence of the surviving patients at 6 months. By multivariate analysis, significant risk factors for both incontinences were age, severity of stroke, diabetes, and comorbidity of other disabling diseases. According to Harari et al. [27] prevalence of poststroke faecal incontinence was 30% [7 to 10 days), 11% [3 months), 11% [1 year), and 15% (3 years). New-onset faecal incontinence during acute state was associated with urinary incontinence (Odds ratio-OR, 19.96; 95% confidence interval -CI, 8.8 to 36.8), Glasgow Coma Score < 15 (OR, 2.84; 95% CI, 1.6 to 5.0), visual field defect (OR, 2.69; 95% CI, 1.6 to 4.6), dysphagia (OR, 2.16; 95% CI, 1.2 to 3.8) and age 65 years and over (OR, 2.16; 95% CI, 1.0 to 4.8). One third of patients with faecal incontinence at 3 months were continent by 1 year (suggesting the presence of a reversible underlying cause); conversely, 63% incontinent at 1 year had been continent at 3 months. Urinary incontinence (OR, 87.6; 95% CI, 41.6 to 184.4), anticholinergic drug use (including antipsychotics, tricyclic antidepressants, oxybutynin, or antiemetics) (OR, 3.1; 95% CI, 1.1 to 10.2) and needing help with toilet use (OR, 3.5; 95% CI, 1.4 to 17.3) were significantly associated with faecal incontinence in stroke survivors at 3 months. Faecal incontinence at 3 months increased the risk of long-term placement (28% vs. 6%) and death within 1 year (20% vs. 8%). Modifiable risk factors for faecal incontinence 3 months after stroke are constipating drug use and difficulty with toilet access.

b) Conservative bowel management (LOE 3)

Venn et al. [28] performed a trial in persons with stroke and compared 4 bowel programmes based on the use of suppositories and scheduled bowel care. 85% of participants successfully achieved effective bowel training within a month. Those assigned to morning suppository schedules were more likely to establish a successful bowel regime than those assigned to evening schedules (P<0.01).

Munchiando and Kendall. [29] compared the effectiveness of two bowel training programs for patients with CVA and determined the length of time required to establish a regulated program. The sample of 48 CVA patients included 23 in the control group who had every-other-day digital stimulation and 25 in the experimental group who had daily digital stimulation. Demographic data showed no significant differences between the two groups. More subjects in the experimental group established regularity. However, the subjects in the control group who did achieve regularity took less time to do it. Subjects with right-side hemiplegia and less mobility required more time to become established. The routine protocol for bowel training in their rehabilitation unit was then changed to include daily digital stimulation.

Recently, a randomized controlled trial evaluated a specialised intervention (structured nurse assessment including history and rectal examination, targeted patient/carer education and treatment recommendations) versus routine treatment of constipation and fecal incontinence in stroke survivors. A single nurse intervention effectively improved symptoms of bowel dysfunction up to 6 months later, changed bowel-modifying lifestyle behaviors up to 12 months later, and influenced patient–GP interaction and physician prescribing patterns .[30]

CONCLUSION (LOE2/3)

- **Faecal incontinence after stroke is prevalent but declines over time.**
- **Faecal incontinence is associated with age, severity of stroke, urinary incontinence, co morbidity, using constipating drugs and functional difficulties.**
- **Suppository and digital stimulation may assist in regulating bowel evacuation.**

RECOMMENDATION (B)

- **Modifiable/treatable causes of faecal incontinence should be evaluated and corrected.**

V. MULTIPLE SCLEROSIS

1. EPIDEMIOLOGY

Even though there are few studies today to confirm it, the impact on the quality of life for patients with vesicosphincteric disorders (VST) due to multiple sclerosis (MS) is probably significant. Moreover, in a recent cross-sectional study (LOE4), Notvedt et al [1] demonstrated that those patients with VST had distinctly lower quality of life scores on the SF36 scale in comparison with the population of MS patients that is asymptomatic. The tools for evaluating quality of life that take into account VST in MS have been validated so that variations in it over the course of the illness can be measured [2-5].

VST is extremely polymorphic, and it appears in the great majority of cases within the first 6 to 10 years of the progression of the illness [6] [7-11]. Once VST has started (2 to 10% of cases as primary symptom [7, 12-14]), they will present a more elevated risk of developing severe follow-on urological problems (LOE4) [15]).

The prevalence of VST in the global population of patients who are suffering from MS is in the order of 30 to 96% [6-8, 10, 11, 13, 14, 16-32] (LOE 2b-4). The size of this interval manifests the differences linked to the type of MS, to the duration of the illness, and to the degree of handicap, as well as to a probable under-evaluation by certain practitioners of the urological problems that develop progressively and slowly.

2. SYMPTOMATOLOGY OF VST IN MS

Urinary symptomatology in MS is polymorphic and, like its incidence, probably subject to change over time. The most frequent urinary symptoms are indisputably overactive bladder (OAB) symptoms: urinary frequency (32 to 99%), urgency (32 to 85%), and urge incontinence (19 to 80 %) (LOE2b-4) [7-11, 13-15, 18-22, 24-34].

Obstructive urinary symptoms also exist to a lesser degree: difficulty of voiding and chronic or acute urinary retention. Dysuria was found in 6 to 79% of the patients, and acute episodes of urine retention were reported in 8 to 73% of the patients (LOE2b-4)[8-11, 13, 14, 18-22, 24-35].

All of these studies were carried out most frequently in a retrospective fashion or on a population of patients coming for a consultation for another reason, which can upwardly bias the estimated frequency of the disorders. There was a cross-sectional study from Marrie et al [5] (LOE4) of 16,858 patients. Of those patients, 9688 (57.5%) had responded to the two questionnaires that were posted (Bowel Control Scale (BWCS) and Urogenital Distress Inventory-6 (UDI-6)). The figures confirm the frequency of urinary disorders in the MS population: urinary frequency (28%), urgency (17%), urge incontinence (14%), and difficulty with bladder emptying (12.5%). Independent of the non-response rate, there are several elements that cause us to think that these figures are in actuality higher. Indeed, 65% of the patients complain of having at least 1 episode of urinary tract infection, and the majority of patients have not been treated or had a specific checkup. One can think of this very elevated rate of episodes, labeled “UTI”, as manifesting the underlying vesicosphincteric disequilibrium in numerous patients. Problems with emptying the bladder are particularly poorly evaluated by patients, with a large number of patients having a significant post-void residual amount without an evident clinical manifestation. In a cross-sectional study (LOE4) carried out in 2004, Kragt et al had also found a proportion of 16% of patients who had a post-void residual (PVR) greater than 100 ml but without any symptoms that were detected by the questionnaires that are normally used in evaluations of MS (EDSS, Guys Neurological disability Scale (GNDS)).

The estimation of the global incidence of these disorders in the body of patients with MS underlines the frequency of VST in this population. In practice, it is therefore important that the tools that are used to evaluate these problems are the most appropriate ones possible, because, all of the authors agree that the fact that VST is often ignored by the doctors who take care of these patients is due to the fact that the patients under-report their symptoms (LOE5). What is more, a certain number of the patients will suffer from uronephrological complications secondary to VST. It is therefore important to be able to isolate the groups of patients that are at risk so that complex examinations that are seen as risky are not imposed upon the entire population of patients who are suffering from MS [8, 29, 35].

In a systematic review of the literature, De Sèze et al [17] found that the duration of the progression of MS was one of the principal factors that influenced the frequency of VST (LOE 2b-4). Thus, the majority of the studies that were carried out in patients who had a duration of the progression of MS of more than 13 years found a more homogenous frequency for the different symptoms that was in the high range in comparison with the other figures cited up until the present: urinary frequency (38.5 to 99%), urgency (44 to 85%), and urge incontinence (63 to 72%) (LOE2b-4). The frequency of obstructive disorders is

likewise markedly more elevated [36-79.5%) [7-10, 14, 18, 20, 25, 28]. A second important factor that is associated with the frequency of VST is the degree of the patient's physical handicap as estimated by the EDSS (LOE2b-4)(Expanded Disability Status Scale) [1, 8, 20, 29, 36-40]. It is difficult to confirm from these studies whether this factor has a role in itself, however, on the other hand, clinical practice indicates this common sense observation. A person who can compensate for the urgency by going to the toilet beforehand will see the appearance of urge incontinence following the appearance of a new motor or visual handicap (LOE5). The appropriate management of this problem can allow the improvement of urinary disorders without any specific action on the bladder or the sphincter. As in those patients who have medullar injuries, the clinical examination does not always allow the discovery of the specific neurological insults that are associated with VST. Certain authors have found an association between the pyramidal syndrome and irritable VST [8, 14, 20, 29]. No neurological presentation has been found that is associated in a manifest fashion with bladder voiding disorders [10, 41, 42]. No correlation between radiological insults on the central nervous system (localization and intensity) and clinical VST has actually been found [36, 43-45]. The analysis of a series of autopsies that were done on patients who had a sacral and lumbar insult (autopsy series) did not find any correlation with clinical VST [46] (LOE5).

Other associations have been indicated, but they have all been controversial. The type of progression for the MS (progressive or by crisis), the age at which MS started, and the sex, the age, the geographical location where the patient lives, and the like do not thus appear to be associated with a more elevated frequency of VST [14, 20, 29, 36, 38-40, 47]. The age of the patient does not have impact anymore. On the other hand, older patients will have the same problems as the general population (benign prostate hyperplasia in men and stress urinary incontinence in women), and those problems will of course often be more difficult to treat than they are in the general population.

3. VST COMPLICATIONS IN MS

It is difficult to precisely establish mortality from uronephrological complications. In a recent study of the causes of death in MS patients in the U.S. that was carried out using death certificates (LOE4), a symptomatic urinary tract infection was considered as a contributing cause to the death in 8.4% of the cases, which made it one of the principal causes that were associated with mortality [48]. In that study, terminal renal insufficiency was not found to be a notable cause of mortality.

a) Infectious complications

The reported frequency of lower urinary tract infections is elevated in the literature, ranging from 13 to 80% [17] [7, 9, 10, 18, 21, 25, 29, 30, 38, 49-52] after at least 10 years of progression of the illness. In the study by Marrie et al, 64.6% of the patients indicated at least one annual episode of urinary tract infection. The diagnoses of symptomatic urinary tract infection is therefore very difficult in those patients who have a neurogenic bladder. Indeed, in close to half of these cases the symptoms that are related to neurogenic detrusor overactivity will be complicated by a lower urinary tract infection, as has been well demonstrated by Lisenmeyer et al (LOE 3c) in spinal cord injury patients (SCI) [53]. There is also an incompressible rate of asymptomatic bacteriuria in many neurological patients [54] (LOE4). The occurrence of febrile urinary tract infection (pyelonephritis, orchitis, or prostatitis) is estimated to be between 2 and 23% (9% on average). In addition to the risk of mortality from certain of these infections that has already been underlined, several retrospective studies (LOE5) report an aggravation of MS following an episode of this type [1, 55, 56]. Neurogenic detrusor overactivity is probably a significant factor in the occurrence of upper urinary tract infections. Game et al [57] have also reported a prospective open study in which the injection of botulinum toxin in the detrusor in patients with MS had allowed a significant reduction of symptomatic urinary tract infections to be observed (LOE3c).

b) Alterations of the bladder

Morphological alterations of the trabeculation, thickening of the bladder wall, and diverticules type were found in 4 to 75% of cases according to the series (30% on average) [9, 10, 14, 19, 21, 25, 27-31, 34, 38, 49, 50, 52, 58, 59]. These alterations did not have pathological consequences that were different from those that are found in the general population (primarily increased risk of symptomatic urinary tract infections). The exact proportion of vesical calculus is difficult to estimate, because the majority of studies do not indicate the precise site of calculi events. It can be estimated to be in the neighborhood of 5%. Several factors are associated with the discovery of morphological alterations of the lower tract: post void residual greater than 100 ml and a progression of MS of more than 10 years in duration [19, 60]. There is no correlation between VST and the morphological anomalies that were found [14].

c) Bladder cancer

The data on the more elevated risk of a vesical tumor in patients with MS are controversial. Indeed, it known that those patients who have a neurogenic bladder have had a more elevated risk of developing a particular bladder tumor: epidermoid carcinoma (LOE2b-4) [61-64]. There are other factors that increase this risk in theory, such as tobacco use, indwelling urinary catheters, untreated vesical calculi, and chronic urinary tract infection. In patients with

MS, the use of treatment by cyclophosphamide can be an additional risk. The risk is even further elevated in those patients who have an indwelling urinary catheter or who have been exposed to tobacco. The risk of bladder cancer appears to be slightly increased in those patients who suffer from MS, as a result of risk factors related to their neurogenic bladder as well as from medullar trauma: indwelling urinary catheter, vesicular calculi, and chronic infections. There are other factors that increase this risk in theory, such as tobacco use and treatment with cyclophosphamide. The several studies that have specifically analyzed the risk of vesical tumor in patients with MS (LOE4-5) allow its incidence to be estimated at around 0.29%, which is two to three times higher than the incidence in the general population [23, 65-67]. The diagnoses of these cancers is particularly difficult in neurological patients, especially if they have been catheterized, because the usual diagnostic tools (cystoscopy, cytology, and BTA test) may not be as accurate as usaul because of the inflammatory change of the bladder [63].

d) Complications of the upper urinary tract

Renal calculi were found in 2-10% of the cases, hydronephrosis was found in 1 to 16% of the cases, and vesicoureteral reflux was found in 2 to 15% of the cases (LOE 2b-4) [9, 10, 14, 18, 21, 25, 27-31, 34, 38, 49, 50, 52, 59]. Contrary to the case in medullar traumatization and in spina bifida, the incidence of terminal renal insufficiency is rare in patients with MS, and does not appear to be greater than what it is in the general population [68]. On the other hand, a certain degree of renal insufficiency is indicated in certain articles, and may be as high as 2 to 3% in those patients whose illness has progressed for more than 10 years [19, 25, 27].

e) Risk factors in urological complications

As we have specified previously, the great heterogeneity of the clinical signs of VST in MS leads to delayed diagnosis of urological complications. Simple clinical surveillance therefore exposes one to the risk of overlooking a complication that could significantly increase the risk of urinary tract infection, such as postmictional residue (LOE4) [42]. De Sèze et al [17] looked at data based on the literature in an attempt to discern the principal risk factors for urological complications. Those results must be considered with prudence, because the majority of the studies that were used in that analysis were retrospective (LOE4). The duration of the progress of MS is the principal risk factor, with an increase in the frequency of disorders appearing after 6 to 8 years of progression of the illness. These data are consistent with two cross-sectional studies (LOE4) that report a duration of the progress of MS that is significantly more elevated in those patients who have alterations of the upper urinary tract [9, 49].

The second significant risk factor (especially infectious) is the method of urinary drainage. The indwelling catheter (LOE2b-4) [9, 25] has been associated with a number of known infectious complications [69]. The utilization of suprapubic catheters was associated with a reduced risk (LOE3c) [70, 71], however, the series that was published was mid-term [5 to 6 years) and not long term follow up. If one relies on the data that is available for the treatment of patients with SCI, then the best urinary drainage methods are intermittent catheterizations and voluntary voiding (when it can be done without residue) (LOE2) [72].

The third classic risk factor, independent of diagnosis with MS, is the occurrence of post void residual, which is associated with a more elevated risk of urinary tract infection, of vesicular calculus, and, over time, of the distention of the upper urinary tract.

The other risk factors, suggested by many authors, are more rarely reported and do not allow for a group analysis. The urodynamic risk factors will be addressed in the following chapter. The progression of MS and the patient's sex are not associated with particular alterations of the upper urinary tract. Men were more disposed to have febrile urinary tract infections (LOE4) [8, 9, 25, 35]. Older patients were more susceptible to presentation with urological complications, due on the one hand to the occurrence of urological pathologies at their age, but also probably due to the longer progression since the start of MS [17]. The same factor could explain the data of certain authors who report more frequent urological complications in those patients who have a more severe handicap (LOE4) [9, 14, 15, 51].

