

## W28: Surgery of Neurogenic Bladder: What's In and What's Out

Workshop Chair: Bülent Çetinel, Turkey

08 October 2015 14:30 - 16:00

Start	End	Topic	Speakers
14:30	14:35	Neurogenic bladder: When and how to operate	Bülent Çetinel
14:35	14:45	Neurotoxins	David Castro-Diaz
14:45	15:00	Bladder augmentation (When and how and the future)	Bülent Çetinel
15:00	15:10	Surgery to improve bladder outlet function	David Castro-Diaz
15:10	15:25	Urinary diversion and stomal surgery	Ervin Kocjancic
15:25	15:45	Neurosurgery for urologists	John Stoffel
15:45	16:00	Live cases discussion and interaction	All

### **Aims of course/workshop**

To provide awareness of neurogenic bladder and its updated surgical treatment alternatives among urologists, nurses, and physical therapists. To emphasize that when conservative measures fail, surgery can achieve the main goals of preserving upper urinary tract integrity, offering good quality of life with reasonable continence, and minimising urinary infection and stone formation

### **Learning Objectives**

1. To have the knowledge that when conservative measures fail in neurogenic bladder, surgery can achieve the main goals of preserving upper urinary tract integrity, offering good quality of life with reasonable continence, and minimising urinary infection and stone formation.

# NEUROGENIC BLADDER: WHEN AND HOW TO OPERATE

Bülent Çetinel MD

Neurogenic lower urinary tract disorder (NLUTD) conventionally mentioned as neurogenic bladder may be caused by a variety of neurological diseases affecting the various parts of the nervous systems controlling the lower urinary tract (1). Although overall prevalence estimates for neurogenic bladder in the general population is scarce, data are available on the prevalence of underlying neurological disorders, and the relative risk for the development of neurogenic bladder in specific neurologic diseases (1). The typical example is multiple sclerosis. Reported prevalence rates of the disease vary between 40 and 220 per 100,000. The prevalence of lower urinary tract dysfunction (LUTD) in patients with MS is about 50–90% (2)

The primary aims for treatment of neurogenic bladder are protection of the upper urinary tract, improvement of urinary continence, and improvement of the patient's quality of life (QoL) (3).

Preservation of the upper tract function is of paramount importance in neurogenic bladder although some important differences have been determined between the upper urinary tract deterioration rates due to different underlying neurological disorders (2,3). Many studies showed that upper urinary tract (UUT) deterioration in patients with MS and LUTD was rare, and classical risk factors for UUT deterioration such as uncontrolled detrusor contractions and detrusor-sphincter dyssynergia (DSD) did not affect the UUT in patients with MS as seriously as LUTD in spinal cord injury (SCI) (2,3).

Golden rule in treatment of neurogenic bladder stated by EAU guidelines ensures that the detrusor pressure should remain within safe limits during both the filling and the voiding phases of micturition (3). This approach has indeed significantly reduced the mortality from urological causes in this patient group (3).

In patients with high detrusor pressure during the filling phase (detrusor overactivity, low detrusor compliance) or during the voiding phase (DSD, other causes of bladder outlet obstruction), treatment must be aimed primarily at conversion of an high-pressure bladder into a passive low-pressure reservoir (3).

The treatment of urinary incontinence is also important for social rehabilitation of the patient and thus contributes substantially to the QoL. It is also pivotal in preventing UTI (3).

Patients with neurogenic bladder, urinary incontinence, and UUT deterioration refractory to conservative and minimal invasive treatment options are candidates for surgical treatment (2,4).

After the introduction of clean intermittent self catheterisation (CISC) by Lapides, surgical treatment alternatives became more widely used (5).

Surgical treatment alternatives aim a) to facilitate storage, and b) to facilitate emptying.

Minimal invasive treatment alternatives facilitating storage are botulinum toxin injections to detrusor muscle, urethral bulking agents, and urethral inserts. Minimal invasive treatment alternatives facilitating emptying are botulinum toxin sphincter injection, sphincterotomy, bladder neck incision, and implantation of urethral stents. Botulinum toxin injections to detrusor muscle, sphincterotomy, and bladder neck incision are the highly recommended minimally invasive treatment alternatives in neurogenic bladder (3).

Surgical treatment alternatives facilitating storage are urethral sling procedures, artificial urinary sphincter implantation, bladder neck and urethral reconstruction procedures (Young-Dees-Leadbetter, Kropp, and Salle procedures), bladder neck/urethral closure, detrusor

myectomy (auto-augmentation), denervation, deafferentation, neuromodulation, bladder augmentation or substitution cystoplasty, and continent diversion (stoma application by several techniques to native bladder, and to augmentation cystoplasty).

Surgical treatment alternatives facilitating emptying are neurostimulation, neuromodulation, and bladder covering by striated muscle (latissimus dorsi, rectus muscle) procedure.

Treatment alternatives such as urethral slings and artificial urinary sphincter implantation increase the bladder outlet resistance and have the inherent risk of causing high intravesical pressure during the filling phase, which may become even higher during the voiding phase. These procedures must be performed only when the high detrusor pressure is, or can be, controlled (3).

Augmentation cystoplasty (AC) mostly result in intermittent catheterisation (IC) being performed after the procedure. Preoperative training of patients for IC was found to be an essential prerequisite of AC (4). Inability to perform IC is an important contraindication for AC (4).

When no other therapy has been successful, and IC is impossible, incontinent urinary diversion must be considered for the protection of the upper tracts and for the patient's QoL (3).

Surgical treatment alternatives for neurogenic bladder such as urethral sling procedures, artificial urinary sphincter implantation, sacral deafferentation, neurostimulation neuromodulation, bladder augmentation, and detrusor myectomy (auto-augmentation) are recommended with grade (B) in EAU guidelines (3)

The present handouts summarise the presentations made by leading experts on this field during 28th workshop in ICS 2015 Montreal meeting, which I had the privilege of chairing.

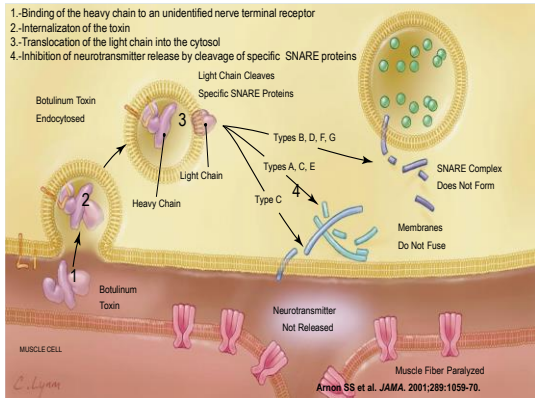
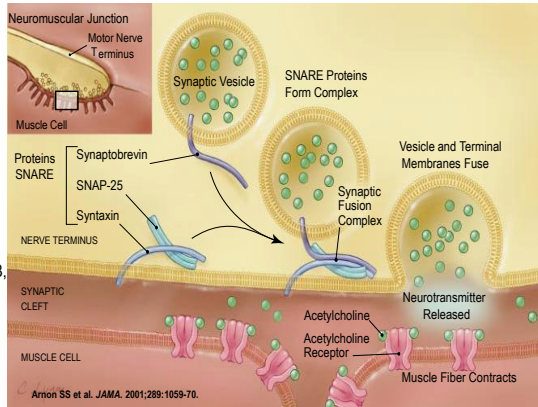
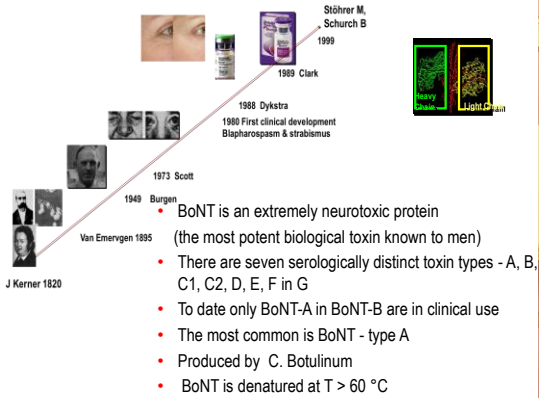
## References

- 1) Drake MJ, Apostolidis A, Emmanuel A, et al. Neurogenic urinary and fecal incontinence. Committee 10. In Incontinence Ed's. Abrams P, Cardozo L, Khoury S, Wein A. 5th Edition 2013
- 2) Cetinel B, Tarcan T, Demirkesen O, et al. Management of Lower Urinary Tract Dysfunction in Multiple Sclerosis: A Systematic Review and Turkish Consensus Report. *Neurourology and Urodynamics* 32:1047–1057 (2013)
- 3) Blok B, Pannek J, Castro Diaz D et al. Guidelines on Neuro-urology. European Association of Urology 2015
- 4) Cetinel B, Demirkesen O, Önder AU, et al. Reconstructive surgery in voiding dysfunction: experience with 69 patients. *Urology*. 56:962-966, 2000
- 5) Lapidus J, Diokno AC, Silber SJ, Lowe BS. Clean intermittent self-catheterization in the treatment of urinary tract disease. *Trans Am Assoc Genitourine Surg* 1971;63:92-96

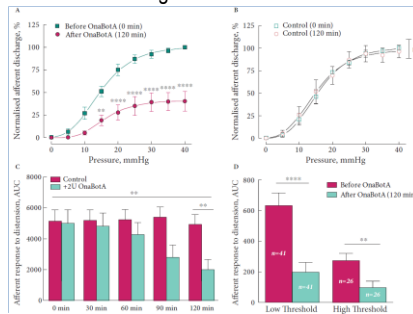


## Neurotoxins

David Castro-Diaz  
University Hospital of the Canary Islands/University of La Laguna



### Effect of botulinum toxin type A in reducing afferent nerve traffic



Adapted from: Collins VM, et al. BMJ 2013 Jun 5; doi: 10.1136/bmj.f2286.

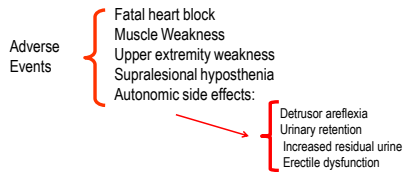
## Botulinum toxin - A

- Three commercially available BoNT-A.
- There are similarities between the two products.
- But different doses, efficacy and safety profiles.
- It needs to be borne in mind that different preparations are not interchangeable!
- Clinically, Dysport® units are not equivalent to Botox® units.
- Botox® vial contains 100 U/5 ng toxin and Dysport® contains 500 U/12,5 ng toxin.

