W5: Neurodegenerative disease's impact on bladder function: A multidisciplinary approach in diagnosis, treatment and improving quality of life

Workshop Chair: Christian Cobreros, Argentina
28 August 2018 09:00 - 10:30

Start	End	Topic	Speakers
09:00	09:05	Introduction	Christian Cobreros
09:05	09:15	Understanding clinical differences in neurodegeneratives disesases	Christian Cobreros
09:15	09:25	Physiotherapy assessment of patients with neurogenic bladder. Keeping the whole patient in mind.	Elizabeth Shelly
09:25	09:35	Video - Urodynamic value in patients. When? Why? Are there any other diagnostic methods that you should use?	Christian Cobreros
09:35	09:45	It is always easy to differentiate urgency from another clinical presentation of these patients (e.g. pain, hypersensitivity, bladder irritation, infection)? How can we avoid over medication?	David Castro-Diaz
09:45	09:55	Oral medication. What do we have today? Is combination better? How to decide when to move to another step?	Christian Cobreros
09:55	10:05	Surgical approach: Botulinum toxine, NTS, Neuromodulation, Bladder augmentation.	Carlos D'Ancona
10:05	10:15	The role of Physiotherapists and a multidisciplinary team in the daily life of patients. Can we improve their quality of life if we work together?	Elizabeth Shelly
10:15	10:30	Case presentations: Interactive activity with the audience and panel	Panel

Aims of Workshop

In the past decades, the aim of the urologist was to treat the neurogenic bladder dysfunction through antimuscarinics and surgical procedures (e.g. bladder augmentation). More recently, new drugs have been approved and new surgical procedures have been developed, but more importantly a new role for the multidisciplinary approach has been established. We will encourge this new concept of treatment to the audience, taking into account differences in incomes of different societes. This a new workshop based on the state of the art knowledge and latest tecniques that are available and with an international pannel of experts we will extent our experience in working under different economic circunstances

Learning Objectives

1- Identify the different patterns of neurological bladdder impacts of neurologic diseases.
2- Transmit the state of the art in treatment and improving quality of life in patients.

Learning Outcomes

After the course, we will expect that the participants will:
Identify basic neurological patterns of bladder activity and malfunction.
Demonstrate technically correct interpretration of urodynamic patterns.
Understand how a multidisciplinary working team will represent a benefit.
Identify, according to each economic possibility, how they can improve the quality of life of their patients.

Target Audience

Urologist, physiotherapist.

Advanced/Basic

Basic

Conditions for Learning

Interactive.

Suggested Learning before Workshop Attendance

ICS teaching module: Cystometry (basic module).
ICS teaching module: Analysis of voiding, pressure flow analysis (basic module).

Suggested Reading

Neurourol Urodyn. 2017 Nov 17. An International Continence Society (ICS) report on the terminology for adult neurogenic lower urinary tract dysfunction (ANLUTD).
Eur Urol. 2014 Feb;65(2):389-98. Detrusor underactivity and the underactive bladder: a new clinical entity? A review of current terminology, definitions, epidemiology, aetiology, and diagnosis.
Curr Urol Rep. 2014 Sep;15(9):433. UTIs in patients with neurogenic bladder.
Eur Urol. 2014 May;65(5):981-90. doi: 10.1016/j.eururo.2013.10.033. Epub 2013 Nov 1. An updated systematic review and statistical comparison of standardised mean outcomes for the use of botulinum toxin in the management of lower urinary tract disorders.
Int Urogynecol J. 2017 Feb;28(2):191-213. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for the conservative and nonpharmacological management of female pelvic floor dysfunction.
Neurourol Urodyn. 2017 Jun;36(5):1243-1260. Epub 2016 Dec 5. Review. International Continence Society Good Urodynamic Practices and Terms 2016: Urodynamics, uroflowmetry, cystometry, and pressure-flow study.
Cochrane Database Syst Rev. 2014 Sep 23;(9):Types of indwelling urethral catheters for short-term catheterisation in hospitalised adults.
Cochrane Database Syst Rev. 2015 Dec 10;(12):Urethral (indwelling or intermittent) or suprapubic routes for short-term catheterisation in hospitalised adults.
Cochrane Database Syst Rev. 2017 Aug 8;8:WITHDRAWN: Intermittent catheterisation for long-term bladder management.
Cochrane Database Syst Rev. 2013 Nov 18;(11): Review. Catheter policies for management of long term voiding problems in adults with neurogenic bladder disorders.

Other Supporting Documents, Teaching Tools, Patient Education etc

Paritcipans will receive the WS presentation in paper so they can engage beforehand in the proposal of the working panel. They will be able to participate in the third part of the WS which will be interactive with the participations of all the public and coordinated by the working pannel.
All asistants will received a USB with all the conferences and the list of suggesting reading.

Understanding clinical differences in neurodegeneratives disesases

Dr Christian Cobreros, MD

Understanding clinical presentations in lower urinary tract dysfunction due to neurological disorders is very challenging. Nevertheless, we do know that a wide variety of neurological conditions, acute or chronic, may affect the functionality of the bladder, or sphincter, or the pelvic floor musculature innervation resulting in different conditions as well as similar ones. Their clinical presentations is determined by the site and the nature of the lesion.

In a simple classification, but a very useful one, is to base the clinical urodynamic findings in terms of the lesion level, we also expected classical symptoms for each level:

- Suprapontine lesion: detrusor over activity due the lack of cortical inhibition, so storage symptoms are to be expected.
- Pontine micturition: if its preserved the control of the coordination of detrusor –sphincter mechanism will be preserved, as this center is the responsible for the coordination of the relaxation of the sphincter and pelvic floor musculature during bladder contraction
- Infrapontine-suprasacral lesions: this patient may present with a variety of clinical presentations due to a complete or partial lesion, in case of cortex and coordinated signal from the pontine center are injured the patient could present with neurogenic and detrusor over activity and sphincter dyssynergia
- Sacral micturition center: when this center is compromise we should expect involuntary contractions of the bladder as if it is a reflex center for bladder contractions
- Infrasacral lesions: In these lesions, even the reflex bladder contractions are lot due to and interruption of the signals between the bladder and all micturition centers, which will result in a clinical manifestation of a neurogenic detrusor underactivity or arreflexic detrusor or even a sphincter deficiency.

Although this systematic and practice review of lesion level of neurogenic urological disease the clinical presentations in neurogenerative diseases may vary form presented above, and this classification although its more useful in traumatic lesions but in the clinical practice in neurogenerative diseases we should expected some evolution of the clinical presentations and in some cases a completed different pattern within the clinical evaluation due to a progressive neurological disease

Suprapontine Lesion (Brain)

Cerebrovascular Accident (Stroke)

- acute phase of CVAs patients
- post-acute (chronic) phase of stroke
- LUT dysfunction following stroke

Degeneration disease and syndromes

- Parkinsonian Syndrome
- Multiple System Atrophy
- Alzeihemer disease
- Intracranial tumors

Spinal cord : Infrapontine-Suprasacral lesions

- Demyelination (multiple sclerosis, transverse myelitis)

Spinal Cord and Peripheral Nervous System: Sacral-Infrasacral Lesion

- Intervertebral Disk Prolapse
- Peripheral Neuropathies (*Diabetes* Diabetes mellitus , radiation therapy)

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Physiotherapy assessment of patients with neurogenic bladder. Keeping the whole patient in mind

Dr Beth Shelly PT, DPT, WCS, BCB PMD

Summary of PT Assessment

- Bladder function and voiding
- Neurological testing
- Mobility and movement
- PFM function
  - Tone
  - Coordination

Intake (Stohrer 1999, NICE 2012, Apostolidis 2017, Unger 2014)

- Social and family - caregiver availability
- Cognitive ability - mini mental test

- Urinary incontinence
  - Predictability of UI
  - Position UI occurs in
  - Other circumstances related to UI
  - Current and past treatments: catheter, pads, pessary, clamp
  - Bother and QOL impact
- Mode of voiding
  - Position
  - Continuous or intermittent stream
  - Hesitancy or weak stream
  - PVR or sensation of incomplete emptying
  - Initiation of voiding
    - Voluntary
    - Increased intra-abdominal pressure: crede, abdominal straining
    - Triggered voiding: tapping, scratching
  - Self-catheterization
- Measured volume bladder diary
  - Record volume of voluntary void
  - Results of any triggered void or bladder expression
  - Record volume of intermittent catheter void
  - Type and volume of fluid intake
  - Occurrence of leak - circumstances
  - Success of urge suppression
  - Sensations of bladder filling - urgency, reduced, absent, abdominal fullness, increased spasticity, autonomic dysreflexia
  - Colored urine test - pyridium

<u>Neurological Physical Examination</u> (Stohrer 1999, NICE 2012, Apostolidis 2017)

- Sensation of S2-5: sharp/dull, light touch
- Reflexes: (Drake 2013)
  - S4, 5 - anal wink
  - L5 to S5 - bulbocavernosus reflex
  - L2 to L4 - knee reflex
  - L5 to S2 - ankle reflex
  - L1, 2 - cremasteric reflex

<u>The whole body - mobility and function</u>

- ROM of lower body for positioning on the toilet
- Sitting balance on toilet
- Mobility for ambulation to the bathroom and transfers on and off toilet
- Finger dexterity for undressing, hygiene and catheter use

<u>PT Physical Examination - PFM</u>

- Full digital assessment of PFM per vagina and or rectum
- Tone – esp the ability to relax fully subjectively assessed with manual palpation
- Voluntary contraction - ability to sustain a PFM contraction

Hypertonic PFM

- An increase in muscle tone related to the contractile or viscoelastic components that can be associated with either elevated contractile activity and/or passive tension in the muscle
- Digital testing
  - Relaxation post contraction
  - Ability to maintain relaxation
  - Descent of PFM with bearing down
  - Resting tension

Devreese tone grading scale – good reliability (Devreese 2004)

- Measured superficial and deep
- Hypotonic
  - Wide and weak
  - Reduced mm bulk, easy drop
- Normotonic
  - Index finger can move
  - Normal smooth suspension

- Hypertonic
  - Tightness with firm band
  - Finger cannot move down

De Ridder – used in MS patients (De Ridder 1998)

- 3 - active relaxation after contraction
- 2 - hypertonic with relaxation after manual elongation
- 1 - spasm unable to relax even after passive elongation
- May be difficult to know what normal resting level is

Hypotonic PFM

- An decrease in muscle tone related to the contractile or viscoelastic components that can be associated with either decreased contractile activity and/or passive tension in the muscle
- Voluntary contraction
  - Strength
  - Endurance
  - Motor control and coordination

Surface EMG (sEMG) assessment of PFM - diagnosis

- Surface EMG measures muscle activation patterns
- Intramuscular or concentric needle EMG would be necessary to diagnose
  - Normal
  - Denervated
  - Reinnervated
  - Myopathic

Surface EMG assessment of PFM

- Ability of the PFM to relax fully when needed – defecation and urination
- Ability of the PFM to contract fully standard contract relax test

Surface EMG (sEMG) assessment of PFM - tone

- Ideally tools such as intra-vaginal pelvic floor dynamometry or Myotonometer are best for full assessment of tone however they are not easily clinically available
- Only the contractile competent of hypertonic PFM can be measured by sEMG
- Amount of muscle activity registered in sEMG signal is limited by adipose tissue, hair, and other factors of skin conductance

Bearing down test

- Bearing down with abdominal bulge = PFM relax
- Bearing down with inward abdominal contraction = PFM contraction
- Paradoxical PFM contraction – PFM contracts during proper bearing down
- Leads to obstructed defecation and urination
- Performed with external peri-rectal electrodes
- Lying down or sitting on a commode

Not a perfect test

- Fear - Patients are reluctant to bear down and fully relax for fear of passing gas
- Position - Lying down on a table and bearing down is not natural
- EMG artifact – skin electrode shear resulting in increased EMG signal

EMG during voiding

- Arrive to clinic with full bladder
- Place external peri-rectal electrodes
- Patient sits on commode with external EMG
- Leave the room and allow machine to save data

Perineal Surface Electromyography Does Not Typically Demonstrate Expected Relaxation During Normal Voiding. (Kirby 2011)

- 6.5% had EMG signal at 0 for the entire study
- 88.2% had EMG activity during flow

Many neurological conditions result in combinations of dysfunctions and various intensities of dysfunctions
It is essential to consider all dysfunctions and work closely with medical professional to determine the correct treatment approach.

More comprehensive chart provided in Unger 2014

Location of Lesion	Type of dysfunction	Simple description	Therapy directed toward
Supraspinal lesions - lesions above the brain stem	Neurogenic detrussor overactivity (NDO) with normal sphincter	Bladder is squeezing too much	Decrease overactive bladder
Spinal lesions	NDO with detrussor sphincter dyssynergia (DSD)	Sphincter is squeezing too much	Decrease PFM tension / spasm and improve PFM relaxation during empting
Lower motor neuron lesions - lesions of the conus medularis or lower	Neurogenic detrussor underactivity (Areflexic bladder) Striated sphincter denervation or weakness	Bladder is not squeezing enough Sphincter is not squeezing enough	Increase bladder contraction during voiding Increase sphincter contraction

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Video - Urodynamic value in patients. When? Why? Are there any other diagnostic methods that you should use?
Dr Christian Cobreros, MD

We do know that videourodynamics it's an invaluable helpful study as to be consider the "gold standard" procedure in the investigation of the urinary tract in patients with neurogenic disorder. This study provides an anatomical and functional way to understand the clinical presentations of the urological disease that is almost difficult to replace. But not in all countries, cities or medical insurance this kind of study is available.

