W32: ICS Core Curriculum (Free): Urodynamic study and its role in treatment of neurogenic bladder in children

Workshop Chair: Jian Guo Wen, China
31 August 2018 14:35 - 16:05

Start	End	Topic	Speakers
14:35	14:40	Introduction of the workshop and speakers	Jian Guo Wen
14:40	14:55	How to perform the paediatric urodynamic study (UDS) and analyse the result, as well as its application in evaluation of neurogenic bladder in children	Jian Guo Wen
14:55	15:10	Pitfalls in performing UDS in children	Stuart Bauer
15:10	15:20	Brief synopsis for drug therapy in children with NB	Stuart Bauer
15:20	15:40	Clean intermittent catheterisation (CIC), electrical neuromodulation in children with NB	Giovanni Mosiello
15:40	16:00	Urodynamically Guided Surgical Procedures for Incontinence in Children with NB	Israel Franco
16:00	16:05	Discussion	Jian Guo Wen

Aims of Workshop

The prevalence of neurogenic bladder (NB) in children is high and the quality of life is poor especially in cases with complications. The urodynamic evaluation not only can accurately reflect the type and severity of NB and urethral dysfunction but is helpful in designing right treatment protocol, predict the risk of upper urinary tract damage and evaluate the post-treatment efficacy. This workshop will introduce the characteristic of paediatric urodynamic study (UDS) and how to perform a good UDS and its application in diagnosis and treatment in children with NB.

Learning Objectives

1. To introduce how to perform the paediatric urodynamic study (UDS) and analyse the result, as well as the indication for the study, especially in the children with NB.
2. To introduce the non-surgical treatment of NB including CIC, electrical stimulation and pharmaceutical therapy, and the application of UDS in guiding these procedures.
3. To introduce the surgical procedures in treatment of NB and the application of UDS in guiding these procedures.

Learning Outcomes

The learner will understand the step and why perform the urodynamic study in children with NB, and how to use this test to help design the right treatment protocol and follow up the children with NB. The mechanism of effect of bladder dysfunction on the upper urinary tract damage as well as advanced knowledges of present procedures including no operative and operative treatment will be further understood.

Target Audience

Urologists, paediatrics, nurses, technicians, and anorectal surgeons.

Advanced/Basic

Advanced

Conditions for Learning

Normal lecture meeting room.

Suggested Learning before Workshop Attendance

Basic knowledge of urodynamic study and neurogenic bladder is required.

Suggested Reading

Guideline of ICCS and ICS on urodynamic study and NB.

14:40 Lecture 1

How to perform the pediatric urodynamic study (UDS) and analyse the result, as well as its application in evaluation of neurogenic bladder in children

Jian Guo Wen, MD, PhD, Professor
The pediatric urodynamic center, First Affiliated Hospital of Zhengzhou University，Zhengzhou, China

Pediatric voiding dysfunction is common in clinical practice. Urodynamic studies（UDS）are objective investigations developed to clarify these abnormality, also the necessary procedure to evaluate neurogenic bladder (NB) before making treatment protocol. However, the specific characteristics in PUDS, such as performing and interpretation of the UDS in infants and children are often challengeable. No doubt, the understanding the procedures of UDS is most important for interpretation of the results of the test. This talk will introduce how to perform UDS and analysis the result, as well as its application in evaluation of neurogenic bladder in children.

1. How to perform the pediatric urodynamic study (UDS) and analysis the result

The common UDS techniques include simple voiding diary, simple investigation (pad testing, uroflowmetry + ultrasound residual), pressure/flow studies (cystometry and video urodynamics) and urethral pressure measurement. How to use the urodynamic equipment and choice the normal materials such as the catheter, infusion liquid, EMG electrodes and wires, electrodes and wire fixing activities are also very important to the study. Recently, the bladder/urethral pressure measurement performed simultaneously has shown a good evaluation of detrusor sphincter dysnergia (DSD) and urethral instability indicating the possibility of replace of pressure/EMG study in the future.
The technique for performing cystometry is introduced in details. Emphasis is placed on correctly setting up the equipment according to ICS and ICCS guidelines, cooperation between the young child and technician or nurse. The primary parameters such as maximum detrusor filling pressure (Pdet.fill.max), detrusor compliance (△C=△V/△P), leak point pressure (LPP), detrusor voiding pressure, detrusor sphincter dyssynergia (DSD), urethral instability and post voiding residual (PVR) should be analyzed. The UDS parameters are varied with the different age, such as maximum bladder capacity which is only 30 ml in newborn, but 390ml in 12 years boys, but the normal voiding detrusor pressure is similar to those of adult in the cases with no DSD.

2. The application of UDS in evaluation of NB in children

Pediatric NB is common and may have different clinical voiding dysfunction. UDS is strongly recommended to evaluate NB by ICS. It can objectively reflect the type and severity of bladder and urethral dysfunction. In children, the spinal level and extent of congenital lesion are poorly correlated with the clinical outcome. UDS and functional classifications have therefore been more valuable for defining the extent of the pathology. The urodynamic parameters including bladder capacity, compliance, the end intravesical filling pressure, the bladder leakage pressure, the presence or absence of reflex detrusor activity, the competence of the internal and external sphincter mechanisms, the degree of detrusor sphincter dysnergia (DSD) and the post-voiding residual urine volume are frequently used to select the treatment protocol, such as biofeedback. CIC, medicine and different operative procedures. UDS is also necessary step to follow up the long-term results of the treatment of NB cases.

14:55 Lecture 2

Pitfalls in performing UDS in children

Stuart B Bauer,MD, Professor
Department of Urology, Boston Children's Hospital, USA

The pitfalls in performing UDS are more frequently confronted in children than those in adults. For right interpretation of the UDS results it is necessary to know what is and how to judge pitfalls during the UDS. This lecture will show different pitfalls and give an explanation of its mechanism of formation and reason as well as possible influence on the diagnosis of bladder dysfunction.

This lecture is designed to emphasize the pitfalls that can arise when urodynamic studies are not performed with the utmost care. Preparation is the first important key; providing the child and parents with a clear reason for undertaking these studies goes a long way to insuring cooperation and reliable results. Having the child arrive with a relatively but not over-distended bladder for the flow rate allows for a representative flow pattern. For smaller children who sit to void, having a foot-rest & a toilet seat that is an appropriate size avoids their need to balance themselves, thus minimizing pelvic floor tightening.

Instructing boys to 'aim' for a specific location on the funnel wall when they void will insure a more even flow and minimize the potential for a staccato pattern if they do not aim. Using the smallest double lumen catheter possible that is well lubricated reduces urethral pain on insertion and when the child voids at the end of the cystometrogram (CMG).
Although it may seem undesirable, placing a rectal balloon catheter to measure abdominal pressure in order to obtain subtracted detrusor pressure is even more critical in youngsters than it is in adults, as children often fidget during the filling phase and may use all their energies to inhibit voiding or even strain (Valsalva) to void, rather than relax their sphincter muscles to let normal voiding take place. These factors can only be ascertained when using a rectal balloon catheter. Additionally,

making sure the child has an empty rectum by administering a laxative 1 – 2 days before the scheduled study insures accurate abdominal pressure recordings with the rectal balloon catheter.

Too rapid an infusion rate during the filling phase of the CMG may cause discomfort, such that the child reflexively tightens the external sphincter muscle, which in turn, may mask detrusor overactivity. It is imperative not to over-distend the bladder during the study and to encourage the child to void in a relaxed manner when they feel full. Sometimes, repeating the study after the child has experienced what it is like to urinate around the catheter will allow for a more relaxed void with representative pressures the second time around.

Attention to these details, with careful explanations of what each of the tests entail, why they are being done, what the medical provider hopes to find and how this may make a difference for future management, are the keys to minimizing artifacts while maximizing results so appropriate and expeditious treatments can be instituted. Examples of all these potential pitfalls will be highlighted during the lecture.

15:10 Lecture 3

Brief synopsis for drug therapy in children with NB

Stuart B Bauer, MD, Professor
Department of Urology, Boston Children's Hospital, USA

Pharmaceutical therapy has been used in treatment of NB for many years. The medicine such anticholinergic, cholinergic, alpha Sympathetic blocker might be used for different types of NB in children but have many differences compared with those in adult. This lecture will give a brief synopsis for drug therapy in children with NB.

The first part of this lecture is designed to review the current state of knowledge regarding the various antimuscarinic medications available for use in children. The presentation will include a brief summary of their mechanism of action and how they lead to effective changes in bladder function during the micturition cycle. A description of what versead effects these medications may produce and why they occur in some individuals and not in others will be included. The differences and effectiveness of tertiary versus quaternary amines, categories which most of the antimuscarinic drugs fall into, will be discussed. The second part of the lecture will focus on drugs that modulate the sympathetic nervous system's control over lower urinary tract function; how and why alpha sympathomimetic agents may produce changes in the proximal urethral resistance and what effect they have on bladder compliance. This part of the lecture will also highlight what is currently known about a new class of bladder modulating drugs, the alpha adrenergic agonists, (mirabegron) and the bladder's response to them taken either individually or in combination with antimuscarinic medication.

An in-depth review of the literature regarding efficacy and safety of all these pharmaceutical preparations for potential use in children will be noted. The emphasis throughout this lecture will be what medicines we have in our armamentarium for children with lower urinary tract dysfunction.

15:20 Lecture 4

Clean intermittent catheterization (CIC) and electrical neuromodulation in children with NB

Giovanni Mosiello, MD, Professor
Pediatric NeuroUrology Research and Clinical Unit,
Bambino Gesù Pediatric Hospital, Rome, Italy

1. Clean intermittent catheterization (CIC) in children with NB

Conservative management of neurogenic bladder is mainly based in clean intermittent catheterization (CIC). The goal of CIC is first of all to preserve renal tract function, optimizing then quality of life and promoting independence of self-care (de Jong 2008). CIC has demonstrated to be useful to preserve bladder function and structure (Bauer). If nowadays this practice is considered worldwide a mainstay of NBD treatment, some concerns exist.

Training of caregiver, by skilled continence nurses or urotherapist is mandatory in order to avoid incorrect practice. CIC must be performed considering a correct size, hand, perineal, genitalia hygiene, correct manouvres to avoid contamination and trauma. Any mental impairment or physical difficulty limiting CIC should be considered.A correct time for starting self-administered CIC, and training modalities of Young children, scholar age, are another critical point, as adherence in adolelescents. Overnight catheter drainage could be considered in some clinical situations, as well as suvrapubic catheter (buttom cistostomy). In the Treatment and prevention of urinary tract infections improving hydration and more frequent catheterizations can be useful. Surveillance is mandatory during puberty because bladder capacity, maximum detrusor pressure and leak point pressure may increase.

Indications for surgical therapy could be related to hand function that preclude self CIC, Physical weight of child makes wheelchair transfers difficult, necessitating a catheterizable stoma as for preserving patient privacy in young people where

caregiver is not . If hydrophilic single use catheter is worldwide recommended, concerns are present in different geographical setting due to economical reason. Commonly critical point remains lack of education and trained health care professionals (Krassioukov, Mosiello).

2. Sacral Neuro Modulation

From the first description in 1988 (Tanagho) a significant number of reports have been published, and Sacral NeuroModulation (SNM) became rapidly a well-accepted treatment in adults. SNM was used in neurogenic bladder dysfunction (NBD) too, and Kessler in a systematic review, analyzing 26 independent studies, stated that there is evidence indicating that SNM may be effective in adults with NB. According to adult's experience is interesting to note the SNM has been used mainly in non NBD , while in pediatrics the first prospective randomized controlled study has been performed in 2004 in NBD (Guys). Actually SNM is not a first-line treatment but rather as a second or better third line treatment for the patients who have failed conservative treatments, still presenting low evidence due to the lack of large series and clinical trial. SNM seems effective in partial acquired lesion, respect to congenital, with disappointing results in myelomeningocele and complete spinal cord injury . SNM is today less invasive, more safe, reliable and effective thanks to a standardized patients selection and surgical approach. The re-operation and complication rates decreased significantly. Limitations remain related to MRI use and height growth. In personal experience of more 60 patients results are very interesting , especially for patients presenting bladder and bowel dysfunctions.

15:40 Lecture 5

Urodynamically Guided Surgical Procedures for Incontinence in Children with NB

Israel Franco, MD
Clinical Professor of Urology
Yale University School of Medicine
Director of Yale New Haven Children's Bladder and Continence Program

Urodynamic study is a useful tool in evaluate neurogenic bladder, especially, used to guide surgical procedures to improve bladder compliance, increase bladder capacity, reduce urinary tract leak pressure, eliminate risk factors for upper urinary tract dilatation, increase or decrease bladder outlet resistance, improve lower urinary tract symptoms.

1. Expanding or enlarging the vessel:

Once medical therapy has been maximized and there is no evidence of continued inability to obtain reasonable capacities the decision needs to be made to make the bladder larger. Botulinum Toxin A injection. Ileal augments: Pros: less mucous production compared to other bowel segments; Cons: thinner muscularis making implantation into more difficult and less secure. Ileocecal augments: Pros: appendix is attached, thereby making catherizable channel easier to make, ureters can be implanted into it along tinea more securely and easier than in ileum; Cons: risk of vitamin b12 deficiency, diarrhea is a potential complication, more mucous production due to cecal segment Sigmoid augments: Pros: thicker muscularis making implantation into it easier, sigmoid is in the pelvis so it can be readily placed on top of the bladder reducing the need to do extensive bowel mobilization; Cons: increased mucous production and greater risk for stone formation; chloride absorption is increased leading to increased risk for metabolic acidosis. Demucosalized augments: Pros: reduced mucous production and no associated metabolic derangements associated with urine absorption; Cons: difficult to perform, requires the use of special form to be placed in the bladder to prevent contraction of the augment. Detrusorraphy: Pros: no issues with mucous production and no associated metabolic derangements associated with urine absorption; Cons: original surgery had low success rate, volume generally not increased with greatest effect on compliance.