4. THE ROLE OF THE URODYNAMIC EXAMINATION IN MULTIPLE SCLEROSIS

The clinical manifestation of vesicosphincteric disorder in MS is heterogeneous, and urodynamic examination is indicated in two situations. The first is in cases in which the patient requests treatment for urinary symptoms that bother him or her. The purpose of the examination is to understand the vesicosphincteric disorder that is causing the clinical symptom and to propose an appropriate treatment. The second situation is one in which the patient is considered at risk and for whom a search for additional urodynamic risk factors is to be carried out.

a) Urodynamic examination before the treatment of urinary symptoms

The most frequently found anomaly is detrusor overactivity, which is found in 34 to 99% of cases. It is defined by the presence of detrusor contractions outside of the bladder filling phase. The second anomaly was detrusor underactivity, which was found in 5 to 37% of the cases [6, 9-11, 18, 20, 22, 24-26, 28-30, 32-36, 38, 50, 52, 59, 73, 74]. In those patients who have urinary symptoms, a normal cystoma-

nometry was found in at the most 30% of the cases [21, 25, 33].

Regarding the sphincter, a vesicosphincteric dyssynergy (VSD) was found in 6 to 82% of the cases (35% on average). It is defined by the absence of relaxation or by the reinforcement of the electrical activity of the external sphincter during vesicular contraction miction, and is the object of needle electromyography of the anal sphincter [58, 75]. VSD is associated indifferently with detrusor overactivity or detrusor underactivity, although the association of detrusor overactivity with VSD (43 to 80% of cases [7, 18, 34, 50, 51]) is more frequent than that of detrusor underactivity with VSD (less than 10% [9, 73]). OAB syndrome seems to more often be the result of DO, especially urgency incontinence [20, 52] (one of the incontinence risk factors that was found was the female sex and the existence of low closure pressure [25]). Obstructive VST was as often associated with DO as it was with detrusor underactivity, and there is also often an associated VSD [10, 20]. VSD does not appear to correlate to the type of urinary symptom [20].

The urodynamic presentations progress through time in a manner that cannot be predicted, especially from the detrusor component. However, VSD, when it is demonstrated in a patient, most often persists without change [26, 59, 73, 76].

b) The urodynamic examination (UDE) in a patient who is considered at risk for urological complications

The role of UDE in this case is much more debated. Certainly, UDE is indicated because of the association of certain UDE anomalies with the possible occurrence of urological complications. The purpose of UDE is therefore the exclusion of an area of risk for the occurrence of complications. Even though this approach is today the most agreed upon, it is useful here to remember that, at least in the case of MS, it has never been evaluated in a strict fashion as part of a prospective protocol. This is explained in part by the fact that sometimes many years will pass before the urological complications occur, which makes the task of evaluation very difficult. The adversaries of preceding in this fashion propose a more pragmatic approach, with regular surveillance of simple criteria (postmictional residue, renal echography) and they propose a therapeutic approach only in those patients who present with a complication. This approach has the advantage of simplicity for the patient and for the doctor. The theoretical risk is that of the late diagnoses of a future complication (indeed, close to 50% of asymptomatic patients have urodynamic anomalies (LOE4)) [21] and of having to therefore propose a therapy to the patient that is more intensive than what could have been proposed had an earlier diagnosis been made.

The three elements of UDE that were strongly associated with urological complications were detrusor overactivity, bladder compliance failure, and VSD [9, 77]. The relationship between DO, bladder compliance failure, and the alteration of the upper urinary tract are classic in neurogenic bladders. The advent of the use of intradetrusor botulinum toxin reinforced the notion of causality between an elevated intravesicular pressure regime and the risk of alteration of the upper urinary tract, because certain authors indicated a disappearance of vesicorenal reflux after injection of botulinum toxin, at which time the intravesicular pressure regime normalized [57]. The relationship between urological complications and VSD is more debated [15, 29, 35]. The practical difficulties of researching this anomaly, the invasive nature of the electromyogram that is necessary for confirmation, and the absence of targeted therapeutic efficacy for VSD mitigate against this systematic search.

5. DIGESTIVE DISORDERS (BOWEL SYMPTOMS) IN MS

a) Epidemiology

Digestive disorders are very frequent in patients who have MS, and, like the urinary disorders that are to blame, when they are significant they have a significant impact on patients' quality of life (LOE4) [1, 5, 78]. What is more, the patients seem to tend to be ashamed of these problems and seldom report them. The clinicians, for there part, have few tools at their disposal for evaluating this impairment. The het effect of these two observations is that it is the patients' digestive disorders that are the most often hidden (:OE3-4) [27, 34].

Taking into account the great diversity of definitions in the several studies that are concerned with this problem, one is obliged to regroup the digestive symptoms into two large groups: those symptoms that can be defined as "retentive", including abdominal pain, flatulence, and constipation on the one hand, and those symptoms that can be defined as "irritant", including false urges to defecate, diarrhea, and/or incontinence of stool and/or gas on the other hand. Digestive disorders of both types were found in 45 to 68% of the cases (LOE 4) [27, 78-82]. The frequency of the "retentive" symptoms was clearly the more elevated, ranging from 31% to 54% [27, 78, 80-82] [79]. The frequency of the irritant symptoms ranged from 6 to 20% [78, 80] [27, 79, 81, 82]. The authors who had sought to flush out the more exceptional episodes of incontinence found a frequency of at least one episode of that type in the months that preceded the interview in 29 to 30% of the cases [27, 79]. Finally, a proportion of about 20% of the symptomatic patients had a combination of irritant and retentive disorders [78, 80] [27, 79, 81, 82]. The figures were clearly more significant than in the general population, where the "retentive" disorders have a frequency that is

estimated to be around 2 to 20% and the "irritant" disorders have a frequency of 2% [83].

b) Risk factors for digestive disorders in MS

There was no factor that allowed the identification of a scalable type of MS that would be at greater risk of developing digestive disorders [78, 80] [27, 79, 81, 82]. Similarly, the duration of the progress of MS does not appear to be a factor that influences the frequency of digestive disorders.

The factor that seems to be the most important is the estimated degree of disability (LOE3c-4) [82, 84]. Thus, Munteis et al [84] found in a case control study (LOE 3c) a frequency of digestive disorders that exceeded 21.2% if the patients had an EDSS between 0 and 1. This frequency exceeded 78% in those patients who had an EDSS that was greater than 4.5.

Other risk factors were suggested (LOE4), but they seemed to have an influence that was less clear, such as being of the female sex, the existence of related urinary disorders, age, and taking anticholinergic treatments [82, 84] [78, 80] [27, 79, 81].

c) Pathophysiology of the digestive disorders of MS

Few studies have been carried out specifically in patients who have multiple sclerosis. One of the difficulties is the frequent existence of related treatments that can themselves bring about the specific symptoms. The colic transit times can be extended or shortened in those patients who present with digestive disorders [85-87]. Several anorectal manometry anomalies were in evidence: reduced tone and compliance, a reduced sensation of filling and incoordination of the external anal sphincter during expulsion, with an onset of the phenomenon known as paradoxical anal sphincter contraction. In patients with faecal incontinence, a decrease in anal canal pressures and hyper-reactivity of the rectal wall have been shown manometrically. In the most recent of these studies, Munteis et al [84] has found that the anomalies that are found the most often are those of maximal sphincter pressure, of anal inhibitory reflex (which occurred later than in the control population), and the presence of paradoxical contraction of the puborectal musculature during straining. These anomalies might be able to allow the proposal of biofeedback reeducation in the concerned patients, however, at present the benefit of this approach has not yet been proven.

VI. SPINAL CORD LESION

1. URINARY INCONTINENCE

a) Epidemiology and prevalence

Spinal cord injury (SCI) including cauda equina injury usually causes impairments of urinary functions such as urinary incontinence (UI) and/or difficulty in urination. During the past 3-4 years, there was no report on epidemiology of urinary dysfunction in acute or post-acute SCI but there were three studies on prevalence of bladder management in chronic SCI persons [1-3] (**Table 20**) and one study in patients with chronic cauda equina lesions [4]. About 8%-11% of chronic SCI persons had normal voiding [1,2], not different from the time after initial rehabilitation [2]; and more normal voiding in tetraplegics then paraplegics [2].

According to the study from Denmark [2], at discharge from the initial rehabilitation period of 233 traumatic SCI patients, bladder-emptying methods were as follows: 12% normal voiding, 57% suprapubic tapping, 19% abdominal pressure, 5% Crédé manoeuvre, 11% CIC, 2% SIC, 8% urethral indwelling catheter (IDC), 0.4% suprapubic catheter (SPC), 0.4% sacral-anterior-root-stimulation (SARS), and 5% use of condom-catheter or diaper. When dividing the patients by years of injury (before 1981 and after 1980), there was a decreasing trend of using suprapubic tapping (drop from over 60% to 45%), abdominal pressure (from over 20% to 15%) and Crédé manoeuvre (drop from over 12% to 1%) but there was an increasing trend of using CIC (rise from 0% to 26%). Over times, 37.5% to 46% of SCI persons changed their bladder-emptying management [2,3]; 28% found their bladder-emptying methods to be a problem; of these 58% were tetraplegic [2]; and the biggest bother bladder management to the subjects was in the compression or straining group (over 50% of the subjects)[1].

There was a statistically significant difference in the frequency of urinary tract infection (UTI) between the bladder management ($P < 0.001$) [1]; the frequency of UTI was high (about 70%) in the mixed group (65% used CIC with other methods) and the CIC group and less (less than 50%) in the groups with catheter free [1]. According to the study financed by Medicon Valley Academy and Coloplast A/S and done in Denmark, of those using CIC, 92% reported using hydrophilic-coated catheters [2] but there was no report about frequency of UTI. However there was a report of reused silicone catheter for CIC in 28 SCI men done in Thailand [5] with the average time of usage of each catheter of 3 years, 36% reported fever with cloudy urine and 64% of foul smell urine; however, where the frequency of CIC is higher, the abnormality of the urethra was lower (P, 0.05) [5].

In 2006, Podnar et al [4] studied 55 patients with chronic cauda equina or conus medullaris injury: 76% of the patients reported LUT dysfunction, 70% had urinary incontinence (UI) (56% of men and 71% of women); and a post void residual (>100 ml) was found in 40% of men and 17% of women. Perianal sensation was abnormal in 96%, electromyography (EMG) of the external anal sphincter (EAS) muscle in 88%, and sacral reflex in 84% of patients; using multiple linear

Table 20. Prevalence of bladder management in chronic SCI

Study (year)	Subjects	Methods of bladder management
Dahlberg et al (2004)[1]	129 traumatic SCI in Finland; mean time since injury 18 years (SD 13)	Normal voiding: 11% Controlled voiding (assisted voiding or incontinence: 12% CIC: 12%; mixed (CIC with other methods):23% Suprapubic tapping 24% Compression or straining (usually with condom catheter): 12% Catheter or conduit: 5%
Hansen et al (2004)[2]	233 SCI in Denmark (82% males, 47% tetraplegics, mean age at the time of follow-up of 50.5 years and mean time since injury of 24.1 years)	46% changed bladder-emptying method Normal voiding: from 12% to 8% CIC: from 11% to 36% SPC: from 0.4% to 6% Suprapubic tapping: from 57 to 31% Crede manoeuvre: from 5 to 19%
Patki et al (2006)[3]	64 traumatic pediatric onset, ambulate SCI; mean follow-up 7 years; mean age 46 years	Spontaneous voiding: initial 62.5%; 47.5% of them deteriorated CSIC: initial 31.2%; 25% of them improved SPC: initial 6.3% 37.5% required a change in urological management 68.7% had abnormal urodynamics at the last follow-up

regression analysis, perianal sensory loss (P=0.0001) and female gender (P<0.02) had a significant positive effect on urinary incontinence score [4].

b) Pathology and disease specific LUT problems

1. Neuro- and bio-chemical regulation of the LUT

Pontari MA et al (2004)[6] analyzed 7 bladder specimens from 6 cervical SCI patients and 1 L1 congenital myelomeningocele (MMC); and compared with results from bladder specimens obtained from 8 organ transplant donors to determine whether the muscarinic receptor subtype mediating contraction shifts from M3 to the M2 subtype as in the denervated, hypertrophied rat bladder; and found that whereas normal detrusor contractions are mediated by the M3 receptor subtype, in patients with NBD, contractions can be mediated by the M2 muscarinic receptor subtype [6]. Haferkamp et al (2006)[7] evaluated the role of neuropeptide Y in 31 patients with NDO and 7 patients with stress urinary incontinence (SUI) and concluded that the reduction of neuropeptide Y-containing nerves, inhibiting the contractile response of the detrusor, may play a role in the development and persistence of NDO in SCI patients. Oner-Iyido?an et al (2004) [8] found that urine 8-iso PGF2alpha concentrations were significantly increased in SCI with hyperreflexic group (median value 0.89 pg/mg creatinine) compared to both normal control (0.52 pg/mg creatinine) and SCI with areflexic groups (P < 0.001); and the lowest concentrations of urinary 8-iso PGF2alpha were observed in the areflexic group (0.22 pg/mg creatinine) [8].

2. Neurophysiology of LUT

In patients with cauda equina lesion, on filling cystometry DO was found in 21% of men and 0% of women, reduced detrusor capacity in 9% of men and 15% of women, and during voiding phase an acontractile detrusor or detrusor underactivity were found in 59% of men and 85% of women [4].

According to the study of viscerosensory pathway of the lower urinary tract (LUT) by Schmid et al (2004)[9], after electrical stimulation (ES) of the posterior urethral mucosa (single square pulses of 0.2 ms, 2 to 3-fold sensory threshold, 60 mA in complete SCI patients), evoked skin sympathetic responses (SSRs) of the hand could be recorded in 14 of 15 sensory incomplete SCI patients with disturbed urethral sensation but not in 13 sensory complete SCI patients with loss of any urethral sensation. Electrically evoked urethral sensations resembled the subjective desire to void at full bladder reported by controls and patients [9].

Later in 2005, Schmid et al [10] did a comparative study of motor evoked potentials (MEP) and evoked pressure curves (EPC) from the urethral compressive musculature (UCM) in 9 healthy persons and 33 patients with neurogenic UI (15 SCL, 14 cauda equina lesion, and 4 multiple sclerosis). In healthy subjects the central latency was 19.0 msec, the peripheral latency was 4.25 msec, and the ratio between central and peripheral latencies was 4.4. In patients with

incomplete SCL, the central latency was significantly delayed (22.7 msec), whereas the peripheral responses were normal; and the ratio (5.5) was increased. Those with a complete SCL showed no UCM reaction after transcranial stimulation, whereas peripheral responses were normal. The increased ratio of 6.0 indicated a SCL. Ten patients with incomplete cauda equina lesions and UI had normal central latencies but prolonged peripheral latencies of 6.7 msec; the ratio of 3.4 indicated a lesion of the sacral caudal roots. In patients with complete cauda equina injury neither central nor peripheral responses could be evoked [10].

According to Dai and Xiao (2005) [11], the thresholds of stimulation on ventral root were 0.02 ms duration, 0.2-0.4 mA, (mean 0.3 mA+/-0.07 mA), compared with 0.2-0.4 ms duration, 1.5-3 mA (mean 2.3 mA+/-0.5 mA) for dorsal root (P<0.01) to cause evoked potentials and EMG. The continuous stimulation for about 3-5 seconds on S2 or S3 ventral root (0.02 ms, 20 Hz, and 0.4 mA) could resulted in bladder detrusor contraction, but the strongest bladder contraction over 50 cm H2O was usually caused by stimulation on S3 ventral root in 7 of the 10 patients [11].

3. Urodynamic studies

Ockrim et al (2005) [12] found that in men with SCI, cystometric variables and detrusor overactivity (DO) remained consistent over sequential studies while in those with LUT symptom of urge, a significant decrease in the number and pressure of involuntary detrusor contractions (IDCs) in consecutive cystometries resulted in a reduction of observed DO from 72% to 63% and 48%, in the three studies. Chou et al (2006)[13] did a retrospective study on urodynamic studies to provide reference ranges for "normal" variability in urodynamic parameters that can be considered as "no real change" from one study to the next. Fifty consecutive individuals with SCI had 2 trials (trial 1 and trial 2) of urodynamic studies done 5 minutes apart, and the following data were collected: maximum cystometric capacity, opening pressure, maximum detrusor pressure, volume voided, and postvoid residual (**Table 21**).

Generao et al (2004)[14] did a retrospective review of SCI cases with 1-year minimum follow up to determine the effect of SCI on the developing bladder and kidneys using video-urodynamics, sonograms. In 42 children (average age at injury of 5.3 years and mean follow up of 5.5 years), 40 used CIC and 37 took antispasmodics. No patient had reflux, hydronephrosis or renal scarring. Safe bladder capacity, the pressure specific volume at 40 cm water or less, was less than the expected capacity in 80%, 58% and 50% of cervical, thoracic and lumbar injured patients but 100%, 76% and 67% of the respectively groups undergoing multiple urodynamics had increasing capacity with time.

