Adult Neurogenic Bladder: Current Evaluation & Advances in Clinical Management

W38, 16 October 2012 14:00 - 17:00

Start	End	Topic	Speakers
14:00	14:45	Introduction, Neuro-Anatomy and Neurophysiology, Neuro-pathophysiologies and Voiding Dysfunction	• Angelo Gousse • Stephen Kraus • Hari Siva G R Tunuguntla
14:45	15:30	Urodynamics and Neurogenic Voiding Dysfunction	• Stephen Kraus
15:30	16:00	Break	None
16:00	17:00	Treatment of Neurogenic Bladder	• Angelo Gousse • Hari Siva G R Tunuguntla

Aims of course/workshop

Aims and objectives of this workshop include: 1. To correlate the various types of detrusor and sphincter dysfunction with the location of the nervous lesions 2. To present the contemporary evaluation (including applied urodynamics) of neurogenic bladder conditions 3. Comprehensive discussion on the current management of clinically significant neurogenic bladder syndromes based on the type of dysfunction and individual comorbidities 4. Presentation of evidence based current therapeutic strategies

Educational Objectives

Knowledge gained from the workshop will be of immense benefit to the practicing Urologists, Neurologists, Internists & Geriatricians with special interest in neurogenic bladder dysfunction, Urology/Urodynamic nurses and continence advisors in the day to day evaluation and management of commonly encountered neurogenic bladder conditions. Participants will be able to correlate the type of voiding dysfunction with the location of nervous lesions and learn the role of urodynamic evaluation in the overall management. Participants will have a comprehensive understanding of therapeutic strategies as practiced in 2011-2012 including pharmacological and surgical treatments (endoscopic, minimally invasive, and open options). Participants will gain knowledge regarding the effect of deep brain stimulation on voiding function. Additionally, neurosurgical, perioperative, and anaesthetic management of these patients will be discussed.

W38, Adult Neurogenic Bladder: Current Evaluation and Advances in Clinical Management (Advanced)

Tuesday – 16 October 2012; 14:00 – 17:00 Hours

Start	End	Topic	Speakers
14:00	14:45	1. Introduction 2. Neuro-Anatomy and Neurophysiology 3. Neuro-pathophysiologies and Voiding Dysfunction a. CVA, Brain tumor, Brain Injury, Deep brain stimulation, Multiple Sclerosis b. Parkinson's disease c. Spinal Cord Injury, spina bifida, spinal cord tumor **d.** Other: herniated disk, HIV 4. Clinical Evaluation	Hari Tunuguntla Stephen Kraus Hari Tunuguntla Angelo E. Gousse Stephen Kraus Hari Tunuguntla Hari Tunuguntla
14:45	15:00	BREAK	
15:00	16:00	1) Urodynamics and Neurogenic Voiding Dysfunction a. Before the urodynamics b. Autonomic dysreflexia c. Problems of storage(bladder) i. Detrusor overactivity ii. Impaired compliance iii. DHIC d. Problems of storage (outlet) i. Incompetent outlet-neurogenic vs SUI e. Problems of emptying (bladder) i. Areflexia ii. Hyporeflexia iii. DHIC f. Problems of emptying (outlet) i. DESD ii. BPH	Stephen Kraus
16:00	16:15	BREAK	
16:15	17:00	1) Treatment of Neurogenic Bladder a. Tube drainage b. Pharmacotherapy (improve storage) c. Intravesical therapy (improve storage) d. Pharmacotherapy (improve emptying) e. Botulinum toxin- i. Bladder ii. sphincter f. Surgery i. Continent ii. Incontinence iii. other g. Role of Neurostimulation & Neuromodulation h. Closing	Hari Tunuguntla Hari Tunuguntla Angelo E. Gousse Angelo E. Gousse Hari Tunuguntla Hari Tunuguntla Hari Tunuguntla Hari Tunuguntla Hari Tunuguntla

Aims of course/workshop

Neuroanatomy and neurophysiology of the lower urinary tract will be briefly discussed initially followed by neuropathophysiology of the cerebral, spinal, and peripheral lesions correlating the same with the clinical symptomatology. This will be followed by clinical evaluation including classic urodynamic findings of various forms of neurogenic voiding dysfunction. In the last part of the workshop, current evidence based therapeutic strategies and advances in the management of adult neurogenic voiding dysfunction will be discussed.

Educational Objectives

Having participated in this course, which will also include case presentations to illustrate the points, you should have an advanced knowledge on the pathophysiology, current evaluation and management of adult neurogenic lower urinary tract dysfunction. In addition, you should become familiar with what can now be offered to the individual patient in your clinical practice.

Adult Neurogenic Bladder: Current Evaluation & Advances in Clinical Management (Advanced)

Introduction, Neuroanatomy & Pathophysiology

Workshop Faculty

Hari Tunuguntla, MD, MS, MCh (Program Chair and Faculty)
Asst Professor & Director, Section of Neuro-Urology, Female Pelvic Medicine & Reconstructive Surgery, Voiding Dysfunction, and Urodynamics
UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ, U.S.A.

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Angelo E. Gousse, MD (Faculty)
Bladder Health & Reconstructive Urology Institute
Miramar, FL, U.S.A.

Neurogenic Bladder

- Abnormal bladder function secondary to central nervous system (CNS) injury or neurologic disease[1-3]
  - **Detrusor muscle overactivity**: sustained high bladder pressure[1]; characterized by involuntary detrusor contractions during the filling phase, which may be spontaneous or provoked[4]
  - **Detrusor muscle areflexia**: detrusor underactivity resulting in urinary retention[2]
  - **Sphincter-detrusor dyssynergy**: inappropriate timing of sphincter contraction[2]

1. Manack A, et al. *Neurourol Urodynam*. 2011;30:395-401.
2. Cruz CD, et al. *ScientificWorldJournal*. 2011;11:214-234.
3. Huang ST. *Incont Pelvic Floor Dysfunct*. 2008;2(suppl 1):25-28.
4. Abrams P, et al. *Neurourol Urodynamics*. 2002;21:167-178.

Current Advances in Evaluation & Management of Adult Neurogenic Bladder (NGB)

Workshop - Aims & Objectives

The attendee should be familiar with:

- Classification and epidemiology of neurogenic bladder (NGB)
- Neuroanatomy/neuropathophysiology of NGB Evaluation and treatment
- Understand specific issues associated with NGB treatment in patients with:
  - central nervous system abnormalities
  - Parkinson's disease
  - spinal cord injury
  - multiple sclerosis

Classification & Epidemiology

Neurogenic Detrusor Overactivity:[1]
Defined as overactivity due to a relevant neurological condition

- **Examples of Neurological Conditions[1-3]:**
  - Multiple sclerosis
  - Spinal cord injury
  - Stroke
  - Parkinson's disease
- **Approximately 4.4 million Americans with a neurologic condition (MS, SCI, PD, and stroke) have DO[4]**
- **Approximately 2.6 million Americans with a neurologic condition (MS, SCI, PD, and stroke) have UI[4]**

MS=multiple sclerosis; PD=Parkinson's disease; SCI=spinal cord injury; DO=detrusor overactivity; UI=urinary incontinence

1. Abrams P, et al. *Neurourol Urodynamics*. 2010;29:213-240.
2. Chancellor MB, et al. *Am J Phys Med Rehabil*. 2006;85;536-545.
3. Cherney I, Yan K. *Cases Journal*. 2009;2:9120.
4. Data on file, Allergan, Inc.

Impact of Bladder Symptoms on Daily Activities From Patient Perspective

Intimacy	Physical	Psychological
• Avoidance of sexual contact and intimacy	• Limitations or cessation of physical activities	• Guilt/depression • Loss of self-esteem • Fear of: ▪ Lack of bladder control ▪ Urine odor
Occupational	**Domestic**	**Social**
• Absence from work • Decreased productivity	• Requirements for specialized underwear • Precautions with clothing	• Reduced social interaction • Planning travel around toilet accessibility

Tubaro A. *Urology*. 2004;64(Supp 6A):2-6.

Clinical Presentations of NDO

Symptoms[1]
- Urgency
- Frequency
- Incontinence

Sequelae[1-4]
- Higher intravesical pressures
- Poor bladder compliance
- Recurrent febrile urinary tract infections
- Stones
- Vesicoureteral reflux
- Hydronephrosis
- Renal failure
- Autonomic dysreflexia

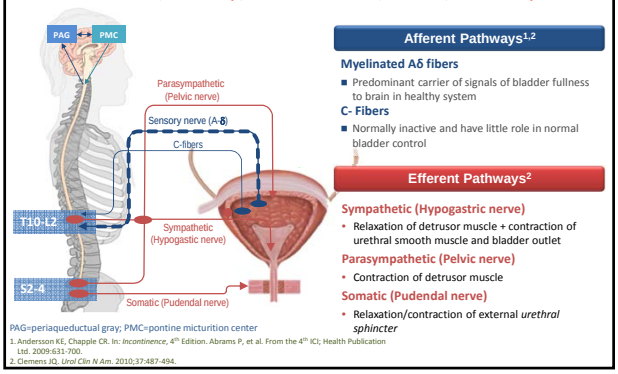
1. Chancellor MB, et al. *Am J Phys Med Rehab*. 2006;85:536-545.
2. Reynard JM, et al. *Spinal Cord*. 2003;41:1-11. 3. de Sèze M. *Mult Scler*. 2007;13:915-928.
4. Gormley EA. *Urol Clin N Am*. 2010;37:601-607.
Images courtesy of Michael Kennelly, MD.

Why Should We Worry???

- **Potentially detrimental to upper tracts**
  - Hydronephrosis
  - Renal failure
- **Urinary incontinence**
  - Social
  - Skin care
- **Other urological issues**
  - UTIs
  - Stones

Normal Neural Circuit:

Afferent (Sensory) and Efferent (Motor) Pathways



PAG=periaqueductual gray; PMC=pontine micturition center

1. Andersson KE, Chapple CR. In: *Incontinence*, 4th Edition. Abrams P, et al. From the 4th ICI; Health Publication Ltd. 2009:631-700.
2. Clemens JQ. *Urol Clin N Am*. 2010;37:487-494.

Normal Micturition Physiology

- Storage
- Evacuation
- Role of Central Nervous System

Keep these components in mind during GU tract w/u and management of NGB

Normal Micturition Physiology

- **Storage**
  - Accommodate urinary volume without bothersome sensation
  - Maintain continence
  - Maintain low intravesical pressures
  - Protect upper tracts
  - Provide appropriate warning & sensation
- **Evacuation**
- **Role of Central Nervous System**

Normal Micturition Physiology

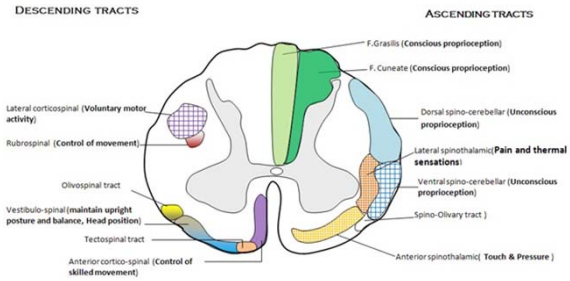
- **Storage**
- **Evacuation**
  - Coordinated event
  - Voluntary control
  - Sustained detrusor contraction of appropriate duration & strength to allow complete emptying
- **Role of Central Nervous System**

Micturition Reflex

- Very coordinated neuromuscular event
- First - sudden, complete striated sphincter relaxation.
- Second - simultaneous detrusor contraction with urethral relaxation.
- Requires integration of the autonomic (parasympatheic, sympathetic) and somatic nervous systems.