2. Containing the Leak

In some cases, the vessel is of adequate size but there is a problem with the outlet resistance and urine just leaks out. This is commonly due to a problem in the function of the bladder neck or external sphincter. Methods to increase outlet resistance are at times necessary alone or in combination with the augmentation of the bladder. The Pros and Cons of following procedures will be introduced. Injection of Bulking agents, Bladder neck slings, Bladder neck reconstruction, Artificial urinary sphincter, Perineal slings

3. The vessel is hypercontractile

In this scenario the bladder is contracting and the pressure generated is higher than the outlet resistance leading to leakage of urine. Medical therapy is the first line treatment and should be optimized especially if bladder volume is adequate without detrusor overactivity. If medical therapy fails Botulinum Toxin A is the next option. Selective Sacral Rhizotomy does not involve bladder surgery and can stop bladder overactivity by removing the sensory arm of the reflex loop. Cord detethering can be an extensive surgery and at times may not make a difference in the bladder overactivity.

Jian Guo Wen

Affiliations to disclose[+]:

Pediatric Urodynamic Center, First Affiliated Hospital of Zhengzhou University,

Department of Pediatric Surgery, Xinxiang Medical University, Urology of Shenzhen Children Hospital , China

[+] All financial ties (over the last two years) that you may have with any business organization with respect to the subjects mentioned during your presentation

Funding for speaker to attend:

- [X] Self-funded
- [ ] Institution (non-industry) funded
- [ ] Sponsored by:

How to perform the pediatric urodynamic study and analysis the result, as well as its application in evaluation of neurogenic bladder in children

Jian G Wen, MD,Ph.D, Prof.

Pediatric UD Center, First Affiliated Hosptial of Zhengzhou University,

Pediatric Surgery, Xixiang Medical University

Urology of Shenzhen Children's Hospital, China

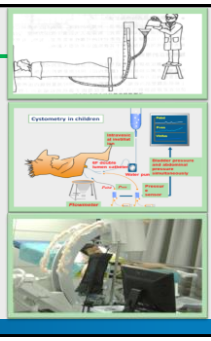
Outline

- How to perform the pediatric urodynamic study (PUDS)
- How to analysis the result of pediatric urodynamic study
- How to apply PUDS in evaluation of neurogenic bladder in children

Difination

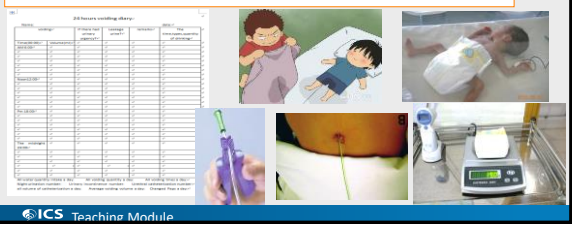
Pediatric urodynamic study (PUDS) is a test that assesses how the bladder and urethra are performing their job of storing and releasing urine.

- voiding diary
- uroflow-PVR
- Pressure/flow
- Video UDS

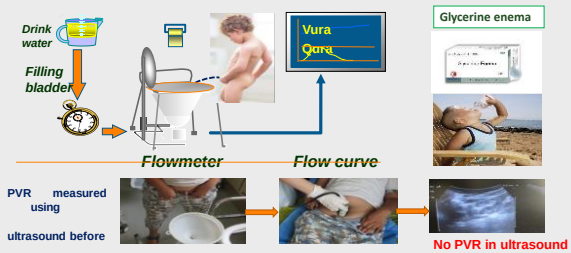


Voiding diary (1day, 2day, 3day)

- How to record in the diary: Time of day,Fluid Intake, Toilet Voids, Drained via Catheter, Leaks, Pad Changes.



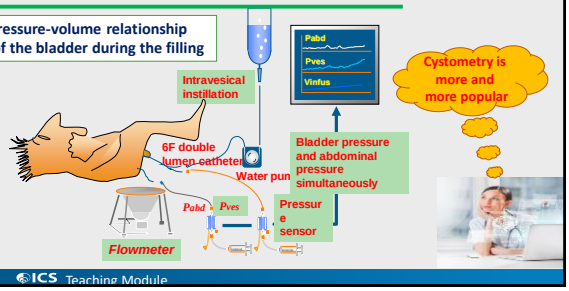
Uroflowmetry



Cystometry: setting

The core contents of PUDS

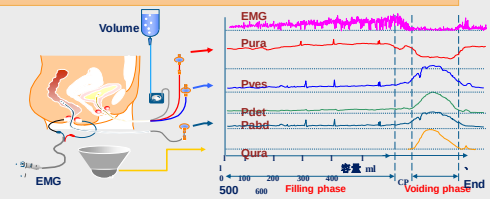
pressure-volume relationship of the bladder during the filling



ICS Teaching Module

Pressur/flow sdudies

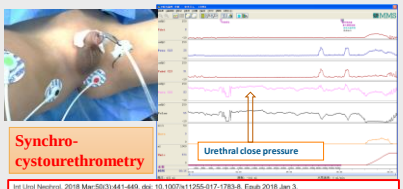
Slow filling (5-10% of estimated bladder capacity/min)



ICS Teaching Module

Synchro-cystourethrometry for evaluating the relationship between urethral instability and overactive bladder

Wensen's fixer



Int Urol Nephrol. 2018 Mar;50(3):441-449. doi: 10.1007/s11255-017-1783-8. Epub 2018 Jan 3.

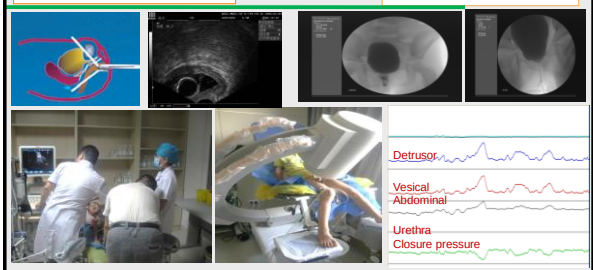
The value of synchro-cystourethrometry for evaluating the relationship between urethral instability and overactive bladder.

Hua C[1,2], Wen Y[1,2], Zhang Y[1], Feng Q[1], He X[1,2], Li Y[1,2], Wu J[1,2], Feng J[1,2], Bauer SB[3], Wen J[4,5].

ICS Teaching Module

Ultrasound UDS

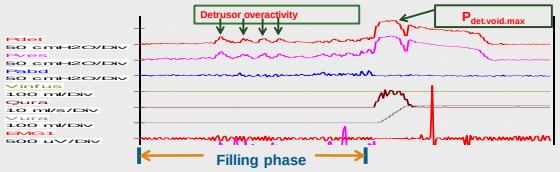
Video UDS



ICS Teaching Module

Interpretation: detrusor overactivity

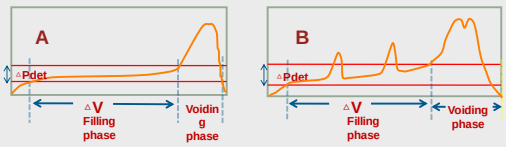
- Detrusor overactivity indicates a detrusor contraction that occurs during the filling phase before expected bladder capacity is reached &, which may occur in 10% of normal children. While in children with VUR, it may be seen in more than half of the infants



ICS Teaching Module

Interpretation: detrusor compliance (△C)

- △C =△V/△ Pdet, △C < 10 ml / cmH_2O indicates decreased bladder compliance, which may due to decreased bladder capacity or increased Pdet or both
- Normally, the end filling pressure < 15 cmH_2O with a slow filling rate



A: The non-linear portions - the beginning & end of the V/Pdet diagram do not contribute to compliance.
B: △V / △ Pdet essentially captures the angle of the line describing the incremental increase in resting pressure

ICS Teaching Module

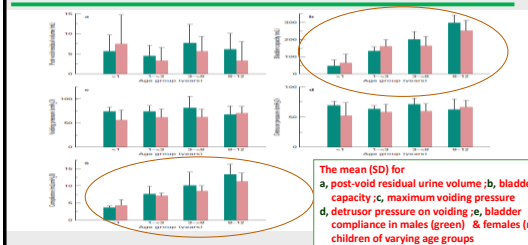
Interpretation: estimated bladder capacity

Bladder capacity (BC), post-void residual (PVR), maximum detrusor pressure during voiding（Pmax.det.void）in the literatures

Age	BC (ml)	PVR (ml)	Pmax.det.void (cmH_2o)
Neonatal			
Premature infant（0.5~7w）	13.2±4.9	1.5±1.0	–
（<4w）	22.6±7.8		
Term infant （1w）	24.6±10.9	1.4±1.1	–
（2w）	23.6±8.7	1.2±1.0	–
Infant			
3 month	53±13	5.7±4.5	50~75
12 month	70±30	7.1±6.3	41~66
24 month	79±31	6.6±7.0	38~60
36 month	128±72	3.3±5.3	38~55

Expected capacity (ml) = 30 + (age in years × 30) in a child > 1 year of age;
Expected capacity (ml) = 38 + 2.5 × age (months) for infants < 1 year old

Interpretation: bladder capacity, compliance



The mean (SD) for
a, post-void residual urine volume ;b, bladder capacity ;c, maximum voiding pressure
d, detrusor pressure on voiding ;e, bladder compliance in males (green) & females (red) in children of varying age groups

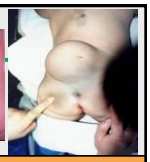
From Wen, etal. British Journal of Urology 1998 81, 468-73

Indications

1. Suspicion of, or overt neuropathic voiding dysfunction, LUT obstruction, DSD.
2. Profound non-neuropathic detrusor-sphincter dysfunction (ie.,dilating ureter(s), high grade vesicoureteral reflux, valve bladder syndrome)
3. Significant PVR with no apparent reason
4. Congenital malformations of the lower urinary tract (ie., exstrophy, epispadias,ureteroceles, mutiple bladder diverticula)
5. The procedure is assumed to effect treatment strategies & for evaluating the treatment response or follow up
6. It is undertaken after history taking, physical examination, voiding diaries & uroflow patch EMG recordings do not answer the questions related to causes, nor provide management schemes for LUTD

Neurogenic Bladder(NB)

NB is a voiding dysfunction due to damage of nerve pathways associated with urination. Most of them is due to spinal bifida

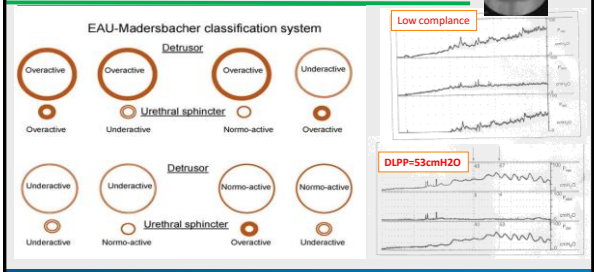


Guidelines for urodynamics and uroneurophysiology tests	GR
Urodynamic investigation is necessary to document the (dys-)function of the LUT [10]	A
The recording of a bladder diary is advisable.	B
Noninvasive testing is mandatory before invasive urodynamics are planned.	A
Video-urodynamics are currently the preferred method for invasive urodynamics in patients with NLUTD. If this method is not available, then a filling cystometry continuing into a pressure–flow study should be performed.	A
For standard urodynamic testing, a physiologic filling rate (see Table 1; eg, not faster than 20 ml/min) and body-warm fluid must be used.	A
Specific uroneurophysiologic tests and provocative manoeuvres (eg, fast-filling cystometry, coughing, tapping, and anal stretch) are elective procedures [10,12].	C

GR = grade of recommendation; LUT = lower urinary tract.

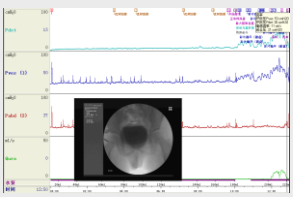
Guidelines for urodynamics and uroneurophysiology tests in NB-EAU

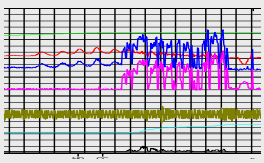
EAU–Madersbacher classification system



VUDS application

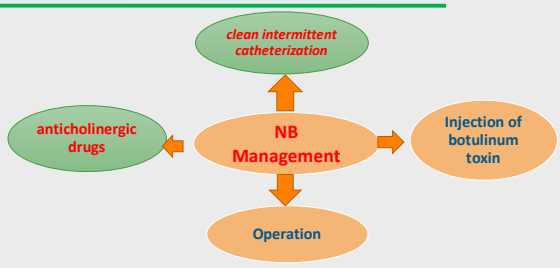
- Video UDS can significantly improve the diagnostic accuracy
- Show the urological shape simultaneously



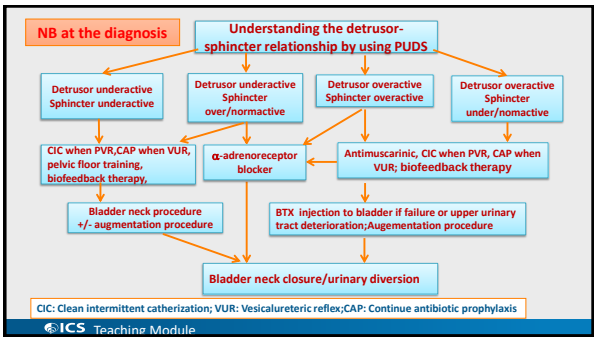


Acontractile detrusor in a child with NB, voiding by abdominal pressure

NB treatment strategy guided by UDS



ICS Teaching Module



ICS Teaching Module

Summary

- PUDS are objective investigations developed to clarify these abnormality
- Understanding the procedures of UDS is most important for interpretation of the results of the test
- It is a necessary procedure to evaluate NB before making treatment protocol and later, follow up

ICS Teaching Module

Thanks for Your time!