Apart from the above-mentioned urodynamic/ cystometric parameters, Ersoz and Akyuz (2004) [15] investigated bladder-filling sensation in 73 consecutive traumatic SCI patients to determine to examine the quality of the preserved sensation and to determine the potential for sensation-dependent bladder emptying in this patient group. Bladder-filling sensation was present to some degree in all incomplete SCI patients, in 82.4% of the patients with complete lesions below T10, and 38.9% of the patients with complete lesions above T11. There were statistically significant differences between three groups with respect to bladder sensation category (P<0.001). About 86% of the patients with incomplete lesions, 53% of the patients with complete lesions below T10 and 22% of those with lesions above T11 had bladder-filling sensation before Pves reached 25 cmH2O and simultaneous bladder capacity of more than 150 ml was present in 61.2, 41.2 and 22.2% of the patients in the groups, respectively. Bladder-filling sensation investigations were reliable in terms of bladder filling sensation category in 36 SCI patients who had second cystometric examination.

Table 21. Shows ranges of variability in urodynamic parameters done in 50 SCI individuals from the study of Chou et al [13]

Urodynamic parameters		Maximum 5th to 95th percentile		Maximum 10th to 90 th percentile		Maximum 25 th to 75 th percentile	
	Mean	Increase	Decrease	Increase	Decrease	Increase	Decrease
Cystometric capacity (mL)	234.63	+213.50	-158.05	+126.40	-74.60	+72.00	-27.00
Opening pressure (cmH_2O)	54.56	+30	-18.00	+13.70	-12.00	+4.00	-9.50
Maximum detrusor pressure (cmH_2O)	60.82	-10.00	+17.35	-27.80	+10.00	-20.00	+4.00
Volume voided (mL)	122.20	+177.25	-176.00	+105.60	-82.00	+50.00	-30.00
Postvoid residual (mL)	176.06	+197.25	-118.00	+131.00	-86.00	+50.00	-30.00

To quantitatively measure bladder mucosal sensory function, Ukimura et al (2004) [16] used neuroselective Current Perception Threshold (CPT) tests in 8 healthy volunteers and 38 patients with NBD. Standardized neuroselective CPT measures were obtained from the left index finger and the mucosa of the posterior bladder wall. The CPT values in the bladder could be determined using the neuroselective measures in all patients but three who had no sensory response (absence of sensation) caused by complete SCI. In the 8 patients with NDO due to incomplete supra-sacral SCI, the bladder CPT value (4.0+/-1.9) at 5Hz was significantly lower ($p<0.01$) than that in the controls (26.2+/-17.7). In the NBD determined to be underactive (n=11, including post pelvic surgery, post infra-sacral level SCI and diabetes patients), the higher CPT values of bladder mucosal sensory functions were found at 5Hz ($p<0.05$), 250Hz ($p=0.07$), and 2000Hz ($p<0.05$) compared to the controls.As described in the section diagnosis of neurogenic urinary incontinence, no fibre specificity has so far been found depending on frequency of current used or current type.

4. Detrusor (external) sphincter dyssynergy, D (E)SD

Schurch et al (2005) [17] assessed types of DSD (according to the Blaivas classification during urodynamic examinations) in 105 chronic SCI males and evaluated the change in the DSD pattern over time. Results showed that those with an incomplete sensory and motor SCL presented with DSD type 1 whereas those with complete sensory and motor SCI lesion had DSD type 2 to type 3. A correlation was also found between the AIS and the DSD type but not between the DSD type and the level of lesion; and at medium to long-term follow-up, a significant change was found in the DSD type [17]. Generally, presence of DSD was determined by increased wire needle EMG activity and/or by dilated bladder neck and proximal urethra during detrusor contraction, in the absence of valsalva or attempt to inhibit voiding.

De et al (2005) [18] did a comparative study to explore the diagnostic congruence for DSD between needle EMG and voiding cystourethrogram (VCUG) in the neurogenic population. They found 60% agreement and 40% disagreement between EMG and VCUG for diagnosis of DSD. Binomial testing demonstrated significant disagreement ($P < 0.000$) in observed proportions [18]. By retrospectively analyzing clinical data consisting bladder and EAS EMG from 41 SCI individuals with NDO, Wenzel et al (2006) [19] found that the onset of bladder contractions was detected within 1 sec of the start of the EAS contraction for both synergic and dyssynergic human subjects; and they concluded that this detection could be used as a control signal to deliver inhibitory ES to arrest nascent bladder contractions and maintain continence [19].

5. Complications related to urethral indwelling catheterization (IDC)

During 2004-2006, at least three papers reporting urinary complications related to prolonged urethral IDC such as follows: the catheter balloon of a Foley catheter inserted only half-way was inflated in the urethra distal to the stricture and a long-term IDC caused urethral erosion and a severe degree of hypospadias (Vaidyanathan et al, 2004) [20]; contracted bladder followed by autonomic dysreflexia (AD), gross hematuria and extravasation of contrast media due to improper technique of voiding cystourethrography (Kovindha et al, 2005) [21]; and continuously incontinent despite a catheter and low bladder compliance leading to a urinary diversion to achieve continence (Stoffel and McGuire, 2006) [22]. In chronic SCI, IDC was associated with higher mean levels of C-reactive protein (CRP) while intermittent catheterization was associated with lower levels of CRP when compared with other methods of bladder management (Frost et al, 2005) [23].

6. Vesicoureteral Reflux (VUR)

VUR seems common among SCI patients with upper motor neuron (UMN) neurogenic bladder. According to the study of Linsenmeyer et al (2004) [24], there was an association of posterior position of ureteral orifices and reflux ($p = 0.004$) but no differences were found with regard to bladder capacity, bladder wall compliance, or voiding pressures between the reflux group and nonreflux group.

7. Stone formation

Linsenmeyer and Linsenmeyer (2004) [25] found that the majority of bladder stones were calcium phosphate (46.8%) or struvite (26.7%). According to the retrospective study in 32 patients with NBD, Matlaga et al (2006) [26] found renal stones were infectious in etiology in 37.5% (12 struvite/carbonate apatite) and metabolic in 62.5%. All with struvite calculi were infected with urea-splitting bacteria.

Stone formation is usually related to IDC. In 2006, there were five papers reporting on such. Ke et al [27] found bladder calculi with a nidus of hair that could have been introduced into the bladder accidentally during the cystostomy catheter replacement. According to the retrospective study of Ku et al [28], over the 17 years 28% and 15% of 140 men were diagnosed with bladder and renal stones for a total of 59 and 25 episodes, respectively; bladder stone was more common in patients injured when aged > or = 24 years than in those injured when aged <24 years (OR 2.5; 95% CI 1.1-5.7; $P = 0.03$); patients with complete injury had a greater risk of renal stone formation than those with incomplete injury (OR 4.1, 95% CI 1.3-12.9; $P = 0.016$); renal stone was more common for patients with urethral catheterization than for those voiding spontaneously (OR 5.7, 95% CI 1.3-

24.6, P = 0.021) and for patients with bladder stone than for those without (OR 4.7, 1.5-15.1; P = 0.01). According to the review by Ost and Lee [29], recurrent UTI, IDC, VUR, and immobilization hypercalcuria were major risk factors for the development of urolithiasis.

According to the retrospective study of Ozawa et al (2005) [30], the incidence of bladder stone in urethral IDC was 1.11 times/100 months, cystostomy was 1.05, contemporary urethral IDC at night time only was 0.96, CIC-wet was 0.61, and CIC-dry was 0.21; and the urethral IDC group had significantly higher incidence of bladder stone than CIC-dry ($p<0.05$).

Linsenmeyer and Linsenmeyer (2006) [31] did a prospective cohort study by examination of IDC for encrustation at the time of removal for cystoscopy and found that 35% of 49 SCI individuals had bladder stones. Catheter encrustation was noted in 13 patients and 11 of them also had bladder stones i.e., a positive result for catheter encrustation had a positive result for bladder stones 85% of the time. Thirty-six individuals had no catheter encrustation; of these, 16% were found to have bladder stones.

8. Bacteriuria

According to the retrospective study, Jayawardena and Midha (2004) [32] suggested that healthy asymptomatic SCI patients who came for annual evaluations should not have routine urine cultures if they are at low risk for UTIs; that is, <6 WBC/HPF in the urine and/or nitrite negative [32]. Svensson et al (2004) [33] studied the occurrence of bacteriuria in SCI patients with NBD who used CIC. Of 344 cultured samples, there were 285 isolates: coagulase-negative Staphylococci (27%), Enterococci (25%), Klebsiella spp (19%), and Escherichia coli (12%); and bacteria grew at concentrations of 10^5-10^8 cfu/L, but only a few at 10(4) cfu/L. Levendoglu et al (2004) [34] prospectively studied in 27 SCI patients who applied CIC during the initial rehabilitation and 40 controls. E. coli was predominantly isolated from the urine and the urethral cultures of both female and male patients; there was concordance between urethra and urine cultures concerning the growth of E. coli (P=0.82); and Pseudomonas was colonized more in male patients [34]. Waites et al (2004) [35] found that among 77.1% of men with bacteriuria, uropathogens were shown in the perineum in 57.4% and in the urethra in 85.2%; differences in the occurrence of uropathogens in men with and without bacteriuria were statistically significant, and organisms were present in higher numbers in men with bacteriuria.

9. Epididymo-orchitis and other complications

Over the 17-year follow-up study of Ku et al (2006) [36], of 140 male patients (24.3% complete, the average age at onset of 24.8 years old, the average time since SCI of 16.9 years), 27.9% were diagnosed with epididymo-orchitis; and in multivariate analysis, patients on CIC had a 7.0-fold higher risk (OR, 6.96; 95%CI, 1.26-38.53; P=0.026); however, a history of urethral stricture lost statistical significance (P=0.074). Nambiar et al (2005) [37] reported a C4 tetraplegia man presenting with a necrotic ulceration on the ventral aspect of the penis and scrotum of 2 days duration and diagnosed with fulminant Fournier gangrene. Vaidyanathan et al (2004) [38] reported cases of a perirenal haematoma due to warfarin and a tumor like of necrotic slough and debris in the bladder.

10. Quality of life (QoL)

Oh et al (2005) [39] conducted a prospective trial involving 132 SCI patients and 150 controls matched to age and sex to determine the psychological and social status of patients using CIC. According to health-related quality of life (HRQOL), the Medical Outcomes Study 36-Item Short-Form General Health Survey (SF-36) scores did not reveal any significant differences between the men and women in the patient group. When patients and controls were divided into two groups according to sex and age, the SF-36 scores of the patients were significantly lower than the controls across both sex and all age groups, other than the energy and vitality scale, the differences for which were not statistically significant in women and those younger than 50 years. Later Oh et al (2006) [40] used the Beck Depression Inventory (BDI) with SCI patients on CIC and control group and found that, the average total BDI scores were 20.3+/-1.0 in the patient group and 11.4+/-0.5 in the control group, respectively ($P<0.001$); 69.6% of 102 the patients reported severe depression; female patients had a 3.8-fold higher risk (OR 13.83; 95%CI 1.42-10.31; P=0.008) of depression than male patients; and those who were unable to perform catheterization independently had a 4.6-fold higher risk (OR 4.62; 95% CI 1.67-12.81, P=0.003) of depression than those who were able to perform self-catheterization.

c) Disease specific treatments

1. Urological follow-up practice

According to retrospective reviews [4,41], there was evolution of bladder management by time, outcomes and complications in both pediatric onset and adult onset SCI; and treatment was not modified during the entire follow-up in very few patients. Regular urodynamic follow-up is warranted for protection of the upper urinary tract (UUT) and maintenance of continence, however, urological follow-up practice varied: in Bochum, Germany, follow-up included urodynamic evaluation, sonography of the UUT and LUT, urine examination, and evaluation of renal function and treatment modifications were based on the urodynamic findings (Nosseir et al, 2007)[42]; in the Spinal Injuries Units of U.K., all units performed routine upper tract screening, ranging from annually to every 3 years (Bycroft et al, 2004)[43].

According to the retrospective chart review of Sepahpanah (2006)[44], the 24-hour creatinine clearance (CCr) was highly variable from one evaluation to the next and the within-subject standard deviation (SD) for CCr was 25.9mL/min; for all comparisons of repeatability, variability, and reliability, serum creatinine was superior to CCr; and renal ultrasound results and post-void residuals were the major factors in changing medical management with regard to renal function preservation. To determine the accuracy of bladder stone detection by abdominal x-rays of individuals with SCI, 13/62 (20.97%) of stones found during cystoscopy were detected by the x-ray; the detection by x-ray was 33% for stones 1.0 cm to 1.49 cm, 33% for stones 1.5 cm to 1.9 cm, and 54% for stones > or = 2.0 cm; and 57% for volumes > or = 1.0 cm^3 [25]. In addition, long-term SCI individual with aged 50 to 60 or more should be screened for prostate and bladder cancer [45,46]; however, PSA cannot be used in patients with IDC and diagnosis should be based on prostatic biopsies [45].

2. Intermittent catheterization (IC)

IC is recommended as the safest method of bladder emptying for SCI persons with NBD [47], especially for those who have sufficient hand skills or a willing caregiver to perform the catheterization [48]. Mizuno et al (2004) [49] reported a paraplegic woman using CSIC for 27 years who had no complications and absence of UI due to underactive and normal capacity bladder. However SCI men on CIC, according to the retrospective comparative study of patients on CIC had a 7.0-fold higher risk of epididymo-orchitis [28].

• Techniques

Previouly, recommended bladder training with CIC was time-dependent, however, some experienced bladder over-distention, especially in those with polyuria that made an IC programme unmanageable [50]. Polliack et al (2005) [51] compared volume-dependent IC (VDIC) following bladder volume measurement by a portable ultrasound device in SCL patients with time-dependent IC (TDIC). After 12-30 days follow-up, the number of IC per patient per day, the time required to perform volume measurements and IC, and their total cost, were approximately 44, 49, and 46% lower in the VDIC group than in the TDIC group. UTI was found in three patients in the TDIC group and in none in the VDIC group.

• Type of catheter

In developed countries, there is a variety of urethral catheters available for SCI individuals.

However, by reviewing all controlled trials comparing methods of using catheters in people with NB, Jamison et al (2004) [52] could not draw any conclusions regarding the use of different types of catheter in managing the NB.

According to the multi-centre RCT of De Ridder et al (2005) [53], 57 SCI male patients completed the 12-month study; 64% of those using the SpeediCath hydrophilic-coated catheter experienced 1 or more UTIs compared to 82% of those using the uncoated polyvinyl chloride (PVC) catheter ($p = 0.02$); and twice as many patients in the SpeediCath group were free of UTI. According to another multi-centre study of Bjerklund Johansen et al (2007) [54], of 378 SCL (the mean duration of IC was 4.6 yr) who completed a 12-d trial of the novel hydrophilic catheter: LoFric Primo, 55.2% of the patients were happy to continue with the novel device, which was 74% of patients using standard PVC catheters and 36% of those using prelubricated PVC ($p=0.04$).

In a developing country, such as Thailand, Japanese reusable silicone catheters were reused and median duration of usage for each catheter was 2 years. Electron microscopic findings of the reused catheters for 2 years revealed encrustation but no obstruction in the lumens and 20% increase in stiffness. Demographic data, urinary management and complications did not have significant relation to the abnormality of the urethrogram or UTI [21].

3. Indwelling catheterization

As mentioned-above, the long-term IDC caused significant complications in SCI patients and some applying CIC experienced incontinence in between catheterization. Therefore, Ozawa et al (2005) [30] applied a contemporary (reusable) balloon catheter at night time only. After a mean follow up of 41 months, the incidence of febrile episode was as follows: CIC-wet 3.36 times/100 months, IDC 2.96, cystostomy 1.26, the contemporary catheter 0.57, and CIC-dry 0.42. The incidence of febrile episode in CIC-wet and IDC were significantly higher than in CIC-dry ($p<0.05$). The incidence of bladder stone was as follows: IDC 1.11 times/100 months, cystostomy 1.05, the contemporary catheter 0.96, CIC-wet 0.61, and CIC-dry 0.21.