Spinal Cord Centers

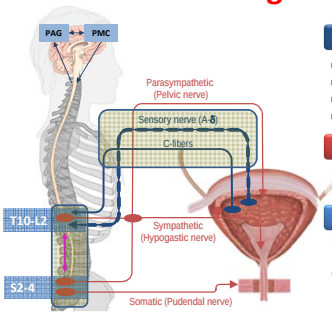
- Sympathetic Input - **T10 - L2** cell bodies form the ***hypogastric nerve***
- **Sacral Micturition Center - S2 - S4**
  - Parasympathetic Nucleus - cell bodies form the ***pelvic nerve***
  - Pudendal Nucleus (Onuf) - cell bodies form the ***pudendal nerve***



Peripheral Nerves

- Hypogastric - sympathetic fibers, chain ganglia, to pelvic plexus
- Pelvic - S2 - S4 ventral roots to the pelvic plexus
- Pudendal - S2 - S4 ventral roots leave the pelvis through Alcock's canal to innervate the striated urethral and anal sphincters
- All are mixed motor and sensory nerves

Pathophysiology Related to Neurogenic Disease



Afferent Pathways[3,4]

- Aδ/C-fibers ratio modification
- C-fibers activated
- Form a spinal reflex circuit in lumbar area
- Voiding escapes outside cerebral control

Efferent Pathways[3]

- Supraspinal inhibitory control on the bladder may be affected

Afferent and Efferent Pathways[5,6]

Both afferent and efferent modifications are believed to potentially contribute to detrusor overactivity

1. Andersson KE, Chapple CR. In: *Incontinence*, 4th Edition. Abrams P, et al. From the 4th ICI; Health Publication Ltd. 2009:631-700.
2. Clemens JQ. *Urol Clin N Am*. 2010;37:487-494.
3. Koelbl H, et al. In: *Incontinence*, 4th Edition. Abrams P, et al. From the 4th ICI; Health Publication Ltd. 2009:255-330.
4. Yoshimura N, Chancellor MB. In: *Campbell-Walsh Urology, 9th edition*. Wein J, et al. eds. Philadelphia: Saunders Elsevier; 2007: 1992-1972.
5. McCombe PA, et al. *Expert Rev Neurotherap*. 2009;9:331-340. 6. Kalsi V, Fowler KJ. *Nature Clin Pract*. 2005;2:492-501.

Neurogenic Bladder: Assessment

Physical Examination[1,2]

- Detailed patient history
- General/Medical exam
- Abdominal exam
- Pelvic/rectal exam
- Focused neurological exam

Bladder/Sphincter Function Tests Can Include[1-4]

- Post void residual (PVR)
- Urinalysis
- Urinary diary
- Ultrasound of urinary tract*
- Urodynamics
- Sphincter Electromyography (EMG)
- Voiding cystourethrogram (VCUG)
- Urethral pressure profiles

*Upper tract imaging.

1. Abrams P, et al. *Neurourol Urodyn*. 2010;29:213-240.
2. Wyndaele JJ, et al. In: *Incontinence*, 4th Edition. Abrams P, et al. From the 4th ICI; Health Publication Ltd. 2009:793-960.
3. De EJB, et al. *Neurourol Urodynam*. 2005;24:6160621.
4. Ahmed HU, et al. *Nat Clin Pract Urol*. 2006;3:368-380.

Work up for the Patient with NGB

- Upper tract evaluation
- Lower tract evaluation
  - Remember concept of filling & emptying
- Labs

Upper GU Tract Evaluation

- **Imaging**
  - Renal sonogram & KUB
  - Nuclear renal scan
  - IVP
  - Cross sectional imaging
- **Renal Function**
  - 24 hr creatinine clearance
  - Nuclear renal scan (total and split function)
  - Serum creatinine unreliable

Lower GU Tract Evaluation

- Voiding/catheterization diary
- Urodynamic evaluation
- Cystoscopy
- **Imaging**
  - fill and voiding cystourethrogram
  - Can be done simultaneous with UDS

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Neuro-pathophysiology of Voiding Dysfunction

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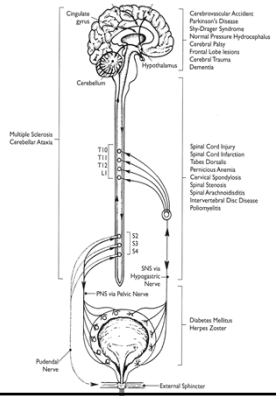
Neuro-pathology of Neurogenic Voiding Dysfunction



Tethered Cord Syndrome

- Impediment of cephalad migration of conus medullaris during vertebral growth
- Associated with short filum terminale, lipoma , adhesions, esp. after repair of dysraphism
- Mitochondrial anoxia and axonal injury[1]
- Lower extremity weakness, spastic gait
- Bowel & bladder dysfunction
- May occur in adulthood[2]
- UDS mandatory

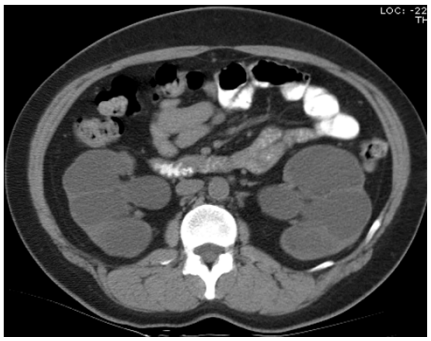
1. *Yamada et al J. Neurosurg 54: 494, 1981*
2. *Adamson et al Br J Urol 71:417, 1993*

Tethered Cord Syndrome

- Detrusor areflexia in 60%[1]
- Recovery after cord release[2]
- Overactivity in up to 30%[3]
- Early, aggressive surgical correction[4]

1. *Kondo et al J Urol 135:313, 1986*
2. *Hellstrom et al J Urol 135:317, 1986*
3. *Flanigan et al Urology 33:80, 1989*
4. *Fukui & Kaizaki Urology 16:539, 1980*

Spina Bifida



Spina Bifida

Myelomeningocele

- Nerve roots/spinal cord with meningeal covering protrudes through posterior vertebral bony arch
- Deficit depends on neural structures affected
- Detrusor may be areflexic; compliance poor 50%
- Bladder neck classically open - incontinent
- Non-relaxing external sphincter - high storage pressure
- These patients are wet but in danger of renal damage

Myelomeningocele

- Early UDS evaluation required (pre-op?)
- Elevated intravesical storage pressure
  mandates early drainage procedure
- ISD (Low LPP) permits
  surveillance with U/S screening
- AUS effective for incontinence
  but must know compliance
- Augmentation to decrease storage pressure
  if anticholinergics ineffective

Sacral Agenesis

- Absence of part or all of 1 or more sacral vertebrae (caudal regression syndrome)
- Neurogenic lower urinary tract dysfunction with 2 or more vertebral bodies affected
- 1% children born to IDDM mothers (terato?)
- M=F
- Normal cord but conus ends abruptly
- Nerve rootlets embedded in dense fibrous tissue

Sacral Agenesis

- Bladder denervation: 50% UMN, 50% LMN
- Cannot be predicted by # of affected vertebrae
- Sacral sensation usually intact
- 25% have no neurologic lesion
- Hyperreflexia vs. Areflexia
- May have DESD
- UDS and imaging important for management

Spinal Stenosis

- 90% of the population will report back pain
- Acquired lumbar stenosis over 65 yrs: 1 per 1000
- Chronic and substantial pain limits activity

Cerebrovascular Accident

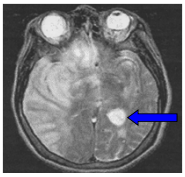
US Incidence/ Prevalence	Estimated 7,000,000 Americans ≥20 years of age have had a stroke[1] An estimated 795,000 people experience a new or recurrent stroke annually[1] Someone in the US has a stroke every 40 seconds, on average[1]
Bladder Dysfunction	In a pooled meta-analysis of 18 studies evaluating a total population of 727 patients who had a stroke, 56% were found to have DO.[2] In another pooled meta-analysis of 93 studies evaluating a total population of 24,198 patients who had a stroke, 32% were found to have UI.[2] Urinary retention observed in up to 29% of patients (n=80) within 4 weeks after a first ischemic stroke[3]
Progression	Among ischemic stroke survivors ≥ 65 years of age (n=108), 50% had some hemiparesis, 31% were unable to walk without assistance, and 26% were institutionalized in a nursing home at 6 months after stroke[4]
Life Expectancy	Median survival time after first stroke is 13.1 years for men and 7.8 years for women aged 55 to 64 years of age[1]

1. Roger VL, et al. *Circulation*. 2011;123:e18-e209.
2. Data on file, Allergan, Inc.
3. Kong KH, et al. *Arch Phys Med Rehabil*. 2000;81:1464-1467.
4. Kelly-Hayes M, et al. *J Stroke Cerebrovasc Dis*. 2003;12:119-126.

Cerebrovascular Accident

- 83/100,000 Americans, hemorrhage or infarction
- Location and size determines effect on the lower urinary tract
- Generally, decreases **inhibitory** control over the voiding reflex
- Initial retention is common
- Urinary frequency, urgency, urge incontinence

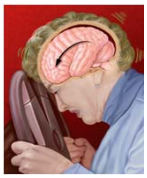
Fun Facts: CVA



- **Incidence: 2.6%** **(Noninstitutionalized)**
  - Male =Female
  - Increases with age (8.1% if > 65 years old)
  - >500,000 CVA occur annually in US
  - 3rd most common cause of death
- **LUT problems-Varies depending on time point**
  - 53% during acute stage
  - 32% at 12 months
- **UI has long term predictive value**
  - Acute stage (7 days) UI: 4x higher risk of institutionalization @1 year
  - UI within first week: 50% mortality at 6 months
  - 2x worse impairment in level of disability in nursing home residents

CDC Website, MMWR 2007
Markinkovic et al, Journal of Urology 2001
Kolominsky-Rabas et al, Neurourology & Urodynamics 2003
Wade & Hewler, Quart J Med 1978
Bean et al, American Journal of Physical Medicine, 2003

Fun Facts: TBI



- Most commonly results from MVA
- Male to female: 5 to 1
- Mechanism
  - Diffuse axonal shearing injury
  - Severs gray matter from white matter & other brain regions
    - Essentially isolates cortex from rest of the brain
  - Results in variety of deficits
    - Cognitive
    - Physical
    - Emotional
    - Behavioral
- Urinary incontinence is most common urologic problem
- Most likely loss of inhibitory control (similar to CVA)

Krimchansky et al, Brain Injury 1999
Oostra et al, Brain Injury 1995
Multi-Society Task Force on Persistent Vegetative State Pt I-II, NEJM, 1994

CVA: Types of Bladder Dysfunction

- Neurogenic Detrusor overactivity
- Detrusor Hyperactivity with impaired contractility
- Alterations in sensation
- Detrusor areflexia
- Sphincter should function normal
  - Level of pathology precludes causes of DESD
  - Question of "uninhibited sphincter relaxation"
  - Pseudo-dyssynergia is possible
- "Normal" pathology
  - BPH
  - OAB
  - SUI

Burney et al, Journal of Urology, 1996
Tsuchida et al, Urology, 1983
Krimchansky et al, Brain Injury 1999
Oostra et al, Brain Injury, 1995

CVA: Types of Bladder Dysfunction

- **May change with time**
  - 47% with retention or overflow incontinence during acute CVA presentation
  - Usually followed by DO
- **Type of CVA (based on 72hr)**
  - 85% of hemorrhagic infarcts with areflexia
  - 90% of ischemic infarcts with DO

Burney et al, Journal of Urology 1996

NGB in Cerebrovascular Accident

- Incontinence rate as high as 51% - 1st year
- Detrusor Hyperreflexia - most common
- Although variable, sensation usually intact
- Pseudodyssynergia - voluntary attempt to hold off a bladder contraction
- Synergistic void - above the Pontine Center
- Consider coexisting pathology - BPH

Parkinson's Disease

US Prevalence	≥500,000 persons currently living in US with PD[1] Affects ≈50% more men than women[1]
Bladder Dysfunction	In a pooled meta-analysis of 11 studies evaluating a total population of 358 patients with PD, 48% were found to have DO.[2] In another pooled meta-analysis of 8 studies evaluating a total population of 4335 patients with PD, 31% were found to have UI.[2]
Type of Disease	A movement disorder associated with loss of dopaminergic neurons in substantia nigra[3]
Age of Onset	Average age of onset is 60 years, and incidence increases with age[1]
Progression	Symptom progression may take 20 years or more[1] Patients with late-stage disease may become wheelchair-bound or bedridden[1]
Life Expectancy	Average life expectancy generally similar to those without PD[1]

1. National Institute of Neurological Disorders and Stroke. Parkinson's disease: hope through research. http://www.ninds.nih.gov/disorders/parkinsons/disease/detail/detail_parkinsons_disease.htm. Accessed July 8, 2011.
2. Data on file, Allergan, Inc.
3. Blackett H, et al. *Parkinsonism Related Disorders*. 2009;15:81-87.