ICS Teaching Module

22

Stuart B. Bauer

ICS 2018 PHILADELPHIA

Affiliations to disclose[†]:

Department of Urology
Boston Children's Hospital

† All financial ties (over the last year) that you may have with any business organization with respect to the subjects mentioned during your presentation

Funding for speaker to attend:

- [X] Self-funded
- [ ] Institution (non-industry) funded
- [ ] Sponsored by:

ICS 2018 PHILADELPHIA

Preventing Pitfalls in Urodynamic Testing in Children

Stuart B. Bauer, MD
Department of Urology
Children's Hospital Boston

Preparation for UDS

ICS 2018 PHILADELPHIA

- Education
  - Parental acceptance
  - Patient understanding
  - Familiarization with components of study
  - Touring the facility beforehand
- Adherence to Protocol
  - Bowel cleanout 1 - 2 days before
  - Lower urinary tract modulating medications
    - Know what medications, dosage & frequency
    - Record when taken prior to study
    - Discontinuation timing if need to know change in function
  - Adequate but not excessive fluid intake prior to flowmetry
  - Have family bring favorite toy / video or provide same

CMG Performance

ICS 2018 PHILADELPHIA

- Attention to Detail
  - 'Zero' transducers
  - Have child void into flowmeter, if toilet trained
  - Empty bladder (aspirate catheter after urine stops draining)
  - Know status of upper urinary tracts
    - Hydronephrosis & hydroureter
    - Presence of reflux
  - Perform U/A & send urine for culture
    - Consider delaying study if (+) U/A
  - Recheck all connections to pump, transducers
  - Have child as comfortable as possible when starting
  - Make sure all channels are recording
    - Test with cough, Credé, initially & throughout filling CMG
  - **Never** 'rush through' the study

CMG Performance

ICS 2018 PHILADELPHIA

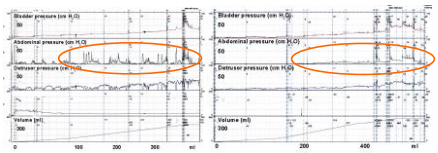
- Attention to Detail
  - Record every event during study
  - Look for DO early in filling as child may suppress them later
  - Encourage child to void
    - Run sink faucet, pour warm water on thigh, perineum
    - Engage parent to work with their child
    - Don't 'give up' easily, when child doesn't want to void
  - If no void, record 'equilibration pressure' 2 minutes after stopping infusion before draining bladder, & compare with max detrusor fill pr. at capacity
  - Record voided volume & residual urine, to know urine production during the study – compare to volume infused
  - Repeat CMG 2nd or 3rd time to answer the questions posed

Cystometrogram Performance

ICS 2018 PHILADELPHIA

- Attention to Detail

CMG without bowel cleanout **CMG with bowel cleanout**



Cystometrogram Performance

ICS 2018 PHILADELPHIA

- Attention to Detail
  - 38 pts underwent 3 CMGs
    - medium (20% EBC/min), slow (2% of EBC/min) then, medium fill again
  - Findings
    - Detrusor Pr. > 40 cm H_2O = occurs twice rate in medium fill
    - Δ in Pr. > 15 cm H_2O = only occurred in medium fill
  - Conclusion
    - Bladder filling rate affects detrusor pressure measurements

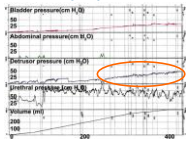
Joseph D: J Urol 1992: 147; 444

Cystometrogram Performance

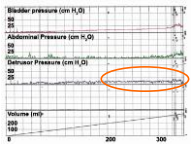
ICS 2018 PHILADELPHIA

- Attention to Detail

CMG with rapid fill – 20 ml/min



CMG with slow fill – 10 ml/min



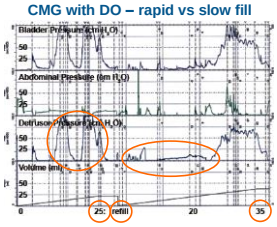
Joseph D: J Urol 1992: 147; 444

Cystometrogram Performance

ICS 2018 PHILADELPHIA

- Attention to Detail

CMG with DO – rapid vs slow fill

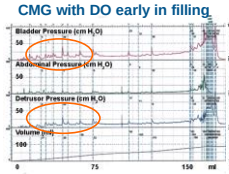


Cystometrogram Performance

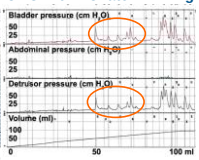
ICS 2018 PHILADELPHIA

- Attention to Detail Early in Study

CMG with DO early in filling



CMG with DO later in filling

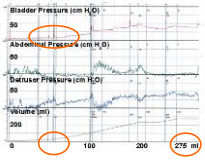


Cystometrogram Performance

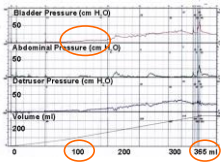
ICS 2018 PHILADELPHIA

- Attention to Detail – Timing of Medicine

CMG 24 hrs after last med



CMG 6 hrs after last med

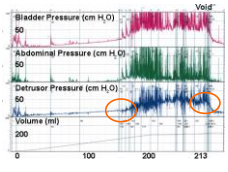


Cystometrogram Performance

ICS 2018 PHILADELPHIA

- Attention to Detail – Know upper urinary tract status

Note detrusor fill & void pressures are normal



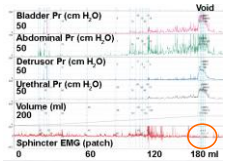
Indications for CMG / Patch EMG

- Indications
  - Obvious non-neurogenic dysfunction
  - Specific question regarding sphincter response to DO
- Contra-indications
  - Evaluating a known / suspected neurologic lesion
  - Repeating study after spinal cord surgery
  - Importance of knowing precise sacral spinal cord function
  - Evaluation after pelvic surgery

Indications for CMG / Patch EMG

6 y/o girl with dysfunctional voiding, daily dampness & recurrent UTI

UDS reveals nl capacity, no overactivity & quieting of the sphincter on voiding

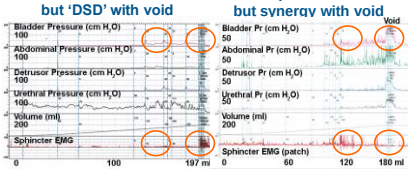


Cystometrogram Performance

- Attention to Detail

CMG + patch EMG – no response to DO but 'DSD' with void

CMG + patch EMG – response to DO but synergy with void



Urethral Sphincter Electromyogram (EMG)

- Attention to Detail

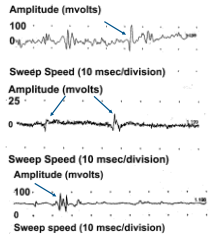
Normal motor units

Fibrillations

- early signs of denervation

Polyphasic potentials

- evidence for re-innervation



Urethral Sphincter Electromyogram (EMG)

- Attention to Detail
  - Indications for Needle EMG
    - Known or suspected neuropathic bladder dysfunction
    - Provides precise information about sacral cord function
    - Clearly differentiates artifact from true dyssynergy
    - Easily comparable to prior studies if concerned about progression (tethering) of condition
  - Contra-indications
    - Can be painful for sensate children
    - Unnecessary for children with just an anatomic abnormality
    - Requires a neurophysiologist for interpretation

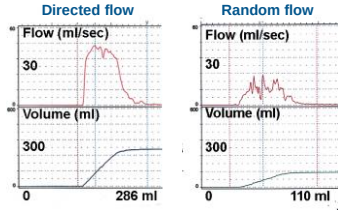
Flowmetry Performance

- Attention to Detail
  - Record timing of prior void
  - Measure bladder volume with 'ultrasound scanner'
  - Have boys 'aim' at a specific location in flow meter
  - Have girls sit comfortably with feet supported
  - Make sure toilet seat is appropriate size to avoid pelvic floor muscle tightening
  - Record residual urine via scanner
  - Encourage 2nd void if pvr is > 30 ml
  - Repeat flowmetry if not normal initially, or if questions regarding its authenticity
    - ICCS recommends 3 uroflows

Bladder Scanner

Flowmetry Performance

- Attention to Detail



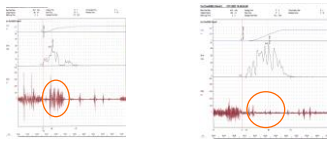
Need to emphasize boys should aim their flow to a specific location

Flowmetry – Importance of Patch EMG

- Attention to Detail

Uroflow / EMG in two 5 y/o girls with LUTS + RUTI

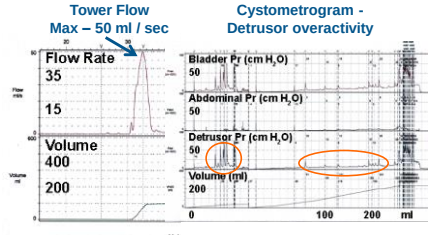
Both suspected of Dysfunctional Voiding (DV)



Girl with urgent voiding has **Dysfunctional Voiding**

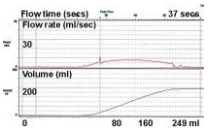
Girl with only mild urge to void despite a voided volume 180% of EBC - study reflects straining to void or **Underactive Bladder**

Predictability of a Flow Rate



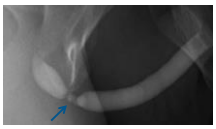
Reliability of a Flow Rate

Slow prolonged flow rate – suggestive of a stricture



Flow rate was repeated 3 times with similar findings before imaging the urethra

Retrograde urethrogram - confirmation of a stricture



Conclusions

- Cannot stress enough the importance of paying attention to detail
- Improves accuracy of findings
- Allows for reproducibility of findings
- Provides efficiency when ordering additional studies
- Directs effective therapy based on findings
- Leads to overall improved results

The End!

Stuart B. Bauer

ICS 2018 PHILADELPHIA

Affiliations to disclose[†]:

Department of Urology
Boston Children's Hospital

† All financial ties (over the last year) that you may have with any business organization with respect to the subjects mentioned during your presentation

Funding for speaker to attend:

- [X] Self-funded
- [ ] Institution (non-industry) funded
- [ ] Sponsored by:

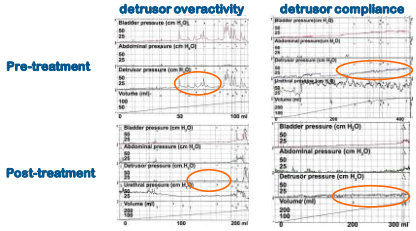
Drugs Modulating Lower Urinary Tract Function

ICS 2018 PHILADELPHIA

- Antimuscarinics (Ach)
  - Mollifies overactive contractions (DO)
  - Increases capacity
  - Lowers urine storage pressures
  - Level 1 evidence of ACh efficacy
    - Andersson *et al*, Curr Opin Urol, 19:380, 2009
- Antispasmotics
- β_3 adrenergic receptors
  - Diminishes detrusor overactivity via sympathetic control on M_2 receptors
- α-adrenergic receptors
  - Modifies bladder neck receptor function

Antimuscarinic Effects on Detrusor Function

ICS 2018 PHILADELPHIA



Antimuscarinic Agents

ICS 2018 PHILADELPHIA

- Oxybutynin (Ditropan, Oxytrol)
- Tolterodine (Detrol)
- Fesoterodine (Toviaz)
- Solifenacin (Vesicare)
- Darifenacin (Enablex)
- Propiverine (Detrunorm)
- Trospium (Sanctura)
- Glycopyrrolate (Robinul)

Muscarinic receptors: 5 subtypes & adverse events

ICS 2018 PHILADELPHIA

- M_1 – brain, eye, salivary glands, sympathetic ganglia
- M_2 – bladder (66%), brain, eye, heart
- M_3 – bladder (33%), brain, eye, GI tract, salivary glands
- M_4 – brain, lung, eye
- M_5 – brain, eye

Problem:
No organ specific 'M' receptor drugs → systemic implications

Antimuscarinic Agents

ICS 2018 PHILADELPHIA

Tertiary Amines

Oxybutynin, tolterodine, propiverine, solifenacin, & fesoterodine:

- Lipophilic → easily absorbed by GI tract
- Easily crosses blood-brain barrier
- 95% metabolized by (cytochrome oxidative system - p450 enzyme)

Quaternary Amines

Trospium, glycopyrrolate:

- No studies in children (~ to oxybutynin in adults)
- Less lipophilic → less absorbed by the GI tract
- Minimized passage through blood-brain barrier → less central side-effects
- Still peripheral side-effects: xerostomia, constipation, tachycardia

Antimuscarinic Agents - Oxybutynin

Oxybutynin (Ditropan [IR / XL], Oxytrol)

- Tertiary amine ↑ affinity 1° for M_3 + some M_2
- Active metabolite (N desethyloxybutynin) has M_1 affinity
  - AE - dry mouth, blurry vision, drowsiness, headache & behavioral Δ's
  - Better tolerated by children than adults
- Direct effect on smooth muscle
- Short $T_{1/2}$ (2 hours)

Prototype anticholinergic

Extensive study in pediatrics (NBD)

ONLY anticholinergic approved by FDA for OAB in children

No placebo-controlled, randomized trials in children

Oxybutynin: Immediate vs Extended Release

81 children with OAB treated with 0.39 mg/kg/day for 1.2 yrs

UDS parameters of flow rate + PVR (scan) & voiding diary monitoring symptom changes

31 (38.3%) became dry but 25 (31%) had little Δ

No differences in bladder cap., flow pattern or pvr noted in those becoming dry vs those without improvement

Side effects seen in 34 (42%)
Constipation, dry mouth, flushing, heat intolerance