Non-proprietary names	Proprietary names	Dose	Status in NDO
OnabotulinumtoxinA	Botox	200 U	BoNT/A brands are not interchangeable
AbobotulinumtoxinA	Dysport	500-750 U	
IncobotulinumtoxinA	Xeomin	200-300 U	

## Botulinum Toxin

- Lethal dose 2000-3000 units
- 200-300 units of Botox is unlikely to produce systemic effects



- Striated muscle function recovery between 2 weeks to 3 months
- Smooth muscle function recovery between 6 and 9 months
- Increasing toxin dilution maximizes the local paralytic effect
- Larger injection volumes increase risk of systemic absorption and weakness

### Botulinum Toxin Contraindications

- Peripheral motor neuropathy (Amyotrophic lateral sclerosis)
- Neuromuscular junction disorders (Myasthenia gravis, Lambert-Eaton myasthenic syndrome)
- Treatment with aminoglycosides and agents interfering with neuromuscular transmission



Higher risk of significant systemic side effects, including severe dysphagia and respiratory compromise

### Botulinum Toxin Resistance

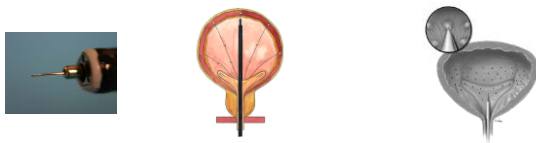
- 5%-17% of patients treated for cervical dystonia develop neutralizing antibodies
  - Higher doses and shorter intervals between doses contribute to the development of clinical resistance
- 3 month interval between treatments  
Smallest dose to achieve the desired clinical effect



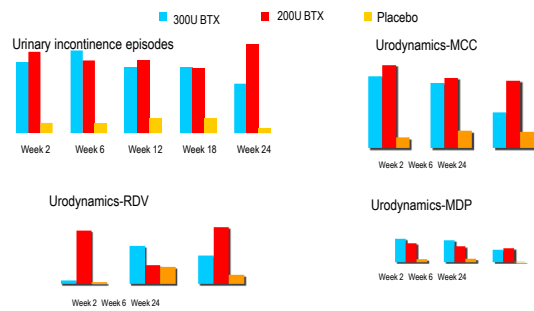
- Factors that influence immunoresistance
- Toxin dose
  - Treatment duration and frequency of immunization
  - Genetic susceptibility
  - Prior immunoresistance to another serotype
  - Prior active immune response to tetanus neurotoxin
  - Quality of the antigen

### BoNTA injection in the bladder

- Dilute 100-200 U of BoNTA into 10-30 ml of saline
- Inject targeting the trigone, base of the bladder and lateral walls
- Rigid cystoscope: 25 Gauge Williams needle,
- Inject approximately 0.5- 1.0 ml into 20 sites
- Submucosal versus intradetrusor

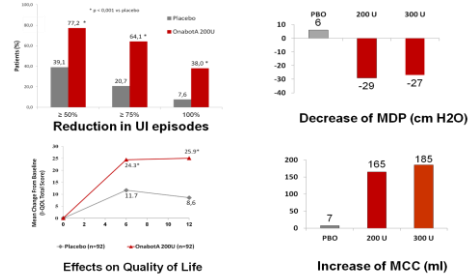


Botulinum Toxin A (Botox®) in neurogenic urinary incontinence: Results from a multi-centre randomized, controlled trial.  
Schurch B & Botox detrusor hyperreflexia study team J. Urol 2005



Clear differences between BTX and placebo, but not much difference between 300 and 200 U BTX

### Onabotulinumtoxin A in Neurogenic patients. Dignity study



Clear differences between BTX and placebo, but not significant difference between 300 and 200 U BTX  
Recommended dose is 200 U  
FDA approval

Cruz F et al, Eur Urol, 2011

### Summary of key findings of the Dignity studies

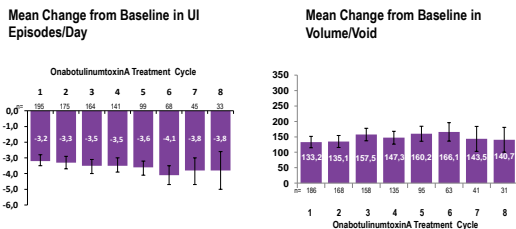
Cruz et al, Eur Urol 2011, Ginsberg et al, J Urol, 2012, Ginsberg et al Adv Ther, 2013, Cruz and Nitti, NAU 2014

- 200 U is the ideal dose for NDO (effective in MS and SCI)
- Incontinence decrease more than > 3 episodes/day (average)
- Dry rate of 37%
- Frequency decreased by 2 voids /day (MS patients voiding spontaneously)
- QoL improved significantly
- MDP decreased more than >30 cm H2O
- Duration around 9 months

Adverse Events	PBO	200 U	300 U
UTI (1st 12 weeks)	18	28	28
UTI (overall)	34	49	50
Urinary retention	3	20	17
CIC due to UR	10	35	42
CIC any reason	22	47	49
Hematuria	3	4	5

### Long-term effects of Onabotulinum Toxin type A 200 U in NDO

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Error bars represent 95% confidence intervals. Baseline UI episodes/day: 4.5. Baseline volume/void: 153.8 mL for 200U group. Data available at Week 6.  
\*Baseline is prior to receiving any treatment in the phase 3 studies for all patients entering the extension study.  
UI = urinary incontinence.

Karsenty G, et al, EJA 2014 (abstract)

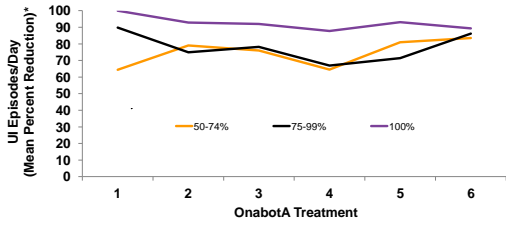
### Positive Response to First OnabotulinumtoxinA Treatment Persists Long-term With Repeat Treatments in Patients with Neurogenic Detrusor Overactivity

Pierre Denys<sup>1</sup>, Roger Dmochowski<sup>2</sup>, Philip Aliotta<sup>3</sup>, David Castro-Diaz<sup>4</sup>, Bertil Blok<sup>5</sup>, Karen Ethans<sup>6</sup>, Manher Joshi<sup>7</sup>, Quanhong Ni<sup>8</sup>, Michael Kennelly<sup>9</sup>

<sup>1</sup>Hôpital Raymond Poincaré, Garches, France; <sup>2</sup>Vanderbilt University Medical Center, Nashville, TN, USA; <sup>3</sup>Western New York Urology Associates, LLC, Cheektowaga, NY, USA; <sup>4</sup>Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain; <sup>5</sup>Erasmus Medical Center, Rotterdam, The Netherlands; <sup>6</sup>University of Manitoba, Winnipeg, MB, Canada; <sup>7</sup>Allergan, Inc., Irvine, CA, USA; <sup>8</sup>Allergan, Inc., Bridgewater, NJ, USA; <sup>9</sup>Carolinas Rehabilitation, Charlotte, NC, USA

**Patients with ≥50% mean UI reduction after onabotulinumtoxinA treatment 1 had consistent mean UI reductions after all subsequent treatments**

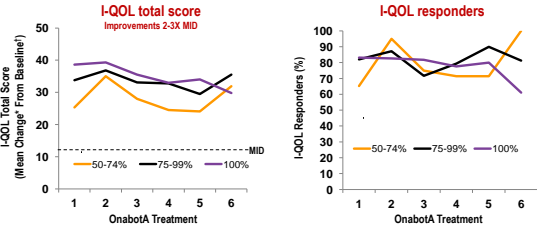
Denys P, Roger Dmochowski, Philip Aliotta, David Castro-Diaz, Bertil Blok, Karen Ethans, Manher Joshi, Quanhong Ni, Michael Kennelly  
EAU, Madrid, 2016



Tx1 Response	n (data available at week 6)					
	1	2	3	4	5	6
50-74%	23	20	17	12	8	5
75-99%	55	47	44	32	20	15
100%	84	73	61	47	34	19

\*Week 6 after each treatment.  
OnabotA = onabotulinumtoxinA; UI = urinary incontinence.

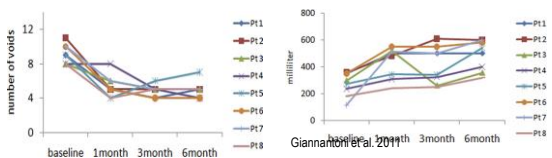
**Patients with ≥50% mean UI reduction after onabotulinumtoxinA treatment 1 also had consistent improvements in QOL after all subsequent treatments**



Tx1 Response	n (data available at week 6)					
	1	2	3	4	5	6
50-74%	23	20	16	14	7	5
75-99%	54	47	46	34	20	16
100%	82	75	60	49	35	18

\*Week 6 after each treatment. †Baseline is prior to receiving any treatment in the phase 3 studies for all patients entering the extension study.

**Botulinum toxin in MS & Parkinson's disease?**



**Questions to follow in MS/PD patients with NDO:**

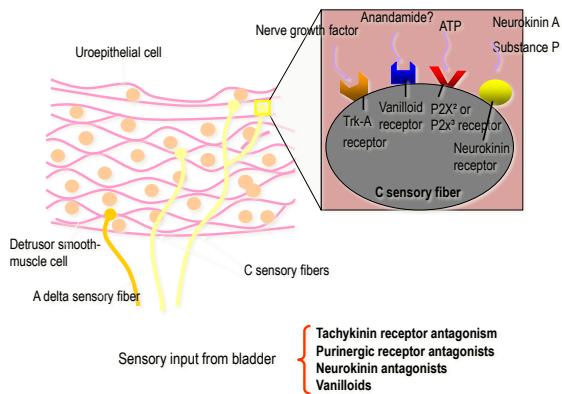
Is it possible to decrease OnabotA dose in MS/PD patients with less severe urinary incontinence and therefore decrease the risk of urinary retention / CIC?  
Study 117 (Onabot 100U vs PBO) funded by Allergan will enrol MS patients with ≥ 2 episodes / 3days



**Recommendations on the Use of Botulinum Toxin in the Treatment of Lower Urinary Tract Disorders and Pelvic Floor Dysfunctions: A European Consensus Report**

Apostolou Apostolida<sup>1,2</sup>, Prekar Dasgupta<sup>3</sup>, Pierre Denys<sup>4</sup>, Sohler Elnel<sup>5</sup>, Clare J Fowler<sup>6</sup>, Antonello Giannantoni<sup>7</sup>, Gilles Karzeny<sup>8</sup>, Heinrich Schulte-Buhlloh<sup>9</sup>, Brigitte Schurch<sup>10</sup>, Jean-Jacques Wyndaele<sup>11</sup>