Parkinson's Disease

- Degenerative disorder - loss of dopamine containing neurons in the substantia nigra and locus ceruleus
- **Bradykinesia, tremor, skeletal rigidity**
- Common cause of voiding dysfunction - detrusor hyperreflexia with sphincter bradykinesia (impaired relaxation)
- Up to 75% have voiding symptoms -
  - LTIS (57%), LTOS (23%)

Parkinson's Disease

- Pseudodyssynergia - often misdiagnosed
- Impaired relaxation may cause hesitancy
- BPH with Parkinson's - CMG, Press-Flow with EMG a must
- PPI 20% in Parkinson's vs. 1% with TURP
- Can reduce risk to 4% if normal sphincter control demonstrated
- Poorly sustained contractions with obstruction is problematic (DHIC)

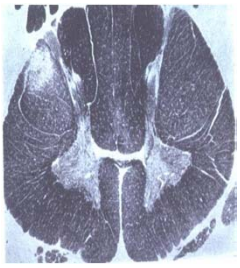
Shy-Drager Syndrome

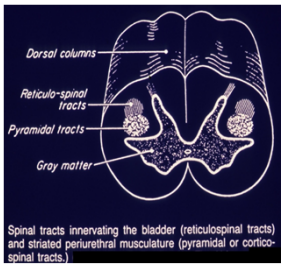
- Uncommon degenerative disorder - atrophy in cerebellum, brainstem, peripheral autonomic ganglia and spinal cord sympathetic neurons
- Orthostatic hypotension, anhydrosis, impotence, Parkinson's like symptoms, voiding and bowel dysfunction.

Shy-Drager Syndrome

- Bladder neck open at rest, detrusor overactivity & denervation of striated sphincter
- Frequency, urgency, urge incontinence or retention may herald the onset of Shy-Drager syndrome.
- Work-up similar to Parkinson's

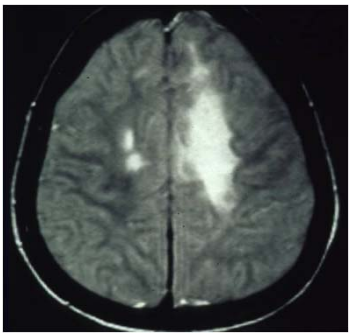
Multiple Sclerosis





Spinal tracts innervating the bladder (reticulospinal tracts) and striated periurethral musculature (pyramidal or cortico-spinal tracts.)

Multiple Sclerosis



Multiple Sclerosis (MS)

US Prevalence	400,000 in 2011[1] At least 2 to 3 times more common in women than men[1]
Bladder Dysfunction	In a pooled meta-analysis of 29 studies evaluating a total population of 2817 patients with MS, 56% were found to have DO.[2] In another pooled meta-analysis of 14 studies evaluating a total population of 2807 patients with MS, 51% were found to have UI.[2]
Type of Disease	An inflammatory demyelinating disease[3] The site of lesions will contribute to UI symptoms[4]
Age of Onset	Most patients diagnosed between ages 20 and 50[1]
Progression	Characterized by irreversible limitation in ambulation, a unilateral aid required for walking, and becoming wheel-chair bound after median times of ≈8, 20, and 30 years, respectively[5]
Life Expectancy	MS patients typically have a near-normal life span[3,5]

1. National MS Society. Who Gets MS? Available at: www.nationalmssociety.org/about-multiple-sclerosis/what-we-know-about-ms/who-gets-ms/index.aspx Accessed May 23, 2011.
2. Data on file, Allergan, Inc.
3. MS International Federation. About MS. Available at: www.msif.org/en/about_ms/what_is_ms.html. Accessed January 5, 2011.
4. McCombe PA, et al. *Expert Rev Neurotherap*. 2009;9:331-340.
5. Confavreux C, et al. *Brain*. 2003;126:770-782.

Multiple Sclerosis

- Focal inflammmatory/demyelinating lesions
- Ages 20-50; temperate climate
- Plaque formation of brain and cord may have autoimmune etiology
- Voiding dysfunction in 90% of MS patients: frequency, urgency, urge incontinence, hesitancy, intermittency, poor stream

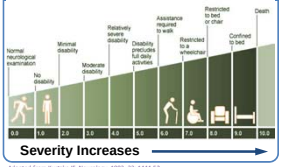
Multiple Sclerosis

- Voiding symptoms/ neurological findings do not correllate with UDS results[1]
- Detrusor hyperreflexia in up to 78%[2]
- Hyperreflexia associated with DESD in 50%[3]
- Up to 40 % patients-impaired contractility (areflexia)[4]
- 55% MS patients may change urodynamic behavior[5]

1. Awad et al J Urol 132:499, 1984
2. GonnorSE et al Urology 25:429, 1985
3. Goldstein et al J Urol 128:541, 1982
4. Mayo & Chetner Urology 39:67, 1992
5. Wheeler et al J Urol 130:1123, 1983

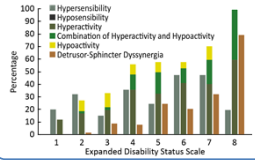
Progression of Multiple Sclerosis

Expanded Disability Status Scale (EDSS)[1]



Adapted from Kurtzke JF. Neurology. 1983; 33: 1444-52.

Relationship Between Urodynamic Abnormality and EDSS[2]



- Bladder symptoms worsen with increasing MS disease duration and disability[2,3]
- Bladder dysfunction in MS patients may become more complicated due to worsening of DO, worsening paraparesis, recurrent UTIs, spasticity, reduction in general mobility, and cognitive impairment[4]

UTI=urinary tract infection

1. Image from University College London NHS Trust. Treatments Overview: Rating scales. Available at: www.msdecisions.org.uk. Accessed July 23, 2011.
2. Koldewijn EL, et al. *J Urol*. 1995;154:169-173.
3. Mahajan ST, et al. *J Urol*. 2010;183:1432-1437.
4. Kalsi V, Fowler KJ. *Nature Clin Pract*. 2005;2:492-501.

Spinal Cord Injury (SCI)

US Incidence and Prevalence	12,000 new cases each year[1] 265,000 (range 232,000-316,000) in 2010[1]
Bladder Dysfunction	In a pooled meta-analysis of 20 studies evaluating a total population of 1228 patients with SCI, 49% were found to have DO.[2] In another pooled meta-analysis of 15 studies evaluating a total population of 2773 patients with SCI, 36% were found to have UI.[2]
Type of Disease	Leading causes are motor vehicle crashes, followed by falls and acts of violence[1]
Age of Onset	Average age at injury is 40.7 years[1]
Life Expectancy	Related to severity of injury[1]

1. National Spinal Cord Injury Statistical Center. Spinal cord injury facts and figures at a glance. Available at: www.nscisc.uab.edu. Accessed May 17, 2011.
2. Data on file, Allergan, Inc.

Traumatic Spinal Cord Injury

Lower urinary tract function varies depending on stage of recovery from SCI

- **Spinal Shock:**
  Detrusor areflexia, Flaccid paralysis,
  Reflexes absent below the level of the lesion
- **Recovery:** Return of reflex detrusor activity
- Stable

Stable Phase

- Absence of further somatic neurorecovery
- Unchanging urodynamic behavior
- Level of lesion MAY correlate w/ expected function
  Upper level SCI: DH+DESD
  Lower level SCI: Areflexia
- Need to diagnose and treat patients effectively to preserve renal function

Remember: ***The enemy of the upper tracts is sustained elevation of intravesical pressure***

Traumatic Spinal Cord Injury

- Objectively evaluates detrusor & sphincter behavior
- Essential to establish management plan
- Do not treat SCI patients symptomatically
- Do not base treatment on supposition
- Remember: Enemy of the upper tracts is sustained elevation of intravesical pressure

NGB in Spinal cord injury

- Incidence: 12,000 newly diagnosed cases every year*

Table 1
Meta-analysis on the associations between injury levels and urodynamic findings in patients with SCI

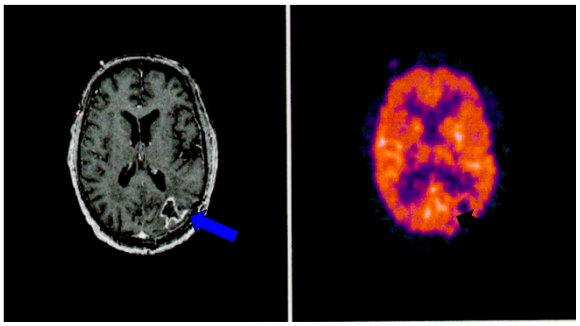
	Level of Injury				
	Cervical	Thoracic	Lumbar	Sacral	*P* Value*
Number of Patients	259	215	137	46	
DO	65%	78%	49%	22%	<.001
DSD	63%	72%	33%	13%	<.001
DA	9%	9%	39%	70%	<.001
Normal	1%	2%	2%	9%	.002

*National Spinal Cord Injury Statistical Center. Facts and figures at a glance. 2009

Brain Tumor

- Both primary and metastatic tumors may cause voiding dysfunction
- The area(s) and level(s) of brain affected will determine the pattern of dysfunction
- Like CVA, most lesions cause disinhibition of the pontine micturition center
- Detrusor overactivity with sphincter synergy is common

Glioma



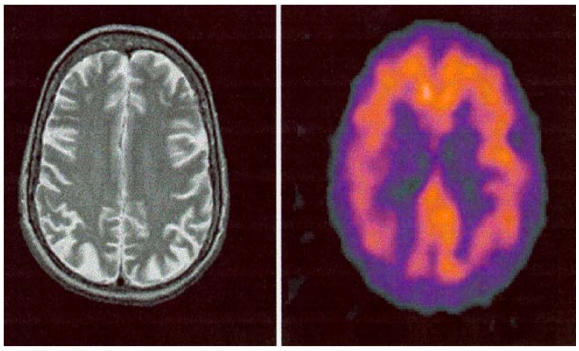
Normal Pressure Hydrocephalus

- Triad - **Gait disturbance, Dementia, Urinary Incontinence**
- Normal intracranial pressure
- Frequency, urgency, urge incontinence, even nocturnal enuresis
- Detrusor overactivity most common finding
- Recovery with shunt may be dramatic, not in all cases

Cerebellar Ataxia Syndromes

- Cerebellar disease causes a variety of motor abnormalities
- Acute forms - tumor, viral, vascular, toxic,demyelinating
- Chronic form - Friedrich's,corticocerebellar degeneration
- Poor coordination, decreased DTR's, dysarthria, dysmetria
- Overactivity to areflexia, DESD in 37%?