Arendonk K, et al: Urology 67: 1049, 2006

27 children with OAB treated with 0.38 mg/kg/day for 19.9 months after failure with regular oxybutynin for daytime incontinence

Symptom improvement: initially all 27 wet daily

- excellent: 44%
- good: 11%
- fair / poor: 44%

Side effects

- 6 of 12 (50%) with SE resolved
- 7 of 15 (46%) without SE developed them

Arendonk K, et al: Urology 68: 862, 2006

Drug Delivery Strategies for Oxybutynin: Minimize Side Effects

Intravesical & transdermal deliveries

- Avoids 1st pass hepatic metabolite
  - N-desethyloxybutynin
- Limitations
  - Local skin irritation
  - Necessity for continual skin adherence
  - Pharmacokinetics for dosing & efficacy have not been established in children
- Intravesical instillation – time consuming, parents often non-compliant

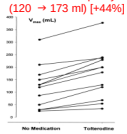
Cartwright P, et al: J Urol 182: 1548, 2009

Other Antimuscarinic Agents - Tolterodine

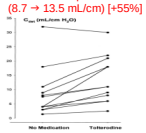
Tolterodine (Detrol [IR / LA])

- Tertiary amine mostly selective for M_3 + M_2 receptors
- Seems to have efficacy similar to oxybutynin
- Does not cross blood / brain barrier → ↓ side effects, so increased dose ≠ ↑ CNS SE
- Moderate $T_{1/2}$ (4 hours)

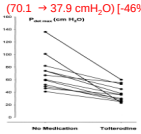
Max Bladder Capacity (120 → 173 ml) [+44%]



Detrusor Compliance (8.7 → 13.5 mL/cm) [+55%]



Mean Max Detrusor Pressure (70.1 → 37.9 cmH_2O) [-46%]



Goessl C, et al: Urol 55: 414, 2000

Tolterodine & LUTS in Neurologically Normal Children

31 children with LUTS, normal pvr + no febrile UTI

Dosing: 0.5, 1, 2 mg BID x 14 days

Voiding diaries to evaluate efficacy:

- Urinary frequency ↓ irrespective of dose
- Incontinence episodes / wk ↓ most in 1 mg group
- PVR changed slightly with ↑ dose (p. = >0.05)

Side effects: 60%, mostly, in 2 mg group

- headache, ↑ HR, visual Δs

1 mg BID is safe, effective for OAB with few SE

Hjalmas K, et al: BJU Int 87: 569, 2001

Tolterodine in Neurologically Normal Children

44 children with LUTS, normal pvr + no febrile UTI

Dosing 1 mg BID x 3 months

DVSS used to evaluate efficacy

DVSS: 14.0 → 6.68 [$p = 0.001$]

Girls: greater ↓ in DVSS than boys

DVSS subgroup measuring OAB symptoms only

- DVSS: 7.63 → 2.59 [$p = 0.001$]

Side effects:

- 14 (31%) dry mouth
- 2 (4%) headache

Good 1st line therapy prior to invasive studies

Ayan S, et al: BJU Int 96: 411, 2005

Other Antimuscarinic Agents - Fesoterodine

ICS 2018 PHILADELPHIA

Fesoterodine (Toviaz)

- Tertiary amine primarily M_3 antagonist with ↑ affinity
- Approved by Health Services of Canada
- Hydrolyzed → active metabolite 5-hydroxymethyl tolterodine
  - by CYP2D6 & CYP3A4 [cytochrome oxidase system]
- Does not cross blood brain barrier so minimal SE
- Prolonged $T_{1/2}$ (24 hours)
- No studies in children
- In adults – classified as 'beneficial'
  - Cochrane review comparing 3 RCT's it to tolterodine
    - Effectiveness similar: 74% vs 66%
    - ↓ adverse events 34% vs 58%
    - Improved subjective symptoms

Madhuvrata P, et al: Cochrane Database Sys Rev CDO05429; 2012

Other Antimuscarinic Agents - Solifenacin

ICS 2018 PHILADELPHIA

Solifenacin (Vesicare)

- Tertiary amine with primarily M_3 affinity
- Rapid onset effect
- Very long $T_{1/2}$ (50 hours)
- Minimal SE - dry mouth, constipation, blurry vision
- Effective in OAB

Currently, a phase III trial of drug for OAB is underway, in neurologically normal & neurologically impaired children ages 5 - 18

Solifenacin for Overactive Bladder

ICS 2018 PHILADELPHIA

- 72 children with OAB [CMG] who failed bladder retraining + anticholinergic Rx in past
- 27 – NBD; 45 – OAB; mean age 9 yrs (4.7 – 13.3)
- Dose (0.19 mg/kg [max 5mg/D] → 0.31 mg/kg [max 10 mg/D]) based on response & PVR
- Voiding parameters: Void vol., incontinence
- UDS parameters: cap (ml), DO (height cm H_2O),
- Subjective experience (QofL): PPBC [Patient/Parent /Bladder/Condition] – 6 point questionnaire
- ICCS criteria for improvement
- Monitored for SE

UDS Δ:

- Capacity ↑: - 146 → 311 ml
- DO height ↓: - 70 → 20 cm H_2O
- Voided/CIC vol $_{mean}$ ↑: 107 → 251 ml
- Incontinence episodes/day ↓: 3.0 → 0.3
- PPBC score ↓: 4.9 → 1.8
- Overall response:
  - 100% dryness – 33.3%
  - > 90% improvement – 58.3%
  - 50 – 89% improvement – 8.3%
- Side effects:
  - mild – 21%
  - moderate – 7%

Bolduc S, et al: J Urol 184: 1668, 2010

Other Antimuscarinic Agents - Propiverine

ICS 2018 PHILADELPHIA

Propiverine (Detrunorm)

- N-oxide is the main therapeutic metabolite
- Easily binds to plasma proteins with steady state levels ~ 4 - 5 days
- Ca^{+2} channel blocker - prevents influx of Ca^{+2} intracellularly that activates a rho kinase → contraction
- Binds to calmodulin which inhibits actomyosin ATPase
- High affinity for M_3 receptor
- Some binding to M_1 without crossing blood brain barrier
  - Few CNS & cardiac side effects d/t ↓ affinity
  - Causes dry mouth (parotid gland affinity - M_1)
- Moderate $T_{1/2}$ (8 hours)

Madersbacher H, Murtz G: World J Urol 19: 324, 2001

Propiverine Efficacy in Children

ICS 2018 PHILADELPHIA

- 2 studies (1 placebo controlled) 74 & 280 children, respectively
- Dose = 0.4 mg / kg BID
- Results
  - ↓ symptoms of wetting in 55%
  - FBC: 153 → 185 ml
- 3 prior older studies of 154 children 80% ↓ in enuresis +/- day symptoms

- Multi-center study comparing propiverine to oxybutynin 621 children w OAB symptoms (no invasive testing)
- Cohort: 437 – propiverine; 184 oxybutynin
- Dose / day: propiverine 15 mg; oxybutynin 10 mg
- Measurements
  - Voiding/day: propiverine [9.2 → 6.6]; oxybutynin [9.1→6.5]
  - Incontinence episodes/week: propiverine [6.2 → 1.8] oxybutynin [6.4 → 1.3]
  - Continence: propiverine (61.6%) oxybutynin (58.7%)
- Side effects: propiverine (2.8%) oxybutynin (9.2%) [*p=<0.001*]

Madersbacher H, Murtz G: World J Urol 19: 324, 2001

Allousi S, et al: BJU Int, 106: 550, 2009

Other Antimuscarinic Agents - Darfenacin

ICS 2018 PHILADELPHIA

Darifenacin (Enablex)

- Tertiary amine primarily M_3 antagonist with ↑ affinity
- Good detrusor effect but may cause constipation
- Does not cross blood brain barrier so minimal SE
- Prolonged $T_{1/2}$ (24 hours)
- No studies in children

Antimuscarinic Agents – Quaternary Amines

ICS 2018 PHILADELPHIA

Trospium (Sanctura)

- Quaternary amine mostly selective for M_3 + M_2 receptors
- More effective than oxybutynin / tolterodine
- Crosses blood brain barrier but low M_1 affinity, thus ↓ SE
- Long $T_{1/2}$ (20 hours)

Trospium for Overactive Bladder

ICS 2018 PHILADELPHIA

- 50 children with OAB tx with varying doss Trospium x 21 days with pre- & post UDS; compared with 8 given placebo
- Randomized dose (10,15, 20 & 25 mg/day); highest dose if wt > 40 kg
- UDS parameters: # of DO, vol. at 1st DO, DO Pr_{max}
- Response grading:
  - excellent: >30% ↑ in 1 UDS finding + dry
  - good: >30% ↑ in 1 UDS finding + >50% ↓ wetting
  - fair: no Δ UDS but >50% ↓ wetting
  - poor: no Δ UDS but <50% ↓ wetting

- Results drug vs placebo
  - Excellent: 16 (32%) vs 1 (12.5%)
  - Good: 21 (42%) vs 2 (25%)

  } 74% [*p=0.006*]
- Urodynamic changes
  - DO reduction: 4.6 → 2.1 (35% no D.O. 54% some ↓)
  - Volume at 1st contraction: 71 → 122 ml
  - Pr_{max} reduction: 47.6 → 19 cm H_2O
  - 4 (8%) had ↑ pvr
- Side effects 4 (8%)

Lopez Pereira P, et al: J Urol 170: 1978, 2003

Other Antimuscarinic Agents – Glycopyrrolate

ICS 2018 PHILADELPHIA

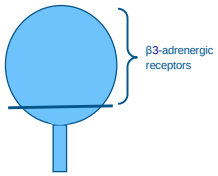
Glycopyrrolate (Robinul)

- Quaternary amine primarily selective for M_3 with low affinity for M_2 receptors
- Moderate $T_{1/2}$ (8 hours)
- Has more cardiac SE than other antimuscarinics
- No studies in children involving bladder function
- 0.5 – 1.0 mg BID seems to be an effective dose

β-Adrenergic Receptor Activity

ICS 2018 PHILADELPHIA

- 1° site for lower urinary tract effect – bladder body
- Agonists: ↓ smooth m. activity →
  - ↑ compliance
  - affects contractility by ↑ intracellular cyclic AMP & Ca^{++}
- Mirabegron: effective in adults with OAB
- No studies in children



β-Adrenergic Agents - Mirabegron

ICS 2018 PHILADELPHIA

Mirabegron – β_3 adenoreceptor agonist

- Blocks detrusor contractility via stimulation of β_3 receptors that inhibit M_2 receptors involved in muscle contraction
- Accomplished by releasing adenylyl cyclase that ↑ intracellular cyclic AMP & Ca^{+2} preventing contraction
- T ½ = 40 hours – 1x/day dosing
- ↓ Aδ & C fiber afferent activity (↑ SCI)
- Rapidly absorbed by GI tract
- Metabolized by cytochrome oxidase enzymes; **must** consider these pharmacokinetics & other drug interactions
- Much fewer adverse events seen than with antimuscarinics

Chapple C, et al: Neurourol & Urodynam 33:17, 2014
Geoffrion R, et al: J Obstet Gynaecol 39: 1221, 2017

β-Adrenergic Agents

ICS 2018 PHILADELPHIA

Mirabegron

- 60% experienced subjective improvement for OAB
- Similar cure rates compared to tolterodine
- When used as 'add-on' therapy → not significantly better but fewer adverse effects when compared with ↑ antimuscarinic dosing

One study - 7 adults with NDO

- Combination with antimuscarinic for antimuscarinic-refractory patients
- 100% ↑ incontinence
- 100% ↑ impaired compliance
- 40% ↓ detrusor overactivity

Geoffrion R, et al: J Obstet Gynaecol 39: 1221, 2017
Wada N, et al: Acta Urologica Japonica 61: 7, 2015

Mirabegron: Prospective, Multicenter, Double Blind, Placebo-Controlled, RCT

ICS 2018 PHILADELPHIA

66 pts (SCI / MS: 18 → 65 yrs)

Urodynamics: comparing drug to placebo:

- Volume to 1st contraction: ↑ [*p = 0.00047*]
- Compliance: ↑ [*p = 0.00041*]
- Capacity: No significant Δ [*p = 0. 061*]
- Det Pr_{max}: No significant Δ [*p = 0.78*]

Subjective findings: comparing drug to placebo:

- ↓ pad weight/ 24 hrs [*p = 0.056*]
- ↑ QoL questionnaire [*p = 0.006*]
- Tx satisfaction (Visual Analog Scale) [*p = 0.00045*]
- Patient perception of ↑ bladder condition [*p= 0.0013*]
- Drug-related adverse events = 3.12%

Krhut J, et al: Neururol Urodynam 37: 2018

Conclusions

ICS 2018 PHILADELPHIA

Plethora of available pharmaceutical agents

No one drug is specific for the bladder → systemic effects

Important to:

a. characterize LUT behavior & symptoms causing the dysfunction

b. Identify & manage bowel behavior prior to initiating pharmacotherapy

Most children respond to behavioral modification & 'urotherapy'

Antimuscarinics & other drugs should be reserved for "refractory" cases

Medical management can help to optimize treatment

The horizon looks promising, as we await drugs specifically targeting the detrusor

The End!