4. Bladder relaxants

Many SCI individuals with NDO experienced high detrusor pressure with incontinence and post-voiding residual, bladder relaxants – antimuscarinic drugs, usually are prescribed for those applying CIC as well as IDC. Tolterodine, 2 mg twice daily [55], controlled release oxybutynin (OXY-XL) [56], doubled dosage of tolterodine ER or Trospium [57] and self-selected dosages (SSD) of tolterodine and oxybutynin [55] showed reduction in degree of UI and increase in IC volumes, and cystometric capacity; but the side effect of dry mouth was differed significantly when comparing tolterodine SSD with oxybutynin SSD ($P < 0.05$) [55].

5. Intravesical vanilloids instillation

According to a review article [58], currently available

intravesical treatment options either act on the afferent arc of the reflex such as local anaesthetics or vanilloids or on the efferent cholinergic transmission to the detrusor muscle such as intravesical oxybutynin or botulinum toxin. Later there were many clinical trials and case series done in SCI with NDO proved the efficacy of intravesical instillations of various concentrations of resiniferatoxin (RTX) by cystometric/urodynamic parameters and degree of UI [59-64]; intravesical capsaicin (CAP) also improved in symptoms and urodynamic parameters [57,61], without a significant difference between the CAP and the RTX groups [61]. When compared RTX with injection of 300 units botulinum A-toxin diluted in 30 ml normal saline, both treatments provided significant reduction in mean catheterization and episodes of incontinence, and a significant increase in mean first involuntary detrusor contraction and in mean maximum bladder capacity at 6, 12 and 24 months after therapy; while botulinum-A toxin significantly reduced also the maximum pressure of uninhibited detrusor contractions more than RTX at all follow-up time points [59].

6. Treatment of DSD

In those using reflex voiding to empty bladder, it is recommended to use non-surgical methods – alpha-blocker and botulinum toxin injection into urethral sphincter [48]. According to the study of Reitz et al (2004) [65], 12 male SCI patients with NDO and DSD received 10 mg of isosorbide dinitrate sublingually and found that nitric oxide significantly reduced external urethral sphincter pressures at rest ($p < 0.05$) and during dyssynergic contraction ($p < 0.05$); and the mean post triggering residual volume was significantly reduced ($p < 0.05$).

7. Prevention of UTI

According to 2 double-blinded, placebo-controlled RCTs [66,67], to determine the effectiveness of cranberry supplement (400-mg cranberry 3 times a day for 4 weeks [66] and 2 g per day for 6 months [67]), at preventing UTIs in SCI individuals with NBD, bacterial count, white blood cell (WBC) count, bacterial counts in urine, urinary pH or episodes of symptomatic UTI did not differ between the placebo and cranberry groups. According to another RCT to determine the effectiveness of methenamine hippurate (MH) (1 g twice-daily) and of cranberry (800 mg twice-daily), MH as well as cranberry did not have a significantly longer UTI-free period compared to placebo Lee et al (2007) [68]. In addition, when taking

phosphorus supplementation, there was no significant change in urine pH during the 2-week period compared to when the patient was off supplementation Schlager et al (2005) [69].

• Antibiotic prophylaxis

Some advocated antibiotic prophylaxis for recurrent UTI [43]. To determine the safety and efficacy of a weekly oral cyclic antibiotic (WOCA) regimen consisting of the alternate administration of an antibiotic once per week over a period of at least 2 years to prevent UTI in SCI adult patients, symptomatic UTI dropped from 9.4 to 1.8 per patient-year; and no severe adverse events and no new cases of colonization with multiple drug resistant bacteria were reported (Salomon et al, 2006) [70].

• Bladder irrigation

Waites et al (2006) [71] conducted a randomized, double-blind comparison of twice daily bladder irrigation using 1 of 3 different solutions for 8 weeks with 30 mL of (a) sterile saline, (b) acetic acid, or (c) neomycin-polymyxin solution in community-residing persons with NBD who used IDC. Results showed that the 3 irrigants had no detectable effect on the degree of bacteriuria or pyuria; no significant development of resistance to oral antimicrobials beyond what was observed at baseline; but all groups had a significant increase in urinary pH.

8. Treatment of UTI

Bycroft et al (2004)[43] found few routinely treating asymptomatic UTI in SCI individuals using catheters; and the range of recommended duration of treatment for symptomatic UTI was 3-14 days (mean 6.3).

9. Electrical stimulation

Lavano et al (2004) [72] reported improvement in bladder emptying and continence in 6 neuropathic patients treated with sacral nerve stimulation (SNS) and results were unchanged during the follow-up (maximum 26 months) in all except 1 patient. Kutzenberger et al (2005) [73] reported a 17-years experience with sacral deafferentation (SDAF) and implantation of sacral anterior root stimulator (SARS). Of 464 paraplegics receiving a SDAF-SARS, complete deafferentation was successful in 94.1% and continence was achieved in 83%. With a mean follow-up of 6.6 years, 420 out of 440 paraplegics used the SARS for voiding (frequency 4.7 per day) and 401 used it for defecation (frequency 4.9 per week); UTI declined from 6.3 per year preoperatively to 1.2 per year postoperatively and kidney function presented stable. Hansen et al (2005) [74] applied automatic event driven ES of the dorsal penile/clitoral nerve triggered by Pdet exceed 10 cmH2O and reported during stimulated filling Pdet never exceeded 55 cm H2O and an average bladder capacity increase of 53% was achieved in suprasacral SCI patients.

d) Guidelines for further research:

Most of the papers relating to epidemiology and pathology of urinary incontinence in spinal cord lesion patients were case series; and few papers were clinical trials or RCTs relating to pharmacological treatments. As UTI is a common complication among SCI individuals, further RCT to prove whether a weekly oral cyclic antibiotic for UTI prophylaxis as well as optimal

dosage, effectiveness and safety of bladder relaxants including drugs for blocking nerves innervating bladder is beneficial in SCI with NBD should be done. Regarding types of catheter, RCT should be conducted to prove whether to reuse catheters is safe. In addition, to make an automatic, event driven electrical stimulation for the treatment of NDO suitable in a clinical setting further investigations are needed.

CONCLUSIONS

- **Bladder contraction in neuropathic patients can be mediated by M2 muscarinic receptor subtype density. (LOE 3)**
- **The strongest bladder contraction was usually caused by stimulation on S3 ventral root.**
- **Skin sympathetic responses and motor evoked potentials seem to be a tolerated diagnostic tool to assess autonomic and somotomotor pathways of the lower urinary tract. (LOE 3)**
- **Over time changing of bladder-emptying method is common and usually depends on renal function. (LOE 3)**
- **Long-term urethral indwelling catheterization leads to bladder and urethral complications including continuously incontinent. (LOE 3)**
- **Encrustation of a catheter is predictive of bladder stones whereas abdominal x-ray is not adequate to detect bladder stones. (LOE 3)**
- **Hydrophilic-coated catheters seem beneficial regarding UTI. (LOE 3)**
- **A reusable silicone catheter may be a suitable and safe choice in developing countries if it is properly cleaned and applied to reduce infection. (LOE 3)**
- **Volume-dependent intermittent catheterization has economic and probably also clinical advantages over time-dependent intermittent catheterization. (LOE 3)**
- **Combined clean intermittent catheterization during the day time with indwelling contemporary balloon catheter used only at night time showed less urinary infection than clean intermittent catheterization with incontinence and permanent urethral indwelling catheterization. (LOE 3)**
- **Clean intermittent catheterization was a risk factor for epididymo-orchitis. (LOE 3)**
- **Increased dosage of Tolterodine or Trospium gave a better effect to control neurogenic detrusor overactivity with incontinence. (LOE 2)**
- **Oral administration of nitric oxide may reduce bladder outlet obstruction due to DSD as shown in one study. (LOE 3)**
- **Serum creatinine is reliable and superior to creatinine clearance. (LOE 3)**
- **Posterior position of ureteral orifices seems associated with vesicoureteral reflux. (LOE 3)**
- **Urethral flora was a significant source for the development of urinary infection. (LOE 3)**
- **Low bacterial concentrations in the urine (10^5cfu/L) of patients who were on intermittent catheterization might be due to contamination. (LOE 3)**
- **Cranberry extract, methenamine hippurate or phosporus supplements were not found to be effective in acidifying urine or preventing urinary tract infection. (LOE 2)**
- **Botulinum-A toxin injection seemed to provide better clinical and urodynamic benefits than intravesical resiniferatoxin. (LOE 2)**
- **A weekly oral cyclic antibiotic seemed efficacious in preventing UTI. (LOE 3)**
- **bacteriuria in persons with neurogenic bladder and using indwelling catheterization. (LOE 2)**

RECOMMENDATIONS

- **Regular/annual urological monitoring to early detect complications and to adjust bladder management in patients with neurogenic bladder dysfunction. (A/B)**
- **Recommend urine culture only there is high risk of urinary tract infection. (C)**
- **Routinely observe catheter encrustation to early detect bladder stone. (C)**
- **Cystoscopy is necessary if bladder stones are suspected. (C)**
- **Change urinary treatment according to urological results and complications. (B)**
- **Combine EMG and VCUG to identify DSD. (C)**
- **Correct instructions about catheterization to prevent complications. (B)**
- **Increase bladder relaxant dosage to control neurogenic detrusor overactivity and incontinence; if side-effect cannot be tolerated, try botulinum toxin injection into the bladder. (B)**

2. FAECAL INCONTINENCE

a) Epidemiology and prevalence

According to Dvorak et al, 2006)[1], in patients with central cord syndrome, bowel and bladder continence was reported by 81% in those with American Spinal Injury Association (ASIA) motor score improvement from a mean of 58.7 at injury to a mean of 92.3 at follow-up. However, neurogenic bowel dysfunction (NBoD) is common among spinal cord injury (SCI) patients. From 2004 to 2007, there were 6 studies reporting epidemiology of NBoD in chronic spinal cord injured (SCI), from various countries [2-6] (more details see section D1 in this chapter). Apart from SCI [2-6], there were other spinal cord lesions (SCL) that causes NBoD such tumors (e.g. a conus medullaris ependymoma and filum terminale lipoma [7]; a clear cell meningioma along the thoracic and lumbar levels [8], neuroblastoma [9]); venous congestive myelopathy, mostly at thoracolumbar and/or conus medullaris levels [10]; transverse myelitis [11]; and iatrogenic [12,13]. Tanaka et al (2006) [11] 77% of 22 transverse myelitis (average age at onset 8.8 years, mean follow-up 7.1 years) had NBoD (**Table 22**).

b) Pathology and disease specific lower gastrointestinal (LGIT) problems

According to electromyography (EMG) of external anal sphincter (EAS), 18 and 22 of 64 patients with cauda equina or conus meduallaris lesions had bilateral and unilateral EMG abnormalities [14]. In addition, it was found that those with no such reflexes had significantly more severe FI than those with spinal sacral reflexes ($p < 0.005$) [5] (see more details in section D2 – III Clinical assessment); FI was found to associate with higher severity of injury[4] whereas constipation was associated with a higher level of injury (cervical OR= 5.6 vs. lumbar) [3] which was due to incapacity to increase the intra-abdominal pressure, and the absence of anal relaxation during the defecation maneuver [5].

According to the anorectal manometry, the maximum anal resting pressure of a 26-lumbosacral SCI patients group with mixed symptoms of constipation and/or FI was slightly lower than that of a 13-normal volunteers control group (Li and Xiao, 2006)[15]. During defecation , 88.5% of the patients but 7.7% of the control group significantly showed pelvic floor dysfunction (PFD). Rectoanal inhibitory reflex (RAIR)

Table 22. Shows prevalence of neurogenic bowel dysfunctions reported in spinal cord injury patients

Study (year)	Countries	Subjects	Prevalence		
			Faecal incontinence	Constipation	Others
Liem et al (2004) [2]	Canada	352 SCI (> 20 years)	41.8% (including diarrhea)	47.9%	
Ng et al (2005)[3]	Australia	110 SCI (duration from injury, median 17 years)	41%	46% (including laxative use)	Abdominal pain 33% Abdominal bloating 22%;
Tongprasert & Kovindha (2006) [4]	Thailand	100 SCI (duration from onset, mean 6 years)	35% (normal subjects: 1.8%, p = 0.0013)	86% (including uses of laxative, enema, etc)	Haemorrhoid 16% (normal subjects, 20%, p =0.338)
Vallès et al (2006)[5]	Spain	54 motor complete SCI (mean duration from onset 6 years)	85%	67%	
Vallès et al (2006)[6]	Spain	109 patients 83% had spinal sacral reflexes (SSR)	31%	27% more in tetra A,B,C	
Pagliacci et al (2007)[6]	Italy	403 SCI (duration from discharge to follow-up, mean 3 years)	2.7% (20.1% partial)		

was identified in both groups. The rectal volume for sustained relaxation of the anal sphincter tone in lumbosacral SCI patients group was significantly higher than the control group. The mean rectal volume to generate the first sensation was significantly higher in SCI patients than in the control group. Regarding constipation, its association with level of injury was supported by many studies [3-5] i.e., upper motor neuron vs lower motor neuron NBoD ($p = 0.0013$)[4]; cervical injury had more than 5 times more frequent constipation than lumbar injury (OR =5.6, $p = 0.02$)[3]; lesion above T7 had more constipation than lesion below T7 ($p < 0.05$)[5]; it was also associated with severity of injury [4] and taking bladder relaxants [4]. In addition, decreased colonic pressure activity was found during sleep in SCI individuals and may contribute to delayed colon transit time after SCI [16].

Furlan and Fehlings (2006) [17] examined the characteristics of the top 100 most frequently cited articles (so-called "citation classics") on traumatic SCI that were published between 1986 and 2003, and compared this selected professional literature with the consumers' perspective on the key issues in SCI research. From a SCI consumers' perspective, the areas of greatest interest included motor function, bowel and bladder control, sexual function, and pain. Motor function was the leading topic in the matching list between professional literature and consumers' perspective. According to Anderson's quality of life (QOL) survey of the SCI population (2004)[18], regaining arm and hand function was most important to quadriplegics, whereas regaining sexual function was the highest priority for paraplegics; and improving bladder and bowel function was of shared importance to both injury groups. Later, according to a web-based survey of 286 SCI population aged 18 years or older completed the survey, results showed that bladder and bowel concerns during sexual activity were not strong enough to deter the majority of the population from engaging in sexual activity (Anderson et al, 2007a)[19]; however, bladder and/or bowel incontinence during sexual activity was a highly significant concern in women with SCI; in addition, the occurrence of autonomic dysreflexia (AD) during typical bladder or bowel care was a significant variable predicting the occurrence and distress of AD during sexual activity. (Anderson et al, 2007b)[20].

Regarding chronic SCI individuals, FI had 10 times more impact on QOL than those with no FI and NBoD had significant impact on their QOL [21]. They had significantly lower Gastrointestinal QOL score as compared with the normal persons [22]. About one-third needed more help with activities of daily living (ADLs) [2]. There were no statistically significant differences in satisfaction or QOL between those with colostomies and those with traditional bowel care programs; however, 55.7% of those with colostomies and 41.7% of those without colostomies were very unsatisfied with their bowel care program [23].

c) Conservative bowel management

According to the "Neurogenic Bowel Management in Adults with Spinal Cord Injury" Clinical Practice Guideline published by the Consortium for Spinal Cord Medicine [24], rectal stimulations help assist elimination of the stool: mechanical stimulations – digital rectal stimulation (DRS) and manual evacuation; and chemical stimulations – suppository and mini-enema (liquid suppository). Korsten et al (2007)[25] used a manometric catheter to assess colonic motility at baseline, during DRS, and after DRS and evacuation of barium oatmeal paste in six subjects with SCI; and results showed that manometric changes in response to DRS were accompanied by expulsion of barium oatmeal paste in every subject by the fifth DRS. In patients with cervical SCI, a significant increase in systolic blood pressure (BP) was induced by insertion of rectal medications and persisted during additional DRS, and the manual removal of stool induced AD were reported; however, systolic BP recovered to pre-program values within 5 min after defecation[26].

Recently, Uchikawa et al. (2007) [27] reported a successful bowel movement in 75% of 20 SCI patients by using a modified washing toilet seat equipped with a camera monitor and an electronic bidet to facilitate precise hitting of the anal area with water streams to stimulate bowel movement for a maximum of 30 minutes. Regarding transanal irrigation, it showed improvement in constipation, FI and symptom-related QOL in SCI individuals [28].