Alzheimer's Dementia

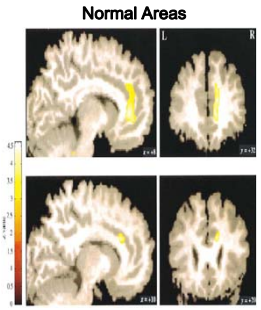


Dementia

- Incontinence approaches 90% in literature
- Atrophy of both white and gray matter
- Although detrusor overactivity may be found, not always the case
- 2/3 with or without cognitive impairment with incontinence were found to have detrusor overactivity (instability)

NGB in Dementia: Detrusor Overactivity - *cerebral effect*

- **Blok et al** ***(Brain 1997)***
  R. Ant Cingulate Gyrus
  - Increased during void
  - Decreased during storage
  - Implies area for "control"
- **Griffiths** ***(Behav Brain Res 1998)***
  Decreased perfusion frontal (esp. Right) in institutional demented
  - Genuine urge incontinence with reduced sensation



Pelvic Plexus Injury

- May occur with any major pelvic surgery
- Pelvic fracture or tumor
- **Neural effect**:

  hypogastric - sympathetic:
  incomplete bladder neck closure

  pelvic – parasympathetic:
  impaired detrusor contractility

  pudendal – somatic: external sphincter

Pelvic Plexus Injury

- Up to 80% will resolve within 6 months
- Best evaluated with UDS
- Beware the development of decentralization
- Silent hydronephrosis risks upper tract damage

Abdominoperineal Resection

- Incomplete emptying (retention) up to 90%
- Pelvic plexus injury impairs contractility
- Treat retention initially with CIC
- Sympathetic defect
  decreases bladder neck tone, ejaculation
- Sphincter weakness results in incontinence

Abdominoperineal Resection

- Up to 40% may have coexisting BPH
- Voiding dysfunction may be transitory
- **Pudendal nerve damage:** external sphincter dysfunction may be permanent
- **For retention:** UDS helps determine
  - –BOO vs. impaired contractility
  - –Sphincter function

Radical Hysterectomy

- Many develop vesicourethral dysfunction
- Effect similar to APR
- Parasympathetic disturbance should be decreased
- Risks increased with cardinal ligament excision
- May develop poor compliance
- Best to monitor upper tracts and storage pressure

Autonomic Neuropathy

- Results from decreased myelinization
- Sensory fibers affected primarily (diabetes)
- Parasthesias, decreased DTRs
- Vasomotor, alimentary tract Sx, diaphoresis
- Acontractile/hypocontractile detrusor
- Positive denervation sensitivity test
- Tx underlying problem will help GU Symptoms

Diabetic Neuropathy

- Voiding symptoms classically after 10 years
- Segmental demyelinization & axonal degeneration
- Classic understanding:
  - –Sensory impairment
  - –decreased contractility
  - –Distention myopathy worsens voiding dysfunction
- Up to 55% diabetics have detrusor hyperreflexia
  33% impaired contractility or areflexia*
- Urodynamics essential in diabetic voiding dysfunction

** Kaplan, Te, Blaivas J Urol 153:342,*

Herpes Zoster

- Varicella affects dorsal root ganglia
- May progress to anterior horns
- Sensory neuropathy
- May progress to somatic
  and visceral motor neuropathy
- Urinary retention may occur
- Usually self-limited

Transverse myelitis

- Uncommon inflammatory condition of the cord
- Grey and white matter involved
- Affects both children and adults
- Bilateral sensory/motor deficits sudden/progressive
- Bowel & bladder dysfunction - incontinence or retention
- ? autoimmune etiology - seasonal clustering
- DA or DH (±DESD)*
- Complete recovery from 3 to 18 months
  Residual deficit common

** Berger, Blaivas, Oliver J Urol 144:103, 1990*

Amyotrophic Lateral Sclerosis

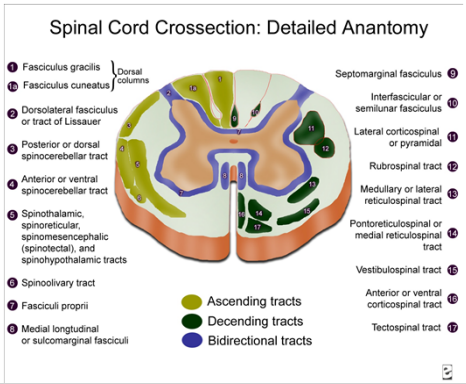
- Progressive neurodegeneration of neurons
  - spinal cord
  - Brainstem
  - cerebral motor
- Upper and lower motor neuron lesions
- May be associated with dementia
- Juvenile forms affect those <30 yrs
- Results in paralysis, respiratory failure
- UMN may have overactivity with sphincteric function preserved

Voiding Dysfunction in AIDS

- Up to 40% AIDS patients - consider other GU pathology (stricture, BPH, prostatitis, calculi)
- HIV encephalitis, Viral meningitis 2º CMV, herpes, Varicella
- *Cryptococcus, Coccidiomycosis, Aspergillus, Mycobacterium*[1]
- Opportunistic CNS infxn- Toxoplasmosis 37%[2]
- Symptoms variable, depending on site of lesion.
  - 36% areflexia
  - 27% hyperreflexia
  - 18% BOO
  - 19% Normal[2]

1. Levy et al J. Neurosurg 62:475, 1985 2. Kahn, Singh, Yang Urology 40:289, 1992

Spinal Cord Tumor



NGB in spinal cord tumors

Weakness:

Upper motor neuron: lesion in precentral gyrus down to lateral corticospinal tracts

Lower motor neuron: lesion in ventral horn cells, neuromuscular junction, or muscles

Mixed: upper+lower weakness

- sensory disturbances
- autonomic disturbances (sweating, sexual, bowel, etc)

NGB after Deep Brain Stimulation

Voiding Function Following Deep Brain Stimulation

- A small device, similar to a pacemaker, is surgically implanted to deliver electrical stimulation to targeted areas of the brain
- Opinion on the effect of DBS on voiding function in PD is divided between improvement and deterioration
- Thalamic deep brain stimulation resulted in an earlier desire to void and decreased bladder capacity, suggesting a regulatory role of the thalamus in lower urinary tract function*

*Kessler TM et al. European Urology 2008; 53(3): 457-670

Adult Neurogenic Bladder: Current Evaluation & Advances in Clinical Management (Advanced)

Urodynamics in Neurogenic Voiding Dysfunction

Workshop Faculty

Hari Tunuguntla, MD, MS, MCh (Program Chair and Faculty)
Asst Professor & Director, Section of Neuro-Urology, Female Pelvic Medicine & Reconstructive Surgery, Voiding Dysfunction, and Urodynamics
UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ, U.S.A.

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Angelo E. Gousse, MD (Faculty)
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Miramar, FL, U.S.A.

Classification of Neurogenic Bladder

- **Urologic/Urodynamic**
  - Failure to Store
  - Failure to Empty
- **Neurologic**
  - "Upper" vs "Lower"
  - Central vs Peripheral
  - "Anything can go"

Rationale for Urodynamic Evaluation

- Baseline functional assessment of LUT
- Identify NGB with risk of complications & may need early intervention
  - High fill pressure/poor compliance
  - DESD
- Assist in developing treatment plan
- Tool for identifying change neuro-pattern

Urodynamics

- **Storage**
  - Sensation
  - Capacity
  - Compliance
  - Stability
  - Continence
- **Emptying**
  - Flow rate
  - Detrusor pressure
  - Straining?
  - Outlet relaxation
  - PVR

Urodynamic Testing: ICS Standard Nomenclature

- **Acontractile Detrusor**
  - Old nomenclature: Areflexia - Atonic, Flaccid
- **Detrusor Overactivity** (old: Bladder Instability)
  - Neurogenic DO
  - DO Incontinence
- **Dyssynergia - Bladder/Sphincter discoordination**
  - Internal urethral sphincter: smooth bladder neck
  - External urethral sphincter: striated Rhabdosphincter

Common Confusion Leak Point Pressures

- **Valsalva or Abdominal Leak Point Pressure-** the intravesical pressure at which urine leakage occurs due to increased abdominal pressure in the absence of a detrusor contraction
- **Detrusor Leak Point Pressure-** the lowest detrusor pressure at which urine leakage occurs in the absence of either a detrusor contraction or increased abdominal pressure

Leak Point Pressures

Valsalva Leak Point Pressure

- Measures Outlet
  - Measure of SUI
- Low (0-60cmH20),
- Gray (60-100cmH20)
- Normal (>100cmH20)

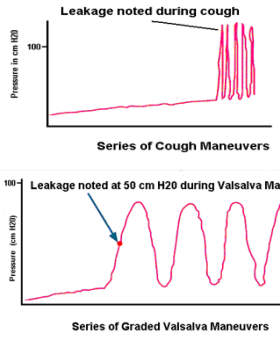
McGuire 1993

Detrusor Leak Point Pressure

- Measures Compliance
  - Measure of bladder ability to safely store urine
- >40cmH20: Risk of damage to upper urinary tract

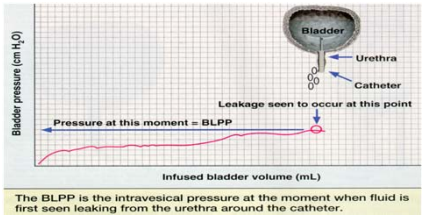
McGuire 1983

Valsalva Leak Point Pressue



- **Cough Manuever**
  - Higher pressure
  - Difficult to localize when leak occurred
- **Valsalva Manuever**
  - Slower rise
  - Allows more exact determination of pressure when leak occurred.

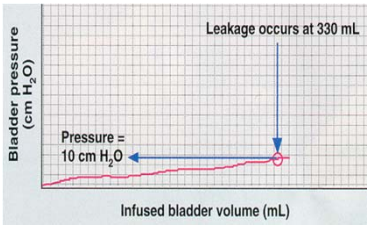
Detrusor Leak Point Pressure



- **DLPP > 40 cm H20**
  - Risk of Upper tract deterioration
    - 68% Vesico-ureteral reflux
    - 81% Hydronephrosis

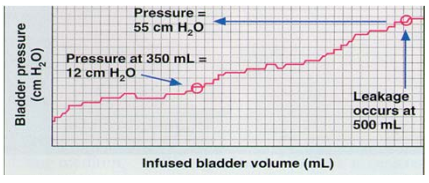
McGuire et al: J Urol 126:205, 1981

Detrusor Leak Point Pressure



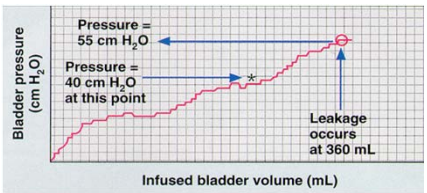
- *Risk of Upper tract damage ?*

Detrusor Leak Point Pressure



- What is the DLPP?
- Does this pose a risk?