We will go in this work shop through formal indications, as well as try to define if there is another studies (less expensive or more available) that could replace video Urodynamics as to give us the more suitable information and the awareness of any complication of our neurological patients in developing countries where this procedure is not always available.

Video Urodynamics

This study as a combination of a urodynamic study and fluoroscopic monitoring in real time helps as to identifies anatomical and functional abnormatlities of the urinary tract.

Filling ciystometry: the visualization of the bladder neck help to determine the level of continence, if its open it may indicate a disorder of the sympathetic bladder innervention resulting in neurogencis sphincter dysfunction. In combination with multichannel urodynamcis detrusor contractions can be measerud as well as con be detected by the images and any leakage of

urine can be detected at earlier time points using fluoroscopy rather than the standard uroflow sensor.

Pressure flow studies: is abolutiely helpful in detecting the point of obstruction when high pressure/low flow exist. In patients that are suspected to have sphincter dyssynergia this study combined with electromyography helps in accurate diagnosis. As well as to identify vesicouretral reflux.

Case presentations

- Patients with Retention Due to Detrusor- Sphincter Dyssynergia DSD
- Intrinsic sphincter deficiency (leakage without urethral hypermobility) in neurological patients
- Peripheral neuropathy
- Vesicoureteral reflux

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It is always easy to differentiate urgency from another clinical presentation of these patients (e.g. pain, hypersensitivity, bladder irritation, infection)? How can we avoid over medication?

David Castro Diaz, MD, PhD

Many different conditions affecting the lower urinary tract function origin in the nervous system and it is important to recognise that lower urinary tract symptoms (LUTS) may be one of the first signs of neurodegenerative disorders such Alzheimer’s disease (AD), Parkinson’s disease (PD), dementia and PD-related disorders, Huntington’s disease (HD), Spinocerebellar ataxia (SCA or Spinal muscular atrophy (SMA).

The symptom “Urgency”, defined as “the complaint of a sudden compelling desire to pass urine, which is difficult to defer”, is sometimes one of the first symptoms indicating a neurodegenerative disorder which may later lead the patient to a fatal outcome. PD patients and others with neurodegenerative disorders, suffer loss of dopaminergic neurons inducing deficit or abnormality of the neurologic control of micturition. More than 60% of patients with PD have LUTS and 30 % refer urinary incontinence. Patients suffering neurodegenerative disorders often express LUTS and its onset may even serve as a diagnostic marker. Patients with bladder pain syndrome/Interstitial cystitis (BPS/IC) and those with hypersensitive bladder, usually refer the symptom of urgency as linked to

fair to pain while patients with neurodegenerative disease or overactive bladder may express urgency as linked to fair to incontinence. However, differentiating urgency from another clinical presentation is not easy particularly in patients with cognitive disorders.

The onset of disease and timescale of symptoms may give clues to the cause of urinary problems. In some cases, LUTS occur early, in the course of disease, whereas in others they may develop later, and could be confused with dysfunctions of a non-neurogenic origin, such as benign prostatic enlargement or bladder outlet obstruction. The extent to which symptoms 'bother' the patient is important and should be determined both subjectively and objectively, through a proper clinical history and the use of a voiding diary, questionnaires and quality of life evaluation. This approach enables us to match therapy with patient´s motivation, and to monitor the success of treatment. The physical status of the patient will have an important influence on the capabilities for maintaining a therapeutic strategy.

Attention should be paid to any medications taken by the patient, as several drugs can have detrimental effects on the urinary tract. For example, diuretics prescribed for hypertension are associated with bladder overstretching. Furthermore, the use of any antihypertensive agent in younger patients should alert the urologist to the likelihood kidney dysfunction due to obstructive urophathy. Drugs that can alter the functioning of the urinary tract include opiate-containing painkillers, which reduce bowel motility and antiparkinsonian agents which act as parasympatholytics and so impair detrusor contractility. Muscle relaxants used to treat spasticity may also cause bladder hypocontractility and urinary retention; alternatively, they can induce pelvic floor laxity leading to stress incontinence.

Sufferers of neurodegenerative disorders and elderly people require taking multiple medications which may have side effects and unwanted drug reactions. Muscarinic receptors antagonists have been shown to cause cognitive disorders in elderly patients and should be used with caution in patients with neurodegenerative disorders preferably choosing those drugs which do not cross the blood-brain barrier. As some commonly used drugs have antimuscarinic properties it is important to avoid overmedication that may increase the exposure to side effects. Potential signs of overmedication include drowsiness, physical complications like dry mouth and ulcers, confusion, withdrawal from family or friends, hallucinations, dizziness or falls, fractures and seizures.

Oral medication. What do we have today? Is combination better? How to decide when to move to another step?
Dr Christian Cobreros, MD

We will review the most current literature on oral medication for neurogenic bladder to treat not only detrusor overactivity, but also to improve bladder capacity, compliance and to treat urinary incontinence.
This medical therapies will be discuss in this section as we do have another section in wich advances therapies as onatoxinabotulinum will be discuss.
At the same time we will go into the improve of quality of life of single drug vs combination and when it's the optimal time to omove to the next step.

- **Drugs that have action in the storage phase**
  - Antimuscarinic drugs
    - Choice of Antimuscarinic agents
      - Side-effects
        - Why do they have such a great drop out?
  - Agonist β 3
  - Its combination better ?
- **Drugs that have action in the pressure flow phase**
  - Alpha blockers
  - Phosphodiesterase inhibitors (PDE5Is)

- **Drugs with different mechanisms of action**
  - Detrusor underactivity
  - Decreasing bladder outlet resistance
  - Increasing bladder outlet resistance

- **Its combination better ?**

- **When to move to the next step**

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Surgical approach: neurostimualtion, botulinun toxin, neuromodulation, bladder augmentation

Carlos D'Ancona, UNICAMP, Brazil

The surgical approach in neurogenic detrusor overactivity is indicated when failures occur in pelvic floor muscles training and drugs administration. The classification of failure is not well defined but we can consider it to be, when the patient is unsatisfied.

Between neurostimuation, neurotoxin, neuromodulation and bladder augmentation, the question is how to choose one of this? Transcutaneous or percutaneous nerve stimulation is a minimal invasive treatment with good response in patients with multiple sclerosis and Parkinson's disease. The botulinum toxin has the advantage that is reversible after 8 to 12 months. Can be use as test before a definite treatment. The results of BT are excellent improving in symptoms, in urodynamics and Quality of Life. There is still the question for how long it is possible to use this treatment. Many papers show that it is effective for more than 10 years.

For neuromodulation treatment, there should be some neuronal connections between the bladder and brain. So, patients with complete spinal cord injury are not a candidate for implantation of neuromodulation. However, patients with multiple sclerosis and Parkinson disease present good results with a long follow up.

Performing bladder augmentation decreased much due to the other techniques used. This technique presents some adverse effects such as bladder stone, urinary tract infection, perforation of the reservoir and others. The advantages of this technique are the long-term good results. Myelomeningocele and spinal cord injury patients have a great life expectancy and this technique should be considered.

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The role of Physiotherapy and a Multidisciplinary team in the daily life of patients. Can we improve their quality of life if we work together?

Dr Beth Shelly PT, DPT, WCS, BCB PMD

Overall Conservative management of neurogenic bladder

- Individualized to the patient in cooperation with caregivers
- Little high level evidence for any one treatment
- NICE guidelines give good outline of evidence related to treatment (NICE 2012)
- Overall goals of treatment is protection of upper urinary tract and improvement in QOL

Therapies to decrease overactive bladder (Wein 2002)

- Bladder training, timed voiding, habit training, prompted voiding, fluid management - a suitable component of a rehabilitation program level C (Drake 2013)
- PFM training with or without biofeedback
- Electrical stimulation

Therapies to decrease PFM tension / spasm and improve PFM relaxation during empting

- Manual stretching of PFM does not appear to have a lasting impact
- Biofeedback-assisted PFM coordination training
  - PFM relaxation
  - Train on the toilet with external EMG during voiding

Therapies to increase bladder contraction during voiding

- Intermittent catheterization - accepted standard (Drake 2013)
- Triggered Reflex Voiding - Provocation of bladder contraction
  - Attempts to initiate reflex detrusor contraction
  - Inappropriate if urodynamics show
    - Signs of reflux
    - Inadequate detrusor contraction – need some intact muscle fibers to provoke
    - Outlet obstruction of any type including PFM tension
  - Reflex voiding may result in autonomic dysreflexia in patients with neurological disorders: paroxysmal HTN, anxiety, sweating, HA, bradycardia
  - Has a limited role and can be potentially dangerous (Drake 2013)
  - Techniques
    - Suprapubic tapping or percussion: 7-8 percussions with intervals of a few seconds (as fast as you can); gross reflex contraction of the detrusor and EUS, when tapping stops the EUS should relax while detrusor contraction continues
    - Thigh scratching
    - Anorectal manipulation
    - Pubic hair pulling
    - Stroking / tickling lower back
- Bladder expression - Increasing intra abdominal pressure
  - Aggressive techniques and dangerous maneuvers done with caution (Drake 2013)
  - Not used in patients with reflux, PFM spasm or DSD
  - Lean forward - Leaning forwards places slight compression on the abdomen, changes the angle of the bladder and urethra, and may encourage empting.
  - Gentle whistling, blowing a toy or balloon – pursed lipped exhaling against mild resistance provides gentle increased intra-abdominal pressure and encourages PFM relaxation and urine empting.
  - Valsalva maneuver – Bearing down with closed glottis significantly increased intra abdominal pressure and may help relax the PFM and encourage bladder emptying. May result in POP or hemorrhoids and should only be used in acute cases with physician monitoring.
  - Credé maneuver – Press down onto the bladder just behind the pubic bone. This can initiate a detrusor contraction but can also increase the chance of POP. It should only be used when other methods fail, with physician instruction, in a patient with hypo or atonic bladder.
- Timed voiding / habit training / bladder training
  - Usually very large voiding intervals need to slowly decrease time between voids
  - Goal is to go to the toilet and try to void every 2 to 3 hours
  - May or may not need to use trigger techniques or catheterization

Ideas and Advice to Help Promote Full Voiding

- Privacy – Paruresis, also called shy bladder, is the inability to urinate in public. Maintaining as much privacy as possible increases bladder emptying for most patients.
- Toilet position - sit fully on the toilet
  - Full relaxation of PFM overflow muscles (adductors and gluteals in particular) is necessary for full PFM relaxation and will increase bladder emptying
  - Sitting relaxed and supported
  - Both feet flat on the floor and fully supported
  - Adequate hip flexion to encourage PFM relaxation
- Relaxation – Take time to fully relax all muscles for full emptying. In some cases it is helpful to distract yourself on the toilet by reading, singing or reciting a poem. This is especially important in patients with anxiety.
- Double voiding - After initial void, stand, move, sit down, and attempt to void again.
  - Toilet Exercises - ideas to encourage full empting, Do not valsalva
    - Sit completely on toilet, relax legs
    - Lean forward bending at the hips 3 times
    - Relax and allow urine to comes out
    - Stand up then sit down (double voiding)
    - Relax and allow urine to come out
    - Several gentle PFM contractions and large relaxation
    - Relax and allow urine to come out
    - Do not push
- Running water - The sound of running water can initiate voiding however over use of the method can lead to OAB and UUI with the sound of water running.