ICS 2018 PHILADELPHIA

ICS 2018 PHILADELPHIA

Antimuscarinics: Relation to 'M' Receptor Affinity

ICS 2018 PHILADELPHIA

Table 2 Affinity (pKi) of antimuscarinic compounds for the human recombinant receptor subtypes M1–M5 (14) [Mean (SEM)]

	M1	M2	M3	M4	M5
Darifenacin	8.2 (0.04)	7.4 (0.1)	9.1 (0.1)	7.3 (0.1)	8.0 (0.1)
Tolterodine	8.8 (0.01)	8.0 (0.1)	8.5 (0.1)	7.7 (0.1)	7.7 (0.03)
Oxybutynin	8.7 (0.04)	7.8 (0.1)	8.9 (0.1)	8.0 (0.04)	7.4 (0.03)
Propiverine	6.6 (0.1)	5.4 (0.1)	6.4 (0.1)	6.0 (0.1)	6.5 (0.1)
Trospium	9.1 (0.1)	9.2 (0.1)	9.3 (0.1)	9.0 (0.1)	8.6 (0.1)

Table 3 Comparison of the M3 : M1 selectivity of the antimuscarinic compounds (14)

	M3 vs. M1	p
Darifenacin	9.3	<0.001
Tolterodine	0.67	<0.05
Oxybutynin	1.5*	<0.05
Propiverine	0.67	<0.05
Trospium	1.5	NS

*Significant but unlikely to be biologically relevant. †Significant selectivity for M1 but unlikely to be biologically relevant.

Darifenacin seems to have ↑ affinity for bladder receptors with least attraction for brain and salivary gland receptors but controlled studies are needed

Parsons M, et al: Int J Clin Pract. 59; 851, 2005

Drug – Food Interactions when treating OAB

ICS 2018 PHILADELPHIA

Of the medicines to treat bladder dysfunction, only trospium's effectiveness was found to be significantly altered by food; therefore, the medication should be taken on an empty stomach.

Oxybutynin is metabolized by CYP3A4

Grapefruit juice is a known inhibitor of the enzyme.

Simultaneous consumption of oxybutynin & grapefruit juice may potentially increase the risk of adverse effects associated with the medication.

The clinical significance of this interaction remains unknown

Pasko P, et al: Int J Clin Pharm 38: 1350, 2016

α-Adrenergic Receptor Activity

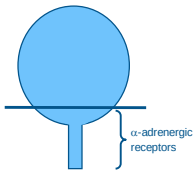
ICS 2018 PHILADELPHIA

Lower urinary tract
- Bladder neck
- Urethra

↑ smooth muscle contractility

↑ outlet resistance

Mediates DO via M_2 receptors



Combination Therapy: α Antagonists & Antimuscarinics

ICS 2018 PHILADELPHIA

No studies in children with LUTS

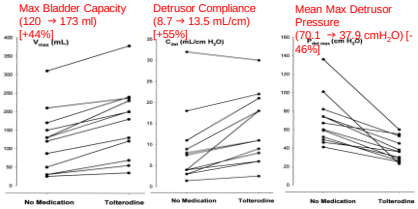
100 adults prospectively randomized propiverine alone vs propiverine + urapidil, assessed by symptom change + QOL questionnaire

Urinary symptoms improved significantly in both groups but no difference between groups

Matsuyama H, et al: Nippon Hinyokika Gakkai Zasshi 98:804, 2007

Tolterodine

ICS 2018 PHILADELPHIA

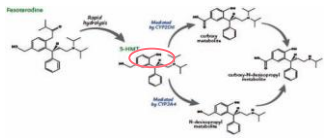


Goessl C, et al: Urol 55: 414, 2000

Fesoterodine

ICS 2018 PHILADELPHIA

Pharmacokinetics
- Active metabolite: 5 hydroxymethyl tolterodine (M_3 affinity)
- Conversion to active form by non-specific esterases CYP2D6 (genetic expression) → ↑ levels 5-HMT in serum vs tolterodine
- Active drug breakdown by CYP3A4 ~ for all antimuscarinics



Clean Intermittent Catheterization and Electrical Neuromodulation in Children with NB.

Giovanni Mosiello

ICS

GIOVANNI MOSIELLO, MD, FEAPU, FEBPS

Affiliations to disclose:

Medtronic: consultant
Wellspect: consultant
Coloplast: consultant
Pfizer: PI in clinical trial
Allergan: PI in clinical trial

Funding for speaker to attend:

- [X] Self-Funded
- [ ] Institution (non-industry) funded
- [ ] Sponsored by: Enter Company Name

ICS

Neurogenic Bladder Dysfunction Management Goal:

Achieve 'normal' bladder function
Healthy kidneys
Bladder empties completely at low pressure
Dry
No UTI

ICS

SPINA BIFIDA

0,3 – 4,5 per 1.000 live births
20% progress to renal failure (first year of life)
Renal Damage in 100% of DSD

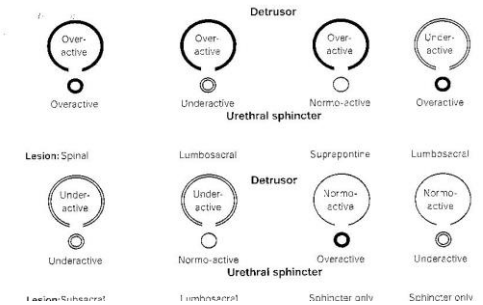
de Jong, Pediatr Nephrol, 2008

ICS

- Spinal Dysraphism
  - Open – myelodysplasia
  - Closed – occult dysraphism
    - Lipoma
    - Lipomningocele
    - Split cord syndrome (Diastematomyelia)
    - Thickened filum terminale
    - Anterior meningocele
  - Sacral Agenesis
  - Associated syndromes
    - Imperforate Anus (~ 40%)
- Central Nervous System Insults
  - Cerebral Palsy
  - Spinal Cord Injury
  - Tumors – Brain (Primary and Metastatic)
  - Tumors – Spinal cord (Primary and Metastatic)
- Metabolic Diseases

ICS

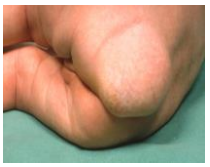
FUNCTIONAL CLASSIFICATION: MADERSBACHER,1990



ICS

Congenital Neuropathic bladder

Spina bifida / LMC / sacral agenesis


SPINA BIFIDA

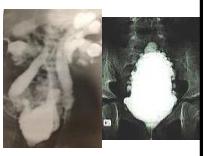
0,3 – 4,5 per 1.000 live births
20% progress to renal failure (first year of life)
Renal Damage in 100% of DSD

de Jong, Pediatr Nephrol, 2008

Dyssynergy
Risk of Upper Tract Deterioration

50% Spina Bifida Aperta
25% Occult Spinal Dysraphism

Pelvic floor behaviour changes from absent activity to overactivity in the first 2-3 months after back closure



de Jong, Pediatr Nephrol, 2008

Neurogenic Bladder Dysfunction in Spina Bifida

" it is disappointing to find, after doing surgery on the back, on the hydrocephalus and on the limb, that the child develops chronic ill because of renal damage "

Zachary, 1972

AT THE BIRTH RENAL FUNCTION= NORMAL

Children with congenital spinal cord lesions "at risk" Urodynamic Patterns

worsening of upper tract through age

44% with Dyssynergia
17% with Synergia
23% with complete Denervation

SB Bauer JAMA, 1984, 252:650
"Predictive values of urodynamic evaluation in newborns with myelodysplasia"

NEUROGENIC BLADDER

The newborn patient:

- Physical examination: anus open or closed?
- Ultrasound, VCUG, urodynamic study ?
- CIC 2dd-5dd, depending on sphincter status
- antibiotic prophylaxis
- oxybutinin

CHILD WITH OVERACTIVE SPHINCTER

Continent on cic

the upper tracts are at risk

dependence on oxybutinin or other medication

good care can reduce % cystoplasties from 90 to 5%

think about continent bladder stoma for cic

CHILD WITH PARALYTIC SPHINCTER

- Safe for the upper tract
- incontinent
- bladder can be too small
- for continence, depending on surgery

Neurogenic Bladder in Children

Initial Evaluation - URODYNAMICS

OPEN Spinal Cord lesions – myelodysplasia

Newborn: PVR (leak / Valsalva) by US /Cath
ability to empty

If cannot empty ICC is started promptly

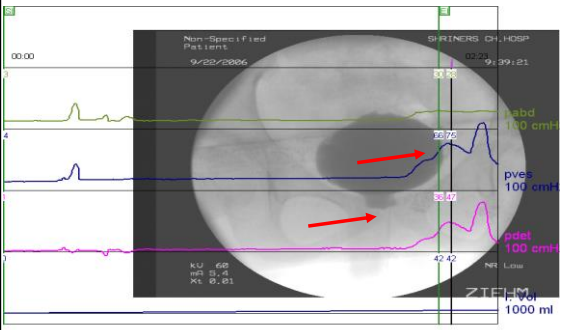
UDS at 2-3 months

CLOSED lesions – occult dysraphism

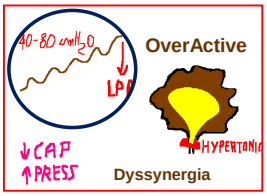
preoperatively (baseline)

Neurogenic Incontinence

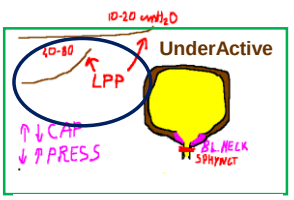
"Videourodynamics is irreplaceable"



"**at risk**" (high pressure) patterns for UUT / renal impairment



Dyssynergia - DSD



Low Compliant (LPP +)

Most important facts

Damage to the upper tracts occurs predominantly in the first months of life

Changes in the properties of the bladder wall occur predominantly in the first year of life

Thus, early start of therapy has enormous benefits!

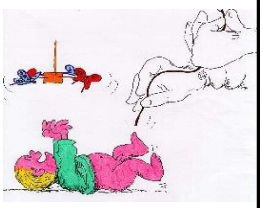
Clean Intermittent Catheterization
Newborn and Infant

Provides adequate means of bladder emptying

Maintains low bladder pressures

Preserves renal function

Useful to deliver antibiotics and/or anticholinergic drugs



ICS

Clean Intermittent Catheterization
Newborn and Infant

- Easily performed by parents / care providers
- Well accepted by children
- Start with 1-2 CIC/day and increase to 4-5/day over time

ICS

Benefits of Early CIC

….Children born with spina bifida can probably use their own kidneys for a lifetime if they start to receive adequate early urological treatment soon after birth. It is necessary to protect the upper urinary tract, ensuring low intravesical pressures…

P. Dik et al, Eur Urol, 2006

ICS

Benefits of Early CIC

….Clean Intermittent Catheterization and anticholinergic medication in newborns at risk maintain the integrity of the upper urinary tract in most myelodysplastic children …..

Kasabian et al, J Urol, 1992

….Identification and treatment of high pressure lower urinary tract significantly decreases the need for further bladder augmentation……

Kaefer et al, J Urol, 1999

ICS

Clean Intermittent Catheterization
Older Children

Self-catheterization can be mastered at school age

Progressing towards independence from family care

ICS

Clean Intermittent Catheterization

- May be difficult to accept by parents and patients
- Well accepted if started early in infancy

ICS

Clean Intermittent Catheterization Concerns

- Indications
- Timing
- Materials
- Training
- Adolescents
- Stoma indications
- Alternatives

CIC is Worldwide used: Italian Validated transl. EAU

Raccomandazioni	LE	GR
In tutti i bimbi iniziare cateterismi intermittenti subito dopo la nascita, tranne nei casi senza nessun chiaro segno di ostacolo alla minzione. Se l'inizio del cateterismo intermittente viene posticipato tenere sotto stretto controllo i pazienti per quanto riguarda IVU od alterazioni dell'alto apparato urinario.	2	B
Usare gli anticolinergici come trattamento iniziale nei bambini con vescica iperattiva. Il miglioramento clinico è frequente ma di solito insufficiente	2	B
Usare le iniezioni di tossina botulinica nel muscolo detrusore come alternativa nei bambini refrattari alla terapia con anticolinergici	2	B
Usare una procedura di ampliamento vescicale, con un segmento di intestino, nel caso di iperattività del detrusore refrattaria alla terapia medica, o di ridotta capacità e scarsa compliance vescicali che provochino danni all'alto apparato urinario ed incontinenza	2	B
Usare l'ampliamento vescicale con procedure aggiuntive sui meccanismi di svuotamento vescicale quando sia la vescica che il collo vescicale siano deficitarii. Il semplice ampliamento vescicale sarà sufficiente nella maggior parte di casi di vescica con bassa capacità ed alte pressioni.	3	B
Ampliare la vescica e creare un'aggiuntiva stomia continente e cateterizzabile dopo interventi sul collo vescicale ed in pazienti con difficoltà nella cateterizzazione uretrale.	3	B
Il follow-up del paziente con vescica neurologica dura tutta la vita ed include non solo il monitoraggio della funzionalità renale e vescicale ma anche l'assicurarsi che le problematiche di sessualità e fertilità ricevano particolare attenzione già in età pediatrica e durante la crescita del paziente fino all'età adulta	3	B

LUTD: disfunzioni del tratto urinario inferiore, NDSD: disfunzione neurogenica vescico-sfinterica
IVU: infezioni delle vie urinarie, RVU: reflusso vescico-ureterale

CLEAN INTERMITTENT CATHETERIZATION AND NEUROGENIC BLADDER TREATMENT IN CHILDREN: A SHORT WORLDWIDE SURVEY.

G MOSIELLO et al (ICCS 2012)

AIM. This preliminary study investigated CIC practice worldwide because different Clinical scenarios around the world due to variable social economic and cultural situations

MATERIAL AND METHODS
Nine multiple choice questions (MPCQ) were defined and addressed to 15 experts in NBD treatment.to describe 15 countries that were evaluated

Italy
Korea
China
Poland
Dubai
Taiwan
India
South Africa
Netherlands
Argentina
Russia
USA
Vietnam
Thailand
Bangladesh

Results

CIC is used in all countries, with the lowest rate in China (15%). Straining in 6/15 countries, suvrapubic in 10/15, Indwelling: 13/15.

Catheters Hydrophilic coated cath.are used in 12/15, Nelaton in 10/15 and rubber catheters in 4/15.