NDOA	GR
Use BoNTA to treat refractory NDO in patients willing to use CISC	A
The aim of treatment is to improve QoL, urodynamic risk factors for renal impairment, or QoL in patients with spinal NDO	A
The diagnosis of NDO should follow the EAU guidelines	A
Patient should be told the treatment does not last indefinitely (8 mo)	A
Repeated treatment has been shown to be efficacious	B

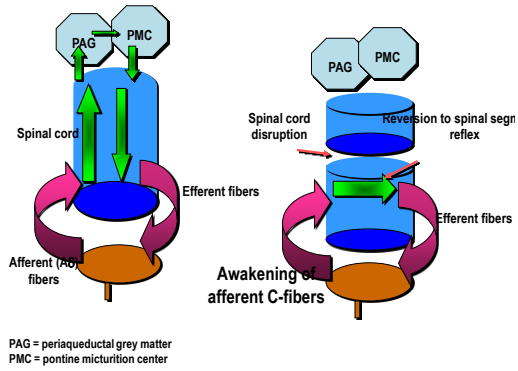


**U A D**

**Trigonal Injection of Botulinum Toxin-A Does Not Cause Vesicoureteral Reflux in Neurogenic Patients**

Frederico Mascarenhas<sup>1,2,3</sup>, Marcelo Cocuzza<sup>2</sup>, Cristiano Mendes Gomes<sup>2</sup>, and Nilo Leão<sup>3,4</sup>  
<sup>1</sup>Department of Urology, Hospital Santo Antonio das Obras Sociais Irmã Dulce, Bahia, Brazil  
<sup>2</sup>Department of Urology, University of Sao Paulo (USP), Sao Paulo, Brazil  
<sup>3</sup>Department of Urology, Federal University of Bahia (UFBA), Bahia, Brazil

**Aims:** We evaluated the effect of botulinum toxin type A (BTX-A) injections in the trigone on the antireflux mechanism and evaluated its short-term efficacy. **Materials and Methods:** Between April and December 2006, 21 patients (10 men and 11 women) were prospectively evaluated. All were incontinent due to refractory NDO and underwent detrusor injection of 300 units of BTX-A, including 50 units into the trigone. Baseline and postoperative evaluation after eight weeks included cystogram, urinary tract ultrasound and urodynamics. **Results:** At baseline, 20 patients had no vesicoureteral (VUR) and one had grade II unilateral VUR. Postoperative evaluation revealed no cases of de novo VUR and the patient with preinjection VUR had complete resolution of the reflux. Ultrasound showed 5 (23.8%) patients with hydronephrosis before BTX-A injection and only one (4.8%) at the follow-up evaluation (p=0.066). After treatment, 9 (42.8%) patients became dry, 11 (52.4%) were improved and one (4.8%) had no improvement. Improved patients received antimuscarinic treatment and 8 (38.1%) became dry, with a final total continence rate of 80.1%. Cystometric capacity increased from 271±92 to 390±189 ml (p=0.002), reflex volume varied from 241±96 to 323±201 ml (p=0.020) and maximum detrusor pressure reduced from 66±39 to 38±37 cm H<sub>2</sub>O (p<0.001). **Conclusions:** Our results confirm the safety of trigone injections of BTX-A in terms of development of VUR and upper urinary tract damage. Whether they are beneficial for patients with NDO or other causes of voiding dysfunction will need further studies. *NeuroUrol. Urodynam.* 27:311-314, 2008. © 2007 Wiley-Liss, Inc.

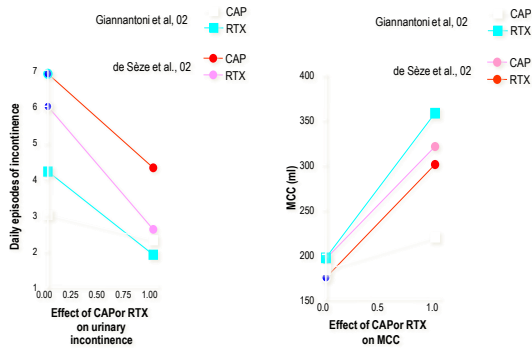


**Vanilloid Effect on C-fibers Neurons**

- Initially activates VR1 receptors
- (Excitation)
- Influx of Na<sup>+</sup> and Ca<sup>++</sup> nerves fire
- Release peptides (Sub-P, CGRP)
- Long-term (Desensitization)
- Inhibits release of peptides
- Neuronal terminal degeneration



**Comparative studies between CAP and RTX**

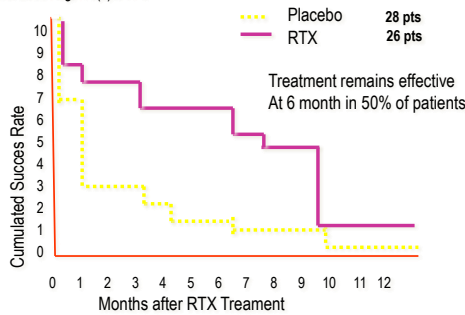


IOS Corp (under sublicense from Afferon Inc)

Phase I clinical trial in patients with UUI due to NVD  
 Found that patients experienced significant incontinence  
 Relief with no reported side effects  
 Phase II 1998 RPCT RTX 4 sites EU and USA  
 23% reduction in frequency  
 64% reduction in incontinence episodes  
 48% increase in bladder capacity, no side effects  
 Improvements last for 2-3 month

*Timari A Exp Opin Invest Drugs 2006*

Therapeutic effect of multiple resiniferatoxin intravesical instillations  
 In patients with refractory detrusor overactivity: a randomized, double-blind, placebo  
 controlled study  
 Kuo HC, Liu HT, Yang WC  
 J. Urol 2006 Aug;176(2):641-5



**Summary**

- OnabotulinumtoxinA has a dual mechanism of action at both efferent and afferent pathways
- Bladder Injections of 200 U of OnabotulinumtoxinA reduce urinary incontinence episodes, increase bladder capacity, decrease MDP and improve QoL of neurogenic patients
- Most common adverse events include UTI, need of IC & haematuria
- It is possible that some MS/PD patients voiding spontaneously can be managed with a lower dose decreasing risk of retention
- Capsaicin and Resiniferatoxin are also effective & safe in Neurogenic patients, unfortunately so far no Industry has been interested in manufacturing

# **BLADDER AUGMENTATION:WHEN, HOW AND THE FUTURE**

Bülent Çetinel MD

## **Summary**

Augmentation cystoplasty (AC) is still the gold standart surgical treatment of neurogenic bladder patients with refractory reduced compliance, small capacity and detrusor overactivity. Literature has been searched with regard to the indications, contraindications, technique, complications, and the tissue engineering approaches of AC.

The results have been discussed.

Although some important progress has been made in tissue engineering AC, conventional augmentation cystoplasty still has an important role in the surgical treatment of refractory neurogenic lower urinary tract dysfunction.

## **Introduction**

Bladder augmentation cystoplasty is used in the adult population for neurogenic bladder dysfunction, as well as for overactive bladder, inflammatory conditions such as tuberculosis cystitis that result in a severely contracted bladder, interstitial cystitis, and reconstruction of iatrogenic bladder injury (1).

Augmentation cystoplasty can be frequently performed by using several bowel segment which is called augmentation enterocystoplasty. The most widely used bowel segment for AC is a detubularised patch of ileum (2). Augmentation enterocystoplasty is a procedure with long-term durability and high rates of patient satisfaction but not without risk of complications and potential increased risk of malignancy (3,4).

Recent studies demonstrated that the use of bladder augmentation procedures has been declining in the UK and the USA (2,5). Although the exact cause for this decline was unknown and likely to be multifactorial, potential reasons might be high risk of complications, potential increased risk of malignancy, newer interventions such as sacral neuromodulation and intradetrusor botulinum toxin injection therapy, increased availability and earlier use of anticholinergics and clean intermittent catheterization (2,5).

Editorial comment on the study of Sclomer BJ et al asked a critical question 'whether this declining trend was beneficial by decreasing the risk of AC related complications, or were the urologists delaying an inevitable operation or risking irreversible upper tract damage' (5,6).

This review aims to update the indications, techniques, complications, and the future of AC.

## **History**

After the first publication of canine model of AC by Tizzoni and Foggi in 1888, von Mikulicz described its first use in humans in 1889 (2). After the introduction of clean intermittent self catheterisation (CISC) by Lapidus, AC became more widely used (7). The first use of the gastric segment for bladder augmentation in humans was reported by Leong in 1978 (8). Apart from bowel segments and stomach other natural tissues such as free fascial grafts, peritoneum, omentum, lyophilised human dura, skin, and pericardium, materials such as gelatin, sponge, teflon, polyvinyl sponge, resin coated paper, collagen/polyglactin membrane and silastic were used with dissappointing results (2).

## **Indications of Augmentation Cystoplasty**

International Consultation on Incontinence in 2012 stated that bladder augmentation was indicated wherever bladder capacity and compliance was reduced, or in the event of detrusor



overactivity, when all conservative treatments (medical treatments, detrusor injections of botulinum toxin and/or neuromodulation of posterior sacral roots) have failed (9).

EAU guidelines on Neurourology declared that bladder augmentation was a valid option to decrease detrusor pressure and increase bladder capacity, whenever more conservative approaches have failed (10).

Bladder augmentation was found to be beneficial in such patients especially with underlying neurological disorders such as spinal cord injury, multiple sclerosis and myelodysplasia (11,12,13,14,15).

### **Contraindications**

Inflammatory and congenital bowel disease (Crohn's disease, congenital anomalies such as cloacal exstrophy, and radiotherapy induced enteritis), or conditions resulting in short bowel (wide bowel resections), and malignant bladder disease constitute contraindications for augmentation cystoplasty (2). Inability to perform CISC because of reduced manual dexterity or cognitive function is a relative contraindication for AC (15).

### **Technique**

Various augmentation techniques using different gastrointestinal tract (GIT) segments, and the alternatives to GIT have been described.