According to the CPG, push up, abdominal massage and a forward-leaning position may aid evacuation by increasing abdominal pressure [24]. Aya? et al., 2006 [29] studied in patients with SCI and showed that abdominal message gave positive effects – increase in frequency of defecation per week, decrease in total colonic transit time and lesser FI. As contraction of the abdominal wall musculature plays a role in normal defecation, Korsten et al (2004) [16] assessed whether an abdominal belt with implanted electrodes would improve difficulty with evacuation in SCI individuals and demonstrated that neuromuscular stimulation of the abdominal wall improved defecation function, including time to first stool and total bowel care time.

Regarding medications to enhance bowel movement, Cisapride, oral does not seem to have clinically useful effects in people with SCI (Coggrave et al., 2006) [30]. Korsten et al (2005) [31] did a randomized, blinded design, to test the efficacy of neostigmine in SCI persons with defecation difficulty by infusing one of three intravenous infusates (normal saline, 2 mg neostigmine, or 2 mg neostigmine + 0.4 mg glycopyrrolate – to prevent neostigmine's muscarinic effects) on separate days and determining on bowel evacuation of the barium paste, heart rate and airway resistance; and results indicated that both neostigmine and neostigmine + glycopyrrolate resulted in prompt bowel evacuation. Studies have shown that neo-

stigmine + glycopyrrolate intravenous admini-stration is safe and well tolerated in persons with chronic SCI [31,32] and studies have been under way to assess the efficacy of neostigmine by other routes [32].

d) Guidelines for further research

Most of the studies reported were case series and used different definitions of faecal incontinence and constipation. Therefore further researches should base on internationally acceptable definitions so that they can be compared. In addition, RCTs on rectal or anal stimulations both mechanical and chemical as well as medications promoting bowel movement are needed.

CONCLUSIONS

- **Constipation is more common than faecal incontinence among established SCI persons. (LOE 3)**
- **Constipation is more common in those with preserved sacral reflexes whereas faecal incontinence is more common in those without sacral reflexes. (LOE 3)**
- **Faecal incontinence has impact on QOL of SCI individual and is highly concerned by SCI women during sexual activity. (LOE 3)**
- **Digital rectal stimulations aid bowel evacuation in individuals with SCI in part by increasing left-side colonic motility. (LOE 3)**
- **Transanal irrigation with water improves constipation and quality of life in individuals with SCI. (LOE 2)**
- **Abdominal massage seems effective in enhancing bowel movement and defecation. (LOE 3)**
- **Anal stimulation by water stream seems effective in stimulating bowel movement and shortening bowel care time. (LOE)**

RECOMMENDATIONS

- **Encourage adherence to the clinical practice guidelines on neurogenic bowel management in adults with spinal cord injury. (A)**
- **Apply mechanical stimulation e.g. digital rectal stimulation to aid bowel evacuation especially in those with preserved sacral reflexes. (B)**
- **Use chemical stimulations when mechanical stimulations fail. (C)**
- **Beware of autonomic dysreflexia during bowel care especially in those with high lesion. (C)**
- **Consider transanal irrigation with water for those with severe chronic constipation and faecal impaction. (B)**

VII. SPINAL CANAL STENOSIS

1. EPIDEMIOLOGY AND PREVALENCE

According to our previous extensive review of spinal canal stenosis (SCS) and incontinence published in the 3rd ICI (2005)[1], about half of the patients with intractable leg pain also had bladder symptoms – urinary difficulty with high post-void residual (PVR) and reduced flow rate and/or incontinence indicating cauda equine syndrome. Such symptoms including urinary incontinence (UI) may usually improve after surgical decompression.

Schkrohowsky et al (2007) [2], one third of patients with achondroplasia developed SCS, especially at lumbar level, requiring surgical intervention; and 77% had UI. According to Johnsson and Sass (2004) [3], in the County of South Jutland, Denmark during a 5-year period (1996-2000), the annual incidence of SCS was 272 per million inhabitants; and of 340 cases diagnosed with SCS during that period, only one patient presented with acute cauda equina syndrome: a 74-year-old woman with SCS from L2 to L4 appeared with urinary retention and fecal incontinence (FI) for the previous 24 hours; after an urgent operation and she recovered within 5 days from her anal sphincter paresis and within 5 weeks from her bladder paresis.

2. PATHOLOGY AND DISEASE SPECIFIC PROBLEMS

Goh et al (2004) [4] carried out a comprehensive retrospective review of the clinical features, radiological changes and outcome of 75 patients with radiologically diagnosed lumbar SCS; imaging of the lumbar spine showed that moderate to severe central spinal stenosis correlated with complaints of weakness and abnormal motor power on clinical examination; and the commonest symptom was numbness or tingling of the legs. According to the study of Inui et al (2004)[5], 58.8% of the 34 patients were diagnosed with positive neuropathic bladder; however there was no difference in the cross-sectional area of dural sac between those with and without neurogenic bladder dysfunctions (NBD) in patients with lumbar SCS; but the antero-posterior diameter of the dural was shorter in those with NBD; and a critical size for the dural sac of patients with NBD was revealed as 8 mm in this study.

Usually signs and symptoms of compressive neuropathy of multiple lumbar and sacral roots, so called ‘cauda equina syndrome’ is an indication for surgical intervention but relatively unknown as a postoperative complication following surgery [6]. Four years after diagnosis, 65% had undergone surgical decompression; a third of patients felt that their symptoms had improved while a quarter felt that they had worsened [4]. Imran and Halim (2005)[7] reported a 63-year-old man who developed acute cauda equina

syndrome due to fat graft compression after decompressive laminectomy, posterior instrumented fusion with pedicle screw fixation for spinal stenosis of L5 and S1 vertebral levels and free fat grafting to cover the exposed dura; three days postoperatively, gradual neurological deficit started with sensory loss and weakness of the affected dermatomes and myotomes, followed by FI on the 12th postoperative day; and immediate removal of the fat graft resulted in recovery from cauda equina syndrome.

Another case was reported by Tubbs et al (2005) [8]; a Caucasian girl who had idiopathic growth hormone deficiency and Klippel-Feil and Duane's syndromes with symptomatic stenosis of the first cervical vertebrae presented with episodes of loss of tone with subsequent falling, facial cyanosis, UI, hand weakness, and difficulties with swallowing; following suboccipital craniectomy and the removal of the posterior arch of the atlas, her symptoms were resolved and UI improved.

3. DISEASE SPECIFIC DIAGNOSIS AND TREATMENTS

To demonstrate narrowing of the lumbar canal with compression of the cauda equina, computer tomography (CT) or magnetic resonance imaging (MRI) is often recommended to reveal either bony or soft tissue compression [9].

Miyata et al (1998) [10] studied the relationship between bladder function and roentgenographic changes in the spinal canals of ossification of posterior longitudinal ligament (OPLL) patients. CO2-filling cystometry, uroflowmetry and PVR were measured and the vertical extent of OPLL and the degree of SCS was estimated by x-ray films and CT. The occurrence of abnormal detrusor activity had no relationship to the degree of canal stenosis, while the occurrence of an areflexic or underactive detrusor correlated with the vertical extent of OPLL [10].

Yamanishi et al (1998) [11] found detrusor overactivity in 14 lumbar canal stenosis patients (29%) and most of them had voiding symptoms and had storage symptoms which seemed to be caused by the irritation of sacral roots. Of 10 patients followed up after surgical decompression, detrusor overactivity disappeared in 5 patients, improved in 1 patient and remained unchanged in 4 patients [11].

Lee et al (1997) [12] did an expansive cervical laminoplasty in patients with nontraumatic cervical spondylosis with myelopathy and found that age greater than 60 years at the time of presentation, duration of symptoms more than 18 months prior to surgery, preoperative bowel or bladder dysfunction, and lower-extremity dysfunction were found to be associated with poorer surgical outcome.

CONCLUSIONS

- **Patients with spinal stenosis, especially at lumbar level, may present with bladder and bowel involvements – urinary retention/ incontinence and faecal incontinence (LOE 3/4)**
- **Lumbar canal stenosis may cause either detrusor underactivity/acontractility or overactivity. (LOE 3)**
- **Imaging helps diagnose spinal stenosis where as urodynamic study help diagnose neurogenic bladder dysfunction. (LOE 3/4)**
- **Acute symptom of incontinence or urinary retention may recover after decompression of spinal stenosis. (LOE 3/4)**

RECOMMENDATIONS

- **Surgical decompression is recommended in patients with spinal stenosis having acute symptoms of urinary retention/incontinence and faecal incontinence. (A)**

VIII. GUILLAIN-BARRE SYNDROME

1. URINARY INCONTINENCE

a) Epidemiology and prevalence

Guillain-Barré syndrome (GBS) is the most common cause of acute, flaccid paralytic disease [1]. The term GBS defines a clinical entity that is characterized by rapidly progressing limb weakness and the loss of tendon reflexes. The disorder affects children and adults of all ages and both sexes. The following stages are observed: progression or acute phase, plateau phase and recovery phase. Despite intensive immunomodulating therapies such as intravenous immunoglobulin or plasma exchange, 4% to 15% of patients with GBS die from this syndrome and nearly 20% have a persistent disability [2]. Therefore, supportive care remains the mainstay of treatment. A recent consensus guideline in supportive care for patients with GBS covers airway problems and tracheostomy, pain, deep vein thrombosis, fatigue, cardiac problems, and bladder and bowel dysfunction [2]. Whereas cardiovascular autonomic dysfunction (mainly reflecting sympathetic adrenergic function) is recognized in up to 60% of GBS patients [3], lower urinary tract (LUT) function has only been studied infrequently in the acute phase of GBS. This is partly because most patients are catheterized as part of their general nursing care to maintain bodily hygiene or to monitor water balance [2].

Sakakibara et al [4] (LOE3/4) studied LUT symptoms in 28 patients with GBS (24 acute inflammatory demyelinating polyradiculoneuropathy, AIDP, 4 acute motor axonal neuropathy, AMAN) during the acute phase. They found that 25% of the patients showed micturitional disturbance. Voiding difficulties were presented by 86%, urinary retention by 43%, nocturnal urinary frequency by 43%, and urge incontinence by 28% of patients suffering from micturition problems. This figure is almost in accordance with the 25% found in the original reports of Guillain and colleagues.[5,6]. Urinary dysfunction in patients with GBS appeared after the occurrence of motor weakness in all cases [4]; whereas in two patients with axonal GBS, it is reported that voiding difficulty and motor weakness appeared almost simultaneously [7,8] (LOE3/4).

Sakakibara et al [4] (LOE3/4) indicated that urinary dysfunction increases with higher Hughes motor grade, although it did not reach statistical significance. Lichtenfeld [9] (LOE3/4) has also reported urinary retention in one-third of patients requiring ventilatory assistance. Even though up to 11% of GBS patients may develop urinary retention at the peak of motor weakness, it will mostly ameliorate along with other neurological signs after supportive patient management, with/without immuno-modulating therapies. In contrast, it is reported that urinary retention failed to recover for 10 months even after one patient (with axonal GBS) regained the ability to walk [8] (LOE3/4).

With regard to subtypes of GBS, it was found that heart rate and plasma noradrenaline concentrations were elevated in AIDP in 7 patients but not in 8 patients with AMAN [3]. This contrasts with the observation of bladder dysfunction in 21% of patients with classic GBS (AIDP) (n=24) but in 50% of those with axonal GBS (AMAN) (n=4)[4]. These findings may reflect the vulnerability of autonomic fiber among these variants, although it is too early to determine urinary function of axonal GBS since the number of such patients was too small.

b) Pathology and disease specific lutproblems

There is a lack of good systemic studies on micturition disorders in GBS during both acute and chronic phases. In a few reports,[10,11,12] detrusor areflexia and disturbed bladder sensation are common, and nonrelaxing urethral sphincter with neurogenic change in the sphincter motor unit potentials is another factor (LOE3/4). Among these, Grimvac et al [12] (LOE3/4) studied uodynamically 4 patients in the acute stage of GBS. All of them had complete urinary retention. They described both detrusor areflexia and detrusor overactivity, as well as detrusor-sphincter dyssynergia. One patient was followed during the chronic stage of the disease showing detrusor overactivity. The most extensive study was performed by Sakakibara et al [4] (LOE3/4) during the acute phase. They performed a urodynamic study on 4 symptomatic patients, and 2 of whom underwent repeated study. Disturbed bladder sensation was noted in one patient, detrusor areflexia in one and absence of the bulbocavernosus reflex in one. In contrast, cystometry also showed decreased bladder volume in 2 and bladder overactivity in 2, one of whom had urgency urinary incontinence and the other urinary retention. GBS primarily affects the large myelinated fibers, but pathology studies have revealed moderate to severe loss of small myelinated fibers and inflammatory cell infiltration in the lumbosacral spinal roots, sympathetic chain, and spinal cord [1,13]. Therefore, one mechanism is postulated for the urinary dysfunction in GBS: peripheral nerve damage and irritation in the sacral autonomic fibers, from either bystander inflammation or immune attack of the autonomic fibers [1,13]. Contrast enhancement in magnetic resonance imaging (MRI) of the cauda equina in GBS has also been reported [14].

Previously Wheeler and colleagues [11] (LOE3/4) found detrusor overactivity in 3 of 7 patients with GBS. However, they used carbon dioxide as a cystometry medium, which is not now recommended since it is an irritant to bladder mucosa. In addition, 2 of his patients with detrusor overactivity had extensor plantar responses, which raise questions regarding the diagnosis of GBS. However, water cystometry findings in the following studies showed detrusor overactivity with clinico-neurophysiologically definite GBS [4]. Whereas GBS patients do not have extensor plantar responses, some axonal GBS patients exhibited increased tendon reflexes [15]. Therefore, another mechanism is postulated for the urinary dysfunction in GBS: immune attack of the inhibitory spinal cord interneurons [15].

c) Disease specific diagnosis and treatment

Urinary dysfunction occurs in up to 25% of GBS patients including urinary retention in 11%, particularly in those with higher Hughes motor grade or those under mechanical ventilation. Therefore, in such patients, we should check post-void residual volume repeatedly by ultrasound echography. We then determine which supportive care is better; including the indwelling urinary catheter. Recovery of LUT function usually occurs along with the recovery of motor weakness in GBS. However, in rare cases it might take months. During the recovery period, not only voiding difficulty but also urinary urgency and frequency could occur. At this stage, urodynamic study is easily performed in order to optimize the therapy for the symptomatic patients. Clean, intermittent catheterization (CIC) is the treatment of choice to prevent over-distention bladder injury.

d) Guidelines for further research

There is only one study about the prevalence of LUT problems in GBS, which is however concentrated on the acute phase of the disease. Therefore a long-

term follow-up of these patients is needed. We still don't know what are the long-term consequences of this disease for the LUT including urinary incontinence.

CONCLUSIONS

- **In the acute phase of GBS, about 25% of patients demonstrate LUT functional problems (LOE3/4).**
- **Both storage and voiding dysfunctions are observed in GBS (LOE3/4).**
- **Recovery of LUT functions occurs along with the recovery of motor weakness. However, in rare cases it might take months (LOE3/4).**

RECOMMENDATIONS

- **Recovery of the LUT functions is expected in GBS; while supportive case including indwelling catheter and the following CIC is the treatment of choice in order to prevent over-distention bladder injury (C).**
- **During and after the recovery of paralysis a detailed functional evaluation of the LUT in symptomatic patients is needed in order to optimize the therapy (C).**

2. FAECAL INCONTINENCE

a) Epidemiology and prevalence

Among various autonomic dysfunctions, whereas cardiovascular dysfunction occurs in up to 60% of Guillain-Barré syndrome (GBS) patients, [3,16] bowel dysfunction is less common, occuring in up to 15% [17,18]. In Burns' study (LOE3/4) [17] in which adynamic ileus was noted in 17 out of 114 GBS patients, cardiovascular symptoms coincided with ileus in only 5 patients, suggesting a different pathomechanism may underlie in these two autonomic dysfunctions. Indeed, in 4 patients, mechanical ventilation and immobilization could be implicated. In 8 patients, preexisting conditions such as prior abdominal surgery or incremental doses of opioids could also be linked to ileus. However, three case reports by Gazulla Abio et al (LOE3/4) [19], Sawai et al (LOE3/4) [20] and Noew et al (LOE3/4) [21] have also shown that paralytic ileus can be the initial presenting symptom in GBS.

b) Pathology and disease specific lutproblems

There is a lack of good systemic studies on bowel disorders in GBS during both acute and chronic phases. However, there are some reports suggesting an involvement of bowel autonomic fibers in GBS. Sawai et al (LOE3/4) [21] performed a detailed bowel function test in a 47-old man with acute motor axonal neuropathy (AMAN) type of GBS who presented with ileus (also called intestinal pseudo-obstruction) by an abdominal X-ray. Sitzmarks showed prolonged total colonic transit time (86.4 hours; normal 16.0-48.0), suggesting slow transit constipation. As indicated in the bladder part, pathology studies of GBS have revealed moderate to severe loss of small myelinated fibers and inflammatory cell infiltration in the lumbosacral spinal roots, sympathetic chain, and spinal cord. Therefore, involvement of bowel autonomic fibers might also occur in GBS [21], as shown in an autopsy case of autoimmune gastroparesis [18].

c) Disease specific diagnosis and treatment

Adynamic ileus or intestinal pseudo-obstruction occurs in up to 15% of patients during a course of GBS, particularly in those with severe motor dysfunction or those under mechanical ventilation [17]. Supportive care remains the mainstay in the treatment of bowel dysfunction in GBS, including laxatives or enemas [22,23]. Recovery of bowel function usually occurs along with the recovery of motor weakness in GBS, after an intensive immune therapy including intravenous immunoglobulins.

d) Guidelines for further research

There is still a lack of a detailed functional evaluation of the bowel in GBS patients. Such studies are needed in order to optimize the therapy in the future.