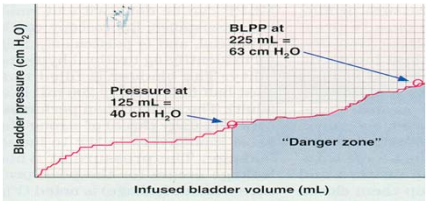
Detrusor Leak Point Pressure



Pt performs self cath for volumes =500 cc

- What is the DLPP?
- Does this pose a risk?

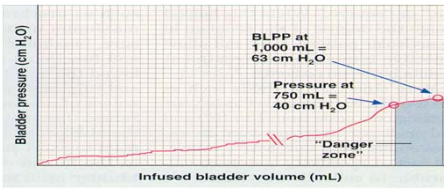
Detrusor Leak Point Pressure



Pt performs self cath for volumes =225 cc

- What is the DLPP?
- Does this pose a risk?

Detrusor Leak Point Pressure



Pt performs self cath for volumes = 500 cc

- What is the DLPP?
- Does this pose a risk?

Classification of Neurogenic Bladder Failure to Store

- **Detrusor Cause**
  - Detrusor overactivity
  - Loss of Detrusor Compliance
- **Sphincter Cause**
  - Denervation
  - Ablation
  - Fixed sphincter (ISD?), open scar

Classification of Neurogenic Bladder Failure To Empty

- **Detrusor function**
  - Is detrusor contraction of significant magnitude to achieve emptying?
    - Areflexia, hypocontractility
    - Hyperactivity with impaired contractility
- **Sphincter function**
  - Is sphincter creating excessive outlet resistance?
    - Detrusor sphincter dyssynergia
    - Mechanical obstruction
    - Fixed sphincter

Urodynamic Patterns of NGB

- Detrusor Areflexia
- Detrusor Overactivity
  - Detrusor-External Sphincter Dyssysnergia
  - Detrusor Hyperactivity with Impaired Contractility
- Hostile Storage
  - Loss of compliance
  - High DLPP
- Don't forget about non-neurogenic void dysfunction
  - SUI, Bladder outlet obstruction

Acontractile Detrusor

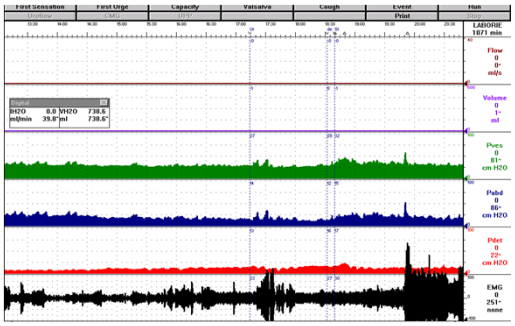
- Variant: Impaired contractility
- Absent/diminished detrusor contraction
- Storage capacity often increased
- May have diminished sensation
- Assuring storage pressure < 40 cm H2O safeguards upper tracts

Detrusor Areflexia

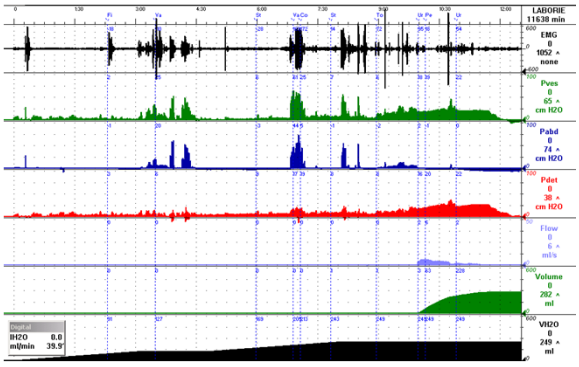
Decentralized Bladder

- Adrenergic overgrowth
- Progressively decreased compliance
- Need to follow DA patients with DLPP
- Upper tract imaging helpful
- Ensure low pressure storage

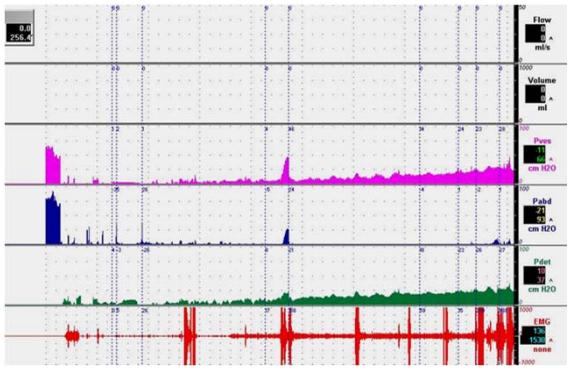
Acontractile Detrusor



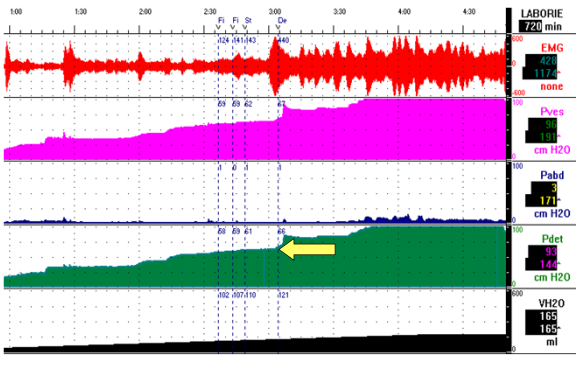
Normal compliance



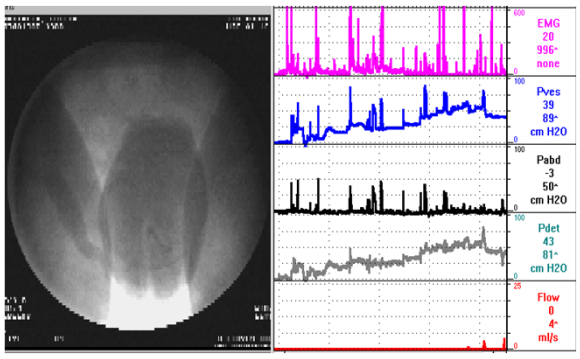
Impaired Compliance



Poor compliance with leak

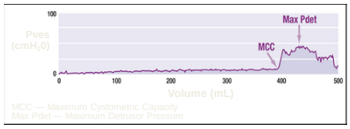


Non-compliant bladder with reflux

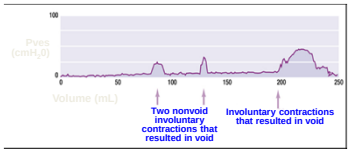


Detrusor Overactivity

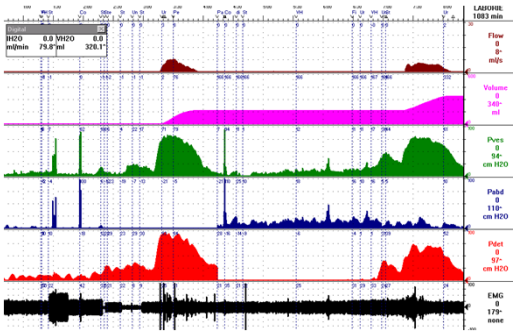
Normal Cystometrogram



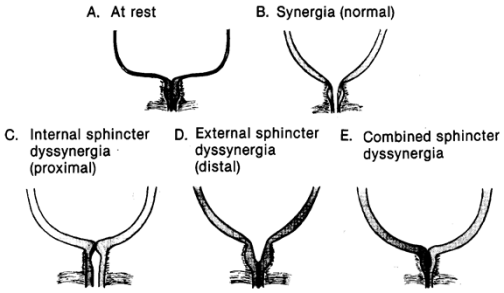
Cystometrogram in patient with detrusor instability



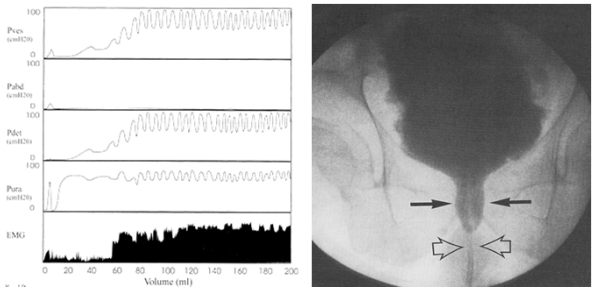
Detrusor Overactivity



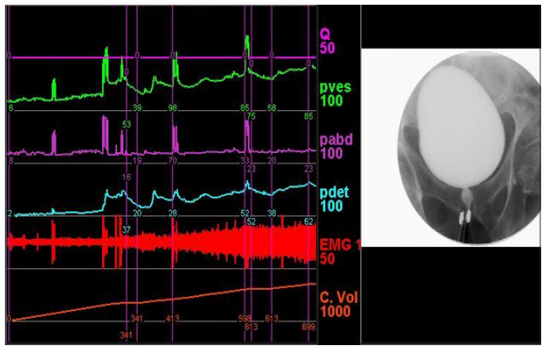
Detrusor External Sphincter Dyssynergia



Detrusor External Sphincter Dyssynergia



Detrusor External Sphincter Dyssynergia (DESD)



Adult Neurogenic Bladder: Current Evaluation & Advances in Clinical Management (Advanced)
Treatment of Neurogenic Bladder

Workshop Faculty

Hari Tunuguntla, MD, MS, MCh (Program Chair and Faculty)
Asst Professor & Director, Section of Neuro-Urology, Female Pelvic Medicine & Reconstructive Surgery, Voiding Dysfunction, and Urodynamics
UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ, U.S.A.

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Angelo E. Gousse, MD (Faculty)
Bladder Health & Reconstructive Urology Institute
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Current Management of Neurogenic Bladder

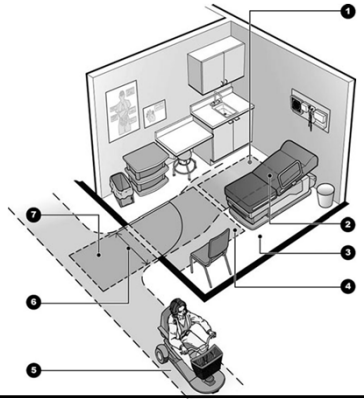
3 major categories:

- **Behavioral/non-pharmacologic interventions**[1-3]
  - Lifestyle interventions
  - Pads, portable urinals
  - CIC/CISC, condom or Foley catheterization for patients with incomplete bladder emptying
- **Pharmacotherapy**[1,3,4]
  - Anticholinergic agents are the standard therapy
- **Surgery**[1,4]
  - Reserved for those who fail conservative therapy
  - Urinary Diversion
  - Bladder Reconstruction

CIC=clean intermittent catheterization; CISC=clean intermittent self-catheterization

1. Abrams P, et al. *Neurourol Urodyn*. 2010;29:213-240.
2. Smith JH, et al. In: *Incontinence*, 4th Edition. Abrams P, et al. From the 4th ICI; Health Publication Ltd. 2009:1025-1120.
3. Wyndaele JJ, et al. In: *Incontinence*, 4th Edition. Abrams P, et al. From the 4th ICI; Health Publication Ltd. 2009:793-960.
4. Chancellor MB, et al. *Am J Phys Med Rehabil*. 2006;85;536-545.