#### *Use of gastrointestinal segments*

Augmentation cystoplasty can be performed by using several bowel segment which is called augmentation enterocystoplasty. The most widely used bowel segment for AC is a detubularised patch of ileum (2,14). When ileum is not convenient for augmentation because of short ileal mesentery and obvious ileal pathology, sigmoid colon is the most common alternative to ileum (2,14). The caecum can be used in its original tubular shape or as a detubularised patch which is called augmentation caecocystoplasty. Where bowel is unavailable or unsuitable, and in patients with metabolic acidosis, stomach is an alternative to bowel, and this procedure is called augmentation gastrocystoplasty (2,8). Recently there has been an increase in reports of malignancy associated specifically with gastrocystoplasty (2,16). Recent increase in the incidence of malignancy, complications of the haematuria-dysuria syndrome, and high incidence of reoperations has reduced the use of stomach for augmentation (2,16).

#### *Alternatives to GIS*

There are alternatives to gastrointestinal flaps for augmentation cystoplasty such as autoaugmentation and ureterocystoplasty. Autoaugmentation was first described by Cartwright, and Snow who reported their series in children with neurogenic voiding dysfunction. The authors resected detrusor muscle off the bladder to create a low-pressure bladder diverticulum (17). Most of the published series of autoaugmentation consist of children, and the results are generally poor (9). The technique of extensive detrusorectomy with rectus muscle hitch and backing to prevent shrinkage and retraction was described (18,19).

When there is pre-existing dilated ureter, ureterocystoplasty may be an option for augmentation mainly for children with neurogenic bladder (9). A study reporting the long term follow-up results associated with the bladder capacity and compliance demonstrated that 24% of the patients required revision surgery with ileocystoplasty for poorly compliant bladders (20).

International Consultation on Incontinence (ICI) in 2012 stated that any segment of the gastrointestinal tract except jejunum might be used for bladder augmentation, while the ileum seemed to give the best results in terms of ease, risk of complications and efficacy, and recommended its use with grade (B)(9). Detrusor myomectomy (autoaugmentation) was not recommended in neurological patients with impaired bladder function by ICI (Grade D)(9).

#### *Technique*

Classically, AC is performed as an open abdominal operation with coronal or sagittal bi-valving of the bladder down to the level of the ureteric orifices, with anastomosis of a detubularised segment of bowel onto the native bladder (2,21).

When the bladder wall is very fibrous and thickened supratrigonal cystectomy should be performed, since otherwise exclusion of the ileal patch may occur (9).

#### *Ureteric reimplantation*

High pressures generated by the neurogenic bladder may result in vesicoureteral reflux (VUR) and may contribute to renal deterioration. Augmentation cystoplasty lowers intravesical pressure and increases bladder compliance during the storage phase, so generally in most of the cases, VUR resolves or improves after AC making an anti-reflux procedure unnecessary (2,14,22).

It was demonstrated that ureteric reimplantation during cystoplasty in children with neurogenic bladder might be required as VUR can persist after bladder augmentation without reimplantation, and be associated with febrile UTI and upper tract scarring (23). International Consultation on Incontinence in 2012 stated that bladder augmentation might resolve low grade VUR, while it recommended ureteric reimplantation in the case of grade 4 or 5 VUR with grade C level (9).

Several techniques such as seromuscular enterocystoplasty and reversed seromuscular ileocystoplasty have been tried both clinically and experimentally to reduce the reabsorption of urine from the intestinal mucosa. These techniques did not gain widespread use (9).

### **Complications (early and long term complications)**

#### ***Early complications***

The mortality rate from AC was reported to be 0–3.2% (2,9). The most frequently reported early complication was prolonged post-operative ileus (9). Transient urinary fistula (0.4–4%), wound infection (5–6.4%), bleeding requiring re-operation (0–3%), and thrombo-embolic complications (1–3%) consist of early complications (2,9,24).

#### ***Long-term complications***

##### *Metabolic complications*

Reabsorption of and secretion of bicarbonate by the bowel segment resulted in acid-base and electrolyte disturbance nearly in all patients with enterocystoplasty, but this complication was not found to be clinically important in majority of the cases (2,9,24). Varying degrees of villous atrophy in the mucosa of augmented ileal segments has been shown (25). These changes may explain the limited acid-base and electrolyte disturbance in these patients. However, clinician must be careful when operating patients with low creatinine clearance levels, since metabolic acidosis is no longer compensated (9). Since the colon patch secretes potassium into the urine, colcystoplasty may be occasionally associated with hypokalaemia (2). Gastrocystoplasty was found to be associated with hypochloremic hyponatraemic alkalosis in nearly 7% of the patients because of hydrochloric acid secretion by the gastric patch (26). Haematuria-dysuria syndrome, peptic ulceration of the bladder, and perforation of the gastric segment are the other complications of gastrocystoplasty due to hydrochloric acid secretion by the gastric patch (2,9).

##### *Diverticulisation of the intestinal patch*

Inadequate bi-valving of the bladder may result in the diverticulisation of the intestinal patch, and surgical revision of the augmentation may be required (27).

##### *Urinary stone formation after augmentation*

The formation of urinary tract stones, especially bladder stones, is a common complication of cystoplasty and occurs in 3–40% (2). Some factors such as bacterial cystitis with urease-producing bacteria ( *Proteus* , *Klebsiella* ), intravesical foreign bodies (staples,

nonabsorbable sutures), excess mucus production, and hypocitraturia may play a role in stone formation (2).

Lower quantity of mucus production, and urinary pH, and the lower incidence of bacteriuria may result in lower incidence of urinary tract stones (28,29)

#### *The risk of malignancy*

The general consensus is that the risk of malignancy is higher in augmented patients than in general population but still there remains controversy as to whether enterocystoplasty is an independent risk factor for cancer development (9,30,31). The incidence of malignancy after augmentation is low and range from 1 to 4.6% (9). Most of the published cases are adenocarcinomas located at the junction of intestinal and bladder mucosa. These tumors have long latency period after augmentation (over 10 years in most cases) (9). Urinary stasis, bacterial conversion of urinary nitrates to nitrosamines, infection, bladder calculi, are the proposed risk factors for the development of malignancy

(30,32,33). Traditionally, malignancy incidence after gastrocystoplasty was found to be generally lower than after enterocystoplasty. However, recent studies report an increased incidence of malignancy associated specifically with gastrocystoplasty (16,34).

It was suggested to perform cystoscopy with or without biopsy and urinary tract imaging in the symptomatic patient with haematuria, suprapubic pain, and recurrent or unexplained UTIs (35).

Due to the risk of complications, International Consultation on Incontinence in 2012 recommended regular follow up for patients with augmentation cystoplasties with grade B (9).

#### *Perforation*

The most serious and life threatening complication is cystoplasty perforation with a reported incidence of 0.8-13%, and with some reporting mortality rates of up to 25% (2,9). Perforation usually occurs on the graft or at the junction of the bladder with the bowel, and often results from the high pressures within the enterocystoplasty, or rarely from traumatic catheterization or urodynamic investigations (9).

#### *Bowel disturbance*

Resection of the large segments of terminal ileum may result in bile acid and fat malabsorption with consequent steatorrhoea and diarrhoea (36). Furthermore this may expose the patients to a vitamin B12 deficiency with possible onset of megaloblastic anemia(37). The use of ileocecal valve and terminal ileum should be avoided to prevent this complication. Since the use of terminal ileum was avoided, and generally small bowel segments less than 50 cm was used in augmentation enterocystoplasty, clinically overt vitamin B12 deficiency is rare after augmentation cystoplasty (9).

Bowel disturbances after augmentation have been reported in 18–54% of the patients (38,39,40). It has been demonstrated that this high rate of intestinal transit disorder after augmentation resulted in nearly 10% of the patients to regret having undergone augmentation surgery (41).

#### *Urologic surgery after augmentation cystoplasty*

A recent retrospective, population based cohort study using administrative data records of adults who underwent enterocystoplasty between 1993 and 2009, identified 243 patients, of whom 61% had a neurogenic bladder, 20% had a simultaneous incontinence procedure and 18% underwent creation of a catheterizable channel (3). This study concluded that repeat urological surgery was common after enterocystoplasty. Patients who had a simultaneous incontinence procedure at enterocystoplasty were more likely to require future surgery, and patients with catheterizable channels were at significant risk for future cystolitholapaxy (3). A large retrospective cohort of children who underwent AC identified 2831 patients. Ten-year

cumulative incidences of cystolithopaxy and reaugmentation were found to be in the ranges of 13.3-35.1%), and 5.2-13.4% respectively (4).

### **Functional outcome of augmentation cystoplasty**

International Consultation on Incontinence (ICI) in 2012 concluded that all series of patients undergoing augmentation cystoplasty for neurogenic bladder reported an improvement in bladder capacity. More than 90% of patients achieved nocturnal and diurnal continence with high satisfaction rates (9). Recent retrospective study demonstrated that protection of renal function, adequate bladder capacity and low detrusor pressure could be achieved using supratrigonal cystectomy and augmentation ileocystoplasty in patients suffering from refractory neurogenic lower urinary tract dysfunction (42).

### **Concomitant procedures**

Surgical correction of concomitant urethral sphincteric deficiency is usually required if demonstrated pre-operatively in patients with neurogenic bladder (2,14,15). Several surgical treatment alternatives such as artificial urinary sphincter (AUS) implantation, conventional, and midurethral tension free slings are available to treat co-existing urodynamic stress urinary incontinence (SUI). (2,14,15). These procedures can be performed concomitantly with AC, or after AC if urinary incontinence persists (14). Closure of the bladder outlet may be performed if above mentioned procedures to manage sphincteric deficiency have failed. On this occasion continent catheterisable stoma using the Mitrofanoff principle must be added to AC for urinary drainage. Closure of bladder outlet in patients with neurogenic bladder, and especially in female patients seemed to be a challenging surgical reconstruction. A single operation did not usually solve all the problems but persistence did almost always result in continence (43). International Consultation on Incontinence (ICI) in 2012 recommended bladder outlet closure to patients who had persistent neurogenic stress incontinence after the other alternatives of sphincter enhancing procedures (Grade B) (9). Good results of concomitant insertion of an AUS cuff only with AC was reported in patients with neurogenic bladder who appeared to need both procedures. The authors deferred insertion of the remaining AUS components at a second procedure if incontinence persisted (24).

If for any reason a patient with neurogenic bladder who appear to need AC, is not able to perform transurethral clean intermittent catheterization, augmentation with stoma using Mitrofanoff or Monti channel may be required (14,15).

### **Kidney Transplantation, and Bladder Augmentation**

A low-pressure, good capacity, and compliant bladder is a prerequisite for a favourable outcome from renal transplantation. Otherwise graft failure will occur due to high-pressures inside the bladder. In patients with neurogenic bladder who have high pressure bladders during filling, and resultant end stage renal failure renal transplantation must be performed in conjunction with bladder augmentation. However the timing of AC in combination with renal transplantation remains controversial. AC before transplantation aims to avoid complications of systemic infection and delayed wound healing associated with immunosuppression (44,45,46). On the other hand AC after transplantation avoids the rare complication of pyocystitis secondary to an under-filled bladder (2). Little statistical difference has been found in terms of acute or chronic rejection between the groups (45).