CONCLUSIONS

- **About 15% of patients demonstrate bowel functional problems particularly in the acute phase, but they can also be presenting symptoms (LOE3/4).**
- **Constipation and intestinal pseudo-obstruction are observed in GBS (LOE3/4).**
- **Recovery of bowel functions usually occurs along with the recovery of motor weakness.**

RECOMMENDATIONS

- **Recovery of the bowel functions is expected in GBS; while supportive case including laxatives or enemas is the treatment of choice (C).**

IX. LUMBAR DISC PROLAPSE

Medline through Pubmed between 1966-2007

• Data base was searched for keywords:

Disc prolapse (or disc hernia), bladder dysfunction, neurogenic bladder, sphincter dysfunction, bowel dysfunction, fecal incontinence, and constipation

1. PATHOPHYSIOLOGY, EPIDEMIOLOGY AND PREVALENCE

Central lumbar disc prolapse compresses sacral nerve

fibers to and from the bladder, the large bowel, the anal and urethral sphincters, and pelvic floor resulting in so-called cauda equina syndrome. Cauda equina syndrome due to central lumbar disc prolapse has been reported to be relatively rare, the incidence being from 1 to 5% of all prolapsed lumbar disc [1-8]. Clinical features of the cauda equina syndrome include low-back pain, bilateral sciatica, saddle anesthesia, and urinary retention, loss of urethral sensation as well as constipation and erectile dysfunction [4,7,9,10]. Those patients with cauda equina syndrome usually have some sensory disturbance in the sacral dermatomes [4,10]. A Retrospective cohort study with prospective clinical follow-up showed that bowel dysfunction at presentation was associated with sexual problems at follow-up [11].

2. DISEASE SPECIFIC DIAGNOSIS AND LUT DYSFUNCTION PATTERNS

The most common urinary symptom associated with lumbar disc prolapse is acute urinary retention [12,13]. At the onset, acontractile detrusor with impaired bladder sensation is a typical urodynamic finding [4,10,12,13,14]. Severe denervation of pelvic floor [12] and external urethral sphincter [10] is also frequently demonstrated. Detrusor overactivity may occur through the irritation of the sacral nerve root [14,15,16]. Urinary disorders usually follow or accompany more obvious neurologic symptoms, such as lumbar pain and perineal sensory disturbances, that lead a proper diagnosis. However, sometimes voiding disturbances may be the only or the first symptom of this condition, which makes it more difficult to diagnose this disease [4,10]. Nevertheless, urgent MRI assessment is recommended in all patients who present with new onset urinary symptoms concomitantly with lumbar back pain or sciatica because it is impossible in a significant proportion of patients to exclude the diagnosis of prolapsed intervertebral disc in the context of referral with suspected cauda equine [17].

3. DISEASE SPECIFIC THERAPY

Emergency surgical decompression has been reported to be important to increase the chance of satisfactory neurological recovery in patients with cauda equina syndrome due to central lumbar disc prolapse [4,18,19]. In a meta-analysis of surgical outcomes, Ahn et al (2000) [7] reported that a significant improvement in sensory and motor deficits as well as urinary and rectal function occurred in patients who underwent the surgery within 48 hours compared with those who had the surgery more than 48 hours after the onset of the cauda equina syndrome. Although there is still a controversy [11], most of other reports support the concept that decompression performed within 48 hours of onset of this syndrome resulted in improved functional outcomes [3,8,20]. However, acontractile detrusor is usually irreversible even after immediate decompression [10,21,22], although many patients can empty their bladder postoperatively, but only by straining or changing their voiding postures [10,22]. In contrast to bladder dysfunction, urethral function shows a better recovery after surgery [10,13].

X. MENINGOMYELOCOELE

Please refer to the chapter on children. We have looked in the scarce literature on adult patients.

1. URINARY INCONTINENCE

a) Epidemiology and prevalence

Myelomeningocele (spina bifida) is one of the most common birth defects of the spine and brain. It occurs in 1-2 births per 1000, involving all levels of the spinal column (lumbar 26%, lumbosacral 47%, sacral 20%, thoracic 5% and cervical spine 2%). Associated Arnold-Chiari malformation is seen in 85% of children, often requiring ventriculo-peritoneal shunting of cerebrospinal fluid. Ingestion of folic acid prior to conception and during the first trimester of pregnancy has significantly reduced the incidence of this problem and other associated neural tube defects. The neurologic defect produced is quite variable and cannot be totally predicted by the vertebral level of the lesion. Additionally the fibrosis associated with myomeningocele closure, may tether the cord. Subsequent growth of the infant or child will produce further neurologic problems, manifesting as changes in bladder, bowel and lower extremity function.

The incidence of urethrovesical dysfunction in myelomeningocele is not absolutely known, but most studies suggest it is very high (>90%). Similarly, anorectal dysfuction is very common, but its exact incidence has not been reported. Congenital neurologic bladder dysfunction with spina bifida and sacral dysgenesis that manifested itself only at middle age in a 48-year-old male is reported by Kaneoya et al (LOE4)[1]. Yamamura et al reviewed the literature of tethered cord of adult onset and found 56 cases published.(LOE 3) [2].

b) Pathology and disease specific LUT problems

The two major consequences of the vesicourethral dysfunction are urinary incontinence and hydroureteronephrosis which can occur early or later in life .

There are many studies documenting the urodynamic characteristics of the vesicourethral unit in myelomeningocele patients but almost all in children. Almodhen and colleagues examined myelomenigocele patients in postpubertal age and correlated these findings with upper urinary tract changes [3] (LOE 3). Of the 26 patients with urinary incontinence before puberty 12 achieved continence following puberty. Hydronephrosis remained stable in 4 patients, improved in 3 and was new onset in 3, whilst vesi-

coureteral reflux persisted in 1 patient, resolved in 4 and was new onset in 1. Regarding the uro-dynamic findings in patients achieving urinary continence following puberty total cystometric bladder capacity increased significantly and maximum detrusor pressure and detrusor leak point pressure showed insignificant changes. This findigs demonstrate that conservative treatment is a viable option for some myelo-meningocoele patients and that with current treatment modalities, including intermittent catheterization no significant upper tract deterioration occurs after reaching the pospubertal age.

In the past much attention has been directed at the significance of dyssynergia between the external sphincter and the bladder, and the associated deterioration of the upper renal tracts in these patients. With the increasing reliance of clean intermittent catheterization in the management of these patients, more emphasis has been placed on the pressure the bladder is able to generate prior to leaking, as a prognostic factor in predicting upper tract deterioration.

c) Disease specific diagnosis and treatment

Urodynamics is the cornerstone in the diagnosis and management of vesicourethral dysfunction in myelomeningocele. As previously stated, urodynamic findings may predict the patients at risk of upper tract deterioration. Controversy continues as when to initiate these studies, either as soon as possible after back closure, at the first sign of upper tract changes or before considering management of incontinence. Studies supporting each position have been reported, although the preponderence of evidence suggests earlier diagnosis of hostile factors is advisable.Taskinen et al [4] examined 30 patients with anorectal anomalies mainly because of fecal or urinary incontinence. All patients underwent spinal magnetic resonance imaging and urodynamic investigation. Major lumbosacral abnormalities were detected in 57% of patients, including 13, 4 and 3 with a tethered cord, syrin-gomyelia and caudal regression, respectively. Significant dysfunction of the LUT in 57% of the cases involved an overactive detrusor in 11, detrusor-sphincter dyssynergia in 4, distended bladder in 4 and lazy bladder in 1. When the spinal cord was normal, 54% of the patients had abnormal urodynamic findings but when the spinal cord was abnormal, 59% had abnormal urodynamics. When the bony spine was normal, 33% of the patients had an abnormal spinal cord but when the bony spine was abnormal, 69% had an abnormal spinal cord. (LOE3).

As hydronephrosis and vesico-ureteric reflux are a consequence of detrusor dysfunction, synchronous fluoroscopic evaluation of the urinary tract is advisable at the time of urodynamics. Similarly, renal ultrasound has become an invaluable routine serial evaluation in these patients, assessing renal growth, development of scarring and, most importantly, hydroureter-onephrosis. Studies suggest a role for repeat urodynamics and ultrasound in this patient population, however, the timing and frequency of these studies still needs to be elucidated.

Although, renal scans are routinely used, especially in the myelomeningocele patient with hydronephrosis, the exact role of this study in these patients is not clear.

Urologic treatment depends on the age of the patient and the nature of the vesico urethral dysfunction as characterized by urodynamics. In a retrospective study urinary sepsis accounted for the majority of admissions (62%), while 38 of 62 patients required 60 surgical procedures[5]. Targeting the primary urological abnormality (the dysfunctional and usually poorly compliant bladder) allowed implementation of effective treatments, including regular intermittent bladder catherisation (52%) in order to preserve upper renal tract function. Associated postural abnormalities complicated both conservative and interventional therapies.

The mainstay of treatment is clean intermittent catheterization and antimuscarinic medication. As continence is not at issue in the neonate and infant, treatment may be postponed, unless upper tract changes are present. Some evidence exists pointing to the fact that early initiation of treatment may prevent subsequent deleterious bladder changes. Recently botulinum toxin was suggested as a possibility to avoid invasive surgery in these patients [6].

Bruschini et al evaluated 104 patients who were not managed and followed-up adequately during their childhood [7] (LOE 3). Reflux and urinary tract damage were found in 30 patients, 6 patients presented signs of upper tract damage without reflux. The cystometry showed detrusor overactivity in 48% of patients, poor compliance in 49% of patients, increased bladder capacity in 2% and normal cystometry in 1%. Detrusor leak point pressure over 40 cm H(2)O was associated with upper urinary tract damage. Patients with a decrease of functional bladder capacity over 33% had more renal scars than their counterparts. Overall, 26 % of urological untreated myelomeningocele patients have kidney damage.

On the other hand there is a work by Olsson and colleagues, evaluating 175 Swedish myelomenin-gocele patients in adult age [8] (LOE 3). Clean intermittent catheterisation for bladder emptying was used by 85%, and 59% used enemas on a regular basis because of the neurogenic bowel dysfunction. Renal dysfunction was than seen only in 1.7% of the adolescents.

Management of incontinence and/or upper tract deterioration mirrors the treatment of neurologic bladder. Variations in this algorithm include the use of vesicostomy in the younger child who has failed conservative measures and has evidence of deteriorating upper tracts. External sphincterotomy

has no place in the management of these patients and the use of the appendico vesicostomy in continent LUT reconstruction(Mitrofanoff) has become very popular. Most studies on surgical management of the myelomeningocele bladder are descriptive (LOE 4) at best. Data from adult and paediatric surveys show renal damage to be the single most prevalent cause of morbidity and mortality; even in children, 30-40% exhibit evidence of renal damage.

Additional factors such as chronic infection and stone formation will then render the kidney more vulnerable to progressive loss of renal mass and subsequent chronic renal failure. Renal transplantation is now considered the optimal treatment for end-stage renal disease in all age groups. Although more prone to complications, recent data on patients with meningomyelocele or severely abnormal LUTs demonstrate excellent patient and graft outcomes. [9] (LOE 3)

d) Guidelines for further research

Further clarification of the role of fetal surgery to repair the neural tube defect is required. Similarly the role of early intervention, conservative or surgical is required. The timing of surgical intervention needs further study as well as better quality of life assessments and risk/ benefit analyses of LUT reconstructive procedures. The development of a tissue-engineered substitute for cystoplasy is being studied. Finally, the fate of the adult myelomeningocele patient, especially those who have undergone reconstruction needs to be documented.

CONCLUSIONS

- **Myelomenigocele is one of the commonest birth defects (LOE 1)**
- **Incidence decreased by folate ingestion (LOE 2)**
- **Most have bladder dysfunction which can lead to incontinence and / or upper tract deterioration (LOE 3)**
- **Majority will derive significant benefit from conservative measures (LOE 3)**

RECOMMENDATIONS

- **Regular surveillance, from infancy, with urodynamics and renal ultrasound is mandatory. However the exact timing is not definied. One must observe the general rules for neurogenic bladder(B)**
- **Early initiation of conservative measures (clean intermittent catheterization, anti muscarinic medication) generally provides protection of the upper urinary tract (B)**
- **Surgery is reserved for failed conservative treatment (B)**

2. FAECAL INCONTINENCE AND BOWEL PROBLEMS

• Methods

Using MEDLINE we identified English-language journal articles and reviews published from 2000 to April 2008, looking for the keywords myelomeningocele, fecal incontinence, management.

a) Pathophysiology

Voluntary control of defecation requires rectal sensation, peristalsis and adequate anorectal sphincter function. Neurological defects in patients with spinal lesions may affect one or more of these components resulting in different types of defecation disorders: fecal incontinence, chronic constipation or both. Incontinence is one of the major stigmas affecting patients born with myelomeningocele [1].

b) Prevalence

Bowel dysfunction occurs in most children with spinal cord impairment from disease or injury.

c) Management (LOE 3)

Although many different regimens have been used to manage this problem none has had universal success. Behavioural modification and laxatives failed to achieve an acceptable result because of the persistence of soiling. A small dose of laxatives alone accomplished nothing while administering a large dose to an incontinent patient only resulted in profound embarrassment [2]. Bearing in mind that none of these patients can resist the push of peristalsis, the most effective therapy is the emptying of the colon, which takes at least 24–48 h to refill again.

The main goal, to empty the colon as much as possible to achieve continence during the next 24–48 h, can be achieved nowadays by two ways, (A) by a retrograde colonic enema (RCE) using a special ballon catheter or (B) an operative procedure which allows an antegrade continence enema (ACE).

1. Conservative

• *The retrograde colonic enema (RCE)*

In neurological fecal incontinence the standard enemas are difficult if not impossible to administer because there is inability to retain the enema which flows out involuntarily through the weak anus during its instillation.

Therefore a catheter system, which allows to perform the retrograde colonic enema, has been developed by industry, the application of which can easily be applied either by the parents or even by children over the age of 7–8 years. Not all children tolerate this procedure, in some of them colonic peristalsis creates pains. However the reported results are good according to Eire et al. [3], in 1998.

Shandling et al. [4] reported 100% success in using the enema continence catheter in the management of his patients with spina bifida.

These authors regard the RCE as one of the best conservative methods of treatment for relieving fecal incontinence originating from myelomeningocele and other neurological problems within intestinal dysfunction.

With ***intravesical electrical stimulation*** (IVES) also concomitant improvement in fecal incontinence was observed in children with myelomeningocele and IVES is regarded by some as another viable option for controlling fecal incontinence in these children [5].

Biofeedback was introduced for use in children with intact rectal sensation [6], but recent trials have reported less encouraging results [7]. "Digital disimpaction" is unpleasant to perform and only succeeds in emptying the distal rectal ampulla.

2. Operative

• The antegrade colonic enema (ACE)

The impact of antegrade colonic enema (ACE) [8] in the management of patients with myelomeningocele was analysed recently by Lemelle et al [1]. 47 patients were treated with ACE, of whom 41 used the method at a mean time of 4.1± 1.9 years after the ACE operation: only six abandoned ACE for conventional management. With ACE, faecal incontinence was significantly improved compared with conventional management and neither retrograde rectal enema nor digital extraction were required.