<u>Therapies to increase sphincter contraction</u>

- PFM training with or without biofeedback
- Overflow or functional PFM training
- Electrical stimulation - may be an option in cases of PFM weakness (not in complete denervation) however no research exists (Drake 2013)

<u>Evidence for conservative management of UI in patients after Stroke</u>

- PFM exercises (PT), timed voiding and prompted voiding (RN), functional bathroom activities (OT) - significant decrease in frequency of accidents and need for assistance to toilet in treatment group as compared to control group. (Couran 2012)
- PFM exercises decrease urinary frequency and UI by pad test RCT (Tibaek 2005)
- PFM exercises added to standard rehabilitation decreased UI by RCT (Skin 2016)
- PFM exercises with bladder retraining - systemic review found little evidence in stroke patients (Dumoulin 2005)
- Restoration of functional mobility - RCT shows benefit in stroke patients (Wilkander 1998)
- UI is a strong predictor of discharge status, functional recovery, and return to social activities. (Dumoulin 2007)

<u>Evidence for conservative management of UI in patients with Multiple Sclerosis</u>

- Best candidate for PT - mild MS, without PFM spasticity or dyssynergia (De Ridder 1999)
- Poor success - elevated PVR (McClurg 2008)
- Guideline recommendations for PFM training
  - Fowler 2009 - UK consensus, grade B
  - Pannek 2012 - EAU guideline, no grade given
  - Cetinel 2013 systematic review and consensus report, grade A
- PFM exercises versus sham - decreased pad weight, number of pads and nocturia (Lucio 2010)
- PFM exercises plus EMG and electrical stimulation vs no treatment RCT (Vahtera 1997)
  - Significant improvement in UI, nocturia, and improved bladder emptying.
  - Men > women
- PFM exercises plus EMG and electrical stimulation vs sham electrical stimulation RCT (McClurg 2008)
  - Significant improvement in UI by pad test, IIQ, UDI, IPPS and decreased PVR
  - 85% in the active group, 47% in the control group
  - PFM strength improved equally in both groups
- Biofeedback assisted PFM exercises are not superior to PFM exercises alone (Klarskov1994)
- Transcutaneous posterior tibial nerve stimulation resulted in significant decrease in urgency, frequency and leakage without increase in PVR - no control group (de Seze 2011)
- TENS to sacral dermatomes (Skeil 2001)
  - Mixed neuro diseases, but mostly MS patients
  - Diary showed significant improvement - decrease in 24 hour frequency, UI episodes and clothing changes
  - Risk for increased PVR

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Workshop 5
Neurodegenerative disease's impact on bladder function:
A multidisciplinary approach in diagnosis, treatment and improving quality of life

ICS 2018 PHILADELPHIA

Understanding urological clinical differences in neurodegeneratives disesases

Dr. Christian Cobreros
Urology Division - Hospital Carlos G. Durand
Buenos Aires - Argentina

Workshop 5
Neurodegenerative disease's impact on bladder function:
A multidisciplinary approach in diagnosis, treatment and improving quality of life

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Affiliations to disclose[1]:

- IPSEN (as PI in clinical studies, phase III)
- ASTELLAS (as PI in clinical study , phase III)

[1] 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:

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

AIMS OF THE PRESENTATION

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NEUROGENIC LOWER URINARY TRACT DYSFUNCTION (NLUTD)

IS ONE OF THE MOST CHALLENGING PROBLEMS IN UROLOGY

THE TYPE OF DYSFUNCTION DEPENDS ON THE LEVEL, INTENSITY, AND EXTENT OF THE INJURY

AND ALSO TIME-LENGHT OF SPECIFIC DISORDER (STROKE, DIABETES, MS)

NEUROLOGICAL CLINCIAL PRESENTATION IS NOT AN STATIC CONDITION

CLASSIFICATION SYSTEM FOR DAY TO DAY CLINICAL PRACTICE

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- SUPRAPONTINE LESIONS
- SPINAL (Infrapontine / suprasacral)
- SPINAL & PERIPHERIC (Sacral / Infrasacral)

EXPECTED SYMPTOMPS AND URODYNAMICS FINDINGS

Pfisterer MH, Griffiths DJ, Rosenberg L, Schaefer W, Resnick NM. The impact of detrusor overactivity on bladder function in younger and older women. J Urol. 2006;175(5):1777-83. Discussion 1783

SUPRAPONTINE LESIONS: STROKE

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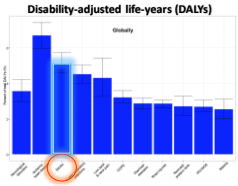
Disability-adjusted life-years (DALYs)



SURVIVORS

10% have no residual effects
40% have mild disability
40% have significant disability
10% require nursing home care

90% Survivors who will required attendance

USA (2018) → 8 M survivors **72 Billions usd/year**
USA (2030) → 30 M survivors **183 Billions usd/year**

Osborn DJ, Reynolds WS, Dmochowski RR. Cerebrovascular accidents, intracranial tumors, and urologic consequences. In: Corcos J, Ginsberg D, Karsenty G, editors. Textbook of the neurogenic bladder. 3rd ed. Boca Raton: CRC Press/Taylor & Francis; 2016. p. 269-4

SUPRAPONTINE LESIONS: STROKE

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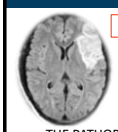

ACUTE UROLOGIC PRESENTATION

Urinary retention may be the first **urologic** event to occur after a CVA **"Cerebral sock"**

THE PATHOPHISIOLOGY OF THIS MICTURITION DISTURBANCE INVOLVES:

- there is often a decreased sensation and awareness of bladder filling
- there is damage to higher cortical centers, especially in the frontal lobe

Burney TL, Senapati M, Desai S et al. Effects of cerebrovascular accident on micturition. Urol Clin North Am 1996; 23: 483–90
Mehdi Z, Bims J, Bhalla A. Post-stroke urinary incontinence. Int J Clin Pract. 2013;67(11):1128–37

SUPRAPONTINE LESIONS: STROKE

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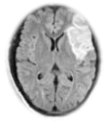
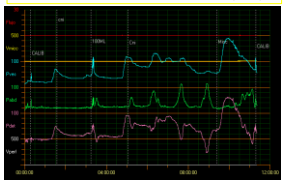


POSTACUTE OR CHRONIC UROLOGIC PRESENTATION

NEUROGENIC DETRUSOR OVERACTIVITY (NDO)



37% to 90% URODYNAMIC FINDINGS IN REPORTS

Comparison of urodynamics between ischemic and hemorrhagic stroke patients; can we suggest the category of urinary dysfunction in patients with cerebrovascular accident according to type of stroke? Neurourol Urodyn. 2010;29(3):387–90

Pfisterer MH, Griffiths DJ, Rosenberg L, Schaefer W, Resnick NM. The impact of detrusor overactivity on bladder function in younger and older women. J Urol. 2006;175(5):1777–83. Discussion 1783

Carlsson CA. The supraspinal control of the uri- nary bladder. Acta Pharmacol Toxicol (Copenh). 1978;43(Suppl2):8–12.

Mehdi Z, Birns J, Bhalla A. Post-stroke urinary incontinence. Int J Clin Pract. 2013;67(11):1128–37

SUPRAPONTINE LESIONS: STROKE

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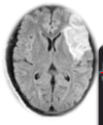
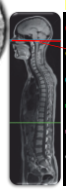


POSTACUTE OR CHRONIC UROLOGIC PRESENTATION

NEUROGENIC DETRUSOR OVERACTIVITY (NDO)



37% to 90% URODYNAMIC FINDINGS IN REPORTS

Urinary incontinence is the most common sequela

Others:

- **Nocturia (36-80%)**
- **Frequency (18-36%)**
- **Urgency (20-30%)**
- **Difficulty in voiding (25%)**
- **Straining (3.5%)**
- **Pain (2.5%)**

Comparison of urodynamics between ischemic and hemorrhagic stroke patients; can we suggest the category of urinary dysfunction in patients with cerebrovascular accident according to type of stroke? Neurourol Urodyn. 2010;29(3):387–90

Pfisterer MH, Griffiths DJ, Rosenberg L, Schaefer W, Resnick NM. The impact of detrusor overactivity on bladder function in younger and older women. J Urol. 2006;175(5):1777–83. Discussion 1783

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Mehdi Z, Birns J, Bhalla A. Post-stroke urinary incontinence. Int J Clin Pract. 2013;67(11):1128–37

SUPRAPONTINE LESIONS: DEMENTIA

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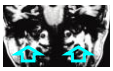
Etiology

Alzheimer's disease

urinary disturbances do occur in Alzheimer's disease but are very uncommon at an early stage

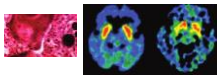
6.5 years after dementia onset



Dementia with Lewy bodies

the onset of urinary incontinence was significantly earlier in patients with DLB

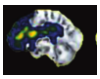
3.2 years after dementia onset



White matter disease

WMD becomes an anatomical substrate in the brain etiology of OAB

5 years after dementia onset



URINARY DISTURBANCES ARE UNCOMMON AT EARLY STAGES OF THIS DISEASES

SUPRAPONTINE LESIONS: DEMENTIA

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Prevalence rate of urinary incontinence in dementia

Campbell et al.,10	urinary incontinence was found in 53% patients with dementia 13% nondemented older individuals	
Ouslander et al.7	65% incontinent subjects	3 episodes per week
	11% incontinent subjects	6 episodes per week
	24% incontinent subjects	1 or more episodes per day
McLaren et al	that 90% incontinent subjects	at least one episode during the 3-week assessment period
		78% had one episode a week

5% in non-dementia elderly populations ---- at least 1 epsiode of UI per week

75% of patients with dementia ---- at least 1 epsiode of UI per week

Ouslander JG, Zarit SH, Orr NK, Muira SA. Incontinence among elderly community-dwelling dementia patients. *J Am Geriatr Soc 1990; 38: 440–5.*

McLaren SM, McPherson FM, Sinclair F, Ballinger BR. Prevalence and severity of incontinence among hospitalised, female psychogeriatric patients. *Health Bull 1982; 39: 157–61.*

Campbell AJ, Reinken J, McCosh L. Incontinence in the elderly: Prevalence and prognosis. *Age Ageing 1985; 14: 65–70.*

SUPRAPONTINE LESIONS: DEMENTIA

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BASAL GANGLIA: PARKINSON'S DISEASE / HUNTINGTON'S DISEASE / MSA

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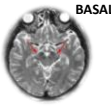
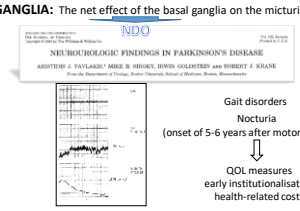


BASAL GANGLIA: The net effect of the basal ganglia on the micturition reflex is inhibitory



Gait disorders

Nocturia

(onset of 5-6 years after motor symptoms)

⇩

QOL measures

early institutionalisation

health-related costs

Bonnet AM, Pichon J, Vidailhet M, Gouider-Khouja N, Robain G, Perrigot M, et al. Urinary disturbances in striatonigral degeneration and Parkinson's disease: clinical and urodynamic aspects. Mov Disord. 1997;12(4):509–13.

Winge K, Skau AM, Stimpel H, Nielsen KK, Werdelin L. Prevalence of bladder dysfunction in Parkinsons disease. Neurourol Urodyn. 2006;25(2):116–22

Herzog J, Weiss PH, Assmus A, et al. Improved sensory gating of urinary bladder afferents in Parkinson's disease following subthalamic stimulation. Brain 2008;131:132–45.

Yeo, L., Singh, R., Gundeti, M. et al. Int Urol Nephrol (2012) 44: 415. https://doi.org/10.1007/s11255-011-9960-y

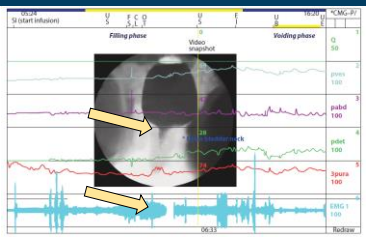
Pavlakis AJ, Siroky MB, Goldstein I, Krane RJ. Neurourologic findings in Parkinson's disease. J Urol. 1983;129(1):80–3

BASAL GANGLIA: *PARKINSON´S DISEASE / HUNTINGTON´S DISEASE / MSA*

ICS 2018 PHILADELPHIA

MULTIPLE SYSTEMIC ATROPHY

- OPEN BLADDER NECK AT THE START OF BLADDER FILLING 53% MSA PATIENTS
- DETUSOR SPHINCTER DYSINERGIA IN 33% MSA PATIENTS
- INCOMPLETE BLADDER EMPTYING IS A SIGNIFICANT FEATURE IN MSA (47%) (>100ml)
- ANOTHER AUTONOMIC MANIFESTATIONS: NOCTURNAL POLIURIA, POSTURAL SYNCOPE

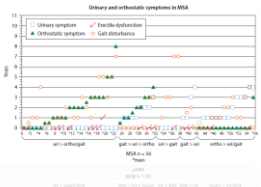


Ito T, Sakakibara R, Nakazawa K et al. Effects of electrical stimulation of the raphe area on the micturition reflex in cats. *Neuroscience 2006; 142(4): 1273–80.*
Ito T, Sakakibara R, Yasuda K et al. Incomplete emptying and urinary retention in multiple system atrophy: When does it occur and how do we manage it? *Mov Disord 2006; 21(6): 816–23.*
Stocchi F, Carbone A, Inghilleri M et al. Urodynamic and neurophysiological evaluation in Parkinson's disease and multiple system atrophy. *J Neurol Neurosurg Psychiatry 1997; 62: 307–11.*
Berger Y, Salinas JM, Blaivas JG. Urodynamic differentiation of Parkinson disease and the Shy–Drager syndrome. *Neurourol Urodynam 1990; 9: 117–21.*
Sakakibara R, Hattori T, Uchiyama T et al. Videourodynamic and sphincter motor unit potential analyses in Parkinson's disease and multiple system atrophy. *J Neurol Neurosurg Psychiatry 2001; 71: 600–6.*

BASAL GANGLIA: *PARKINSON´S DISEASE / HUNTINGTON´S DISEASE / MSA*

ICS 2018 PHILADELPHIA

In MSA disease Urinary Symptoms preceeds motors manifestations



This indicates that many of these patients seek urological advice early in the course of their disease.