The concern with cystoplasty in patients with kidney transplantation is the increased risk of UTI in these immunosuppressed patients, which could lead to urosepsis and ultimately graft rejection (2).

### **Pregnancy and Augmentation**

Vaginal delivery should be recommended to women with AC. Caesarean section should be reserved for obstetric indication only, to avoid possible injury to the pedicle of the augmenting bowel preferably with the involvement of an urologist (2). Elective caesarean

section should be offered to those women with an AC in conjunction with bladder outlet procedure, to avoid pressure and ischaemic damage to the continence mechanism during vaginal delivery (47). On the other hand, Creag TH et al demonstrated that vaginal delivery has also been proven safe in this subset of patients (48).

Close monitorization of women with AC and pregnancy was proposed because of higher rates of complications, including UTI, upper tract obstruction requiring intervention, and pre-eclampsia (49). On the other hand, pregnancy has not been found to have any long-term deleterious effect on renal function and AC despite higher rates of complications (49).

### **Future**

Even if augmentation cystoplasty is currently considered as the gold standard surgical treatment in refractory neurogenic detrusor overactivity, it is associated with serious complications such as bowel and, metabolic disturbances, urolithiasis, cystoplasty perforation and malignant diseases. To avoid these complications new therapeutic alternatives such as tissue engineering approaches are needed (50). After considerable experience derived from preclinical bladder reconstruction studies using tissue engineering by use of biomaterials supplemented with cells and/or growth factors, some clinical studies of AC using tissue engineering have been reported (51).

Bladder tissue engineering uses biomaterials (scaffolds) classified as biological or synthetic (50). Biological scaffolds are described in the two sections as naturally derived biomaterials (collagen and alginate), and acellular tissue matrices (bladder submucosa, small intestine submucosa (SIS), derma, bladder and gallbladder) usually extracted from pigs. Synthetic scaffolds comprise several materials, such as polyvinyl sponges, teflon, vicryl (polyglycolic acid, PGA) matrices, silicone and silk derivatives. Given the contrasting findings of biological and synthetic scaffold implantation, some authors suggested the use of cell adjunction (seeding) from several sources (autologous cells, stem cells, human cell reprogramming ) to improve bladder tissue regeneration and functional outcomes in bladder tissue engineering (50)

Very recent systematic review of the preclinical tissue engineering bladder reconstruction studies found that scaffolds with seeding did not result in a better bladder volume than acellular constructs (51). In fact, this systematic review showed a slight decrease in bladder volumes in the group with cellular constructs.

Furthermore this systematic review concluded that preclinical research in healthy animals appeared to show the feasibility of bladder augmentation by tissue engineering. The authors also stated that in view of the disappointing clinical results based on healthy animal models new approaches should also be evaluated in preclinical models using dysfunctional/diseased bladders (51).

In the first clinical study concerning AC by use of autologous cell seeded collagen or composite collagen-polyglycolic acid scaffold in 7 young patients with myelomeningocele, Atala et al concluded that engineered bladder tissues wrapped in omentum after implantation, could be used in patients who need cystoplasty (52). On the other hand in a recent clinical phase II prospective study in 10 children with refractory neurogenic bladder due to spina bifida, autologous cell seeded biodegradable scaffold was used for bladder augmentation, and the results were disappointing. The authors concluded that autologous cell seeded biodegradable scaffold did not improve bladder compliance or capacity, and serious adverse events surpassed an acceptable safety standard (53). Actually, when we had a closer look to the results of Atala et al, it was evident that all patients except one had hypocompliance even after tissue engineered cystoplasty (52).

The bladder is a complex organ particularly because of its sophisticated innervation, and specific storage (good compliance (elasticity) in association with volume ) and emptying

functions (good and sufficient contractility). Although at present bladder tissue engineering is far away from achieving these functions, it might become a reality in the future (51).

### Conclusions

Bladder augmentation is indicated whenever bladder capacity and compliance was reduced, or in the event of detrusor overactivity, when all conservative and minimally invasive treatments have failed. Inflammatory and congenital bowel diseases, conditions resulting in short bowel, and malignant bladder disease constitute contraindications for augmentation cystoplasty. Various augmentation techniques using different gastrointestinal tract (GIT) segments, and the alternatives to GIT have been described. The most widely used bowel segment for AC is a detubularised patch of ileum. Although many complications such as metabolic disturbances, perforation, increased risk of malignancy, and urinary stone formation could be seen after AC, all series of patients undergoing augmentation cystoplasty for neurogenic bladder reported an improvement in bladder capacity. Several adjunctive surgical treatment alternatives are available to treat co-existing SUI. Augmentation with stoma using Mitrofanoff or Monti channel may be required in patients who are not able to perform transurethral CIC. To avoid these complications new therapeutic alternatives such as tissue engineering approaches are needed. Although at present bladder tissue engineering is far away from achieving normal storage and emptying functions of micturition, it might become a reality in the future

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## Surgery to improve bladder outlet

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	Filling	Voiding
Bladder	Normal Overactive Idiopathic Neurogenic	Normal Underactive Acontractile
Urethra	Normal Incompetent	Normal Obstructive } Overactive Mechanical

Incontinence, retention, poor voiding

- Complications**
- Infection
  - Lithiasis
  - Neoplasm
  - Reflux
  - Renal insufficiency

## Surgery to improve bladder outlet

A) Failure to empty

Surgery to decrease outlet resistance  
 (Sphincterotomy, stents, botulinum-A toxin)

B) Failure to store

Surgery to increase sphincteric resistance  
 (Bulking agents, slings, artificial sphincter)

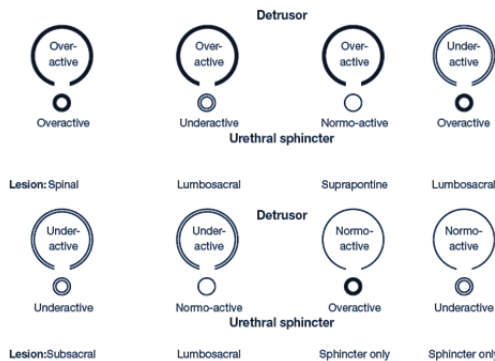
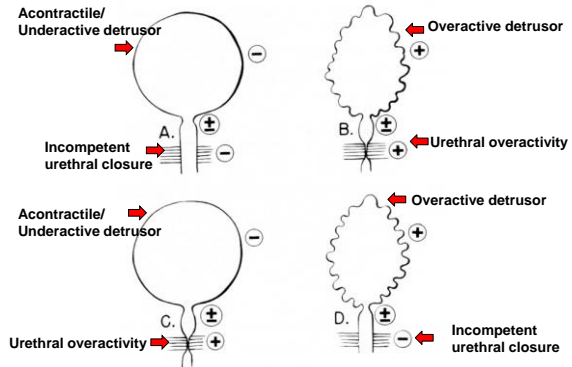


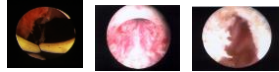
Figure 2.1. Madersbacher classification system (107,122) with typical neurogenic lesions

M. Stöhrer, D. Castro-Diaz, E. Chartier-Kastler, G. Del Popolo, G. Kramer, J. Pannek, P. Radziszewski, J.-J. Wyndaele

Guidelines on Neurogenic Lower Urinary Tract Dysfunction



## •Sphincterotomy



Main goal: To reduce intravesical pressure

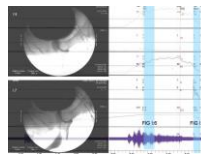
Indications: Difficulties for intermittent catheterization  
Inadequate bladder drainage resulting in UUT damage

- Following a successful sphincterotomy an improvement on bladder function and stabilization of the upper tract can be expected in 70-90% of patients
- Complications include: bleeding, clot retention, urethral stricture, impotence, reoperation (30-60%)
- Laser / vaporization sphincterotomy seems to produce lower complications rate

## Relieving obstruction in NDO + DSD?

Sphincterotomy  
Urethral stenting

- Good long term urodynamic results
- Significant reduction of Pdet
- Stent complications may arise
- Recurrent sphincterdyssynergia is possible
  - Urodynamic FU



Hamid R et al. BJU 2003  
Mehta SS et al. Spinal Cord 2006



Incrustations & Stone formation  
Urethrocutaneous fistula

van der Merwe A 2012

## BoNT/A injections in the urethral sphincter

n = 68	100-200 U	Before treat	After treat	p value
Retention requiring catheterization		41	7	
Postvoid residual urine volume (ml)		240	88	0.01
Maximal voiding pressure (cm H2O)		81	52	0.01
Maximal cystometric capacity (ml)		198	241	ns
Stress Urinary incontinence		2	3	

Smith et al, Urology, 2005

## Sphincter injection technique

Dilute 200 units BoNT-A with 4 ml saline  
Men: transurethral injections in the striated sphincter (25-G Williams needle at the 3, 6, 9 and 12 o'clocks  
Flush with 0.3 ml of saline to not waste any toxin in needle

Dilute 100-200 units BoNT-A with 4 ml saline  
Women: periurethral injection using a 22-G spinal needle at 3, 6, 9 and 12 o'clock  
Depth 2cm and approximately 5-10 mm parallel to urethra

## SPHINCTERIC STENT VERSUS EXTERNAL SPHINCTEROTOMY IN SPINAL CORD INJURED MEN: PROSPECTIVE RANDOMIZED MULTICENTER TRIAL

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### ABSTRACT

**Purpose:** In a prospective randomized multicenter trial we compared the treatment results of conventional external sphincterotomy with those of UroLume sphincteric stent prosthesis placement in men with spinal cord injury and external detrusor-sphincter dyssynergia.  
**Materials and Methods:** We randomized 57 men with spinal cord injury in whom urodynamics verified external detrusor-sphincter dyssynergia into 2 groups to undergo either sphincter defating procedure. We compared the primary urodynamic parameter of maximum detrusor pressure, and secondary urodynamic parameters of bladder capacity and post-void residual urine volume in men who underwent sphincterotomy or sphincteric stent placement. Parameters were measured preoperatively, and 3, 6, 12 and 24 months postoperatively. Patients completed questionnaires regarding voiding sensation and quality of life issues at each followup visit.  
**Results:** Demographic data of the 56 patients treated with sphincterotomy and the 31 treated with sphincteric stent placement were statistically similar. Preoperatively mean maximum detrusor pressure plus or minus standard deviation in sphincterotomy and stent cases was 98.2 ± 27.6 and 95.7 ± 27.7 cm. water, respectively (p = 0.73). At 12 months mean maximum detrusor pressure decreased to 48.9 ± 16.4 and 52.6 ± 31 cm. water in the sphincterotomy and stent groups, respectively (p = 0). Preoperatively mean bladder capacity in sphincterotomy and stent cases was 245 ± 158 and 251 ± 145 ml, respectively (p = 0.87). Bladder capacity did not change significantly in either treatment group throughout followup. Preoperatively mean post-void residual urine volume in the sphincterotomy and stent groups was 212 ± 163 and 168 ± 114 ml, respectively (p = 0.33). Residual urine volume decreased in each group at some but not all followup evaluations. The duration of hospitalization was greater for sphincterotomy than stenting (p = 0.038). Six stents required explantation.  
**Conclusions:** The UroLume stent is as effective as conventional external sphincterotomy for treating external detrusor-sphincter dyssynergia. However, sphincteric stent placement is advantageous because it involves shorter hospitalization and is potentially reversible.