Accessible Exam Room



NGB: Conservative Treatment

- Stress incontinence due to sphincter incompetence
  - Behavioral
  - timed voiding
  - external appliances
- Detrusor overactivity with detrusor sphincter dyssynergia:
  - intermittent catheterization (CIC)
  - bladder relaxants
  - Indwelling catheter + bladder relaxing drugs
- Detrusor overactivity with negligible post void residual & no DESD:
  - Behavioral
  - bladder relaxants
  - CIC
  - triggered voiding (if urodynamically safe)
  - External appliances
  - indwelling catheter + bladder relaxants
- Detrusor underactivity with post void residual: CIC; alpha blockers; intravesical electrical stimulation
  - bladder expression (if urodynamically safe)

Pharmacotherapy (improve storage)

- To improve storage (oral, transcutaneous, and intravesical)
- To improve emptying (oral)

Surgical Management

- Suprapubic tube drainage
- Augmentation Cystoplasty
- Continent Urinary Diversion
- Incontinent Urinary Diversion
- Others

Failure to Store

- **Detrusor Cause**
  - Detrusor Hyperreflexia
  - Loss of Detrusor Compliance
- **Sphincter Cause: *Incompetent outlet***
  - Denervation
  - Ablation
  - Fixed, open scar

Pharmacologic Therapy *for Failure to Store*

- Anticholinergic agents
- Musculotropic agents
- Tricyclic antidepressants
- Alpha-adrenergic agonist

Musculotropic Relaxants

- **Oxybutinin chloride** - 5mg TID
  - Oral as well as transdermal
  - Can also use intravesically
- **Tolterodine SA**- 4 mg Qday
- **Solifenacin**- 5-10 mg Qday
- **Darifenacin**- 7.5 -15 mg Qday
- **Trospium** XR- 60 mg Qday
- **Fesoterodine** 4-8 mg Qday

Table 1 Summary of anticholinergic trials in neurogenic patient population using systematic study design

Study (year)	Study arms	Patients, *n*	Method	Findings
Gajewski and Awad [33] (1986)	Oxybutynin vs propantheline	34	Prospective, randomized trial	Significant mean increase in maximum cystometric capacity in the oxybutynin arm; 21% of oxybutynin group and 27% of propantheline group discontinued therapy due to side effects
Petersen et al. [34] (1989)	Prazosin vs Placebo	18	Randomized, crossover trial	Treatment arm noted no change in urodynamic parameters
Stöhrer et al. [35] (1991)	Trospium vs placebo	61	Multicenter, double-blind trial	Significant ($P<0.001$) improvement in maximum cystometric capacity, compliance, and maximum detrusor pressure over placebo; no effect on maximum flow rate or residual volume
Wyndaele and Van Kerrebroeck [36] (1995)	Cisapride	21	Double-blind trial	No statistically significant change in urodynamic parameters between treatment arms
Yasuda et al. [37] (1996)	Urapidil, 30 or 60 mg, vs placebo	136	Prospective, randomized, double-blind trial	Urinary frequency decreased only in group receiving urapidil; flow rate and residual urine improved in the treatment arms; however, no difference in subjective symptoms was noted in all 3 groups
Yamanishi et al. [38] (1999)	Urapidil vs placebo	149	Double-blind trial	Significant decreases in residual urine, pressure at maximum flow, and urethral resistance in treatment arm; however, flow rates were unchanged
Abrams et al. [39] (2003)	Tamsulosin vs placebo	263	Randomized, double-blind trial with open-label comparative stage	0.4- and 0.8-mg doses were well-tolerated; suggestion of improvement in bladder storage and emptying but did not reach statistical significance
Ethans et al. [40] (2004)	Tolterodine vs oxybutynin vs placebo	10	Prospective, double-blind, crossover trial with open-label comparative stage	Tolterodine and oxybutynin were similar in efficacy at self-selected doses; both were superior to placebo
Bennett et al. [1] (2004)	Oxybutynin	39	Prospective trial with dose escalation	Statistically significant decrease in number of voids per day, nocturia, and incontinence episodes; no change in residual urine volume; doses up to 30 mg were well-tolerated and efficacious
Menarini et al. [41] (2006)	Trospium	80	Double-blind trial	Daily dose of 45 mg "can be considered the standard"; no significant differences in urodynamic parameters for dose escalation group

Stansell LG et al. Curr Bladder Dysfunct Rep (2011) 6:37–44

Anticholinergics in NGB

Meta-analysis

- Compared with placebo, anticholinergics result in better patient-reported cure/improvement
- Higher incidence of adverse events (dry mouth)
- No difference in withdrawal of treatment due to adverse events
- None of the different agents /dosages assessed was superior to another.
- Treatment associated with a reduction in maximum detrusor pressure, which ***can*** be beneficial for long-term renal function

Madhuvrata P, et al. *European Urology* 2012

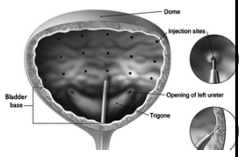
Surgery for Failure to Store

- **Denervation procedures**
  - Central - subarchnoid blocks
  - Peripheral - sacral rhizotomy
  - Perivesical - bladder denervation
- **Bladder augmentation**
- **Urinary Diversion**

Botulinum Toxin Type A

- For bladder & sphincter

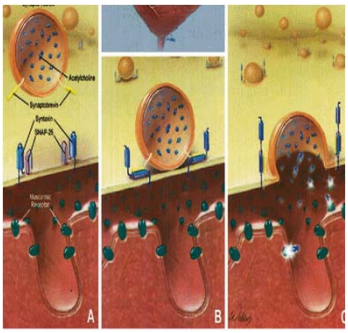
Botulinum Toxin



- Most potent bio toxin known to man
  - 1897 van Ermengen, outbreak of sausage poisoning
  - Clostridium botulinum (Gram + Anaerobe)
  - 7 distinct toxins (A-G)
- Blocks presynaptic release of acetyl-choline from cholinergic nerve terminals
- **Two chains (light and heavy)**
  - 150 kDa (100 kDa connects to 50 kDa via disulfide bond)
  - Heavy chain binds molecule to target cell membrane (nerve terminal)
  - Light chain internalized and inhibits neurotransmitter release

Smith, JU, 2005
Rackley CUR 2004

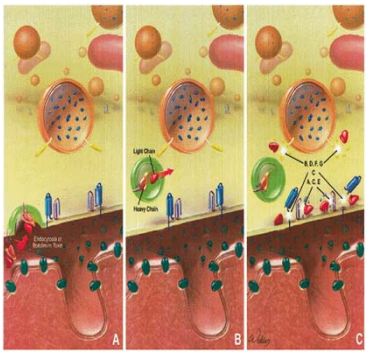
Presynaptic Release of AcetylCholine



- Vesicle with ACH
- **SNAP Complex**
  - Inside presynap
  - Binds vesicle
  - Exocytosis of vesicle and release of ACH

Smith, JU 2005

Botox Inhibits Presynaptic Release of ACH



- Heavy chain gets light chain toxin inside presynaptic cell
- Light chain binds up SNARE complex
- Vesicle unable to exocytose

Smith, JU 2005

Preparations

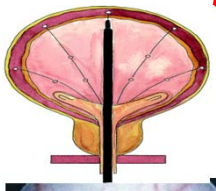
TABLE 1
Comparison of commercial BTX preparations

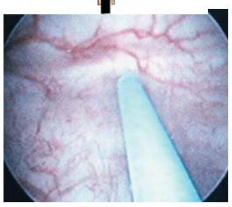
	BTX-A (Botox)	BTX-A (Dysport)	BTX-B (Myobloc)
Serotype	A	A	B
Complex molecular wt. (size)	900 kDa	~900 kDa	~700 kDa
Package (U)	100	500	2,500/5,000/ 10,000
Neurotoxin protein per vial (ng)	~5	12.5	25/50/100
Formulation	Vacuum dried	Lyophilized	Solution
pH	~7	~7	5.6
Year of FDA approval	1989	1991	2000

- BTX-A
- 100-300 units
- Intramuscular detrusor inject
  - 0.2-1.0 cc
  - 10-30 injections
- Care in prep

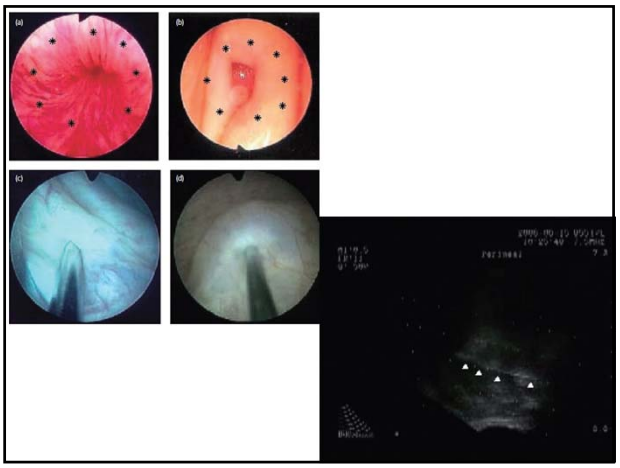
Rackley, CU 2005

Intravesical injection of Botulinum Toxin *technique*



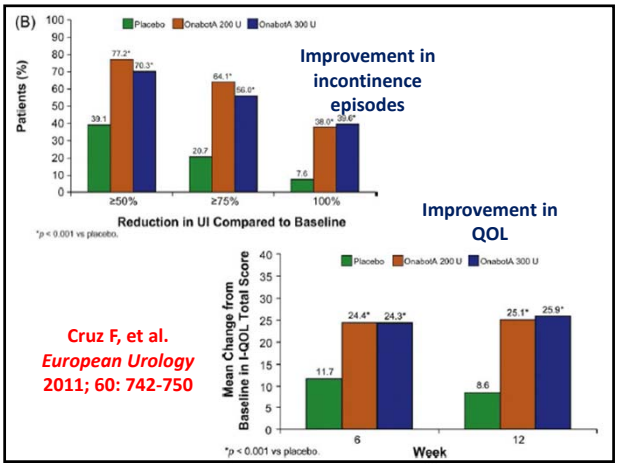


- **My preparation**
  - 100 units (DO/OAB)
  - 200-300 for NGB
  - 30 ml volume
  - 30 injections
  - Collagen inject scope
- **Problems**
  - Invasive
  - Temporary-requires repeat cystoscopy and injections
  - "feel" for the inject
    - Too deep: inject in serosa or outside bladder
    - Too shallow: waste into lumen



Study	Design	Outcome	Evidence level
Neurogenic bladder			
Schurch *et al.*[15]	Open *n* = 21 (BTX-A)	1 Bladder capacity increased 2 Bladder pressure decreased	III
Schulte-Baukloh *et al.*[16]	Open *n* = 20 (BTX-A)	1 Bladder capacity increased 2 Bladder pressure unchanged (decrease at 2–4 week follow up)	III
Riccabona *et al.*[17]	Open *n* = 15 (BTX-A)	1 Bladder capacity increased 2 Bladder pressure decreased	III
Reitz *et al.*[22]	Open *n* = 200 (BTX-A)	1 Bladder capacity increased 2 Bladder pressure decreased	III
Giannantoni *et al.*[23]	Randomized, non-controlled *n* = 12/13 (BTX-A/RTX)	1 Greater reduction in incontinence episodes and greater increase in bladder capacity in BTX-A group	II
Pistolesi *et al.*[19]	Open *n* = 1 (BTX-B)	1 Bladder capacity decreased 2 Bladder pressure decreased	IV
Reitz and Schurch[18]	Open *n* = 2 (BTX-B)	1 Improvement in urodynamic and clinical parameters	IV
Non-neurogenic bladder			
Dykstra *et al.*[20]	Open *n* = 15 (BTX-B)	1 Urinary frequency decreased	III
Rapp *et al.*[21]	Open *n* = 35 (BTX-A)	1 IIQ and UDI symptom scores decreased	III
Interstitial cystitis			
Smith *et al.*[24]	Open *n* = 13 (BTX-A)	1 Improvement in symptom scores and urodynamic parameters	III