Yamamoto T, Sakakibara R, Uchiyama T et al. Questionnaire-based assessment of pelvic organ dysfunction in multiple system atrophy. *Mov Disord 2009; 24: 972–8.*
Sakakibara R, Hattori T, Uchiyama T et al. Urinary dysfunction and orthostatic hypotension in multiple system atrophy: Which is the more common and earlier manifestation? *J Neurol Neurosurg Psychiatry 2000; 68*
Abrams P, Cardozo L, Fall M et al. The standardisation of terminology of lower urinary tract function: Report from the Standardisation Sub-committee of the International Continence Society. *Neurourol Urodyn 2002; 21: 167–78.*

MULTIPLE SCLEROSIS

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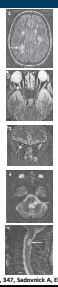

- Cerebrum → Cognitive impairment, reasoning, and executive function; Afective (mainly depression); LATE :Dementia
- Optic nerve → Unilateral painful loss of vision
- Brainstem → Clumsiness and poor balance; Limb incoordination and gait ataxia; Diplopia Nystagms; Impaired speech, swallowing, Dysarthria
- Cerebellum and cerebel-lar pathways → Tremor → Postural and action tremor, dysarthria
- Spinal cord → Weakness Upper motor neuron signs; Stiness and painful spasms Spasticity; **Bladder dysfunction**; Erectile impotence; Constipation

Modified from The Lancet, 347, Sadovnick A, Eberg G, Dyment D, Rish N, Canadian Collaborative Study Group. Evidence for genetic basis of multiple sclerosis, 1728–30, Copyright 1996

MULTIPLE SCLEROSIS

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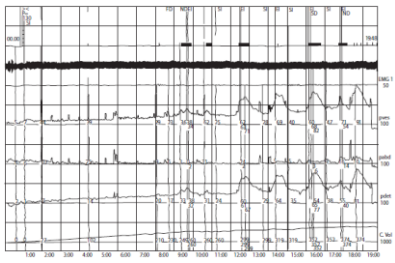

Detrusor Overactivity

↓

symptomatically by urinary frequency urgency Nocturia and urge incontinence

These findings correlate well with the high incidence of intracranial and cervical spinal plaques

TAKE HOME MESSAGES

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IN NEURODEGENERATIVE DISEASES:

- **URODYNAMICS ASSESMENT IS NECESARY FOR DETECTING NDO WITH BLADDER OBSTRUCTION AT THE SAME TIME**
- **UROLOGICAL MANIFESTATIONS CON PRECEED OTHER MANIFESTATIONS FOR YEARS**
- **CLINICAL AND URODYNAMICS FINDINGS CAN CHANGE OVER TIME SO YOU MUST BE CAREFULLY AND GET INVOLVED IN THE CLINICALS MANIFESTATIONS OF YOUR PATIENTS TO DETECT ANY CHANGE AS SOON AS IT PRESENT**

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THANK YOU

Dr Beth Shelly PT, DPT, WCS, BCB PMD

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Affiliations to disclose†:

Analitica – advisory board

Bewell – focus group participant

† 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
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Physiotherapy assessment of patients with neurogenic bladder. Keeping the whole patient in mind.

Dr Beth Shelly PT, DPT, WCS, BCB PMD
www.bethshelly.com
International Continence Society Annual Meeting
August 28, 2018 Philadelphia, PA
Workshop 5

My Practice

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Freestanding, out patient PT practice in the Midwest (USA) specializing in PFM dysfunction of all types

Kids – elderly

Male, female

All types of community dwelling patients with neurological conditions that affect the LUT

Most common dx – MS, Parkinson's, Alzheimer's

Summary of PT Assessment – The Whole Patient

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Bladder function and voiding

Neurological testing

Mobility and movement

PFM function
- Tone
- Coordination

Social and family – caregiver availability
Cognitive ability - Mini mental test

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Urinary Incontinence

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Predictability of UI

Position UI occurs in

Other circumstances related to UI

Current and past treatments: catheter, pads, pessary, clamp

Bother and QOL impact

Mode of Voiding

Position
Continuous or intermittent stream
Hesitancy or weak stream
PVR or sensation of incomplete emptying
Initiation of voiding
- Voluntary
- Increased intra-abdominal pressure: crede, abdominal straining
- Triggered voiding: tapping, scratching

Self-catheterization

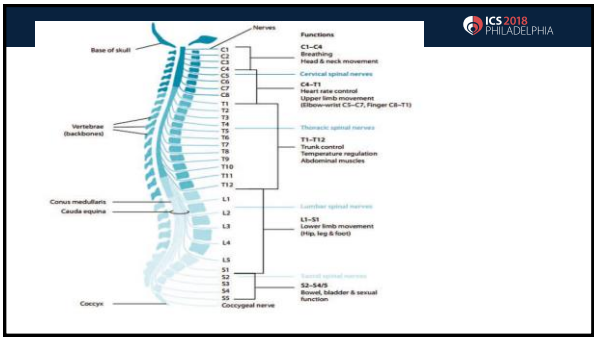
Measured Volume Bladder Diary

Record volume of voluntary void
Results of any triggered void or bladder expression
Record volume of intermittent catheter void
Type and volume of fluid intake
Occurrence of leak - circumstances
Success of urge suppression

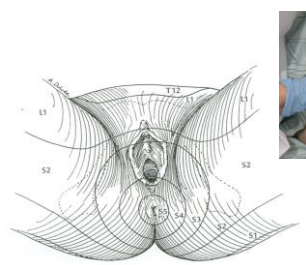
Measured Volume Bladder Diary

Sensations of bladder filling
- Urgency
- Reduced
- Absent
- Abdominal fullness
- Increased spasticity
- Autonomic dysreflexia

Colored Urine test – Pyridium



Sensation of S2-5: sharp/dull, light touch



Reflexes: (Drake 2013)

S4, 5 - anal wink
L5 to S5 - bulbocavernosus reflex
L1, 2 - cremasteric reflex
L2 to L4 - knee reflex
L5 to S2 - ankle reflex

PT Physical Examination – the Whole Body

ROM of lower body for positioning on the toilet
Sitting balance on the toilet
Mobility for ambulation to the bathroom
Transfers on and off toilet
Finger dexterity for undressing, hygiene and catheter use

PT Physical Examination - PFM

Full digital assessment of PFM per vagina and or rectum
Voluntary contraction - ability to sustain a PFM contraction
Tone – esp the ability to relax fully subjectively assessed with manual palpation

Hypertonic PFM

An increase in muscle tone related to the contractile or viscoelastic components that can be associated with either elevated contractile activity and/or passive tension in the muscle

Digital testing
- Relaxation post contraction
- Ability to maintain relaxation
- Descent of PFM with bearing down
- Resting tension

Devreese tone grading scale – good reliability

Measured superficial and deep

Hypotonic
- Wide and weak
- Reduced mm bulk, easy drop

Normotonic
- Index finger can move
- Normal smooth suspension

Hypertonic
- Tightness with firm band
- Finger cannot move down

De Ridder – used in MS patients

3 - active relaxation after contraction

2 - hypertonic with relaxation after manual elongation

1 - spasm unable to relax even after passive elongation

May be difficult to know what normal resting level is

Hypotonic PFM

An decrease in muscle tone related to the contractile or viscoelastic components that can be associated with either decreased contractile activity and/or passive tension in the muscle

Voluntary contraction
- Strength
- Endurance
- Motor control and coordination

EMG (EMG) assessment of PFM

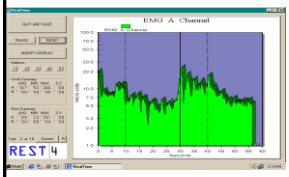
Intramuscular or concentric needle EMG would be necessary to diagnose
- Normal
- Denervated
- Reinnervated
- Myopathic

Surface EMG measures
muscle activation patterns

Surface EMG assessment of PFM

Ability of the PFM to relax fully when needed – defecation and urination

Ability of the PFM to contract fully - standard contract relax test



Surface EMG (sEMG) assessment of PFM - tone

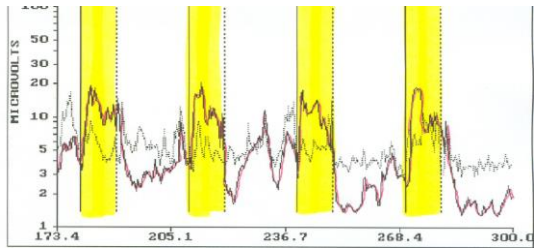
Ideally tools such as intra-vaginal pelvic floor dynamometry or Myotonometer are best for full assessment of tone however they are not easily clinically available

Only the contractile component of hypertonic PFM can be measured by sEMG

Some patients with normal sEMG will have hypertonicity through the passive component

Amount of muscle activity registered in sEMG signal is limited by adipose tissue, hair, and other factors of skin conductance

Hypertonic PFM



Bearing down test ? utility

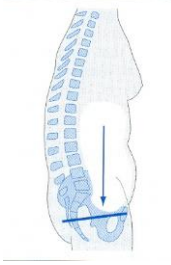
Normal -

Bearing down with abdominal bulge = PFM relax

Paradoxical PFM contraction -

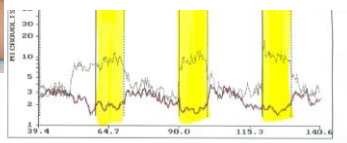
PFM contracts during proper bearing down

Leads to obstructed defecation and urination



Bearing down test ? utility

Performed with external peri-rectal electrodes
Lying down or sitting on a commode



Not a perfect test

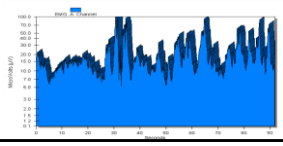
Fear - Patients are reluctant to bear down and fully relax for fear of passing gas

Position - Lying down on a table and bearing down is not natural

EMG artifact – skin electrode shear resulting in increased EMG signal

EMG during voiding - ? utility

Arrive to clinic with full bladder
Place external peri-rectal electrodes
Patient sits on commode with external EMG
Leave the room and allow machine to save data



Not a perfect test

Perineal Surface Electromyography Does Not Typically Demonstrate Expected Relaxation During Normal Voiding. Kirby 2011

6.5% had EMG signal at 0 for the entire study
88.2% had EMG activity during flow

Summary of PT Assessment

Bladder function and voiding

Neurological testing

Mobility and movement

PFM function
- Tone
- Coordination

Diagnosis made by the Physician

Neurogenic detrussor overactivity (NDO) with normal sphincter
NDO with detrussor sphincter dyssynergia (DSD)
Neurogenic detrussor underactivity (Areflexic bladder)
Striated sphincter denervation or weakness

Physicians should provide information on pathophysiology and exact nature of voiding dysfunction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Questions
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Workshop 5
Neurodegenerative disease's impact on bladder function:
A multidisciplinary approach in diagnosis, treatment and improving quality of life

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Video - Urodynamic value in patients. How? When? Why? Are there any other diagnostic methods that you should use?

Dr. Christian Cobreros
Urology Division - Hospital Carlos G. Durand
Buenos Aires - Argentina

Workshop 5
Neurodegenerative disease's impact on bladder function:
A multidisciplinary approach in diagnosis, treatment and improving quality of life

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Affiliations to disclose†:

- IPSEN (as PI in clinical studies, phase III)
- ASTELLAS (as PI in clinical study , phase III)

† 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:

- [ ] Self-funded
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Dr. Christian Cobreros
Urology Division - Hospital Carlos G. Durand
Buenos Aires - Argentina

Videourodynamics GOALS OF TREATMENT

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Various goals of treatment of patients With NLUTD

- ✓Upper urinary tract preservation or improvement
- ✓Absence or control of infection
- ✓Minimal or no incontinence
- ✓Low storage pressures with adequate bladder capacity
- ✓Avoidance of indwelling catheter or stoma
- ✓Low voiding pressures with adequate emptying ability if not performing intermittent catheterization
- ✓Social acceptability and adaptability of bladder management
- ✓Vocational acceptability and adaptability of bladder management.

✓Wein AJ, Dmochowski RR. Neuromuscular dysfunction of the lower urinary tract. In: Wein AJ, Kavoussi LR, Novick AC, editors. Campbell-Walsh urology, vol. 3, 10th edition. Philadelphia: WB Saunders; 2012. p. 1909–46.

Videourodynamics Definition

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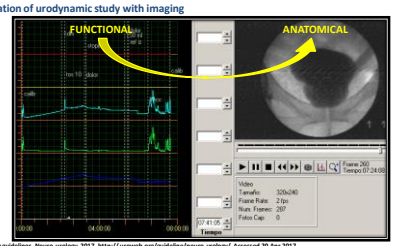
Video-Urodynamics is a combination of urodynamic study with imaging

Considered the *optimum procedure for urodynamic* investigation in patients suffering from neurogenic lower urinary tract dysfunction NLUTD



European Association of Urology (EAU). Non-oncology guidelines. Neuro-urology. 2017. http://uroweb.org/guideline/neuro-urology/. Accessed 20 Apr 2017
Gajewski JB, Schurch B, Hamid R, et al. An International Continence Society (ICS) report on the Terminology for adult neurogenic lower urinary tract dysfunction (ANLUTD). *Neurourology and Urodynamics*. 2018;37:1152–1161.
Djurhuis PL, Groutherz DA. Neurogenic lower urinary tract dysfunction: how, when, and with which patients do we use urodynamics? Urol Clin North Am. 2014;41(3):445–52. ix

Videourodynamics

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2018

Videourodynamics WHEN ?

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Video-urodynamic (VUD) can be defined as the combination of filling cystometry and pressure flow study with imaging. It is the gold standard for urodynamic investigation in neurourological disorders

GR A

Guideline Statement 12.