In most cases, ACE was performed using the appendix or the caecum. Among the

47 patients operated with the ACE procedure, six patients (12,8%) stopped performing antegrade enema for various reasons, from conduit problems due to stomal stenosis or catheterization difficulties, lack of motivation or "too long time to empty the enema" in one case. Antegrade colonic enema was applied before, concomitantly or after urinary incontinence surgery in 5, 27 and 10 cases respectively. Antegrade enema was performed at most three times a week, tap water was used in the majority of patients. Mean volume for ACE was 1.2 L (range 0,25–3,0 L). Mean enema time for colonic washout with ACE was 50 ± 19 min (range 15–90 min), however mean washout duration for ACE tended to be shorter with implantation of the conduit on the left-segment of the colon.

Casale et al. [9] were unable to find any differences in the continence rate or stomal complications between total reconstruction (ACE and continent urine stoma) or staged reconstruction. However, because of shared pathology the authors believe, that most patients benefit from intervention in the gastrointestal and the genitourinary tract. Therefore, a major advantage of total continence reconstruction is avoidance of the morbidity of a second major surgical procedure (LOE 3).

Nevertheless, conventional treatment should be tested first, and the efficacy of retrograde enemas may be a predictor of the efficacy of ACE on bowel management. Moreover, percutaneous endoscopic insertion is fully reversible and does not present drawbacks and encountered with the catheterizable conduit [2]. Nevertheless, experience with the Malone procedure has proved that a suitable continent and catheterizable conduit can be obtained with an appropriate technique. In selected and motivated patients, and with the help of a specialist nurse providing close support in the postoperative period, surgical ACE procedure might be preferred according to the surgeon´s experience.

• ***Sacral neuromodulation*** has been recently described also in the therapy of these patients, but the persistence of continence control and tolerance of the patient need to be evaluated for a prolonged period of time(). Sacral neuromodulation may only be successful in a small selected number of patients, in whom preserved anatomy of the sacral nerves permits placement of the electrodes on the sacral nerves [10].

d) Quality of life – QoL (LOE 3)

As no absolute indication has been defined for ACE, other criteria should be used to evaluate clinical outcome of bowel management, including health – related quality of life (HRQoL). This assessment should be performed prospectively when ACE produce is planned and performed during pre and post-operative periods.

According to Eire et al. (1998) ACE procedure and RCE can be the best options for achieving the best social integration. For wheelchair users and other selected patients the ACE (being faster and easier) is better than the retrograde continence enema which needs some help in its use [3,6].

CONCLUSIONS (LOE 3)

- **Neurologic bowel dysfunction and bowel problems incl. fecal incontinence and constipation are prevalent among myelomeningocele patients.**
- **Fecal incontinence and methods of bowel care affect the QoL and social activities of myelomeningocele patients.**
- **The main goal, to empty the colon as much as possible to achieve continence during the next 24–48 h, can be achieved nowadays either by retrograde colonic enema (RCE) using a special ballon catheter or by an operative procedure which allows an antegrade continence enema (ACE).**

RECOMMENDATIONS B/C

- **Colorectal problems deserve more attention in the treatment of myelomeningocele patients**
- **Appropriate bowel programme/management should be properly designed to each person after adequate counselling.**

FURTHER RESEARCH

The development of a disease-specific HRQoL measure for use with myelomeningocele has been proposed by Parkin et al. [11]. In addition specific questionnaires should be designed to assess fecal incontinence.

XI. DIABETES MELLITUS

1. URINARY INCONTINENCE

a) Epidemiology and prevalence

Diabetes is one of the commonest causes of polyneuropathy. Amongst different types of polyneuropathies in diabetic patients "diabetic cystopathy" occurs in 43% to 87% of insulin-dependent diabetics, with no sex or age differences. It is also described in about 25% of diabetic patients on oral hypoglycemic treatment. A Scandinavian study showed that in patients who have had diabetes for 10 years, the prevalence of diabetic cystopathy in those who were insulin-dependent was 2 to 4 per 1000 and in those on oral hypoglycemic agents was 1 to 3 per 1000. The correlation between diabetic cystopathy and peripheral neuropathy ranged from 75% to 100%. Nephropathy was seen in 30% to 40% of cases [1] (LOE 3)

Diabetes duration, treatment type, peripheral neuropathy, and retinopathy were significantly associated with severe incontinence in multiple regression models adjusted for age, education, and history of UTI [2] (LOE 3). Lewis et al in a cross-sectional studies of 50-90 years old women found that insulin dependent diabetes was strongly associated with urinary incontinence, while non insulin dependent diabetes was not [3] (LOE 2).

b) Pathology and disease specific LUT problems

Van Poppel et al had neuropathological examination of bladder biopsies done on 14 patients with severe insulin-dependent adult-onset diabetes and compared with the acetylcholinesterase and S100 staining of 38 control specimens. A decrease in acetylcholinesterase activity, due to axonal degeneration was found in all cases. An increase in S100 positivity was found in the majority and is due to Schwann cell proliferation as a regeneration attempt after demyelination or axonal degeneration. When acetylcholinesterase activity decreases and an S100 density increase is found in a patient with diabetes, this combination is highly suggestive of diabetic cystopathy amenable to early symptomatic treatment [4] (LOE 2).

Since the peripheral nerves are involved, the clinical manifestations of diabetic cystopathy might be very different. Usually there is reduced sensation of bladder fullness, and decreased frequency of voiding. This is followed by slowing of the urinary stream and difficulty in voiding due to impaired detrusor contraction. Post-voiding dribbling may also occur. The impaired bladder emptying and urinary retention predispose to urinary tract infections. No prospective studies referring specifically to the problem of functional disturbances of the LUT in diabetic patients were performed.

Yamaguchi et al. recently studied 84 diabetic cystopathy [5]. In addition to large post-void residual and decreased sensation, urinary urgency, detrusor overactivity (DO), and increased bladder sensation were seen in 55%, 42%, and 14%, respectively. The frequency of DO in patients with increased bladder sensation was 58%. DO increased with age, but not with the duration of diabetes. A brain MRI was performed in 32 cases. The frequency of multiple cerebral infarction in patients with DO was 76.5%. They concluded that urinary urgency (overactive bladder symptom) is not uncommon in diabetic cystopathy. Both central and peripheral mechanisms are involved, e.g., MCI due to diabetic cerebral vasculopathy for the DO, and, to a lesser extent, peripheral nerve irritation for the DO and increased bladder sensation [5] (LOE 3).

c) Disease specific diagnosis and treatment

Since diabetic polyneuropathy occurs in most patients after prolonged insulin-treatment and in about a quarter of patients treated with oral hypoglycemic drugs, it would be interesting to know the patients who are at risk of developing diabetic cystopathy without performing extensive functional tests of the LUT.

Ishigooka et al [6] (LOE 3) described the results of the ice-water test in diabetic patients with and without cystopathy . 12.5% patients without cystopathy and 25% of patients with cystopathy did not feel the ice water sensation. Ueda et al [7], (LOE 2) performed studies evaluating sympathetic skin response in correlation with cystometry.

They found that patients without sympathetic skin responses had increased residual urine and decreased detrusor contraction pressure, while patients with a lower amplitude of sympathetic skin response and more prolonged latency than controls had a significant decrease in detrusor contraction pressure. The changes within the bladder functions were observed as early as within one year from the diagnosis of diabetes.

Beylot et al [8], (LOE 2) found that the presence of residual urine in diabetic patients, after exclusion of co morbidities, was strongly associated with peripheral neuropathy.

No specific treatment has been described in regards to the population of patients with diabetic cystopathy. Therefore general rules as for the other bladder conditions with impaired (absent) detrusor contractions should be followed.

d) Guidelines for further research

No good epidemiological studies of the true incidence of diabetes related functional disorders of micturition were performed. The same is true for the treatment of diabetic "neurologic bladder". There are no studies referring to the theoretically effective prompted voiding, and intravesical electrostimulation

CONCLUSIONS

- **Diabetic cystopathy occurs in up to 80% of insulin dependent diabetes mellitus (LOE3)**
- **Urinary incontinence is strongly associated with insulin dependent, but not with insulin independent diabetes (LOE 2)**
- **Patients with diabetic cystopathy generally have impaired detrusor contractions and increased post-void residual (LOE ?)**
- **Overactive bladder is not uncommon in diabetes, presumably reflecting both central and peripheral mechanisms (LOE 3)**
- **Recurrent urinary tract infections might be a long term problem (LOE ?)**

RECOMMENDATIONS

- **Post void residual and urine dipstick (optional culture) in all patients with insulin dependent diabetes mellitus should be performed yearly (C)**
- **In case of increased post-void residual prompted voiding, intravesical electrostimulation might be useful (C/D)**
- **Treatment of choice for acontractile bladder in this group remains intermittent catheterization (B/C)**

2. FAECAL INCONTINENCE

Caruana et al [1] (LOE 3) found that diabetes patients with faecal incontinence showed increased thresholds of phasic external sphincter contraction compared with controls ($P<0.05$) and had reduced resting and maximal voluntary anal sphincter pressures compared with controls ($P< 0.05$). Increased thresholds of conscious rectal sensation in some incontinent patients with diabetes may contribute to faecal incontinence by impairing the recognition of impending defecation. Nakayama et al [2] (LOE 3) found that age and diabetes have an independent negative influence on faecal incontinence after stroke. It could be due to an abnormal internal-anal-sphincter function in diabetes patients with faecal incontinence [3] (LOE 3).

Talley [4] (LOE 3) studied gastro-intestinal symptoms, frequent abdominal pain, bowel-related abdominal pain, reflux, dyspepsia, constipation, diarrhea, and fecal incontinence in diabetes patients. There was a clinically significant decrease in QoL scores in diabetics compared with population norms across all subscales. The impact on QoL in diabetes was predominantly observed in type 2 diabetics. For all the Short Form-36 subscales, GI symptom groups were significantly (all $p < 0.0001$) associated with poorer QoL in diabetes, independent of age, gender, smoking, alcohol use, and type of diabetes.

Russo found that acute hyperglycaemia inhibits external anal sphincter function and decreases rectal compliance, which could explain the ethiopatogenesis of faecal incontinence [5] (LOE 3)

CONCLUSIONS

- **Faecal incontinence in diabetes patients may be due to impaired anorectal sensation and/or decreased anal closing pressure after hyperglycemic episodes (LOE 3)**
- **Gastro-intestinal symptoms impact negatively on health-related QoL in diabetes mellitu (LOE 3).**

RECOMMENDATIONS

- **Patients with diabetes and fecal incontinence should have anorectal manometry performed before introducing the therapy for fecal incontinence (C/D)**
- **More studies on neurologic bowel dysfunction and management in diabetes are needed before giving further recommendation (B).**

XII. PERIPHERAL NEUROPATHY DUE TO IATROGENIC LESION (FOCAL NEUROPATHY)

1. EPIDEMIOLOGY AND PREVALENCE

LUT dysfunctions can occur from damage to the nerves innervating the pelvic organs, anywhere in the course of these nerves through the cauda equina, the spinal nerve roots, the sacral plexus, or to the various individual nerves that arise from the plexus

Most injuries to these nerves are iatrogenic. Extensive pelvic surgery as abdomino-perineal resection for rectal cancer, radical hysterectomy, and aortoiliac surgery are all likely to damage the pelvic parasympathetic nerves to the bladder and genitalia. Of course this listing is not complete and practically any surgery performed within the pelvis could damage some nerves e.g. adenomectomy, radical prostatectomy, prolapse surgery. Complications of these procedures are described elsewhere in this in the relevant chapters

Additionally pelvic irradiation, apart from causing damage to the irradiated tissue could cause damage to the adjacent nerve fibers, resulting in altered functions.

A variety of types of voiding ,erectile and fecal dysfunctions can result.

a) Hysterectomy (simpe and radical)

It is difficult to atribute certain dysfunctions to neuronal damage alone, taking into account the altered, after hysterectomy, static and dynamic functions of the pelvic structures.

Parys et al [1] (LOE 3) studied 126 women after simple hysterectomy. The results show that 47.0% had detrusor overactivity, 36.7% had urethral obstruction, and 24.8% stress incontinence. Sekido et al [2](LOE 3) described 9 women treated with radical hysterectomy more than 10 years before the study. Obstructive voiding symptoms and/or urinary incontinence were observed in 7 patients. Cystometry revealed impaired bladder sensation, detrusor acontractility, straining on voiding, and impaired relaxation of the sphincter in all assessable patients. In addition, decreased bladder compliance was observed in 5 patients. Axelsen [3] (LOE 2) studied 100 women after radical hysterectomy and found that these women who reported incontinence had lower urethral pressure. In a prospective study of over 1000 women Jackson et al found hysterectomy to be an independent risk factor of incontinence [4] (LOE 2).

There is however significant lack of long term observations of patients after radical hysterectomy in terms of lower urinary tract neurogenic dysfunctions.

b) Abdominoperineal resection

Retrospective analysis of 52 patients after abdominoperineal resection was performed by Eickenberg et al [5] (LOE 3). Neurologic bladder dysfunction of various degrees was found in 50 per cent of all patients but represented a long-term problem in only 10 per cent

Baumgarner et al [6], (LOE 3) studied 86 consecutive cases of abdominoperineal resection and described 11 cases of various functional problems of micturition. All these studies however lack specific tests of the LUT functions and are not prospective.

However curative total mesorectal excision with autonomic nerve preservation can be done with high rates of preservation of such function: Pocard et al. [7] (LOE 3) investigated 20 patients, 13 men and 7 women following curative total mesorectal excision with autonomic nerve preservation for rectal cancer. There was no difference in preoperative and postoperative LUT function, International Prostatic Symptom Score or urodynamic results, nor in the results of the quality of urinary function questionnaire. Also sexual activity and potency were unchanged in these men. Therefore the authors conclude that autonomic nerve preservation is possible and does not impair urinary and sexual function. Also Kim et al [8] (LOE 3) showed relative safety in preserving sexual and voiding dysfunction with total mesorectal excision with pelvic autonomic nerve preservation. Evaluation was based on uroflowmetry, voided volumes and residual volume, symptoms were evaluated with the IPSS: There were significant differences in max. urinary flow rate and voided volume before and after surgery, however no differences in residual volume before and after surgery were apparent. The IPPS however increased after surgery from 6.2 +/- 5,8 to 9.8 +/- 5,9 (= < 0,05).

Similar results are reported by Turaldo et al. [9] (LOE 3) evaluating incidence and pathogenesis of LUT dysfunction after surgical treatment of rectal cancer in a series of 219 patients with normal urinary function preoperatively: in the immediate follow-up only 17 patients with dysfunction were observed, 14 stage II, 2 at stage III and 1 at stage IV according to Astler-Koller classification; six months later only 8 patients had claimed urinary dysfunction and 1 required catheterisation. However no urodynamic studies were performed. There was no correlation of those with LUT dysfunction with staging, radiotherapy, size of tumuor, surgical technique, however worst functional results were observed in patients who underwent abdomino-perineal resection. Lim et al have found that not only surgery but also preoperative irradiation could cause lower urinary tract and anorectal dysfunctions. The maximum resting anal pressures were unchanged after chemoradiation, but the maximum squeeze anal pressures were reduced after chemoradiation. They conluded therefore that preoperative chemoradiation for rectal cancer carries a significant risk of pudendal neuropathy, which might contribute to the incidence of fecal incontinence after restorative proctectomy for rectal cancer [10] (LOE 3).

2. PATHOLOGY AND DISEASE SPECIFIC LUT PROBLEMS

Focal injury to peripheral innervation of the bladder and/or sphincter results in decentralization or denervation of the above mentioned organs. Therefore detrusor hypocontractility (acontractility) and/or sphincteric deficiency will be the result of such a damage. This in turn will result in impaired bladder

emptying and/or stress incontinence. No prospective studies referring specifically to the problem of functional disturbances of the LUT in focal iatrogenic neuronal injury in patients after hysterectomy or colorectal surgery have been performed.

3. INFLUENCE ON FECAL INCONTINENCE

Iatrogenic faecal incontinence can be caused by sphincter damage caused by childbirth, anorectal surgery, trauma, fistulae and abscesses. Vaginal delivery can cause not only sphincteric, but also neuronal damage to the innervation of the anal sphincter [11] (LOE 3)

There is a significant paucity of the epidemiological data regarding fecal incontinence after pelvic surgery.