### Conclusions

- Similar outcomes on both groups
- Shorter hospitalization with stents

## Botulinum toxin injections for DSD

Author	N	Success
'88 Dijkstra	10	64-91%
'90 Dijkstra	5	100%
'96 Schurch	24	88%
'99 Schurch	6	100%
'99 Schurch	10	95%
'98 Petit	17	71%
02 De Seze	13	100%
05 Gallien**	86	0%

Adapted from Sahai et al. NeuroUrol Urolyn 2005

\*\* placebo controlled, randomized, double blind, multicenter study

- For female retention
  - No effect (Fowler 1992)
- For voiding dysfunction
  - Success in 67-95% (Phelan 2001, Kuo 2003)

## BoNT-A for DSD Why Use It

- Unmet medical need  
Medication: Alpha blocker, muscle Relaxant  
Catheter: Clean cath or indwelling  
Sphincter ablation: sphincterotomy and stent (men only)
- Neurorecovery is main theme in SCI medicine (avoid irreversible procedures)
- Non-neurogenic voiding dysfunction  
Sacral neuromodulation is only alternative

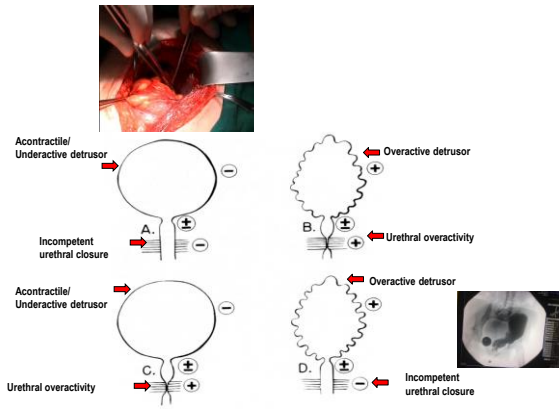
## Surgery to improve bladder outlet

### A) Failure to empty

Surgery to decrease outlet resistance  
(Sphincterotomy, stents, botulinum-A toxin)

### B) Failure to store

Surgery to increase sphincteric resistance  
(Bulking agents, slings, artificial sphincter)



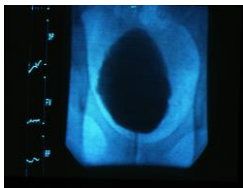
### Evaluation of Intrinsically Incompetent Sphincter

- Boney Test
- Q-Tip Test
- Maximum urethral closing pressure
- Leak Point Pressure
- EMG
- Videourodynamics

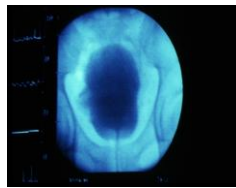


### Bladder Augmentation in Women with Neurogenic Bladder

Is there evidence of concomitant SUI?

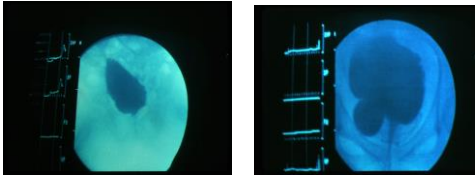


Detrusor overactivity + High LPP

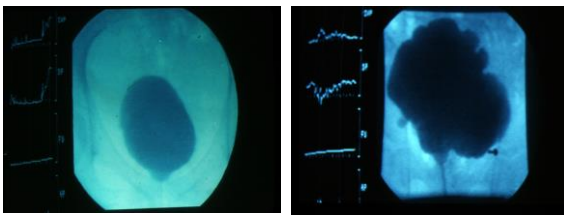
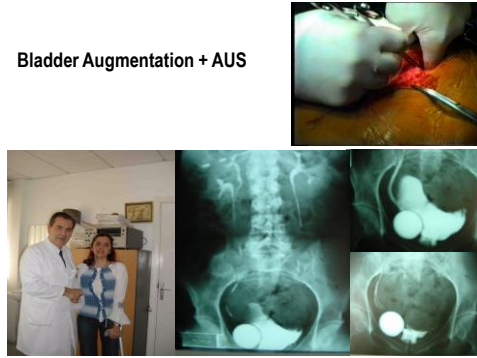


Bladder Augmentation

Clam cystoplasty + AUS-800 implantation

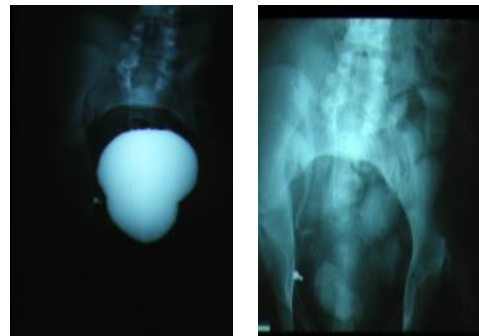


Bladder Augmentation + AUS



Detrusor overactivity + LPP ?

Bladder Augmentation + Cuff

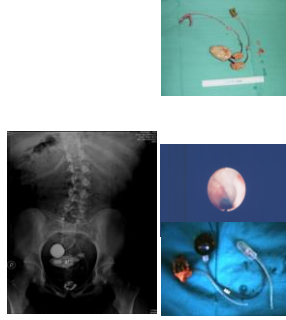


## Artificial Urinary Sphincter

### Complications

- Erosion
- infection
- Malfunctioning
- Incontinence
- Upper tract damage

Continence rate = 70-93%  
Reoperation rate = 35%-54%



## Surgery to increase sphincteric resistance

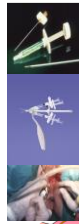
### Slings

- Many reports communicating the success of pubovaginal slings for female neuropathic patients
  - Need of Intermittent catheterization
  - High continence rate
  - Few complications including difficulty with catheterization, ventral hernia at the graft harvest site, bladder calculus
  - detrusor overactivity
  - Erosion is more frequent with heterologous materials
  - Role of synthetic MUS ? To be determined!
- Hamid R 2003—11 patients  
Patki P 2008—9 patients in combination with BTX-A  
Abdul-Rahman A-& Hamid R 2010—12 patients



## Bulking agents for NVD = No data

- Not for primary treatment ?
  - Salvage procedure after failed sling?
  - Literature
    - Mostly Company driven
    - Heterogeneous populations
    - No comparative studies
      - Should be compared to pelvic floor therapy?
      - Should be compared to sling surgery?
- 60% dry



NVD

## Surgical Treatment of Neurogenic Stress Urinary Incontinence: A Systematic Review of Quality Assessment and Surgical Outcomes

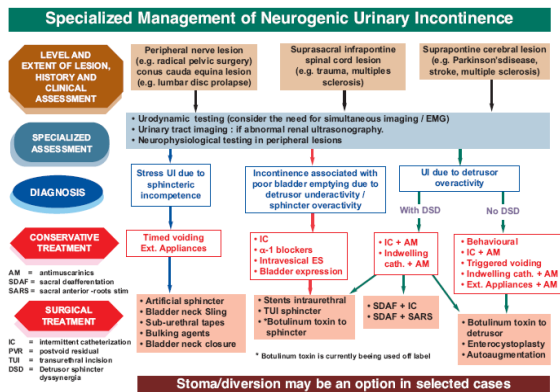
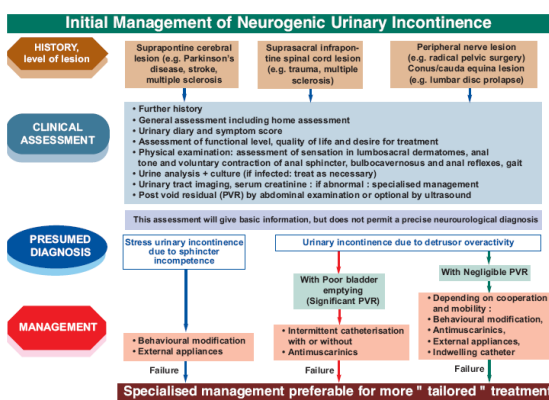
Fawzy Farag,<sup>1,2</sup> Martin Koenigs,<sup>3</sup> Karl-Dietrich Sievert,<sup>3</sup> Dirk De Ridder,<sup>4</sup> Wout Feitz,<sup>1</sup> and John Heesakkers<sup>1</sup>  
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<sup>3</sup>Department of Urology, University of Tuebingen, Tuebingen, Germany  
<sup>4</sup>Department of Urology, UZ Leuven, Leuven, Belgium


Neurourology and Urodynamic

27 patients failing fascial sling  
Bladder neck injection after failure of primary sling procedures has limited value in patients with neurogenic lower urinary tract dysfunction. Repeat bladder neck injection yields no additional benefits. De Vocht J Urol 2010



Better outcome in children . Alova 2012





**Management of UTI's in neurogenic patients**  
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 Academic hospital Pitié-Salpêtrière, AP-HP, Paris, France  
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 Rehabilitation center, Garches, AP-HP, Garches, France

ICS 2015  
 Montreal

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**Objectives**

- Overview of the general discussion about urinary infection in the neuropath
  - Urinary contamination
  - definition
- How to deal with the main clinical situation
  - Self catheterisation
  - Urinary diversion
- Is urinary infection a infectious proble or a neurouroloigical problem?