When available, clinicians may perform fluoroscopy at the time of urodynamics (videourodynamics) in patients with relevant neurologic disease at risk for neurogenic bladder, or in patients with other neurologic disease and elevated PVR or urinary symptoms. (*Recommendation*; Evidence Strength: *Grade C*)

Guideline Statement 19.

Clinicians may perform videourodynamics in properly selected patients to localize the level of obstruction particularly for the diagnosis of primary bladder neck obstruction. (*Expert Opinion*)

Videourodynamics HOW ?

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Neurogenerative diseases

- Elderly
- carry multiple comorbidities
- well, poor, or no mobility
- inhability to comunicate
- impaired bladder sensations
- inhability to express or understand their needs or sensations

CHALLENGING

Videourodynamics HOW ?

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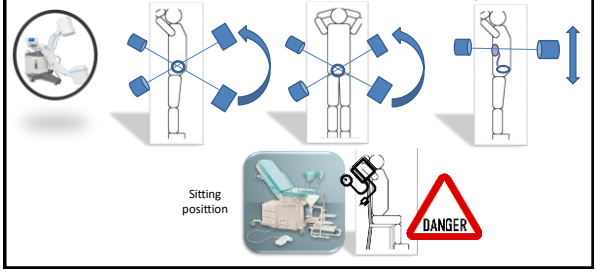
POSITION



Videourodynamics HOW ?

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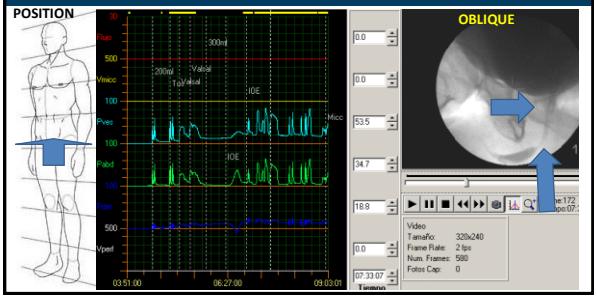
POSITION



Videourodynamics HOW ?

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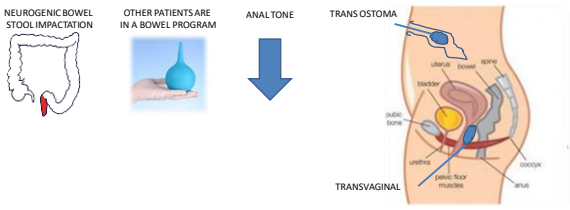
PROPER RECTAL PREPARATION



Combs A, Nitti V. Significance of rectal contractions noted on multichannel urodynamics. NeurourolUrodyn 1995;14:73–80.
Ozawa H, Nagai A, Akiyama H, et al. Significance of rectal contractions during multichannel urodynamic study. Nippon Hinyokika Gakkai Zasshi 1997;88:874–9.
Cho S-Y, et al. The Clinical Significance of Rectal Contractions That Occur During Urodynamic Studies. Neurourology and Urodynamics 29:418–423 (2010)

Videourodynamics HOW ?

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FILLING RATE : 10 mL / min
Or less possible
Below 100 ml/min

BODY-WARM SALINE SOLUTION

MORE DILUTION POSIBLE OF CONTRAST SOLUTION

ELECTROMIOGRAPHY

LESS POSSIBLE EXPOSURE TO RADIATION

Kozomara M, Bellucci CH, Seifert B, Kessler TM, Mehnert U. Urodynamic investigations in patients with spinal cord injury: should the ice water test follow or precede the standard filling cystometry? Spinal Cord. 2015;53:800–802

Videourodynamics COMUNICATION

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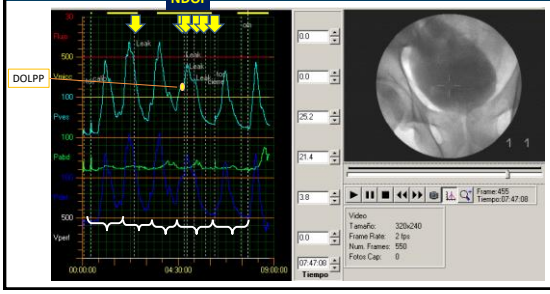
Videourodynamics NDO

PHASIC DETRUSOR OVERACTIVITY

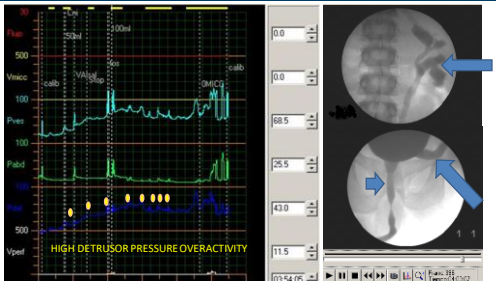
NDOI

DOLPP

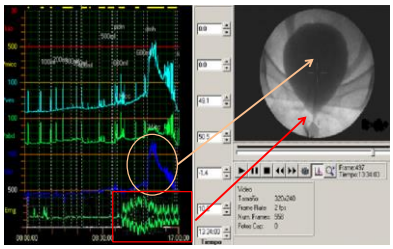


Videourodynamics

SUSTAINED DETRUSOR OVERACTIVITY



Videourodynamics



Urodynamics in NLUTS How often ?

Follow up studies

IT IS RECOMMENDED A YEARLY FOLLOW-UP FOR SYMPTOM AND CLINICAL CHECK

- ❑Serum chemistry to evaluate kidney function
- ❑renal and bladder ultrasound
- ❑abdominal radiograph

ALTHOUGH THERE IS NOT A RECOMMENDATION ON ROUTINE IMAGING STUDIES IN NLUTS PATIENTS

Good Urodynamic Practice Guidelines

"the initial test suggests an abnormality, leaves cause of troublesome lower urinary tract symptoms unresolved, or if there are technical problems preventing proper analysis."

The European Association of Urology

"essential in following up the natural history of the disease or for checking the efficacy of treatment."

Videourodynamics CONCLUSIONS

- immensely helpful in localization of the site of obstruction when high pressure/low flow state exists
- should be done at baseline and might be incorporated into follow-up for individual cases
- strongly considered in patients with impairment of renal function or structural change in the upper urinary tract , particularly in SCI patients

National Institute for Health and Clinical Excellence (NICE). National Clinical Guideline Centre. Urinary incontinence in neurological disease: management of lower urinary tract dysfunction in neurological disease. 20 Apr 2017.
Watanabe T, Chancellor M. Neurogenic voiding dysfunction. In: Nitti VW, editor. Practical Urodynamics. Philadelphia: W.B. Saunders; 1998. p. 142–55.
Brucker B, Kelly C, Nitti V. Evaluation of neurogenic lower urinary tract dysfunction: basic urodynamics. In: Corcos J, Ginsberg D, Karsenty G, editors. Textbook of the neurogenic bladder. 3rd ed. Boca Raton: CRC Press/Taylor & Francis; 2016. p. 373–82.
Drake MJ. Management and rehabilitation of neurologic patients with lower urinary tract dysfunction. Handb Clin Neurol. 2015;130:451–68.

Workshop 5
Neurodegenerative disease's impact on bladder function:
A multidisciplinary approach in diagnosis, treatment and improving quality of life

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It is always easy to differentiate urgency from another clinical presentation of these patients (e.g. pain, hypersensitivity, bladder irritation, infection)? How can we avoid over medication?

David Castro-Díaz
Spain

David Castro-Diaz

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Affiliations to disclose†:

Allergan
Astellas
Boston Scientific
Contura

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

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Neurodegenerative disorders

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- **Alzheimer's disease** (**AD**) and other **dementias**.
- **Parkinson's disease** (**PD**) and **PD**-related disorders.
- **Prion disease**.
- **Motor neurone diseases** (**MND**)
- **Huntington's disease** (**HD**)
- **Spinocerebellar ataxia** (SCA)
- **Spinal muscular atrophy** (SMA)

Parkinsonian syndromes include PD and atypical parkinsonism.
Atypical parkinsonism includes multiple system atrophy (MSA), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), and dementia with Lewy bodies (DLB).

Neurodegenerative disorders

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- **Increase number of people with Neurodegenerative disorders due to worldwide aging**
- **24.2 million people living with dementia in 2001 & 4.6 million new cases anually[1]**
- **Predicted to double every year to 80 million cases by 2040[2]**
- **Total cost of brain disorders in 2010=798 billions€ in Europe (105b for dementia&14b for PD)[3]**
- **Need for medical care and hospital visits & reduce QoL among elderly**
- **High rate of dementia & dependence (PD and ND 70% in within 8 years[4]**

Symptoms of advanced disease & comorbidity expected to rise accordingly

1.-Ferri 2005, 2.-Matthews 2013, 3.-Olesen 2012, 4.-Aarsland 2005

Neurodegenerative disorders

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Bladder dysfunction
- **Integrated part of the syndrome**
- **Due to other conditions**
- **A consequence of the treatment given**

Comorbidity – ↑Complications
Cognitive dysfunction & dementia– ↑LUTS impact
LUT dysfunction rarely link to the neurologic disorder

Neurodegenerative disorders

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- **Multiple phenotypes sharing burden of disease progression without hope for cure**
- **It is important to identify symptoms & complications leading to further loss of mobility and poorer QoL**
- **Mixed pathology is common**
- **Psychological factors & cognitive deficit interfere with copying**
- **LUTS have major impact on patients to stay independent**

Neurodegenerative disorders

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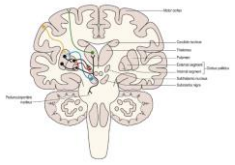
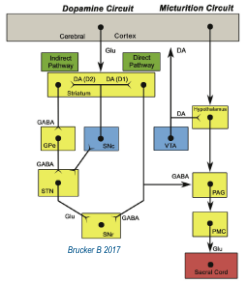


Crossman AR 2015



Brucker B 2017

Degeneration of dopaminergic neurons of substantia nigra & depletion of striatal dopamine
Dopaminergic striatal activity induces selective disinhibition
Dopaminergic loss leads to hyperactivity of Gpi & excessive input to thalamus & cortex-decrease activity of PAG, thalamic-insula pathway→**Neurogenic detrusor overactivity** (Winge K 2015)

Suprapontine and pontine lesions and diseases

Neurological Disease	Frequency in General Population	Type and Frequency of Neuro-Urological Symptoms
Cerebrovascular accident (Strokes)	450 cases/100,000/yr. (Europe)10% of cardiovascular mortality.	Nocturia - overactive bladder (OAB) - urgency urinary incontinence (UUI) - detrusor overactivity (DO), other patterns less frequent. 57-83% of neuro-urological symptoms at 1 month post stroke, 71-80% spontaneous recovery at 6 months. Persistence of urinary incontinence (UI) correlates with poor prognosis.
Dementias: Alzheimer's disease (80%), Vascular (10%), Other (10%).	6.4% of adults > 65 yrs.	OAB - UUI – DO 25% of incontinence in Alzheimer's disease, > 25% in other dementias: Lewy body, NPH, Binswanger, Gaushala, Pick Disease. Incontinence 3 times more frequent in geriatric patients with dementia than without.
Parkinsonian syndromes (PS) -Idiopathic Parkinson's disease (IPD): 75-80% of PS. Non-IPD: Parkinson's-plus (18%): -Multiple system atrophy (MSA), -Progressive supranuclear palsy, -Corticobasal degeneration, -Dementia with Lewy bodies. Secondary Parkinson's (2%)	2nd most prevalent neurodegenerative disease after Alzheimer's disease. Rising prevalence of IPD with age MSA is the most frequent non-IPD PS.	**LUTS frequency 30% at onset, 70% after 5 yrs. Storage phase symptoms: Nocturia (78%) OAB - UUI - DO . OAB and DO at the initial phase, intrinsic sphincter deficiency and impaired contractility appear as the disease progress. Complications of neuro-urological symptoms (infections) account for a major cause of mortality in MSA Impaired detrusor contractility seems to be the urodynamic finding distinguishing MSA from IPD**
Brain tumours	26.8/100,000/yr. in adults (> 19 yrs.), (17.9 benign, 8.9 malignant).	Incontinence occurs mainly in frontal location (part of frontal syndrome or isolated in frontal location).
Cerebral palsy	Cerebral palsy: 3.1-3.6/1,000 in children aged 8 yrs.	62% of women and 58% of men with cerebral palsy suffer from UI,70% DO. Recurrent urinary tract infection (UTI) and radiologic abnormalities in > 10% of cases
Traumatic brain injury	235/100,000/yr.	44% storage dysfunction. 38% voiding dysfunction, 60% urodynamic abnormalities.