Smith, Nature/Urology 2004



Cruz F, et al.
European Urology
2011; 60: 742-750

Table 1 Therapeutic effects of urethral sphincter BoNT-A injections of different voiding dysfunction

Disease	*n*	No. excellent	No. improved	No. failure
DSD	29	8 (27.6%)	15 (51.7%)	6 (20.7%)
Dysfunctional voiding	20	6 (30%)	14 (70%)	0
Non-relaxing urethral sphincter	10	8 (42.1%)	7 (36.8%)	4 (21.1%)
Cauda equine lesion	8	5 (62.5%)	1 (12.5%)	2 (25%)
Peripheral neuropathy	14	5 (35.7%)	6 (42.9%)	3 (21.4%)
Idiopathic detrusor underactivity	13	8 (61.5%)	4 (30.8%)	1 (7.7%)
Totals	103	40 (38.8%)	47 (45.7%)	16 (15.5%)

Table 2 Main therapeutic effects of lower urinary tract dysfunction and causes for dissatisfaction with detrusor BoNT-A treatment

Main therapeutic effects of LUTD	Patients	Causes of dissatisfaction to treatment	Patients
Complete dry	29 (58%)	Persistent severe incontinence	6 (12%)
Increase bladder capacity	36 (72%)	Increased PVR	25 (50%)
Decrease incontinence	45 (90%)	Difficult urination or retention	16 (32%)
Less urgency episodes	31 (62%)	Need CIC/CISC	5 (10%)
Less AD	5 (71%)†	Nocturnal incontinence	10 (20%)

†Just seven patients presented with symptoms of autonomic dysreflexia at baseline.

Kuo YC et al. Int J Urol 2012

Botulinum Toxin Type A
side Effects: rare

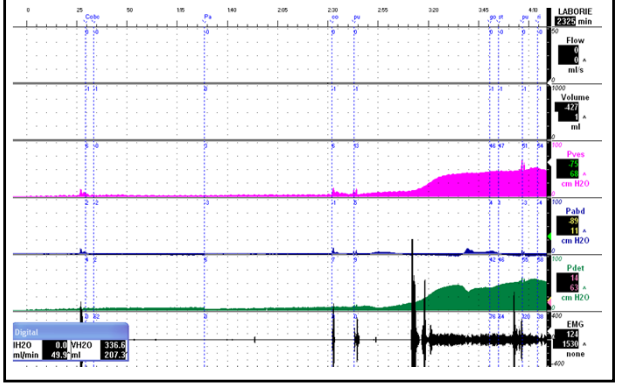
- Lethal dose 2800 unit (40 unit/kg in 70 kg)
  - Detrusor doses well below
- Allergic reactions
- Flu like symptoms
- ***Avoid other agents that impair neuromuscular transmission***
  - Curare like compounds
  - Aminoglycosides
  - Myasthenia Gravis (relative)

Smith, JU 2005

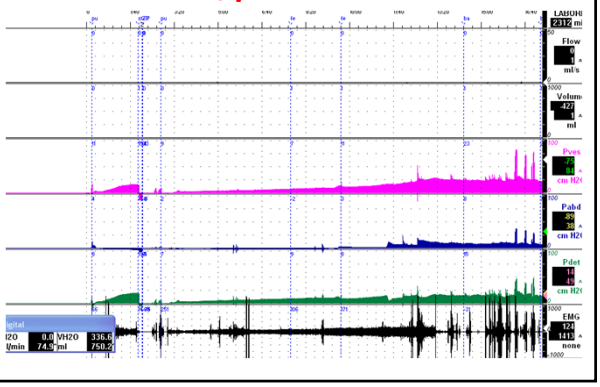
Cost an Issue

"I was very ill and my HMO wouldn't pay for human parts."

T8 SCI - with Severe DO



T8 SCI - s/p botulinum toxin



Surgery for Failure to Store

- **Denervation procedures**
- **Bladder augmentation**
  - **Alternatives**
    - autoaugmentation
    - ureterocystoplasty
- **Urinary Diversion**

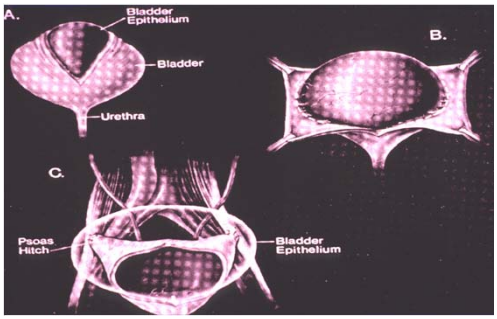
Mymectomy

Auto-augmentation

- Popularized by Snow and Cartwright (1989)
- Strip the bladder muscle leaving the mucosa intact
- Essentially creates a large, wide-mouthed diverticulum
- Long-term success in patients with neurogenic bladder dysfunction still?

Detrusor Myomectomy

Auto-Augmentation



Augmentation Cystoplasty

Indications:

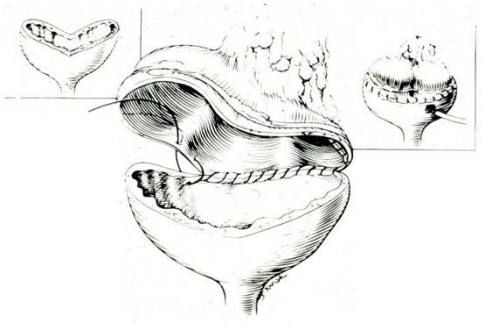
- Intractable detrusor overactivity causing incontinence
- Ability /motivation to perform CIC
- Desire to convert from reflex voiding to an intermittent
- catheterization program
- High risk for upper tract deterioration
  - hydronephrosis and/or high pressure VU reflux
- detrusor sphincter dyssynergia

Scientific evidence–III
Grade of recommendation–C
Strength of panel opinion–Strong

Augmentation Cystoplasty

- Can use small or large bowel
- Transverse bladder incision facilitates placement of the augmentation
- **Reflux**: *consider reimplantation for high grade reflux, +/- grade 3, grades 4 or 5*
- Small but real risk of carcinoma in the augmented bowel segment

Ileal Augmentation Cystoplasty



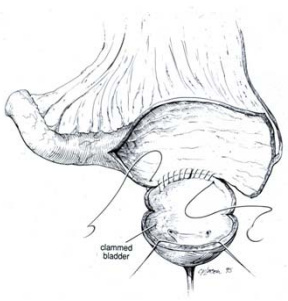
Cutaneous Ileocystostomy

- Tetraplegic male who cannot maintain condom catheter because of penile retraction
- Women without dexterity to self-cath
- An ileal conduit ***"bladder chimney"*** provides low-resistance to outflow
- Avoids complications of foreign body
- Risks less than cystectomy /ileointestinal anastomoses

Cutaneous Ileocystostomy

- A short isolated ileal segment
- Boari flap anastomosis of bowel segment and bladder dome - avoid a waist
- Distal ileum forms incontinent urostomy
- Consider pubovaginal sling in women

Ileo-Vesicostomy

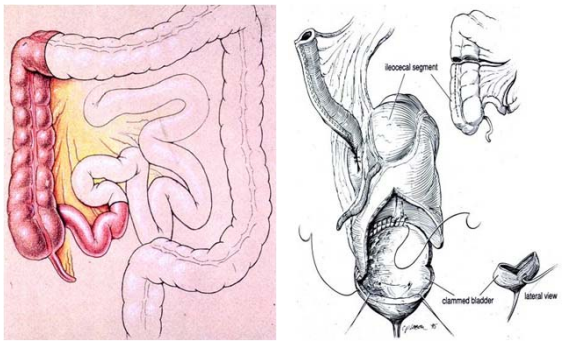


- Short isolated ileal segment
- Wide anastomosis of bowel segment & bladder dome - *avoid waist*
- Distal ileum forms incontinent urostomy
- Must have competent outlet Consider pubovaginal sling in women

Continent Augmentation Cystoplasty

- Utilize ileocecal segment
- Continent cutaneous stoma
- No ureteral reimplantation if no reflux
- Preserves fertility potential
- No transfer needed to do self cath
- No need for urethral catheterization although it's still available

Continent Catheterizable Augmentation *Indiana Augment*



Surgery for Failure to Store

- **Denervation procedures**
- **Bladder augmentation**
- Urinary Diversion

Continent Urinary Diversion - Indications

- Patients who cannot access their native urethra due to congenital
- abnormalities, spasticity, obesity, contracture, or tetraplegia, or who
- require closure of an incompetent bladder neck
- Females with tetraplegia with urethral erosion from indwelling catheter
- Males with SCI with unsalvageable bladders secondary to urethral fistula & sacral pressure ulcers
- Individuals with bladder cancer requiring cystectomy

Scientific evidence–III
Grade of recommendation–C
Strength of panel opinion–Strong

Continent Urinary Diversion

- Indiana Pouch with RLQ / umbilical stoma
- Lower urinary tract is essentially unsalvageable
- Good hand function
- Reasonable life expectancy
- Motivated to undergo the procedure

Ileal Conduit Urinary Diversion

- Generally, method of last resort
- Requires life-long monitoring of renal function
- Be wary of use in children or young adults
- Pyocystis
- Squamous cell carcinoma of the native bladder

Outlet Incompetence *female*

- **Urethral Closure**
  - Transvaginal
  - Retropubic
- **Pubovaginal Sling**
- **Artificial urinary Sphincter**

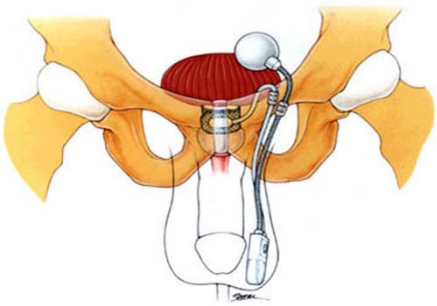
Outlet Incompetence
male

- **Urethral Closure**
  - Perineal Approach
  - Retropubic Approach
- Male Sling
- Artificial Urinary Sphincter

Artificial Urinary Sphincter

- Higher risk for erosion or infection in the neurogenic population
  - Does not mean should not be option
- Need motivated, compliant patient
- Carefully assess hand function
- Catheterization is possible, however, it does increase the risk of complications

Artificial Urinary Sphincter



Failure To Empty

Should think of treatment of neurogenic lower urinary tract dysfunction in components:

1. **Detrusor function:** Is detrusor contraction of significant magnitude to achieve emptying?
2. **Sphincter function:** Is sphincter creating excessive outlet resistance?