The correct "**single use**" catheter is reported regularly only in 6/15 countries while in 10/15 the one day reuse is reported. In 4/15 catheters are reused for a month or more

When patients are **not performing regularly CIC,** the most common **causes** are economical reason, catheter access difficulties and a need for education and a lack of specialized nurses.

Conclusion :short survey suggested that CIC concerns are present worldwide.

Solutions

Common guidelines, outreach/regional programs could be useful for increasing CIC .

Spinal Cord (2015), 1

www.nature.com/sc

LETTER TO THE EDITOR

Reply to Krassioukov *et al.*

G Mosiello[1,3], I Jansen[2] and M De Gennaro[1,4]

Spinal Cord (2015) **00**, 1. doi:10.1038/sc.2015.56

valuated athletes participating in paralympic games who performed lean intermittent catheterization (CIC), focusing on urinary tract nfections (UTIs) and catheter reuse, demonstrating a higher incidence f UTI in individuals who reused catheters. Furthermore, they valuated the relationship between country of residence and catheter euse, showing a significant relationship (higher frequency of reuse nd of UTI in developing nations).

In 2012, in the year of the London Paralympic Games, we involved group of worldwide experts (Center of Physical Reabilitation, Spinal Unit, Pediatric Urology Department) to understand, by their daily experience, CIC concerns in pediatric and young adult populations.[2]

We used a nine multiple choice questionnaire to define the situation Italy, Korea, China, Poland, EAU, Taiwan, India, South Africa, the Netherlands, Argentina, Russia, the USA, Vietnam and Thailand, valuating in this way different clinical scenarios related to diverse ocial, economic and cultural situations.

Same conclusion evaluating athletes of paralympic games have bee described by Krassioukov on his paper on the " the Good , the Bad and the Ugly of CIC".
This reinforced our belief to increase health education in low resources area, as well as encourage future research on UTI prevention.
Main role of scientific societies for educational program

CIC

ORIGINAL ARTICLE

Self-catheterization during adolescence

What are the problems?

GUNDELA HOLMDAHL, ULLA SILLÉN, KATE ABRAHAMSSON, ANNALENA HELLSTRÖM, SONJA KRUSE & EWA SÖLNER

Pediatric Urology and Nephrology Centre, Queen Silvia Children's Hospital, Göteborg, Sweden

The acceptance of CIC treatment decreases when the child gets closer to adolescence.

-problems and complications related to CIC in adolescence: median age of 16.5 yrs

Because **one of the main problem associated with self-catheterization during adolescence is non-compliance**

A poor CIC routine can cause UTIs,

adolescent must be supported and motivated to return to regular catheterization.

ICS

INDICATIONS FOR STOMA

Transfer for each cic

wheel-chair females

privacy of the patient

Appendix for simple cases

ileum tube when appendix is insufficient (Monti)

ureter etc. when available

complication rate is relatively high (20-50%)

ICS

Alternatives to Trans-Urethral CIC

Appendicostomy

- Provides an easily self-catheterizable stoma also in wheel-chaired patients

ICS

Reconstructive Urology

Techniques Used to Create Continent Catheterizable Channels: A Comparison of Long-term Results in Children

Pepijn D. Polm, Laetitia M.O. de Kort, Tom P.V.M. de Jong, and Pieter Dik

RESULTS

A total of 143 patients with 151 CCCs were identified; of these, 117 CCCs met the inclusion and exclusion criteria (67 APV, 31 TBF, and 19 Monti). Median follow-up was 85 (range 3-229) months and median age at time of surgery was 9 (range 1-17) years. Neurogenic bladder was the most common underlying pathology (90 cases, 77%).

CONCLUSION

A CCC is an elegant solution for children who cannot perform urethral CIC; however, 52% of our sample required surgical revision. Because we found no differences in time to surgical revision between APV, TBF, and Monti, we conclude that a TBF CCC is a good alternative for the APV. If the appendix is not available and bladder volume is sufficient, a TBF channel should be preferred to a Monti stoma.

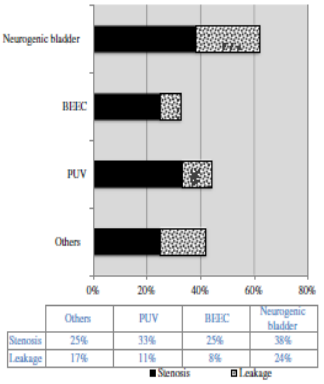
Table 3. Complications of continent catheterizable channels per technique

	APV n = 67 (%)	TBF n = 31(%)	Monti n = 19 (%)	Total n = 117 (%)	*P* Value
Stenosis	27 (40)	9 (29)	3 (16)	39 (33)	.119
False channel	4 (6)	4 (13)	2 (11)	10 (9)	.481
Incontinence	7 (10)	1 (3)	6 (31)	14 (12)	.013
Incontinence with low pressure*	1 (2)	0	3 (16)	4 (3)	.018

APV, appendicovesicostomy; TBF, tubularized bladder flap.
* Detrusor leak point pressure < 20 cmH_2O.

Journal of Pediatric Surgery

Bladder continent catheterizable conduit (the Mitrofanoff Long-term issues that should not be underestimated



	Others	PUV	BEEC	Neurogenic bladder
Stenosis	25%	33%	25%	38%
Leakage	17%	11%	8%	24%

■ Stenosis ■ Leakage

Alternative

Button Cystostomy

Cystostomy button is a continent catheterizable silicone device currently used as a gastrostomy button to deliver enteral nutrition.

de Badiola, F.I., et al., *New application of the gastrostomy button for clinical and urodynamic evaluation before vesicostomy closure.* J Urol, 1996. 156(2 Pt 2): p. 618-20.

ICS

Button Cystostomy: Is it Really a Safe and Effective Therapeutic Option in Pediatric Patients With Neurogenic Bladder?

Giovanni Mosiello, Ana Ludy Lopes Mendes, Maria Luisa Capitanucci, Antonio Maria Zaccara, and Mario De Gennaro

Table 1. Underlying pathologies

Neurogenic Disease	No. of Patients
Wolf-Hirschhorn syndrome (deletion of 4p)	2
Spina bifida and myelomeningocele	7
Down syndrome	1
Menkes syndrome (defect of the *ATP7A* gene)	2
Microcephaly and congenital tetraplegia	4
Hydrocephalus and tetraplegia	1
Tetraplegia and gangliosidosis II	1
Cranial trauma	2
Encephalopathy and severe cerebral palsy	6
Cauda equina regression syndrome	2
Beals auriculo-osteodysplasia syndrome	1
Mowat-Wilson syndrome (*ZEB2* gene mutations)	1
Anorectal malformation with sacral agenesis	1
Osler-Weber-Rendu syndrome with chronic renal failure and ischemic neuropathy	1
Nonobstructive chronic urinary retention	3

CONCLUSION

Cystostomy button has to be considered a safe and effective alternative treatment in pediatric patients suffering from bladder neurological dysfunction. This drainage method is easy to manage and well accepted by patients and caregivers, eliminating most of the social uneasiness created by CIC or suprabubic cystostomy and improving patients' satisfaction and quality of life.

This procedure has been used as a first- or a second-line treatment in severely impaired neurological patients or in patients declining CIC or with complications related to catheterization. In most of the cases, button cystostomy has been successfully used as a temporary measure for a more definitive procedure for bladder drainage such as Mitrofanoff procedure.

ICS

Different surgical steps of button cystostomy placement.
A, B: The bladder is puncturing twice percutaneously and the polypropylene 2-0 monofilament suture is inserted C,D: The loop created inside the bladder and the traction of the bladder wall; E: visualization of the traction inside the bladder. F: Amplatz dilator sizing the cystostomy; G) Cystostomy button in place

ICS

RESULTS

Author	N° Pts°	Technique	Complications	Mean follow-up	Satisfaction
De Badiola[3] (1996)	3	Open	None	30 days	Not Evaluated
Milliken[14] (2007)	17	open	1 wound infection 4 leakage after the insertion period	16 months	Yes
Bradshaw[12] (2014)	30	Open	7 UTI, 1 UTI and leak, 2 Wound infection 1 Wound infection and granulation, 5 Leak 3 Granulation	18 months	Yes
Haider[11] (2008)	12	Percutaneous	None	11 months	Yes
Lacreuse[4] (2010)	21	Percutaneous	1 bladder lithiasis and peristomal leakage, 3 UTI 1 UTI and peristomal leakage, 5 peristomal leakage	24 months	Yes
Hitchcock[5] (2006)	21	Open	1 UTI, 2 button side infections, 3 leakage 1 leakage and side infection, 1 UTI side infection 2 UTI granulation, 2 granulation **(Two revision for button displacement and for persistent leakage)**	30 months	Not Evaluated
Our Series	35	Open and percutaneous	1 button decubitus, 6 UTI, 1 UTI button side infection 1 stone with UTI, 1 button leakage and UTI 1 difficulties in bladder emptying and UTI 1 button leakage **(Two reoperations: one for button decubitus and one for bladder stone)**	37 months	22 patients on-going cystostomy button are satisfied

ICS

Alternatives to Trans-Urethral CIC

Button Vescicostomy

- When CIC is not accepted or tolerated in the older child

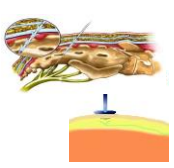
- Provisional mean of bladder emptying while familiarizing with CIC in the infant

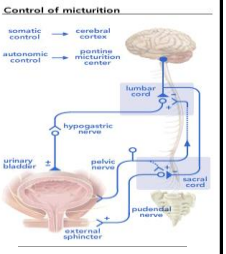
ICS

Review Article

Current State of Nerve Stimulation Technique for Lower Urinary Tract Dysfunction in Children

Mario De Gennaro,* Maria Luisa Capitanucci, Giovanni Mosiello and Antonio Zaccara





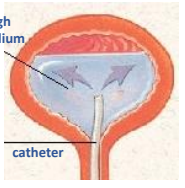
THE JOURNAL of UROLOGY®

ICS

✓ Low Invasive ES

Intravesical Electrical Stimulation - IVES

- **1878** Saxtorph
- **1975** Katona F, Berenyi M: IVES in NB



- **1970 -1980** several NRCTs, few pts, conflicting results:
  - improvement rate : 0-80%
  - cure rate :0-25%

ICS

PTNS

Author, Year	Pts.	Study Type	LUTD	Clinical Outcome (%)	UD Outcome (%)
Hoebeke P, **2002**	32	NRCT	OAB	25 cured 35 improv.	- -
De Gennaro M, **2004**	23	NRCT	OAB DV **NB**	80 improv. 71 improv. **NO improv.**	62.5 normal BC 50 normal PVR **NO improv.**
Capitanucci ML **2009**	44	NRCT	OAB DV	41 cured 71 cured	33 normal Vvol 57 normal PVR

- ✓ Good results in OAB and DV (refractory to conventional treat.)
- ✓ NO results in NB (limited number of pts.)

Tibial nerve stimulation for treating NEUROGENIC LUTD: systematic Review , Schneider 2015MP

PTNS
ADULT

469 pts in 16/1943 Studies: 4 RCT, 9 PCS, 2 RCS 1 CR

Multiple sclerosis, Parkinson's disease, cerebrovascular accident, spinal cord injury

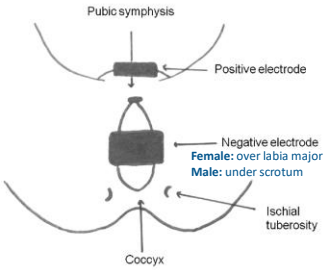
PTNS	Increase in MCC	Increase in BD at I DO	Decrease in Max detr. press.	Decrease N°. Void.	Decrease N°. leak	Decrease in PVR
ACUTE	56 - 132	44 – 92	5-15	-	-	-
CHRONIC	49 - 150	93 - 121	4-21	3 - 7	1 - 4	15 - 55 ml

Conclusions : Early data suggest PTNS might be effective and safe for treating NLUTD, but more reliable evidence is required

✓ **Non Invasive ES**

Functional Electrical Stimulation - FES

- 15 min./session
- 3 sessions/week
- Tot. Session: 15



Kajbafzadeh AM, 2009

FES

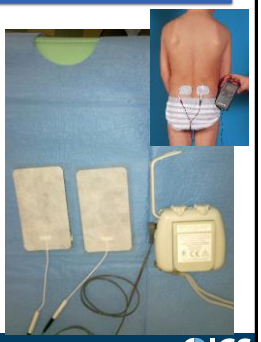
Author, Year	Pts.	Study Type	LUTD	Clinical Outcome (%)	UD Outcome (%)
Trsinar B, **1996**	.	RPT	OAB	75 improv.	BC augmented -
Kajbafzadeh AM, **2009**	30	RPT	**NB**	**78 cured**	Max detr. press. augmented
Kajbafzadeh AM, **2014**	44	RPT	**NB**	Incont. score improved	DLPP increased

- ✓ Reasonable results in OAB and NB
- ✓ **Is stimulation of anal/genital region really non-invasive in children ?**

✓ **Non Invasive ES**

Transcutaneous Electrical Nerve Stimul. - TENS

- Surface Electrodes at S2-S3 level
- 2 hour/day
- 1 – 9 months
- Frequency 2 Hz



TENS

Author, year	Pts.	Study	LUTD	Results (%) CLINICAL	Results (%) UD
Balcom AH, **1997**	29	NRCT	**NB**	Sensation improv.	BC augment.
Hoebeke P, **2001**	41	NRCT	OAB	76 improv. 56 cured	BC augment.
Barroso U, **2006**	36	NRCT	OAB DV	59 cured -	- PVR improv.
Malm-Buatsi E, **2007**	18	NRCT	OAB	60 improved 13 cured	Vvol normalized
Hagstroem S, **2009**	27	RCT	OAB	61 improv.	Vvol unchang.
Fajardo de Oliveira L, **2013**	45	RCT	PMNE	61.8 improv.	-
Quintiliano F , **2014**	28	RCT	OAB	46 cured	-