EAU Guidelines 2018

LUT Symptoms in Parkinson Disease

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Lower urinary tract symptoms in patients with Parkinson's disease (PD)

Study	n in study Questionnaire	Nocturia (%)	Frequency (%)	Urgency (%)	Urge incontinence (%)	Incomplete emptying (%)	Intermittency (%)	Note
Campos-Sousa et al. (2003)	PD: 61 IPSS	63.9	36.1	32.8	NA	18	13.1	PD more symptoms than control persons
Sakakibara et al. (2003b)	PD: 105 Non-validated	Men: 6 Women					NA	
Barone et al. (2009)	PD: 1072 NMSS	34.6					NA	Not specific non-motor questionnaire
Bonnet et al. (2007)	PD: 35 Non-validated	NA					NA	
Hattori et al. (2092)	PD: 110 Non-validated	Irritativ					e symptoms: 11	
Bagah and Mohammed (2011)	PD: 49 IPSS	Irritativ 77					6.1	Referred for urologic evaluation
Sammeur et al. (2009)	PD: 110 IPSS	81					44	
Uchiyama et al. (2011)	PD: 50 Non-validated	38					NA	All untreated
Winge et al. (2006)	PD: 107 IPSS + DAN-PSS	IPSS: 4 DAN-PSS: 86	DAN-PSS: 71	DAN-PSS: 68	DAN-PSS: 46		NA	
Ramenuyr et al. (2008)	PD: 15 Interview by advisor	NA	NA	53	27	NA	NA	

IPSS, International Prostate Symptoms Score; DAN-PSS, Danish Prostate Symptoms Score; NMSS, Non-Motor Symptoms Scale; NA, not available.

Symptom	Frequency (%)
Nocturia	34,6-63-9
Frequency	16-46
Urgency	12-46
Incomplete emptying	8-40
Intermittency	6.1-44

Adapted from Winge K, 2015

LUTD In PD follow the onset of motor disturbances by 4 to 6 years[1]

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Storage Symptoms

Nocturia is the most common complaint = 60%
Urgency = 33% to 54%
Frequency= 16% to 36%
Urinary incontinence= 26% ♂ and 28% ♀[1]

Voiding Symptoms

Reported less commonly than storage symptoms
Hesitancy & poor stream 44% to 70% ♂
Straining to void 18 % ♀[2]

1.-Bonnet AM 1997,2.-Campos-Sousa RN 2003, 3.-Sakakibara R 2001

First symptoms in multiple system atrophy

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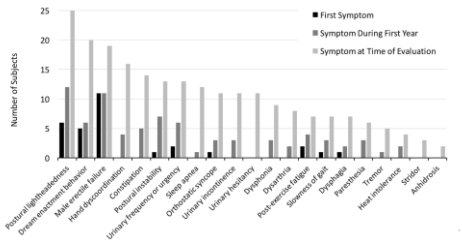
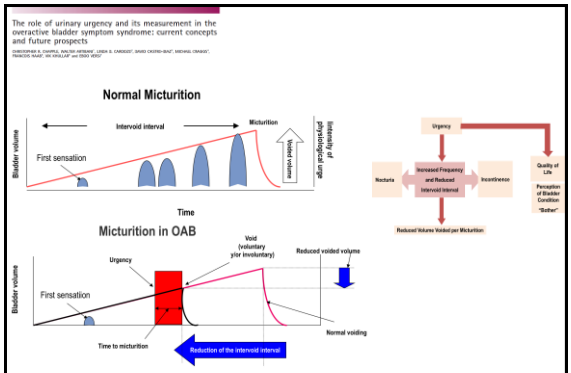


Number of MSA subjects from the cohort of 30 subjects reporting specific symptoms: as the very first symptom (black), during the first symptomatic year (medium grey), and at the time of evaluation (light grey)

Mckay JH 2018



Chapple CR et al. BJU Int 2005;95: 335–40.

What Causes Urgency?

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- Central mechanisms
- LUT mechanisms
  - Myogenic
    - Overt detrusor contractions
    - Micromotions
    - Abnormalities of myofibroblasts
  - Neural
  - Urothelium
- Viscerocutaneous or pelvic floor causes

Khasar J Nsci 28:5721-30 2008

OAB vs BPS

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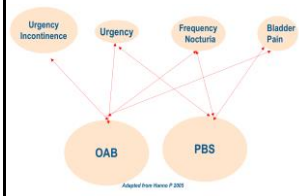
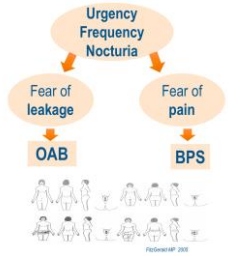


15% incidence of detrusor overactivity in IC patients (Kirkemo, Urology, 1997)



Urodynamics

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Urodynamic findings in PD and BPH/BOO		
Urodynamic parameter	Parkinson Disease	BPH/BPO
Detrusor overactivity	Phasic at low volume	Mostly terminal
DOA incontinence	More common	Less common
Pressure flow	Non-obstructed voiding	Obstructed voiding
Sphincteric activity	Bradykinesia	Normal guarding reflex
Postvoid residual	Insignificant	Can be elevated

Adapted from Defreitas GA 2003

Urodynamic abnormalities may differentiate between MSA and PD

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Urodynamic Parameter	PD	MSA
Detrusor overactivity	At small fill more profound	At larger fill less profound
Sensation	More sensate	Delayed
DESD	Rare	Common
Straining/weak stream	Rare	Common
Voiding efficiency	Preserved	Impaired
PVR	Insignificant	High
Bladder neck on VUD	Closed	Open

Adapted fromBrucker B 2017

Pharmacotherapy for LUTD

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- Alpha adrenergic agonists: (Retention & related symptoms)
- Alpha adrenergic antagonist: (SUI)
- **Antimuscarinics agents** (UR & constipation)
- Angiotensin converting enzyme (ACE) inhibitors (cough)
- Calcium channel blockers (UR & constipation)
- Cholinesterase inhibitors (increase bladder contractility)
- Diuretics
- Psychotropic drugs
- Opioid analgesics
- Other drugs (pyridines, gabapentin, glitazones, non-steroidal anti-inflammatory agents)

Older people and patients with neurodegenerative diseases take multiple drugs
Many of them are over-the counter (OTC) medications, vitamins or supplements
Adverse drug reactions result in > 700.000 visits to emergency/year

Antimuscarinics & Cognitive Function

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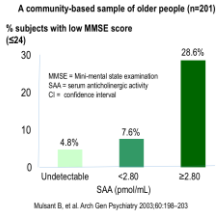
JAMA Neurol. 2016 Apr 18. doi: 10.1001/jamaneurol.2016.0560. [Epub ahead of print]

Association Between Anticholinergic Medication Use and Cognition, Brain Metabolism, and Brain Atrophy in Cognitively Normal Older Adults.

Risacher SL, McDonald BC, Tallman EF, West JD, Farlow MR, Unverzagt FW, Gao S, Boustani MA, Crane PK, Petersen RC, Jack CR Jr, Jagust WJ, Aisen PS, Weiner MW, Saykin AJ; Alzheimer's Disease Neuroimaging Initiative

- AC+ participants showed lower mean scores on Weschler Memory Scale-Revised Logical Memory Immediate Recall
- AC+ participants had a longer Trail Making Test
- AC+ participants had a lower executive function composite score test
- AC+ participants had reduced total cortical volume and temporal lobe cortical thickness and greater lateral ventricle and inferior lateral ventricle volumes

Subjects with higher serum anticholinergic activity have lower cognitive performance scores



Mulsant B, et al. Arch Gen Psychiatry 2003;60:198–203

Antimuscarinic treatment in PD´s patients

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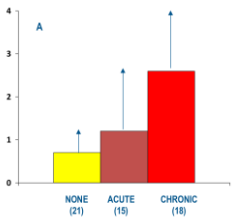
Comparison of senile plaque in Parkinson´s disease cases grouped according to antimuscarinic drub treatment **none, short-term (<2 a), long-term (>2 a)**



Amyloid plaque densities are more than 2.5-fold higher in cases treated with antimuscarinic medication in the long-term compared with untreated or short-term treated cases.

Klausner, A.P. 2007

Commonly used drugs with anticholinergic properties

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Of 25 drugs commonly prescribed to older patients, 14 produced detectable anticholinergic effects

- Ranitidine
- Codeine
- Dipyramidole
- Warfarin
- Isosorbide
- Theophylline
- Nifedipine
- Digoxin
- Lanoxin
- Prednisolone
- Cimetidine
- Furosemide
- Captopril
- Dyazide

The drugs in this study that showed no detectable anticholinergic effects were: Hydrochlorothiazide, Propanolol, Salicylic acid, Nitroglycerin, Insulin, Ibuprofen, Diltiazem,Atenolol,Metoprolol,Timolol

Tune LE, et al. Am J Psychiatry 1992;149:1393–4

How to avoid over medication

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Recommendations of the American Geriatrics Society

Ask before taking an OTC
Make a list and keep it updated
Review your medications
Ask questions (why, how, when, etc.?)
Organize your medications
Follow directions
Report problems
Medication dont´s

Health in Aging Foundation 2015

Workshop 5
Neurodegenerative disease's impact on bladder function:
A multidisciplinary approach in diagnosis, treatment and improving quality of life

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Oral medication
What do we have today ?
Its combination better ?
How to decide when to move to another step ?

Dr. Christian Cobreros
Urology Division - Hospital Carlos G. Durand
Buenos Aires - Argentina

Workshop 5
Neurodegenerative disease's impact on bladder function:
A multidisciplinary approach in diagnosis, treatment and improving quality of life

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Affiliations to disclose†:

- IPSEN (as PI in clinical studies, phase III)
- ASTELLAS (as PI in clinical study , phase III)

† 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:

- ☐ Self-funded
- ☐ Institution (non-industry) funded
- ☒ Sponsored by: **PROMEDON**

Dr. Christian Cobreros
Urology Division - Hospital Carlos G. Durand
Buenos Aires - Argentina

AIMS OF ORAL TREATMENT IN PATIENTS WITH NDO

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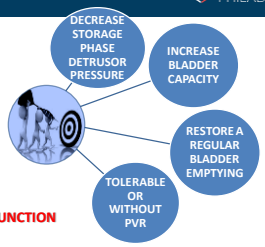
This presentation leads primary to specific issues in pharmacothaerapy in neurogenic patients

IN THIS NEUROGENICS SUBPOPULATION THE MOST IMPORTANCE CAUSE OF UI

NDO
And/or
INCOMPETENCE IN URETHRAL CLOSING FUNCTION



ORAL MEDICATION WILL BE HELPFULL IN MILD DEGREES OF NDO WHEN SYMPTOMPS ARE MORE PROFOUND FURTHER TREATMENTS WILL BE NEEDED

Stohrer M, Blok B, Castro-Diaz D, Chartier-Kastler E, Del Popolo G, Kramer G et al. EAU guidelines on neurogenic lower urinary tract dysfunction. Eur Urol 2009; 56, 81–88.

Oral bladder relaxants: Antimuscarinics

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Oxibutinine	Propiverine	Trospium	Tolterodine	Solifenacine	Darifenacine	Fesoteradine	Imidafenacine
agent with a pronounced muscle relaxant activity and local anesthetic activity Bennett et al. Franco et al. Gajewski et al Lee et.al	Stöhrer et al. NDO Propiverine vs Oxybutynin were equally effective in increasing bladder capacity and lowering bladder pressure Better tolerability achieved significance for dryness of the mouth (LOE1).	quaternary ammonium derivative with antimuscarinic actions not pass the healthy blood-brain-barrier Significantly * reduce the number of urinations *increase cystometric capacity * increase mean effective volume of the bladder * reduce the incidence of urgent voids	competitive muscarinic receptor antagonist a high selectivity in vitro and exhibits selectivity for the urinary bladder over the salivary glands Ethans in enhancing bladder volume and improving continence, but with less dry mouth	Solifenacin has been the antimuscarinic that has been more studied in OAB Krebs and Pannek (2013) SONIC Zesiewiczet.al. (2015)	High relative selectivity for the M3 receptor compared with other anticholinergics. Dariferacin has been extensively studied in OAB, but not in neurogenic bladder dysfunction	Prodrug Active metabolite 5-HMT Phase 3 trials have evaluated fesoteradine in OAB	Sakakibara et. al N: 62 Mean age: 70 yo NDO UDS+ cognitive tests Q: ameliorated urinary urgency night-time urinary frequency and improve quality of life UDS : increased bladder capacity but NDO did not change significantly three cognitive measures did not change significantly

Antimuscarinics

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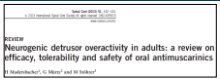
REVIEW
Neurogenic detrusor overactivity in adults: a review on efficacy, tolerability and safety of oral antimuscarinics

LARGE PLACEBO CONTROL STUDIES
- Oxibutinine
- Propiverine
- Trospium

30 – 40 % in CISTOMETRIC BALDEER CAPACITY
30 – 40 % decrease in MAXIMUM DETRUSOR PRESSURE

More capacity
Less pressure

BIAS
All based on **Urodynamcis measurements**
Other parameters were not adequately investigated:
- •IC inbetween cathteterization
- •log term data, patients are in AM therapy for decades

REFRACTORY PATIENTS FOR AN ORAL ANTIMUSCARINIC CAN I USE DOUBLE THERAPY WITH ANTIMUSCARINCS ?

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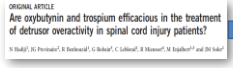
Neuro-urology
Effective Treatment of Neurogenic Detrusor Dysfunction by Combined High-Dosed Antimuscarinics without Increased Side-Effects

Amend et al , 2008
With combined high-dosage antimuscarinic medications, 85% of the patients who previously demonstrated unsatisfactory were treated successfully with combination of AM. The appearance of side-effects was comparable to that of normal-dosed antimuscarinics.