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**UTI in neurogenic patients**

- Probably first or second cause of death in the SCI population
  - Soden et al (2000). Spinal Cord; De Vivo (1993) Arch Phys Med
- First cause of rehospitalization : 43% for tetraplegic patients
  - Vaidyanathan S. Spinal cord, 1998,36:838-46

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**UTI in neurogenic patients**

- 80 % were treated for symptomatic UTI five years after injury
  - Biering-sorensen et al (1999). Scand Urol Nephrol 33: 157-161
- 34 % of patients with SCI suffered of pyelonephritis after 29 yrs of follow-up
  - Ku 2005 Urol Res
- Few data in MS patients but primary discharge diagnosis in MS older than 65 yrs
  - Fleming ST (1994) J Clin Epidemiol

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**Definition of UTI: Which criteria?**

- Various biological and clinical criteria used in the litterature
- Symptoms are not specific (leakage, dysuria, chills, spasticity, autonomic dysreflexia....)
- Asymptomatic Bacteriuria is frequent in this population
- No consensus on the criteria in the litterature

Prevention and Management of Urinary Tract Infections in Paralyzed Persons  
 Agency for Health Care Policy and Research 1999

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**Population are not comparable**

- Disease
- Sex, age
- Type of voiding management
  - from indwelling caths, CIC, to reflex micturition
- Association to immunosuppressive drugs (MS patients)
- Risk for upper urinary tract
- Acute SCI vs non acute SCI patients
- Bladder management

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### And ...

- High number of patients with multidrug resistant bacterial isolated in this population
- 33% of species isolated from 766 samples. More frequent in young male patients with condoms and indwelling catheters
  - WAITES KB Arch Phys Med 2000



### Management of bacteriuria

- **Very strong consensus for not treating patients with bacteriuria without symptoms**
  - very high level of asymptomatic bacteriuria
  - Bakke 1997 BJU Waites 1993 Arch Phys Med
- **Except for invasive urologic procedures such as urodynamics, cystoscopy**
  - Esclarin de Ruz 2000 J Urol, Darouiche J Hosp Infect 1994
- No consensus for MS patients under immunosuppressive drugs except for medicolegal issues



### A innovative multidisciplinary concept

Journal of Antimicrobial Chemotherapy  
doi:10.1093/jac/dk010


JAC

**Prevention of urinary tract infection in spinal cord-injured patients: safety and efficacy of a weekly oral cyclic antibiotic (WOCA) programme with a 2 year follow-up—an observational prospective study**

Jérôme Salomon<sup>1</sup>, Pierre Denys<sup>2</sup>, Corinne Merle<sup>1</sup>, Emmanuel Chartier-Kastler<sup>2</sup>,  
Christian Perronne<sup>1</sup>, Jean-Louis Gaillard<sup>3</sup> and Louis Bernard<sup>1\*</sup>

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Received 17 August 2005; returned 20 September 2005; revised 13 December 2005; accepted 27 December 2005



Inclusion criteria

Patients >18 years old  
Spinal cord injury with controlled neurological bladder activity  
Self-clean intermittent catheterization (5/day)  
Frequent UTI

∪

At inclusion

Complete medical history, including allergy  
Hospitalization (number, length)  
UTI (severity, number, type)  
Antibiotic therapy (number, length, type)  
Analysis of weekly urine sample culture for 6 weeks  
Testing for MDR bacteria in anal and urine samples

∪

Antibiotic cycling choice

According to allergy and antimicrobial susceptibility  
2 antibiotics (A, B): a heavy dose once weekly  
Week A: antibiotic A  
Week B: antibiotic B  
Trimethoprim/sulfamethoxazole (TMP) 320-1600 mg or  
Cefixime (CFX) 400 mg or  
Fosfomicin trometamol (FSF) 6000 mg or  
Nitrofurantoin (NTF) 300 mg or  
Amoxicillin (AMX) 3000 mg  
Gram-negative bacteria: TMP or CFX or NTF or FSF  
Gram-positive bacteria: FSF or AMX

∪

Follow-up under WOCA

Clinical: efficiency, UTI, hospitalization, antibiotic courses, allergy and tolerance  
Bacteriological: urine sample culture, modification of ecology, MDR bacteria.

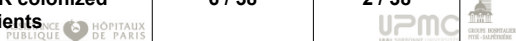
∪

WOCA unchanged or modified




### Results

Variables	Before WOCA	Under WOCA	p
UTI /year/person	9.4	1.8	0.0002
Severe UTI /year/person	0.74	0.31	0.04
Hospitalization /year/person	0.23	0.09	0.0012
Broad spectrum ATB	77 %	12 %	0.0001
MDR colonized patients	6 / 38	2 / 38	



### Ideal treatment goals of symptomatic UTI

- Better treatment of symptoms
- Lower rate of relapse
- Lower rate of reinfection
- And lower rate of resistance



### Antibiotic therapy for patients with symptomatic infections

- Criteria for treatment remain unclear
- Few interventional studies
- Duration of treatment
  - One study 3 vs 14 days ciprofloxacin 250 mgr BID
  - Better biological relapse and symptomatic relapse at Week 6 with 14 days
  - But reinfection rate with another species is the same in the two groups (Dow G CID 2004)
  - 14 days of norfloxacin induced 16% of resistance Waites KB 1991 Urology
- But what about 5, 7, 10 days and with other antibiotics ?
- Recommendations for non neurogenic 3 = 7 days for symptoms longer duration is better for bacteriological cure Cochrane Data base 2006

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### Antibiotic treatment for symptomatic UTI

- Unclear strategy symptomatic UTI, prostatitis and pyelonephritis
- Duration of treatment undefined clearly
- Diagnosis of acute prostatitis vs pyelonephritis remains uncertain (K Everaert Spinal Cord 1998) in case of fever despite the value of PSA
- But information and algorithm of treatment is clearly requested for patients and GP because
  - A lot of variation even in the same country Bycroft NeuroUrol 2004
  - Information may reduce UTI in the population of SCI patients Carstens J Spinal Cord Med 2004
  - Urological follow up is crucial in ensuring that adequate bladder drainage is achieved avoiding indwelling catheters

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### Key messages

- Voiding management and bladder control are key points for urinary tract prevention in neurogenic patients
- Presence of bacteriuria does not mean infection:
  - Definition has to take into account general symptoms and presence/absence of general signs of infection (fever?)
- If a treatment has to be used, WOCA or similar program have to be promoted
- As a GP practice, strong efforts have to be made to promote a well balanced information on this topic

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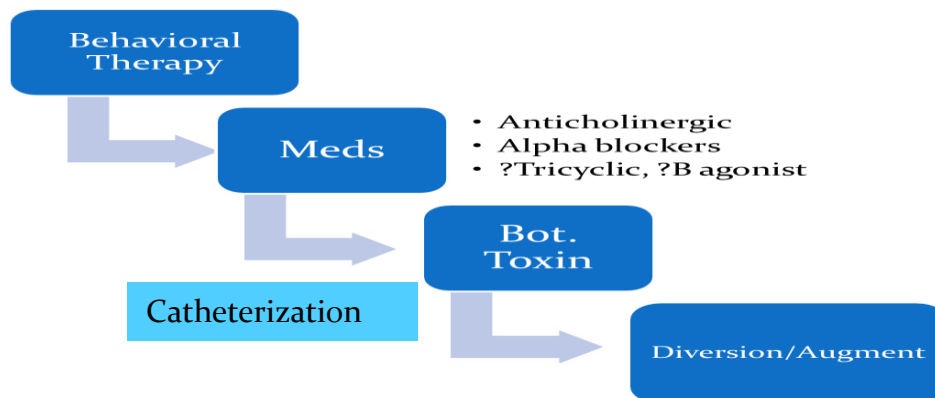
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## Neurosurgery for the Neurourologist:

### Introduction:

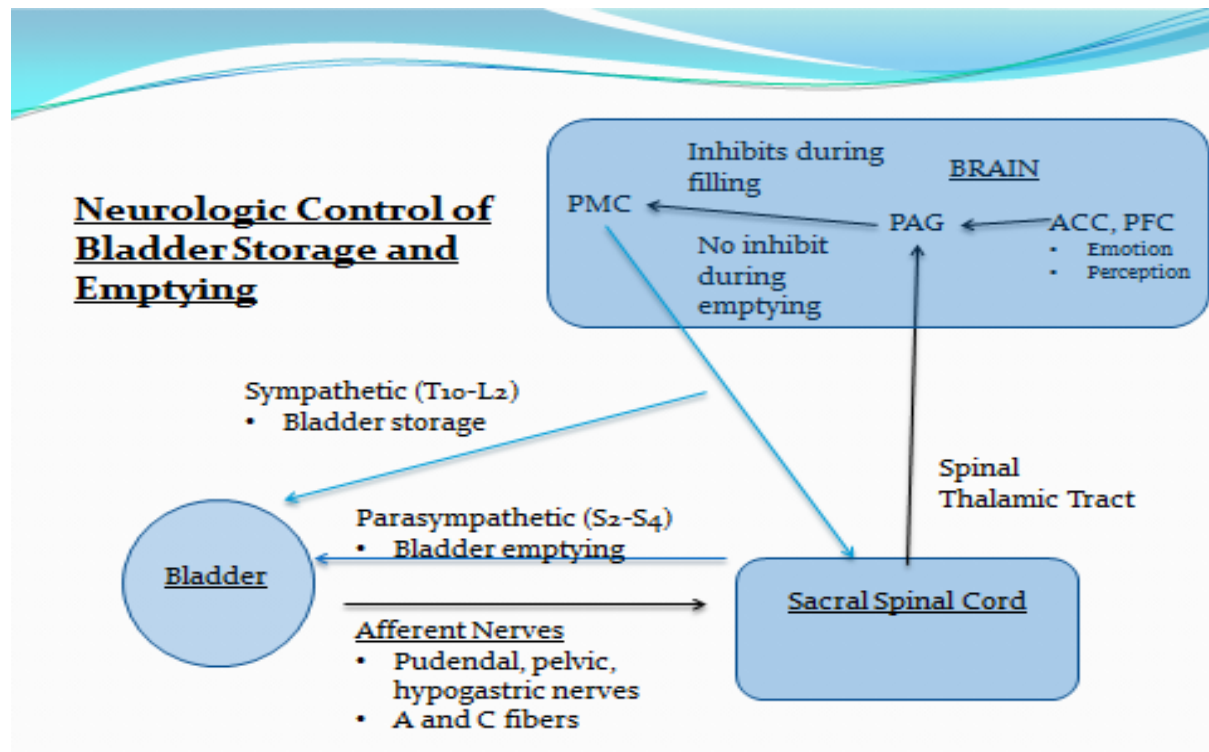
Patients with neurogenic bladder symptoms attach a high priority to managing urinary incontinence and/or retention. In a cross sectional survey, paraplegia neurogenic bladder patients considered restoration of bladder function as a high impact quality of life issue, ranking it second in importance after restoration of sexual function (1). The treatment algorithm for the symptomatic neurogenic bladder generally follows a predictable progression of behavioral therapy and medication, followed by botulinum toxin and then surgical options.