Neuromodulation

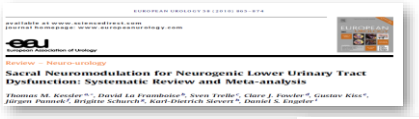
Concept: *NM, applied in urology to chronic diseases, modules the reflexes pathways which control the activity of:*

- Detrusor
- Rectum
- Pelvic floor
- sphincters

Neuromodulation

Overactive bladder
Dysfunctional voiding
Underactive bladder (lazy bladder)
Neurogenic bladder dysfunction

Foecal incontinence
Chronic constipation



Sacral Neuromodulation for Neurogenic Lower Urinary Tract Dysfunction: Systematic Review and Meta-analysis

25/563 included for meta-analysis

A pooled success rate of 68% for the test phase and of 92% for permanent SNM as well as a pooled adverse event rate of 0% for the test phase and of 24% for permanent SNM

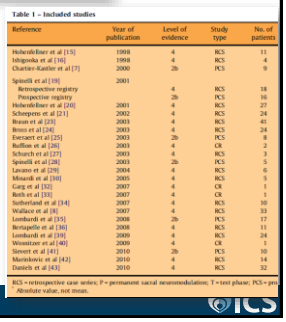


Table 1 – Included studies

Reference	Year of publication	Level of evidence	Study type	No. of patients
Hohenfellner et al [15]	1998	4	RCS	11
Ishigooka et al [16]	1998	4	RCS	4
Chartier-Kastler et al [7]	2000	2b	PCS	9
Spinelli et al [19]	2001			
Retrospective registry		4	RCS	18
Prospective registry		2b	PCS	16
Hohenfellner et al [20]	2001	4	RCS	27
Scheepens et al [21]	2002	4	RCS	24
Braun et al [23]	2003	4	RCS	41
Brines et al [24]	2003	4	RCS	24
Everaert et al [25]	2003	2b	PCS	8
Ruffion et al [26]	2003	4	CR	2
Schurch et al [27]	2003	4	RCS	3
Spinelli et al [28]	2003	2b	PCS	5
Leuano et al [29]	2004	4	RCS	6
Minardi et al [30]	2005	4	RCS	5
Garg et al [32]	2007	4	CR	1
Roth et al [33]	2007	4	CR	1
Sutherland et al [34]	2007	4	RCS	10
Wallace et al [8]	2007	4	RCS	33
Lombardi et al [35]	2008	2b	PCS	17
Bertapelle et al [36]	2008	4	RCS	11
Lombardi et al [39]	2009	4	RCS	24
Wiesinger et al [40]	2009	4	CR	1
Sievert et al [41]	2010	2b	PCS	10
Marinkovic et al [42]	2010	4	RCS	14
Daniels et al [43]	2010	4	RCS	32

RCS = retrospective case series; P = permanent sacral neuromodulation; T = test phase; PCS = pro
* Absolute value, not mean.

Different outcome measures

Neurogenic Bladder

leaking episodes per day (number and degree)
Number of pads replaced per day
Post void residual
N° of intermittent catheterisms per day

Neurogenic Bowel

- Episodes of faecal incontinence per day
- Number of defecation per day
- Wexner score

SACRAL NEUROMODULATION FOR NEUROGENIC BLADDER DYSFUNCTION IN CHILDREN

J. M. GUYS

JOURNAL OF UROLOGY
172, 1673–1676, October 2004

This study was based on the rationale that residual neurogenic activity can subsist in the medullary cone of patients with congenital neurogenic bladder due to defects such as spina bifida and that the level of response depends on the extremely variable extent of intact nerve structures.

Guys JM, Haddad M, Planche D et al.
Sacral neuromodulation for neurogenic bladder dysfunction in children
J Urol 2004

First multicenter study published on SNM in children

42 patients with spina bifida, randomized NMS vs conventional treatment

Other than 1 child who achieved continence with CIC, the study failed to demonstrate significant beneficial effects.

More regular fecal transit and reduced urinary leak were observed in 50% of patients, and bladder sensation was reported in 14%.

A significant increase in leak point pressure was observed in the implant group.

Sacral Neuromodulation in Children With Urinary and Fecal Incontinence: A Multicenter, Open Label, Randomized, Crossover Study
***M. Haddad,* R. Besson, D. Aubert et al.,* THE JOURNAL OF UROLOGY 2010**

A total of 41 patients underwent trial assessment between April 2004 and September 2007, mean age 12.22± 5.09 years.

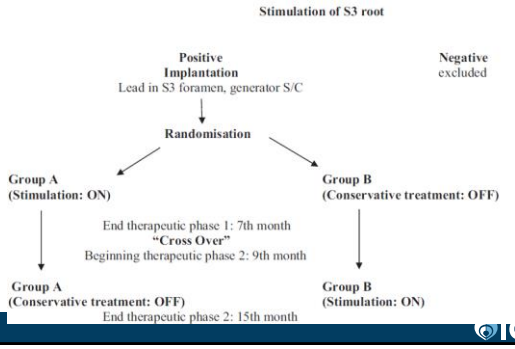
The S3 root was detected in only 33 patients who were randomized, overall implantation success was 81%.

Incontinence was urinary only in 9 patients, fecal only in 5 and mixed in 19. A total of 17 patients with urinary incontinence were on CIC.

The most frequent underlying etiologies were: spina bifida in 10 patients, sacral agenesis in 8, miscellaneous neurological anomalies in 7 (including 2 tumors), and congenital colonanal and urinary malformations in 5.

Patients were randomly divided into 2 treatment groups

Sacral Neuromodulation in Children With Urinary and Fecal Incontinence: A Multicenter, Open Label, Randomized, Crossover Study
***M. Haddad,* R. Besson, D. Aubert et al.,* THE JOURNAL OF UROLOGY 2010**

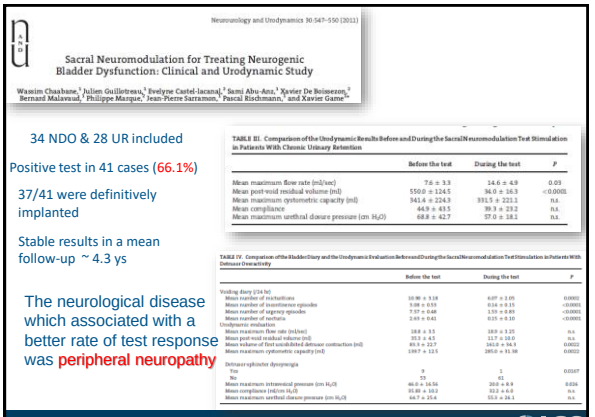


Sacral Neuromodulation in Children With Urinary and Fecal Incontinence: A Multicenter, Open Label, Randomized, Crossover Study
***M. Haddad,* R. Besson, D. Aubert et al.,* THE JOURNAL OF UROLOGY 2010**

Clinical response was significantly better when SNM was ON than OFF (75% vs 21%, p 0.001). No patient was scored as a responder when SNM was OFF and nonresponder when SNM was ON.

A significant increase in cystometric bladder capacity was observed during stimulation (delta 24.27 ml vs 37.45 ml, p 0.01). The bladder was significantly more overactive with than without neuromodulation (1 vs 0.36, p 0.001). No significant difference was noted between other urodynamic and rectomanometric variables

The procedure was well tolerated: two types of complications occurred, ie infection (4 cases) and electrode migration (2). No patients dropped out of the study due to worsening urodynamic parameters with upper tract deterioration.



34 NDO & 28 UR included

Positive test in 41 cases (66.1%)

37/41 were definitively implanted

Stable results in a mean follow-up ~ 4.3 ys

The neurological disease which associated with a better rate of test response was peripheral neuropathy

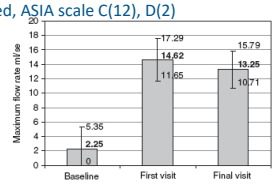
Clinical concomitant benefits on pelvic floor dysfunctions after sacral neuromodulation in patients with incomplete spinal cord injury

Spinal Cord (2011) 49, 629–636
G Lombardi,

- 75 incomplete SCI lesions were selected
- 37 at least 2 chronic (bowel, urinary, erectile) dysfunction
- 14 (8 NOUR, 6 UI) implanted, ASIA scale C(12), D(2)

➢ 5/8 NOUR only ICC, 3/8 2-3 ICC + void (high PVR) residual detrusor contraction

➢ 2/8 no cath 6/8 only one cath/day



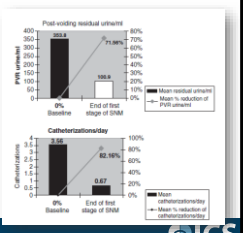
Urodynamic results on N-NOUR, 10 YEAR

Spinal Cord. 2014 Mar;52(3):241-5. doi: 10.1038/sc.2013.155. Epub 2014 Jan 7.
Sacral neuromodulation for neurogenic non-obstructive urinary retention in incomplete spinal cord patients: a ten-year follow-up single-centre experience.
Lombardi G[1], Musco S[1], Celso M[1], Del Corso F[1], Del Popolo G[1].

Retrospective study
36/84 incomplete SCL were responders to SNM

A statistically significant increase in Qmax ml per sec and decrease in post-voiding residual urine per ml were documented. (P<0.01).

First sensation of bladder filling at baseline represented a statistically significant parameter for the success of the first stage SNM (P<0.05)



Although the results of SNM in neurological patients are promising, the evidence level of the studies is generally low, and RCTs are lacking.

OPBG: personal experience 2018 :55 pts
Long –term follow-up

14 Neurogenic,
Incomplete neurologic lesion
Mixed bladder emptying regime (spontaneous and CIC)
7 Congenital NBD 7 Acquired NBD
Motivated patients and families

A

Response = Patients satisfaction + one or more of the following criteria:
- <50% Incontinence episodes
- <50% Post voiding residual
- <50% Need for CIC
- >50% Increase voided volume

OPBG

- 14 children, mean age 16.1 (10-21) yrs.
- Total success 71,4%
- 86% Acquired NBD positive response
- 57% Congenital NBD positive response
- Limited number :no statistical difference between the two groups

A

literature

Groen - Hoebeke et al., 2012
5 pts. 3 Congenital, 2 Acquired

Haddad – Besson et al., 2010
30 pts

Sievert-Amend et al., 2010
1 pt. Acquired Complete lesion

Wosnitzer-Walsh et al., 2009
1 pt. Acquired Incomplete lesion

Guys – Haddad et al., 2004
21 pts. 16 Congenital, 5 Acquired

Schurch-Reilly et al., 2003
2 pts. Acquired Complete

Total: 57 pt.

- Total response 70,4 %
- 18 Congenital
- 14 Acquired
- 25 Not specified

B

Results

Evaluation of our patients together with patients found in literature

- Total 71 patients
- Total response: 71,4% (OPBG) and 70,4% (literature)
- Response incomplete SCI: 75% (OPBG) and 100% (literature)
- Response complete SCI: 0% (literature)
- Response myelomeningocele: 0% (literature)
- Response closed spina bifida: 57% (OPBG)

A + B

Sacral Neuromodulation in Children
Concerns

Prospective Evaluation of Sacral Neuromodulation in Children: Outcomes and Urodynamic Predictors of Success

Matthew D. Mason,* Heidi A. Stephany, Daniel P. Casella, Douglass B. Clayton, Stacy T. Tanaka, John C. Thomas, Mark C. Adams, John W. Brock III and John C. Pope IV

http://dx.doi.org/10.1016/j.juro.2015.11.084
Vol. 195, 1239-1244, April 2016
Printed in U.S.A.
www.jurology.com | 1239

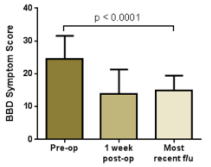


Figure 2. BBD symptom scores before and after SNM. f/u, followup.

Results: During 45 months 30 patients were enrolled. Median age was 8.3 years at enrollment. Median followup was 14.8 months. Patients had significant improvement in quality of life and symptom scores, which persisted at the most recent followup. Patients who had uninhibited detrusor contractions on preoperative urodynamic assessment had significantly greater improvement in symptoms. Of the patients 23% had a complication requiring reoperation, most commonly neurostimulator lead breakage in those with a significantly lower body mass index.

Conclusions: Sacral neuromodulation significantly improves quality of life and symptom severity in children with refractory bowel bladder dysfunction. Children gain greater benefit if they show uninhibited bladder contractions on preoperative urodynamic evaluation. Children have a high rate of lead breakage requiring operative revision, which was seen after minor trauma in those with a lower body mass index.

ICS

Occult spina bifida ?

ICS

Is MRI possible for follow-up use in for neurogenic patients? For Kavia and coll.

YES

- 1) In patients implanted can run in safe mode a spinal MRI up to 1.5 Tesla
- 2) you can switch off the sacral neuromodulator during an MRI and then reprogram it after examining diagnostic

Never adverse events or changes in stimulation parameters set.

ICS

Sacral nerve stimulation: a promising therapy for fecal and urinary incontinence and constipation in children☆

Jason P. Sulkowski [a,b], Kristine M. Nacion [a], Katherine J. Deans [a,b], Peter C. Minneci [a,b], Marc A. Levitt [b], Hayat M. Mousa [b,c], Seth A. Alpert [b,c], Steven Teich [b,c]

In this prospective study they have treated 29 patients with a mixture of neuropathic and non neuropathic BBD.
Outcomes at 17 weeks shown an overall improvement of 62% (87,5% improvement in gastrointestinal symptoms and 78,5% in urinary parameters

Table 1
Baseline characteristics of patients who underwent placement of sacral nerve stimulator (SNS).