Double anticholinergic therapy for refractory neurogenic and non-neurogenic detrusor overactivity in children: Long-term results of a prospective open-label study

Nadeau et al , 2014
Dual therapy in children with mielomeningocele (between combinations of oxybutynin, tolterodine and trospium) to be effective and well tolerated in a few patients with NDO
- **Urodynamic capacity improved**
- **Maximal pressure of contractions decreased ($p < 0.0001$)**

20 % of drop out for adverse events ***36 months of F-UP***


ORIGINAL ARTICLE
Are oxybutynin and trospium efficacious in the treatment of detrusor overactivity in spinal cord injury patients?

NDO and OAB in spinal cord injury patients on IC . Neither the monotherapy nor a combination of Oxybutynin with Trospium allowed full continence

Nadeau G et al Double anticholinergic therapy for refractory neurogenic and nonneurogenic detrusor overactivity in children: long-term results of a prospective open-label study. Can Urol Assoc J 2014; 8(5-6):175-80.
Amend B, et al. Effective treatment of neurogenic detrusor dysfunction by combined high-dosed antimuscarinics without increased side-effects. Eur Urol. 2008 May; 53:1021-8

What about patients with cognitive impairment in this population?

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ANTIMUSCARINIC AGENTS

BLOOD-BRAIN BARRIER

PROVOKE COGNITIVE IMPAIRMENT

BIAS IN RESEARCH TRIALS

HOW MUCH ?

CLINICAL TRIALS ARE PERFOM IN PATIENTS WITH INTACT HEMATO ENCEPHALIC BARRIER

THIS POPULATION IS PROBABLY ELDERLY SO IMPLICATIONS OF DRUG-DRUG INTERACTIONS MAY APPLY

IT´S BLOOD-BARRIER INTACT IN STROKE, DEMENTIA, OR OTHER NEUROLOGICAL DESESASE?

IN DEMENTIA CONCOMITANT TREATMENT WITH DOPENEZIL SHOULD BE AVOID

What about antimuscarinics drug interactions?

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SLOW GASTROINTESTINAL MOTILITY

POTENTIALLY CAN ALTER THE ABSORTION OF OTHER DRUGS

MACROLIDE ANTIBIOTICS
AZOLE ANTIFUNGALS
CYCLOSPORIN
VINBLASTINE

CHOLINESTERASE INHIBITORS

were more likely to then be prescribed a bladder antimuscarinic than those residents with dementia not given a cholinesterase inhibitor

PRESCRIBING CASCADE

Antimuscarinics

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Propiverine	Trospium	Tolterodine	Solifenacine	Darifenacine	Fesoteradine	Imidafenacine
Stöhrer et al. NDO Propiverine vs oxybutynin	quaternary ammonium derivate with antim	a competitive muscarinic	Solifenacin has been the antimuscarinic	High relative selectivity for the	Prodrug Active metabolite	Sakakibara et. al N: 62 Mean age: 70 yo NDO UDS + cognitive tests
were equally effective in increasing bladder capacity and lowering bladder pressure	Significantly * reduce the	a high selectivity in	Krebs and Pannek			Q: ameliorated urinary urgency
Better tolerability achieved significantly for dry the most (LOE1).	cystometric capacity * increase mean patients not pass the healthy blood-brain-barrier	the urinary bladder over bladder volume and improving continence, but with less dry mouth	Zesiewicz et.al. (2015)	studied in OAB, but not in neurogenic bladder		measures did not change significantly

ANTIMUSCARINC DRUGS IMPROVES BLADDER STORAGE FUNCTION

HIGH INCIDENCE OF SIDE EFFECTS ALTHOUGH CONTROLLED-RELEASED HAVE LESS SIDE EFFECTS THAT INMEDIATE REALESE PRESENTATIONS

IN PATIENTS WITH COGNITIVE IMPAIRED, ANTIMUSCARINICS SHOULD BE PRESCRIBED WITH A WARNING, CAUSE THERE ARE PROVES THAT OXINBUTININE CAUSED SIGNIFICANT MEMORY DETERIORIATION

Beta 3 adrenoreceptor agonist

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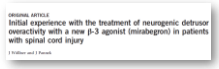
M of A: activation of adenylyl cyclase with the subsequent formation of cAMP down-regulation of ACh release, resulting in an inhibitory control of parasympathetic activity



N: 15 NDO SCI
Retrospective study
Mirabegron for a period of at least 6 weeks

Bladder evacuation per 24 h → 8.1 vs 6.4, P=0.003

Incontinence episodes per 24 h → 2.9 vs 1.3, P=0.027

Improvements in
- **bladder capacity** → from 365 to 419 ml
- **Compliance** → 28 to 45ml cm/H20
- **DP storage phase** → 45.8 vs 30 cm H20

Mirabegron is an alternative in NDO if antimuscarinics are contraindicated

Cognitive impairment should not occur

Wöllner J, Pannek J. Initial experience with the treatment of neurogenic detrusor overactivity with a new beta-3 agonist (Mirabegron) in patients with spinal cord injury. Spinal Cord 2015

WHAT IS SAID IN THE GUIDELINES ?

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	EAU-2015	AUA/SUFU-2014	NICE-2013
AMs	1. Either IR or ER preparations may be used initially	ER formulations should be preferred over IR, because of the lower rates of dry mouth	Oxy IR, tolterodine IR, or darifenacin should be used as 1st line drugs
	2. ER preparations should be used if initial trials of IR fail		All other preparations to be used as 2nd-line, the choice to be guided by local acquisition costs
	3. Consider using transdermal OXY if oral AMs cannot be tolerated due to dry mouth		
	4. Early review (of efficacy and side effects)		
Mirabegron	Use in patients with UUI Patients should be warned there is uncertainty about the long-term side effects	2nd-line treatment alternative to AMs Also, if a patient experiences inadequate symptom control and/or unacceptable AEs with one AM medication	3rd-line option in patients who have failed a trial of at least two AMs
Combination of AMs or AM + MIR	?	?	?

What is "refractory to pharmacotherapy" or "drug" ?

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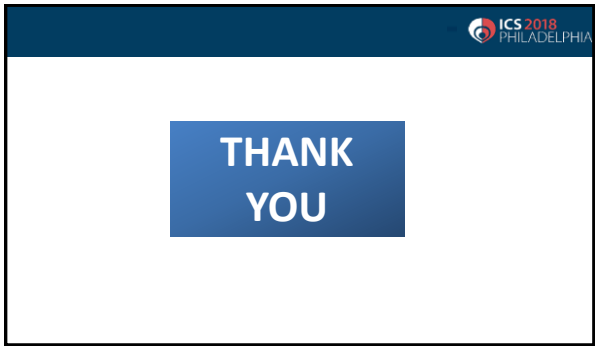
FURTHERMORE, THE MANAGEMENT IN THIS SITUATION IS INCONSISTENTLY NAMED

second-line treatment ?	third line management ?	step-up treatment ?
ICI guidelines	AUA guidelines	FDA
after attempting to treat OAB for 3 months with an AM, taking the step toward "second-line" therapy is worthwhile and justified	BTX-A , PTNS and SNM May be offered carefully in counselled patients who are "refractory" to 1° and 2° line treatments	injections for adults with OAB who "cannot use or do not adequately respond to a class of medications known as anticholinergics."

So independently of the definitions → HOW DO WE TREAT THIS PATIENTS WHEN ORAL TREATMENT FALIED OR ADVERSE EVENTS CAN NOT BE TOLERATED ?

Nitti VW, Kopp Z, Lin AT, et al. Can we predict which patient will fail drug treatment for overactive bladder? A think tank discussion. Neurourol Urodyn. 2010;29:652–657.
Gormley EA, Lightner DJ, Faraday M, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: aUA/ SUFU guideline amendment. J Urol. 2015;193:1572–1580.
http://www.fdagov/newsevents/newsroompress announcements/ucm336101htm.


ICS 2018
PHILADELPHIA
THANK
YOU

Neurodegenerative Disease: Surgical Approach

Carlos D'Ancona
Professor of Urology

Carlos D'Ancona

Affiliations to disclose†:

Ibsen - clinical trial

† 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:

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

Definition of failure

Quality of Live

Combination of clinical and urodynamics

- Urinary incontinence
- Pdet.max > 40 cmH_2O

Peyronnet B. et all. Progres en Urologie. 2015, 25: 1219-24.

Definition of success

1. Protection of upper urinary tract
2. Improvement of urinary incontinence
3. Restoration (or part) of LUT function
4. Improvement of patient's QoL

Blok B. et all. EAU Guideline, 2018.

Surgical approach

Botulinum toxin

Sacral neuromodulation

Bladder augmentation

- Continent urinary diversion

Prospective and randomized study of SCI

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Group I
- 33 patients
- Oxibutinin 5mg three times a day

Group II
- 28 patients
- 300 U. Intradetrusor Onobotulintoxin A

Ferreira R, D'Ancona C, Oelka M, CarneiroMR. Einstein (Sao Paulo) 2018, 16: 1-7

Aetiology

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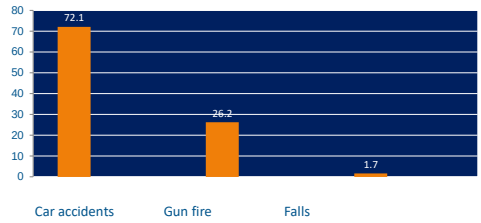

Maximal cystometric capacity

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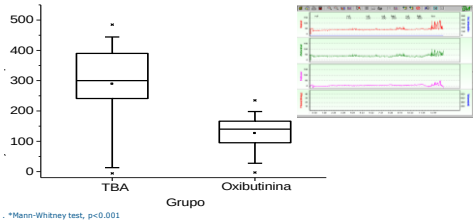

. *Mann-Whitney test, p<0.001

Ferreira R, D'Ancona C, Oelka M, CarneiroMR. Einstein (Sao Paulo) 2018, 16: 1-7

Pdet.max

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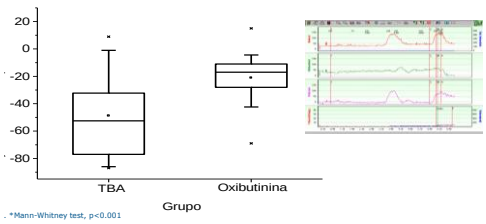

. *Mann-Whitney test, p<0.001

Ferreira R, D'Ancona C, Oelka M, CarneiroMR. Einstein (Sao Paulo) 2018, 16: 1-7

UI episodes decreased

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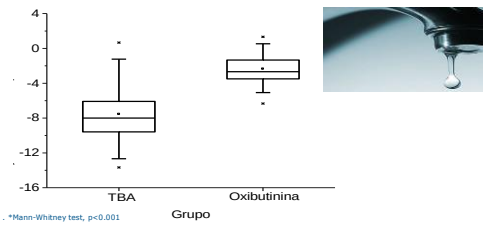

. *Mann-Whitney test, p<0.001

Ferreira R, D'Ancona C, Oelka M, CarneiroMR. Einstein (Sao Paulo) 2018, 16: 1-7

QoL – ICIQ-SF

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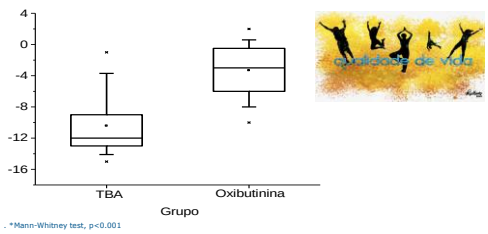


. *Mann-Whitney test, p<0.001

Ferreira R, D'Ancona C, Oelka M, CarneiroMR. Einstein (Sao Paulo) 2018, 16: 1-7

Conclusion

The oral use of oxybutynin and the intradetrusor injection of BoNT A showed a significant improvement in urodynamic parameters, the number of urinary leakage in 24 hours and a lower impact on the quality of life of patients with spinal cord injury treated in this study.

Comparing the objective response (urodynamic study) and subjective (quality-of-life questionnaires) of the two drugs, BoNT A proved to be more effective than oxybutynin in all evaluated parameters, as well as having a better tolerability profile.

Ferreira R, D'Ancona C, Oelka M, CarneiroMR. Einstein (Sao Paulo) 2018, 16: 1-7

How to prevent failures?

Journal of Pediatric Urology
Volume 11, Issue 1, February 2015, Pages 27.e1-27.e4

Botulinum injection is useless on fibrotic neuropathic bladders

S. Tiryaki [a], I. Yagmur [a], Y. Parlar [a], K. Ozel [b], C. Akyildiz [c], A. Avanoglu [a], I. Ulman [a]

Patients with low detrusor compliance and loss of contractility was considered as fibrotic bladder did not respond well to BoNT A.

Conclusion – BoNT A

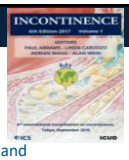
BoNT A declines the rate of augmentation cystoplasties

Decreases intravesical pressure while increases storage capacity

Urodynamic evaluation to prove that the detrusor pressure returns to a safe level

Prakas NS, Lopetegui DM, Gomez C. Curr Urol Rep. 2017, 18: 64.