Valsalva & Crede Maneuvers

- Unphysiologic
- Outflow resisted by same mechanisms that assure continence
- No bladder neck opening - outflow resistance may increase
- Risks damage to pelvic floor
- May increase risk to upper tracts
  esp. w/ poor compliance/ established reflux

Avoid Crede/Valsalva

- Detrusor sphincter dyssynergia
- Bladder outlet obstruction
- Vesicoureteral reflux
- Hydronephrosis

Scientific evidence–III
Grade of recommendation–C
Strength of panel opinion–Strong

Urecholine

- Never proven to generate detrusor contraction in patients with *acontractile detrusor*
- May increase basal tone of bladder wall
- Largely ineffective in treatment of *acontractile detrusor*
- May increase storage pressure and susceptibility to upper tract damage

Failure To Empty

- Tube drainage
- Intermittent Catheterization
- Sphincterotomy
- Ileal Conduit
- Ileal-Vesicostomy
- Neuro-Prosthesis (Sacral Stimulation)

Tube Drainage (urethral & suprapubic)

- *Consider clean intermittent catheterization (CIC) for individuals who have sufficient hand skills or a willing caregiver to perform the catheterization*
  Scientific evidence: III; Grade of recommendation: C
- Alternative to CIC (e.g., SP tube) indicated in:
  - Abnormal urethral anatomy - stricture, false passages, and bladder neck obstruction.
  - Bladder capacity less than 200 ml.
  - Poor cognition, little motivation, inability/unwillingness to adhere to the CIC time schedule or the fluid intake regimen
  - adverse reaction toward having to pass the catheter into the genital area multiple times a day.

Intermittent Catheterization[1]

- Need to assure low-pressure storage
- Urodynamics essential to check compliance and leak point pressure[2]
- Hydronephrosis and reflux may resolve[3]
- Urinary tract becomes colonized[4]
- Treat only clinical UTI (fever, hematuria, epididymitis)
- Complications of strictures, false passages

1. Lapides et al J Urol 107:458, 1972
2. McGuire & Savastano J Urol 129:775
3. Wyndaele & Maes J Urol 143:906, 1990
4. Maynard & Diokno J Urol , 1984; 1983, 32:943

When to avoid CIC ?

- Inability to catheterize themselves
- An unwilling (to perform
- CIC) caregiver
- Abnormal urethral anatomy (urethral stricture, false passages, and BNO)
- Bladder capacity <200 ml
- Poor cognition, little motivation & inability or unwillingness to adhere to catheterization time schedule
- High fluid intake
- Adverse reaction to passing a catheter into the genital area multiple times daily
- Tendency to develop autonomic dysreflexia with bladder filling (despite
- Treatment)

Scientific evidence–III
Grade of recommendation–C

Complications of CIC

- Urinary tract infections
- Bladder overdistention
- Urinary incontinence
- Urethral trauma with hematuria
- Urethral false passages
- Urethral stricture
- Autonomic dysreflexia (lesions at T6 and above)
- Bladder stones

Indwelling Catheter - Indications

- Poor hand skills
- High fluid intake
- Cognitive impairment or active substance abuse.
- Elevated detrusor pressures managed
- with anticholinergic medications
- Lack of success with other, less invasive bladder management methods
- For temporary management of vesicoureteral reflux
- Limited assistance from a caregiver

Scientific evidence–III
Grade of recommendation–C
Strength of panel opinion–Strong

Indwelling Catheterization
Risks

- Chronic infection, stone formation
- Tissue erosion (traumatic hypospadias, bladder neck/urethral destruction)
- Bladder wall fibrosis, urothelial neoplasia
- Vesicoureteral reflux, hydronephrosis
- Neprolithiasis, renal failure

Avoid indwelling catheterizationexcept as last resort

Comparisons of long-term complications between IC and chronic indwelling catheterization in patients with SCI

Investigators	F/U (y)	Complication	IC	Chronic Indwelling Catheter	*P* Value
Weld and Dmochoski[24]	18		n = 92	n = 150	
Weld et al[25]		Patients with complications	27%	51%	<.01
		Decreased bladder compliance	26%	77%	<.01
Larsen et al[26]	12		n = 86[a]	n = 56	
		Renal-related	6 cases[b]	20 cases[b]	<.01
		Urinary tract infection	46 cases[b]	48 cases[b]	<.01
		Stones	16 cases[b]	52 cases[b]	<.01
		Urethra-related	20 cases[b]	30 cases[b]	<.01

Jeong SJ et al. Urol Clin N Am 37 (2010) 537–546

Indications for suprapubic tube

- **Urethral abnormalities**
  - **stricture, false passages, bladder neck obstruction, or urethral fistula**
- **Urethral discomfort.**
- **Recurrent urethral catheter obstruction**
- **Difficulty with urethral catheter insertion**
- **Perineal skin breakdown due to urine leakage secondary to urethral**
- **incompetence**
- **Psychological considerations - body image**
- **Personal preference; desire to improve sexual genital function**
- **Prostatitis, urethritis, or epididymoorchitis**

Scientific evidence–III
Grade of recommendation–C
Strength of panel opinion–Strong

External Sphincterotomy

- **Establishes low-pressure drainage** without indwelling foreign body
- Ensure pt can use external collection device
- Historical **risks**
  Hemorrhage 5-23%
  Recurrent obstruction 12-26%
  Erectile dysfunction 2.8-64%
- **Chemical sphincterotomy**
  – Botox denenveration

Contraindications for Chemical Sphincterotomy (botulinum toxin)

- Neuromuscular disease
- Known allergy to or previous adverse effect from botulinum toxin
- Current aminoglycoside therapy
- Insufficient hand skills or caregiver assistance
- Patient unable to maintain a condom catheter
- Female patient

External Sphincterotomy

- **Contact Nd:YAG laser**: risks much lower
- **Complications:** rare
  - 23 hr admission (for bleeding, AD)
- Bladder neck dysfunction/internal sphincter dyssynergia may persist
- **Follow up**:
  - upper tract imaging
  - UDS

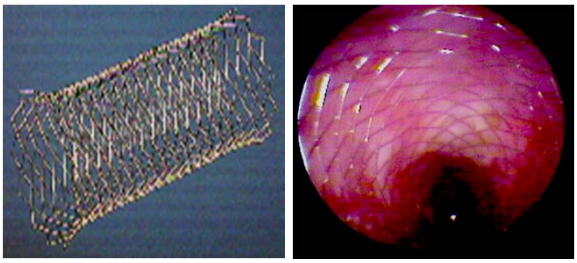
Sphincter Stent Prosthesis

- Lengths 2, 2.5, 3 cm
- 22 French cystoscopic insertion tool
- Use 0º telescope
- Proximal margin at verumontanum
- Distally into bulbous urethra (5 mm)
- Overlapping stents may be needed

Sphincter Stent Prosthesis

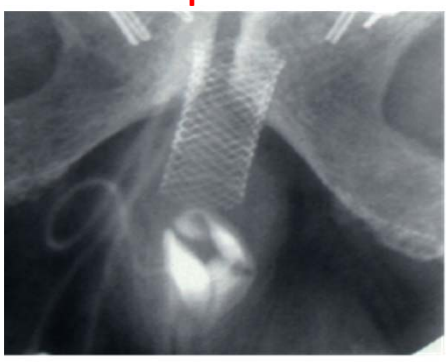
- Acceptable alternative to sphincterotomy
- Results equivalent
- May have less morbidity
- Sphincter ablation potentially reversible
- Learning curve favorable (2-5 patients)
  - *beware chronically dilated prostatic urethra*
- Serial evaluation mandatory
  - pelvic radiograph
  - Cystoscopy
  - UDS
  - U/S

Urolume Sphincter Stent

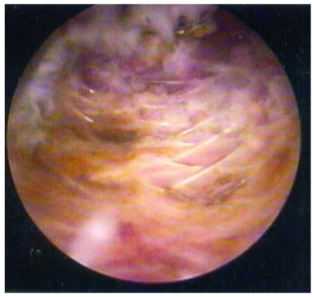


Urolume Sphincter Stent

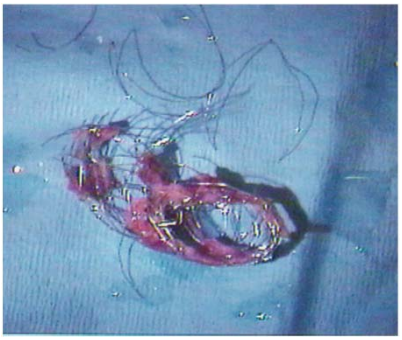
Urolume Sphincter Stent



Epithelialized Urolume



Explanted Urolume



Neurostimulation

Sacral nerve root stimulation

Issues

- Uninhibited reflex voiding controlled - esp. women
  - hyperreflexia abolished by rhizotomy
  - capacity, compliance increased
- Continence good if bladder neck intact
- Residual urine (< 60 ml) acceptable
- Decreased incidence of UTI
- Improves VU Reflux & hydronephrosis
- Voiding pressure may be elevated by sphincter stimulation

Neurostimulation

Sacral nerve root stimulation

Requires intact parasympathetic efferents

- **When to perform?**
  - Comlete SCI: after 1 year
  - Incomplete SCI: after 2 years
- **Technique:**
  - Intradural
  - extradural techniques
  - rhizotomy
- **Surgery challenging** – requires:
  - L2-S4 laminectomy
  - intraop stimulation
  - meticulous dissection
- **Dyssynergic sphincteric contraction problematic**
  - Anodal block may be effective

Cauda Equina Syndrome

Review Criteria for the Diagnosis and Treatment of Acute Cauda Equina Syndrome

SURGICAL PROCEDURE	CONSERVATIVE CARE	CLINICAL FINDINGS		
		SUBJECTIVE	OBJECTIVE	DIAGNOSTIC
		AND	AND	
Lumbar decompression at the earliest safe opportunity	Conservative care alone is rarely indicated	Partial or complete loss of bowel and/or bladder function (incontinence or retention not otherwise explained) AND/OR Acute low back pain AND/OR Bilateral/unilateral sciatica AND/OR Sexual dysfunction	Diminished or absent anal sphincter tone AND/OR Saddle anesthesia AND/OR Numbness and/or weakness involving both legs or multiple nerve roots in one leg AND/OR Urinary retention, incontinence, and / or patulous anus AND/OR Reduced or absent bulbo-cavernosus reflex or anal wink AND/OR Gait disturbances	A radiographic study demonstrates that a lesion with mass effect on the cauda equina is present in the spinal canal, compressing multiple lumbo-sacral nerve roots (usually large mass effect). Lumbar MRI is the diagnostic procedure of choice. CT or CT myelography may provide useful information, especially when MRI cannot be done or is limited by hardware artifact

UTI in Neurogenic Bladder

- For those on intermittent catheterization
  - 10^2 colony forming units (cfu)
- For those using clean-void specimens
  - catheter-free males who use external condom collecting devices: 10^4 cfu
- From indwelling catheters
  - any detectable concentration

Gribble, 1994

What is on the Horizon ?

- Lumbar to Sacral Nerve Rerouting
- Spinal cord Regeneration
- Stem Cell Transplantation

Take Home Points

- Voiding dysfunction associated with a wide range of neurologic conditions
  - Impairs patient daily activities considerably
- Alterations in afferent and efferent neuronal pathways impact bladder function
- Management considerations include maintaining low bladder pressures, preventing infection, and preserving upper tract function
- Current management includes behavioral interventions, anticholinergic therapy, and surgery

Take Home Points

- Antimuscarinic agents are first-line therapy & oxybutynin is the only antimuscarinic agent approved specifically for neurogenic detrusor overactivity
- Onabotulinumtoxin A intradetrusor injection was approved by the US FDA in 2012 for neurogenic detrusor overactivity (MS and SCI)
- Clean intermittent catheterization is a safe treatment for urinary retention in SCI and MS
- Sacral nerve stimulation is approved for idiopathic OAB but not for neurogenic bladder dysfunction
- Bladder augmentation / urinary diversion is reserved for those failing conservative therapy
- Long-term follow-up is important as changes in detrusor compliance and urodynamic patterns may occur over time

Notes

Record your notes from the workshop here