	SNS placement participants (N = 29)
Male, n (%)	13 (44.8)
Race, n (%)	
White	26 (89.7)
Non-white	3 (10.3)
Age, median (IQR)	12.1 (9.4, 14.1) years
Symptoms, n (%)	
Gastrointestinal	27 (93.1)
Urinary	19 (65.5)
Both	17 (58.6)
History, n (%)	
Idiopathic	19 (65.5)
Hirschsprung's disease	1 (3.4)
Syrinx	1 (3.4)
Imperforate anus	8 (27.6)
With tethered cord	1 (3.4)
With myelomeningocele	1 (3.4)

Data are presented as medians and interquartile ranges (IQR) for continuous variables and frequencies and percentages for categorical variables.

In conclusion: The short term improvement in symptoms and QoL in this stud that the SNS may be a promising therapy in pediatric patients with both gastrointestinal and urinary dysfunction that has been refractory to standard medical management

ICS

Sacral Neuromodulation in Children
Concerns

Experience from adults offered this treatment modality suggests future positive development in children to be likely.

Level of evidence: 3.

Grade of recommendation C

THANK YOU

ICS

Urodynamically Guided Surgical Procedures for Incontinence in Children with Neurogenic Bladder

Israel Franco, MD
Clinical Professor of Urology
Director of the Yale/ New Haven Health
Children's Bladder and Continence Program
New Haven CT, USA

Yale SCHOOL OF MEDICINE

Urodynamic studies (UDS) in children

- Non-invasive
  - History, dairies and uroflow
- Invasive UDS
  - Measuring detrusor pressures related to filling and voiding

Study Lower Urinary Tract functions and dysfunction:
- Can give better understanding of signs and symptoms
- Can establish diagnosis
- Can give guidance to management
- Can change the management

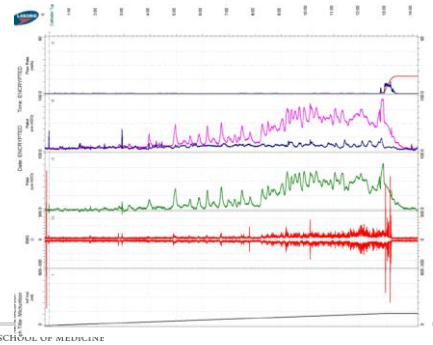
Management of Children with NB

- Pharmacologic
  - Bladder directed
    - Anticholinergics
    - Alpha blockers
    - Beta 3 agonists
    - Botulinum Toxin A
  - Neurologically directed
    - Intrathecal baclofen (GABA Agonists)
    - Oral Baclofen
    - benzodiazepines

Management of Children with NEUROGENIC BLADDERS

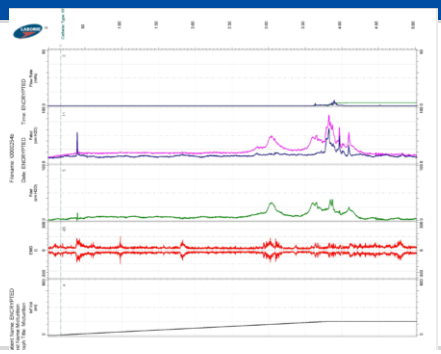
- Neurosurgical management
  - Primary decompression and untethering
  - 2nd decompression and untethering
- Urologic Management
  - Bladder Pressure management
    - Abatement of detrusor overactivity
    - Lowering of end filling Bladder Pressure
  - Continence procedures
  - Facilitation of Catheterization
  - Incontinence procedures
    - External sphincterotomy
    - Urethral overdilation

Detrusor Overactivity in 5 YO with previous back surgery. What Do You Do?



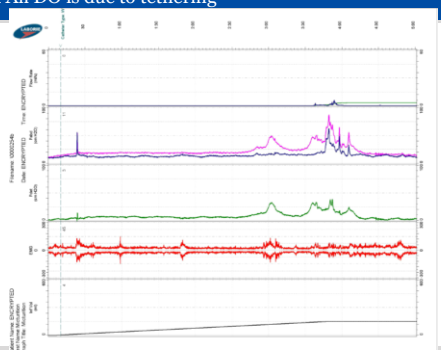
MS s/p dethering for dermal sinus

Is this a tethered cord or not?

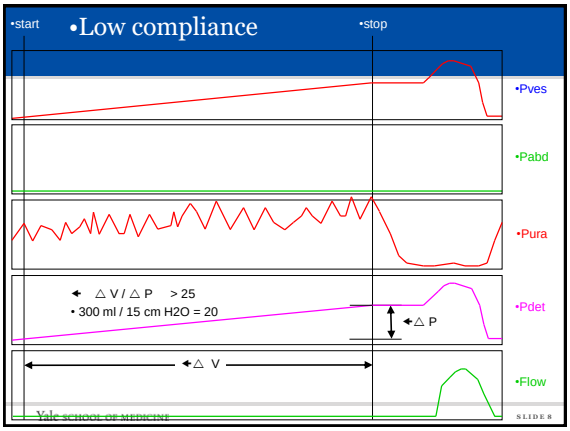


In some cases must rule out NP Causes for wetting.

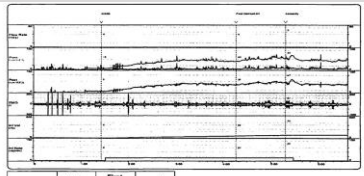
Not All DO is due to tethering



•Low compliance

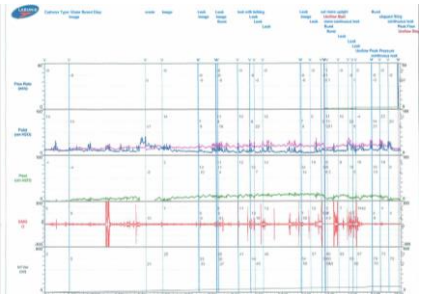


28 mo female with recurrent UTI's and high grade reflux



	Units	First Sensation	capacity
Time	mm:ss	4:16	5:19
Inf Vol	ml	55	76
Pves	cmH2O	40	54
Pabd	cmH2O	4.8	6.8
Pdet	cmH2O	35	47
Flow Rate	ml/s	0.0	0.0
Void Vol	ml	-0.2	-0.3
Inf Rate	ml/min	20	20

28 mo female with recurrent UTI's and high grade reflux
Post Botulinum Toxin A injection



Low capacity low compliance bladder
RX options:

- Botulinum Toxin A: these injections are one simple step that can allow the surgeon to get additional volume out of some bladders.
- Ileal augments
  - Pros: less mucous production compared to other bowel segments
  - Cons: thinner muscularis making implantation into more difficult and less secure,
- Ileocecal augments
  - Pros: appendix is attached, thereby making catherizable channel easier to make, ureters can be implanted into it along tinea more securely and easier than in ileum
  - Cons: risk of vitamin b12 deficiency, diarrhea is a potential complication, more mucous production due to cecal segment

Low capacity low compliance bladder RX options:

- Sigmoid augments
  - Pros: thicker muscularis making implantation into it easier, sigmoid is in the pelvis so it can be readily placed on top of the bladder reducing the need to do extensive bowel mobilization
  - Cons: increased mucous production and greater risk for stone formation, chloride absorption is increased leading to increased risk for metabolic acidosis.
- Demucosalized augments
  - Pros: reduced mucous production and no associated metabolic derangements associated with urine absorption
  - Cons: difficult to perform, requires the use of special form to be placed in the bladder to prevent contraction of the augment

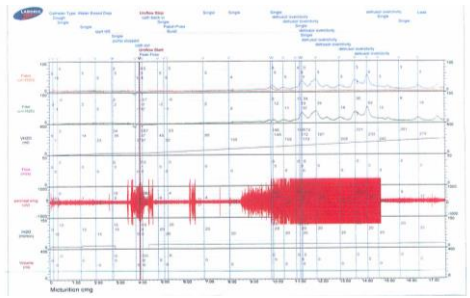
Low capacity low compliance bladder RX options:

- Detrusorraphy
  - Pros: no issues with mucous production and no associated metabolic derangements associated with urine absorption
  - Cons: original surgery had low success rate, volume generally not increased with greatest effect on compliance.
- Ureteral Augments
  - Pros: no issues with mucous production and no associated metabolic derangements associated with urine absorption
  - Cons: volume gains are minimal to modest at best.

Considerations before performing surgery

- How many times has the patient had intraabdominal surgery
- Do they have a shunt?
- Is there adequate bowel to perform an augmentation cystoplasty
- Is there reflux present
- What about the size and width of the ureters

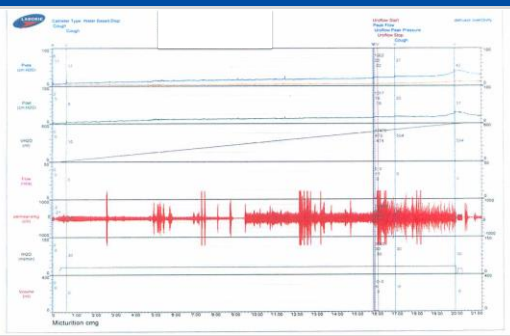
14 yo female with persistent urinary incontinence after a mitrofanoff procedure



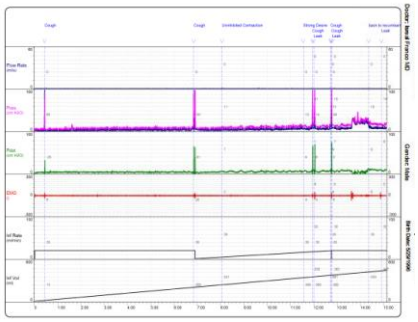
What are our options in this case?

- Eliminate DO
  - Meds
  - Botulinum Toxin A
  - Bladder augmentation
- Low outlet resistance
  - Bladder neck reconstruction
  - Bladder neck sling
  - Bulking Agents

14 yo with persistent urinary incontinence after a mitrofanoff procedure
Post op Botulinum Toxin A injection and Bladder Neck sling



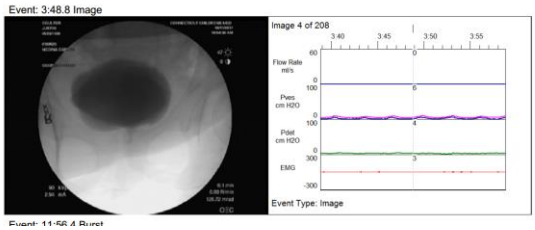
22 yo male with persistent urinary leakage after BLADDER NECK sling and Bladder augmentation



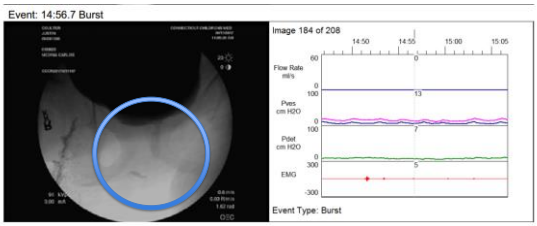
Leaks occur at

360 ml 8 cm
383 ml 13 ml
430 ml 18 cm

22 yo male with persistent urinary leakage after BLADDER NECK sling and Bladder augmentation



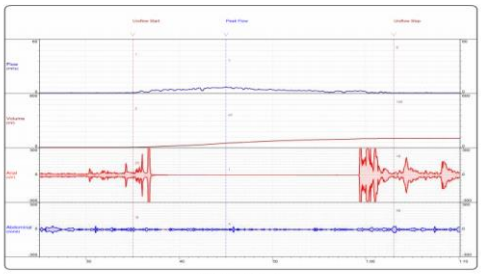
22 Yo Male With Persistent Urinary Leakage After BLADDER NECK Sling And Bladder Augmentation



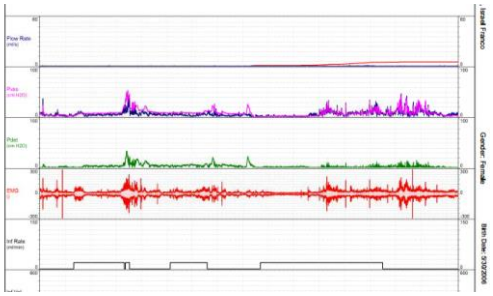
What type of patients need help catheterizing?

- Neurogenic bladder patients with difficult access
  - Wheelchair bound patients especially females
  - Obese patients
  - Patients with tortuous urethras
  - Patients with slings
- Non Neurogenic patients
  - Prune belly patients
  - Non neurogenic neurogenic bladder patients
  - Underactive bladder patients

12 yo girl with vesicostomy for non neurogenic neurogenic bladder



12 yo girl with vesicostomy for non neurogenic bladder



Combined medical and surgical treatment

- Non functioning left kidney
- Left lap nephrectomy
- Mobilizied ureter and brought ureter to skin to be able to cath via ureteral stoma

- Now is perfectly dry
- Performing CIC via ureteral stoma
- Is voiding normally after treatment of bladder neck dysfunction with flomax and Prozac

Conclusions

- Urodynamic studies are critical in helping you select the surgical procedure that best suits the problem
- Video urodynamics are critical in evaluating patient with urinary incontience issues
- Urodynamics does not delineate neurogenic from non neurogenic detruosr overactivity
- Not all patients with DO have a tethered cord

0022-5347/04/1714-1652/0
THE JOURNAL OF UROLOGY®
Copyright © 2004 by AMERICAN UROLOGICAL ASSOCIATION
Vol. 171, 1652–1653, April 2004
Printed in U.S.A.
DOI: 10.1097/01.ju.0000116066.72132.9a

LAPAROSCOPIC APPENDICOVESICOSTOMY (MITROFANOFF PROCEDURE) IN A CHILD USING THE DA VINCI ROBOTIC SYSTEM

ROBERTO PEDRAZA, ADAM WEISER AND ISRAEL FRANCO
From the Department of Pediatric Urology, New York Medical College, Valhalla, New York