However, there is growing evidence that neuromodulation or stimulation could potentially play a larger role in treating neurogenic bladder urinary symptoms. These contemporary treatments are evolutions, in part, of a robust investigational history dating back greater than 150 years. Notable historical events in neuromodulation and stimulation include Giannuzzi's work on spinal cord stimulation in dogs which identified the hypogastric and pelvic nerves as peripheral innervation of the bladder (2) and Kilvington of Melbourne's 1909 attempts in reconnecting several spinal cord fibers to rectal and bladder peripheral nerves in dogs (3).

In this course, we will first review the central and peripheral neurologic regulation of the bladder and then examine the current literature on efficacy of peripheral/central neuromodulation and surgical neurologic rerouting for improving neurogenic bladder storage and/or emptying.

## Neurologic Regulation of the Bladder:



The bladder initiates signaling by responding to stimulation of pressure/stretch (myelinated A $\delta$  fibers) and/or pain/temperature (unmyelinated C fibers) to the urothelium. Afferent nerve fibers, arising from urothelium and suburethelium, carry signaling information to the spinal cord mainly through the pelvic nerve with some additional information carried by the hypogastric, and pudendal nerve(4). The sensory information enters the spinal cord through the S2-S4 dorsal nerve roots in the sacrum. It is then transmitted cranially through the spinal cord by the thoracolumbar tract and synapses to midbrain periaqueductal grey (PAG) region. Information is next relayed to the hypothalamus, thalamus, lateral pre frontal cortex, anterior cingulate cortex, and insula which combine input to suppress the PAG and the pontine micturition complex (PMC). Suppression of the PAG and PMC promotes storage by stimulating the hypogastric (sympathetic) and pudendal nerves to relax the bladder and increase urinary sphincteric tone. When the decision is made to void, the pre-frontal cortex suppression is removed and pontine micturition complex initiates caudal signaling to inhibit the hypogastric (detrusor) and pudendal nerve and initiate a detrusor contraction via stimulation of the pelvic nerve (5)

Neuromodulation:

Mechanism of action:

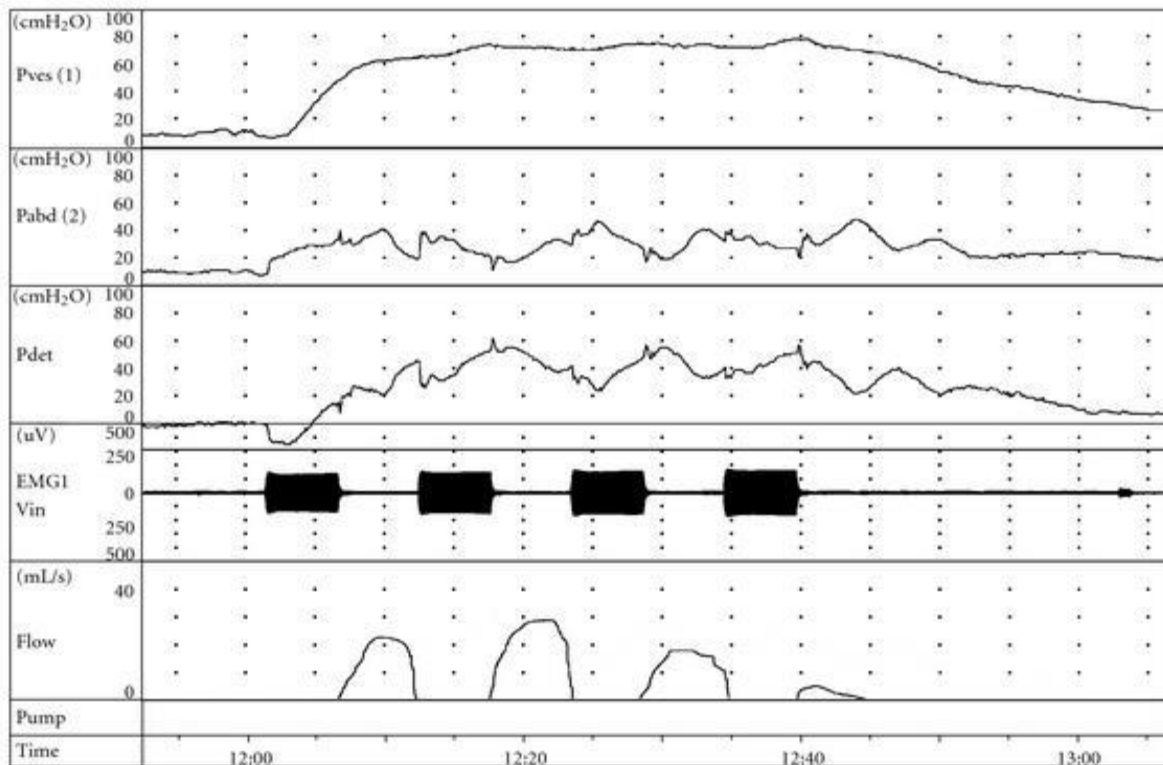
It is postulated that some types of overactive bladder, including neurogenic, may be influenced by the sensitization of normally silent afferent C-fibers. This may cause activation of interneurons at the level of the spinal cord and stimulate a voiding reflex. Neuromodulation is thought to improve bladder storage by increasing A delta fiber stimulation and re-establish suppression of the C fiber signaling and aberrant interneuron stimulation. The normal storage pathways are then utilized active.

Sacral/Pudendal Neuromodulation:

There are few studies examining the efficacy of sacral or pudendal neuromodulation for treating neurogenic bladder symptoms. Lombardi implanted sacral nerve stimulators in 85 incomplete spinal cord injury patients who suffered from urinary retention. 36 of 85 patients responded to the treatment and were able to experience voiding. Over a 3 year follow up, 11 patients subsequently developed device failure (6). Sacral Neuromodulation for detrusor overactivity has had better reported outcomes. Chen et al reported the outcomes of implantation in 23 neurogenic bladder patients 65% improved urinary frequency/urgency, 69% improved urinary incontinence symptoms, and 75% improved constipation symptoms (7). Pudendal nerve stimulation has likewise been examined for treating detrusor overactivity and limited studies have demonstrated improvement in storage and capacity (8,9). However the efficacy studies remain sparse in larger neurogenic bladder populations.

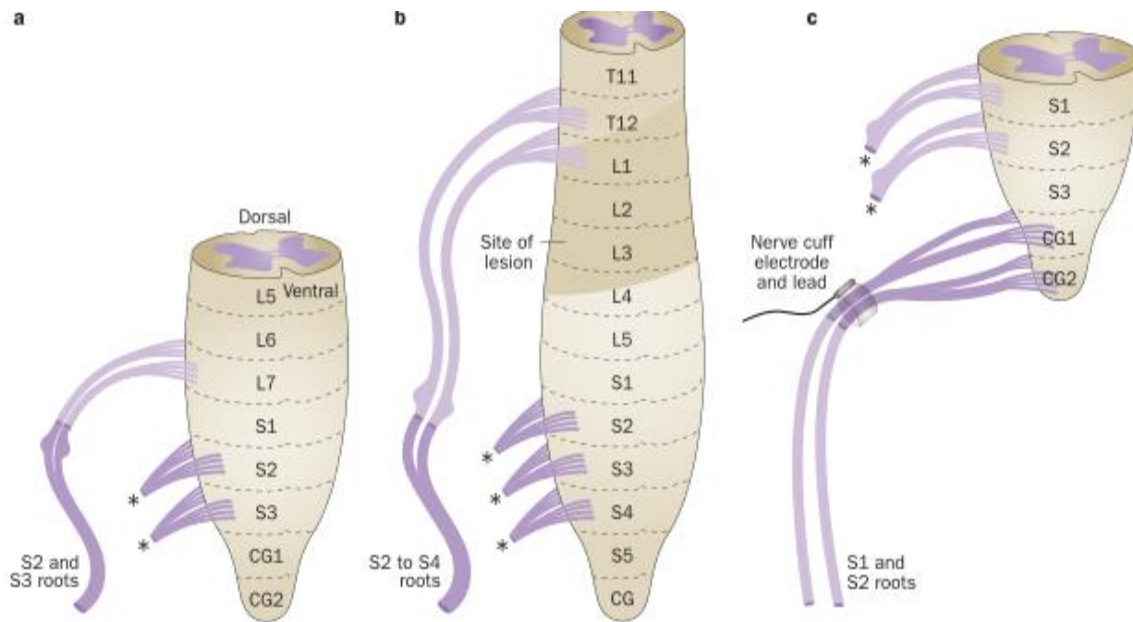
Finetech-Brindley Posterior/Anterior Stimulator

The Finetech-Brindley stimulator is best indicated for patients with a complete spinal cord injury and an intact neural pathway between the sacral cord nuclei of the pelvic nerve and the bladder. A posterior rhizotomy is performed during this procedure which will cause complete loss of sensation in a neurologically intact person. The stimulator electrodes are surgically implanted on the sacral nerve roots and intermittent, external stimulation initiates detrusor contractions. As seen in the below tracing, however, the stimulation needs to be intermittent because external sphincter and pelvic floor contractions as likewise initiated during a detrusor contraction. Pulsing the stimulation allows for intermittent relaxation of the external sphincter and micturition. Single institution studies have demonstrated high patient satisfaction and durable voiding with this device (10).



**Nerve ReRouting/Detrusor Myoplasty:**

Nerve re-routing remains an active area of research for treating neurogenic bladder dysfunction. Xiao has described a somatic-L5 and autonomic S2/3 ventral nerve root microanastomosis 15 suprasacral spinal cord injury patients symptomatic from detrusor sphincter dyssynergia. In 10 of these patients, the bladder storage and emptying became more normalized (11).



Xiao procedure: From Gomez-Amaya et al, Nature Reviews 2015

Gakis has attempted to improve neurogenic urinary retention by creating a cutaneous/myogenic pathway by harvesting a latissimus dorsi free flap, placing the muscle over the bladder, and anastomosing the thoracodorsal nerves and vessels to the 12<sup>th</sup> intercostal nerve and epigastric vessels. 17 of 24 patients treated with this technique had restoration of bladder function and a mean PVR of 24 cc. (12)

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## Notes