Conclusion – BoNT-A



BoNT A injection into the detrusor muscle improves clinical and urodynamic parameter. LoE 1 and QoL LoE 1

Second line treatment

Increase PVR, need CIC, higher incidence of UTIs

Grade of recommendation A

Sacral neuromdulation

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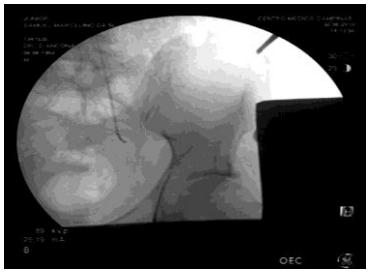

Int Urogynecol J (2016) 27:347–354
DOI 10.1007/s00192-015-2771-0

REVIEW ARTICLE

Sacral neuromodulation: an effective treatment for lower urinary tract symptoms in multiple sclerosis

Federica Puccini[1] · Alka Bhide[2] · Suzy Elneil[3] · G. Alessandro Digesu[2]

- Overactive bladder symptoms due to neurogenic detrusor overactivity is the most common LUTS, occurring in 60 – 80 % of MS patients
- MS should be carefully evaluated however, there is a lack of randomized controlled trials
- SNM is usually offered if the course of the underlying neurological disorder can be considered stable or slowly progressive and patients are not likely to require repeated magnetic resonance scans

Int Urogynecol J (2016) 27:347–354
DOI 10.1007/s00192-015-2771-0

REVIEW ARTICLE

Sacral neuromodulation: an effective treatment for lower urinary tract symptoms in multiple sclerosis

Federica Puccini[1] · Alka Bhide[2] · Suzy Elneil[3] · G. Alessandro Digesu[2]

- It has been reported that the loss of efficacy over time is a result of a new relapse.
- One study found that patients with relapsing disease required and adjustment of the stimulation parameters.
- Magnetic resonance is not recommended after SNM

Wollner J, Krebs J, Pannek J.
Spinal Cord 2016, 54: 137-140.

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Incomplete spinal cord injury

Low risk upper urinary tract damage

MS patients should be carefully selected

Regular urodynamics follow up needed

Conclusion SNM

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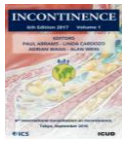
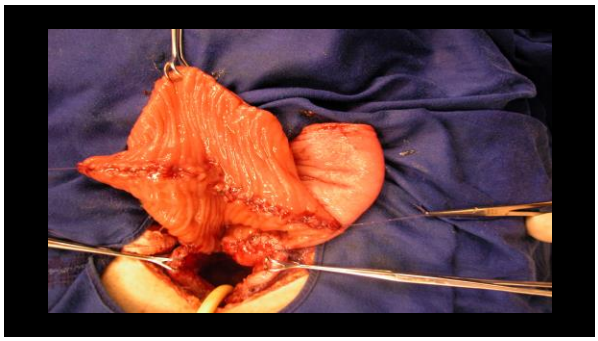


Limited available data

Can have a inhibitory effect on NDO

Grade of recommendation B



Reasons to perform bladder augmentation

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Elevated filling pressure

Diminished bladder capacity

Not responsive to other treatments

Kurpad R, Kennelly MJ. Current Urology Report. 2014, 15: 444

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Current Urology Reports
April 2016, 17:27 | Cite as

Indications for Augmentation Cystoplasty in the Era of OnabotulinumtoxinA

Authors | Authors and affiliations

Evan Shreck, Kevin Gioia, Alvaro Lucioni

It is very effective

88% satisfaction score in spinal cord injury and multiple sclerosis

Failure of conservative treatment

Onabotulinumtoxin A failure

More permanent solution

INTERNATIONAL JOURNAL OF UROLOGY

Original Article: Clinical Investigation | Full Access

Augmentation cystoplasty: Urodynamic and metabolic outcomes at 10-year follow-up

Kwun-Chung Cheng, Chi-Fai Kan, Peggy Sau-Kwan Chu, Chi-Wai Man, Bill Tak-Hing Wong, Lap-Yin Ho, Wing-Hang Au

Change in bladder capacity	+ 130%
Change in bladder compliance	+ 87%
Change in presence of detrusor overactivity	-54

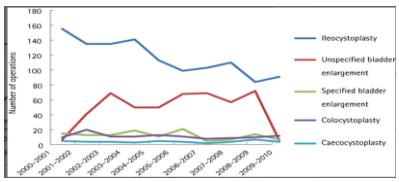
BJUI

REVIEW ARTICLE

The past, present and future of augmentation cystoplasty

Suzanne M. Biers, Suzie N. Venn† and Tamsin J. Greenwell*
Department of Urology, Leicester General Hospital, Leicester, †Institute of Urology and University College London Hospital, London, and *Department of Urology, St. Richard's Hospital, Chichester, West Sussex, UK

Accepted for publication 26 July 2011



Research and Reports in Urology

Dovepress

REVIEW

Neurogenic bladder in spinal cord injury patients

2015, 7: 85-99

CIC to empty the bladder (72.5%)
UTI episodes (65%)
Urinary incontinence (10%)
Stones in the reservoir (32.5%)
Upper tract stones (22.5%)

Conclusion –cystoplasty augmentation

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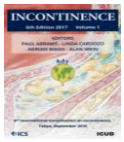
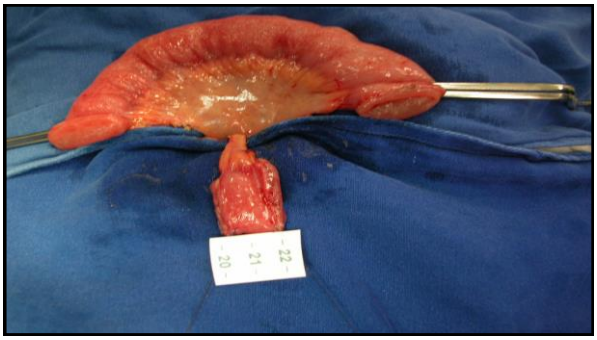
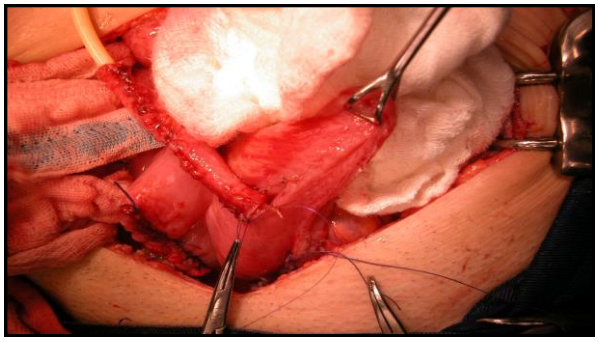


- >90% achieved nocturnal continence
- 91-100% achieved diurnal continence
- QoL improved rates 90%
- 92% satisfaction in long term follow up





Neurourology and Urodynamics 35:1046–1050 (2016)

Long-Term Complications of Continent Cutaneous Urinary Diversion in Adult Spinal Cord Injured Patients

Marie-Aimée Perrouin-Verbe,[1] Emmanuel Chartier-Kastler,[1] Alexia Even,[2] Pierre Denys,[2] Morgan Roupret,[3] and Veronique Phe[1,4]

- 29 SCI patients
- 66 months follow up
- **9 (31%)**
  - 1 stoma stenosis
  - 1 tube stenosis
  - 2 patients developed fistulae between the tube and the skin
  - Three patients had bladder stones
  - Two patients remnant stress urine leakage
- 100% catheterizable stoma
- 96% achieve continence

Conclusion

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Great benefit in wheelchair women patients

The role of Physiotherapy and a Multidisciplinary team in the daily life of patients. Can we improve their quality of life if we work together?

Dr Beth Shelly PT, DPT, WCS, BCB PMD
www.bethshelly.com
International Continence Society Annual Meeting
August 28, 2018 Philadelphia, PA
Workshop 5

Overall Conservative Management of Neurogenic Bladder

Individualized to the patient in cooperation with caregivers

Little high level evidence for any one treatment

NICE guidelines give good outline of evidence related to treatment (NICE 2012)

Overall goals of treatment is
- protection of upper urinary tract
- improvement in QOL

PT best with incomplete lesions

Individualized Treatment

Therapies to decrease overactive bladder

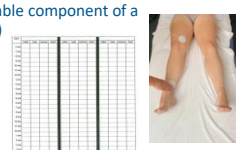
Therapies to decrease PFM spasm

Therapies to increase bladder contraction

Therapies to increase PFM contraction

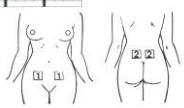
Therapies to Decrease OAB

Bladder drills and fluid management - suitable component of a rehabilitation program level C (Drake 2013)
- Bladder training
- Timed voiding
- Habit training
- Prompted voiding



PFM training with or without biofeedback

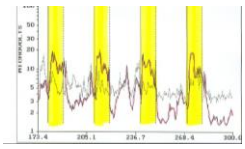
Electrical stimulation



Therapies to decrease PFM tension / spasm and improve PFM relaxation during empting

Manual stretching of PFM does not appear to have a lasting impact

Biofeedback-assisted PFM coordination training
- PFM relaxation
- Train on the toilet with external EMG during voiding



Therapies to increase bladder contraction during voiding

Intermittent catheterization - accepted standard (Drake 2013)

Triggered Reflex Voiding - Provocation of bladder contraction
- Suprapubic tapping, pubic hair pulling
- Thigh scratching, stroking lower back
- Anorectal manipulation

Bladder expression - Increasing intra abdominal pressure
- Lean forward, gentle whisling
- Valsava, Crede

Timed voiding / habit training / bladder training

Ideas and Advice to Help Promote Full Voiding

Privacy – Paruresis, also called shy bladder, is the inability to urinate in public. Maintaining as much privacy as possible increases bladder emptying for most patients.

Toilet position - sit fully on the toilet

Full relaxation of PFM overflow muscles (adductors and gluteals in particular) is necessary for full PFM relaxation and will increase bladder emptying

Sitting relaxed and supported

Both feet flat on the floor and fully supported

Adequate hip flexion to encourage PFM relaxation

Relaxation

Take time to fully relax all muscles for full emptying.

Distract yourself on the toilet by reading, singing or reciting a poem.

This is especially important in patients with anxiety.

Double voiding

After initial void, stand, move, sit down, and attempt to void again.

Toilet Exercises - ideas to encourage full empting, Do not valsalva

Sit completely on toilet, relax legs in abduction

Lean forward bending at the hips 3 times

- Relax and allow urine to comes out

Stand up then sit down (double voiding)

- Relax and allow urine to come out

Several gentle PFM contractions and large relaxation

- Relax and allow urine to come out

Do not push

Running Water

The sound of running water can initiate voiding however over use of the method can lead to OAB and UUI with the sound of water running.

Empting Better

Therapies to increase sphincter contraction

PFM training with or without biofeedback

Overflow or functional PFM training

Therapies to increase sphincter contraction

Electrical stimulation - may be an option in cases of PFM weakness (not in complete denervation) however no research exists (Drake 2013)

Evidence for conservative management of UI in patients after Stroke

Significant decrease in frequency of accidents and need for assistance to toilet in treatment group as compared to control group. (Couran 2012)

- PFM exercises (PT)
- Timed voiding and prompted voiding (RN)
- Functional bathroom activities (OT)

PFM exercises decrease urinary frequency and UI by pad test RCT (Tibaek 2005, **Tibaek 2017**)

Evidence for conservative management of UI in patients after Stroke

PFM exercises added to standard rehabilitation decreased UI by RCT (Skin 2016)

Restoration of functional mobility - RCT shows benefit in stroke patients (Wilkander 1998)

PFM exercises with bladder retraining - systemic review found little evidence in stroke patients (Dumoulin 2005)

Evidence for conservative management of UI in patients with Multiple Sclerosis

Best candidate for PT - mild MS, without PFM spasticity or dyssynergia (De Ridder 1999)

Poor success - elevated PVR (McClurg 2008)

Guideline recommendations for PFM training

- Fowler 2009 - UK consensus, grade B
- Pannek 2012 - EAU guideline, no grade given
- Cetinel 2013 systematic review and consensus report, grade A

Evidence for conservative management of UI in patients with Multiple Sclerosis

PFM exercises versus sham - decreased pad weight, number of pads and nocturia (Lucio 2010)

PFM exercises plus EMG and electrical stimulation vs no treatment RCT (Vahtera 1997)

- Significant improvement in UI, nocturia, and improved bladder emptying.
- Men > women

PFM exercises plus EMG and electrical stimulation vs sham electrical stimulation RCT (McClurg 2008)

- Significant improvement in UI by pad test, IIQ, UDI, IPPS and decreased PVR
- 85% in the active group, 47% in the control group
- PFM strength improved equally in both groups

Evidence for conservative management of UI in patients with Multiple Sclerosis

Biofeedback assisted PFM exercises are not superior to PFM exercises alone (Klarskov 1994)

Transcutaneous posterior tibial nerve stimulation resulted in significant decrease in urgency, frequency and leakage without increase in PVR - no control group (de Seze 2011)

Evidence for conservative management of UI in patients with Multiple Sclerosis

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TENS to sacral dermatomes (Skeil 2001)

- Mixed neuro diseases, but mostly MS patients
- Diary showed significant improvement - decrease in 24 hour frequency, UI episodes and clothing changes
- Risk for increased PVR

Questions

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