Studing of anorectal reflexes and performing anorectal manometry could predict function restoration.[12,13] (LOE 3)

4. DISEASE SPECIFIC DIAGNOSIS AND TREATMENT

The only test in this specific patient population was described by Nordling et al [14] (LOE 3). In patients after radical hysterectomy, those who had a completely denervated bladder had a greater rise in maximum urethral pressure during noradrenaline infusion (exceeding 20 cm H2O) than normal subjects (1 to 15 cm H2O). Therefore authors concluded that urethral supersensitivity to noradrenaline may be a promising test in diagnosing damage of the sympathetic nervous innervation of the LUT.

Since the major cause of focal neuropathy is surgical intervention, the best method is to avoid peripheral neuronal injury during surgery. The detailed knowledge of pelvis neuroanatomy and meticulous preparations of the structures adjacent to the possibly affected nerves was shown to be the best technique [15-19] (LOE 3). An interesting method of intraoperative identification of the vesical branches of the pelvic nerves during radical hysterectomy was described by Kuwabara et al [20] (LOE 3). Postoperative compliance of the detrusor in cases where this method was implemented demonstrated less decrement from preoperative values than in cases with the conventional method. These patients required also significantly fewer days to achieve residual urine volumes less than 50 ml after surgery.

If, however, the injury to the nerves innervating the bladder/urethra complex should occur, the treatment should be based on general principles described elsewhere and on the results of functional examination of the LUT. Nerve sparing surgery seems to have favourable effect on bladder functions and continence in patients after radical hysterectomy [21, 22] (LOE3). Thus it seems that it is the nerve function, rather than the biomechanics of the urethrovesical complex, which are responsible for incontinence.

Nerve sparing technique and intraoperative identification of parasympathetic nerves seem also to play a role in rectal cancer surgery. Kneist and Junginger studied 62 patients undergoing mesorectal excision .Pelvic autonomic nerve preservation (PANP) was assessed macroscopically and with the aid of intraoperative electrical stimulation of pelvic autonomic nerves .

In 46 patients preservation of parasympathetic nerves was confirmed and these patients remained unchanged in early and long-term urinary function opposite to the remaining patients without confirmed preservation of the nerves [23] (LOE 3).

Zanolla et al [24] (LOE 2) suggested that early implementation of rehabilitative treatment (prompted voiding) allows satisfactory functional recovery of the bladder activity in 91% of the symptomatic patients after radical hysterectomy. Another interesting issue is the feasability of the use of the artificial urinary sphincter in patients after colorectal surgery, hysterectomy and or radiotherapy for the treatment of stress incontinence. Only one study on this subject was identified [25] (LOE 3), describing a series of patients after radical prostatectomy and amongst them a patient after abdominoperineal resection with adjuvant radiation [16].

Authors concluded that this method of incontinence therapy should be the method of choice, however there is a significantly greater risk of revision (38% versus 22% in the literature for low risk groups). Fecal incontinence after colorectal surgery, if not resulting from sphincter damage could be succesfully treated by sacral neuromodulation [26] (LOE 3).

5. GUIDELINES FOR FURTHER RESEARCH

No good epidemiological, prospective studies of the true incidence of peripheral injury related functional disorders of micturition were performed. Neither the descriptive studies of the disorders were performed. No specific, injury related therapy was described. There is a strong need for registry database of urinary and fecal incontinence after different types of pelvic surgery in order to establish the true prevalence and prepare guideliness on treatment/ prophylaxis

CONCLUSIONS

- **Injury to the bladder/sphincter innervation occurs in 30-50% of patients after extensive pelvic surgery (LOE 3)**
- **Pelvic irradiation could cause nerve damage attributing to the altered bladder/bowel functions (LOE 2).**
- **Fecal incontinence due to iatrogenic innervation damage could occur after complicated labor, anorectal surgery and pelvic irradiation (LOE 3)**

- **Focal injury results in impaired detrusor contractions and external urethral sphincter deficiency or detrusor/sphincter dyssynergy (LOE 3-4)**
- **The key issue in avoiding these complications are nerve sparing techniques and intraoperative nerve identification(LOE 3)**

RECOMMENDATIONS

- **Patients after extensive pelvic surgery demonstrating functional disorders of micturition should be properly evaluated due to a variety of possible disorders (C)**
- **Early rehabilitation of the LUT and of the anal sphincter might improve voiding in a majority of patients (C)**
- **In case of increased post-void residual after prompted voiding, intravesical electrostimulation might be useful (C/D)**
- **Treatment of choice for acontractile bladder in this group remains intermittent catheterization (B/C)**
- **Surgeons should aim for autonomic nerve preservation when performing surgery for rectal cancer. Post-operative post-void residual urine measurements as well as a targeted history on micturition before and after are mandatory in order to avoid secondary myogenic damage of the detrusor by chronic urinary retention.(B)**

XIII. SYSTEMIC LUPUS ERYTHEMATOSIS

As the literature contains only a case report of faecal incontinence, this will not be described here

1. URINARY INCONTINENCE

a) Epidemiology and prevalence

Nervous system involvement occurs in about half of patients with systemic lupus erythematosis (SLE). Seizures and psychiatric disorders are most common manifestations; spinal cord lesions are uncommon. Symptoms of LUT dysfunction can occur, however data on prevalence are not available.

b) Pathophysiology

Neurological manifestations of systemic lupus erythematosis are subacute encephalomyelopathy, subacute myelopathy (rarely) and chronic encephalomyelopathy.

c) Disease specific diagnosis

Sakakibara et al. (LOE 4) [1] published the findings of 6 women and 2 men, mean age 23 years, suffering from SLE for 2-25 years under immunosuppressant therapy. All 8 patients had urodynamic abnormalities, 5/8 showed decreased urinary flow, 3/8 increased post-void residual urine, 2/8 increased max. urethral closure pressure, 5/8 showed detrusor overactivity, and 5/8 impaired detrusor contractility; furthermore detrusor-sphincter dyssynergia was found in 4/8, and neurologic motor unit potentials of the external sphincter in two of four patient studied. They found detrusor overactivity more common in patients with brisk deep tendon reflex (80 %) than in those without (33 %). Repeated studies during a follow-up period between 2 months and 8 years showed deterioration in 3/8 including loss of bladder sensation, development of a low compliance bladder and decreased bladder capacity (LOE 4).

Yu et al. studied 152 women with SLE and found a significant relationship between central nervous system involvement and the adapted AUA index score. The most common urodynamic finding was a small cystometric bladder capacity (<150 ml; n = 7 patients), followed by a a weak urinary flow rate (<12 ml/second; n = 6 patients). In 3 of 7 patients with small cystometric bladder capacities, imaging studies documented a contracted bladder with marked hydroureteronephrosis [2] (LOE 3)

CONCLUSIONS

- **Half of the patients with systemic lupus erythematosis show nervous system involvement. In 30 % of them subacute and chronic encephalomyelopathy may cause LUT dysfunction with variable patterns including reduced bladder capacity, detrusor overactivity, impaired detrusor contractility, pathologic voiding pattern and increased post-void residual urine (LOE 4).**

RECOMMENDATIONS

- **The dysfunction pattern may change over time, therefore urological follow-up is recommended. (C)**
- **Urodynamics are necessary to define the underlying pathophysiology of the urinary symptoms (C).**
- **Patients with SLE and voiding dysfunctions should be managed expectandly, accordingly to the urodynamic results (C).**

XIV. HERPES ZOSTER

As the literature contains only a case report on faecal incontinence this will not be described here

1. URINARY INCONTINENCE

a) Epidemiology and prevalence

Incidence of LUT dysfunction is as high as 28 % if only lumbosacral dermatome-involved patients are considered. The overall incidence is 4 % [1]. Despite such high prevalence only case reports are avaliable.

b) Pathophysiology

Herpes zoster in the lumbosacral dermatomes may manifest according to Chen et al., based on 17 patients, as cystitis-associated (12/17), neuritis-associated (4/12) and myelitis-associated (1/17).

c) Disease specific diagnosis

Two case reports describe urodynamics findings in herpes-zoster patients. Usually patients develop complete urinary retention, with or without overflow incontinence due to detrusor acontractility and lack of bladder sensation. Repeated urodynamic studies at week 10 after the onset of the disease demonstrated a return of the detrusor contraction, which returned to normal after 14 weeks [2,3] (LOE 4).

Herpes zoster associated voiding dysfunction is a transient phenomenon and is not uncommon in patients with lumbosacral dermatome involvement. As long as voiding is unbalanced the treatment with intermittent catheterisation or indwelling catheter placement is recommended in order to avoid secondary damage to the LUT due to infection or chronic urinary retention. The disease usually is of a benign clinical course and almost every patient will either regain normal voiding or, at least balanced bladder function.

CONCLUSIONS

- **P28 % of patients with Herpes zoster in the lumbosacral dermatoms show LUT dysfunction with impaired voiding as the most common symptom.(LOE 4)**
- **PThe most common symptom is overflow incontinence due to detrusor acontractility and lack of bladder sensation (LOE 4)**
- **PVoiding dysfunction has a transient course and almost every patient will either regain normal voiding within 3-4 months or at least balanced bladder function.(LOE 3).**

RECOMMENDATIONS

- **Till functional recovery takes place treatment with intermittent catheterisation or indwelling catheter are recommended (C).**

XV. HIV

1. EPIDEMIOLOGY AND PREVALENCE

HIV virus belongs to the family of retroviruses. This family of viruses is known for latency, persistent viremia, infection of the nervous system, and weak host immune responses. HIV has high affinity for CD4 T lymphocytes and monocytes. HIV binds to CD4 cells and becomes internalized. The virus replicates itself by generating a DNA copy by reverse transcriptase. Viral DNA becomes incorporated into the host DNA, enabling further replication. HIV enters the nervous system early, at the time of initial infection, and may immediately cause symptoms, or may cause symptoms any time during the person's lifetime.

All parts of the nervous system may be involved. Neurological disorders could be HIV-related, due to secondary infections, malignancies, metabolic or nutritional problems and to therapy.

It is estimated that without anti-retroviral treatment, up to 80% of patients are symptomatic in terms of nervous system and for 30%, neurological symptoms are the initial clinical problem.

Neurological syndromes may be the sole clinical problem or cause of death. The following brain symptoms were described: meningitis, dementia, stroke, seizures, degenerative disorders. For spinal cord both transverse myelitis and progressive myelopathy were observed.

Taking all these information together it is evident that nervous system involvement in HIV infection should be reflected to a various degree in the LUT [1].

Shin et al (LOE3) described a higher prevalence of incontinence in HIV-positive patients in nursing homes as compared to HIV-negative [2]. Whether this represents a true trend or is an observation related to the terminal stage of the disease and associated comorbidities remains to be elucidated.

Gyrtrup et al (LOE 3) found voiding problems in 12% of HIV-infected patients, mostly in advanced stage of the disease [3].

2. PATHOLOGY AND DISEASE SPECIFIC LUT PROBLEMS

As already described virtually all parts of the body could by involved in AIDS patients ,either as the primary location of HIV infection or secondary to HIV-related complications.

Among these different manifestations particular attention should be paid to the primary locations as they develop early in the stage of the disease.

HTLV-I associated myelopathy (HAM) affects up to 3% of HIV positive patients and is manifested by slowly progressive spastic paraparesis, including deterioration of bladder problems [4](LOE 2). Another interesting primary demonstration of HIV infection is lumbosacral polyradiculopathy, described by Matsumoto et al (LOE 3)[5]. In this case report voiding difficulties and lower limb paresis were the primary manifestation of HIV infection.

Also Mahieux et al (LOE 3) described a case of acute myeloradiculitis due to cytomegalovirus as the initial manifestation of terminal stage [6].

Begara et al (LOE 3) performed urodynamic studies in 10 patients with AIDS and voiding disorders and found that the most common symptom was urge incontinence and the most common urodynamic finding was detrusor-external sphincter dyssynergia [7]. In 3 patients they found demonstrable functional disorders of the LUT (2 patients had detrusor over-activity: one of them had a history of encephalopathy from HIV and the other patient had polyneuritis; the third patient had myelitis and a urodynamically diagnosed sympathetic decentralization. Detrusor areflexia was described in 2 HIV-positive patients by Menendez et al [8](LOE 3). One of them had an ascending myelitis of probable herpetic origin, the other had a cerebral abscess caused by Toxoplasma gondii.

3. DISEASE SPECIFIC DIAGNOSIS AND TREATMENT

Since during the course of the disease all parts of the nervous system can be involved, either as the primary location or secondary to AIDS-related complications, no disease specific diagnosis or treatment can be proposed. It is important to observe that sometimes functional disorders of the LUT can be the first manifestation of the HIV infection.

When managing the patient with HIV infection one must bear in mind that both storage and voiding problems can occur and that both should be treated according to the results of urodynamic studies.

4. GUIDELINES FOR FURTHER RESEARCH

All rapports about HIV and voiding problems are rather anecdotal and no good prospective studies exist. The need for such studies is particularly important, when realizing that it takes up to 20-30 years from HIV infection to AIDS full manifestation and that new antiviral treatment modalities could prolong the life of a patient with HIV significantly.

Particular attention should be paid to primary nervous system involvement by HIV and to related voiding dysfunction as well as to the voiding dysfunctions that could be the side effects of HIV drug therapy.

5. FAECAL INCONTINENCE

As diarrhoea is common in HIV infected patients, the faecal incontinence can also occur, mostly due to anal sphincter weakness. Again the true incidence of HIV neuropathy relatad faecal incontinence is not known and further studies are needed [9], (LOE 4)

CONCLUSIONS

- **HIV can influence the nervous system and the LUT functions in two ways: as primary infection site or secondary to AIDS related complications (LOE2/3)**
- **Nervous system manifestation of HIV infection can by the only sign and it is therefore important to take the possibility of HIV infection into consideration when facing unusual signs and symptoms from the LUT without any other obvious cause (LOE 3)**
- **HIV/AIDS is a progressive disease and dynamic changes to the LUT functions can occur during the evoluation of the disease (LOE 2)**
- **Faecal incontinence in HIV/AIDS patients is usually associated with diarrhoea, however the true incidence is not known (LOE 4)**

RECOMMENDATIONS

- **Patients with HIV and nervous system pathological signs and symptoms should be evaluated towards functional LUT problems (B)**
- **Due to the variety of LUT functional damage in HIV patients urodynamic study is essential for tailoring the optimal therapy (C)**
- **No HIV specific therapy of LUT problems and faecal incontinence exist. Due to variety of functional damage therapy should be individually tailored, accordingly to the results of functional/imaging studies (C)**

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B. PATHOPHYSIOLOGY

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C. NEUROLOGIC URINARY INCONTINENCE

C. I. EPIDEMIOLOGY NEUROLOGIC URINARY INCONTINENCE

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C. II. SPECIFIC DIAGNOSTICS NEUROLOGIC URINARY INCONTINENCE

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C. III. CONSERVATIVE TREATMENT NEUROLOGIC URINARY INCONTINENCE

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C. IV. SURGICAL TREATMENT NEUROLOGIC URINARY INCONTINENCE

2. SURGERY FOR NEUROLOGIC URINARY INCONTINENCE ASSOCIATED WITH POOR BLADDER EMPTYING DUE TO DETRUSOR UNDERACTIVITY

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3. DENERVATION PROCEDURES FOR TREATING REFLEX URINARY INCONTINENCE DUE TO NEUROLOGIC DETRUSOR OVER ACTIVITY

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C. IV. SURGICAL TREATMENT NEUROLOGIC URINARY INCONTINENCE

4. SURGERY FOR STRESS UI DUE TO NEUROLOGIC SPHINCTERIC INCOMPETENCE

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5. SURGICAL ALTERNATIVES EXCLUDING DENERVATION PROCEDURES TO TREAT REFLEX INCONTINENCE DUE TO NEUROGENIC DETRUSOR OVERACTIVITY

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C. IV. SURGICAL TREATMENT NEUROLOGIC URINARY INCONTINENCE

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D. IV. SURGICAL TREATMENT NEUROLOGIC FAECAL INCONTINENCE

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E. SPECIFIC NEUROLOGIC DISEASES

I. DEMENTIA

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a) Alzheimer's Disease

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E 2. DEMENTIA, CONSTIPATION AND FECAL INCONTINENCE

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E. II. MULTIPLE SYSTEM ATROPHY
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E. VI. SPINAL CORD LESION

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