Urinary incontinence

Presented By: Dr. Rex O. Ajayi, M.D.

Lower Urinary Tract Function

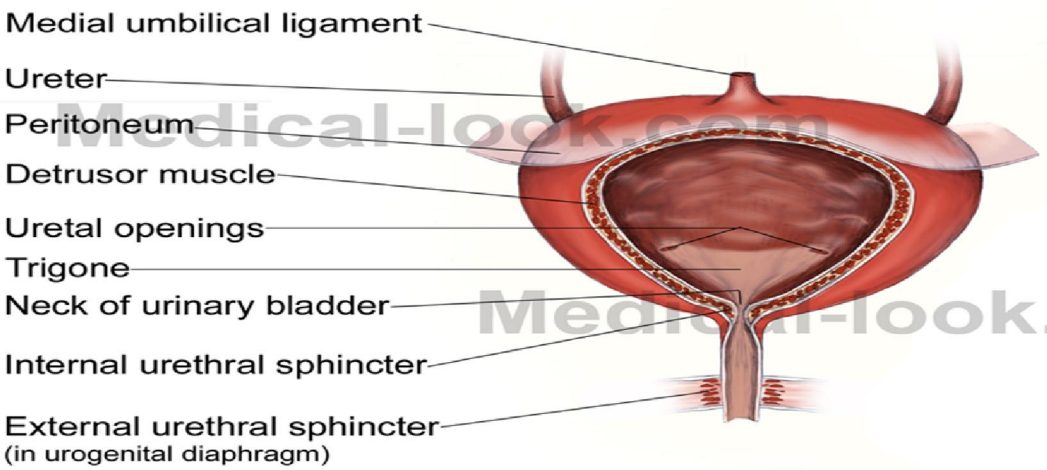
- Low pressure urine storage without leakage
- Complete, periodic, voluntary expulsion of urine
- Involves coordination of peripheral autonomic (parasympathetic, sympathetic), somatic, and central nervous systems
- UNIQUE

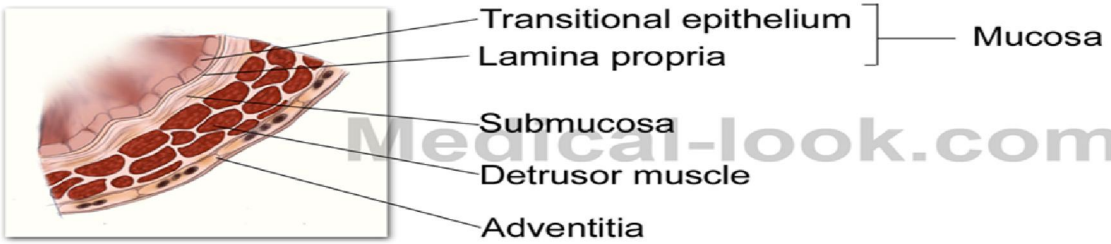
Bladder Anatomy

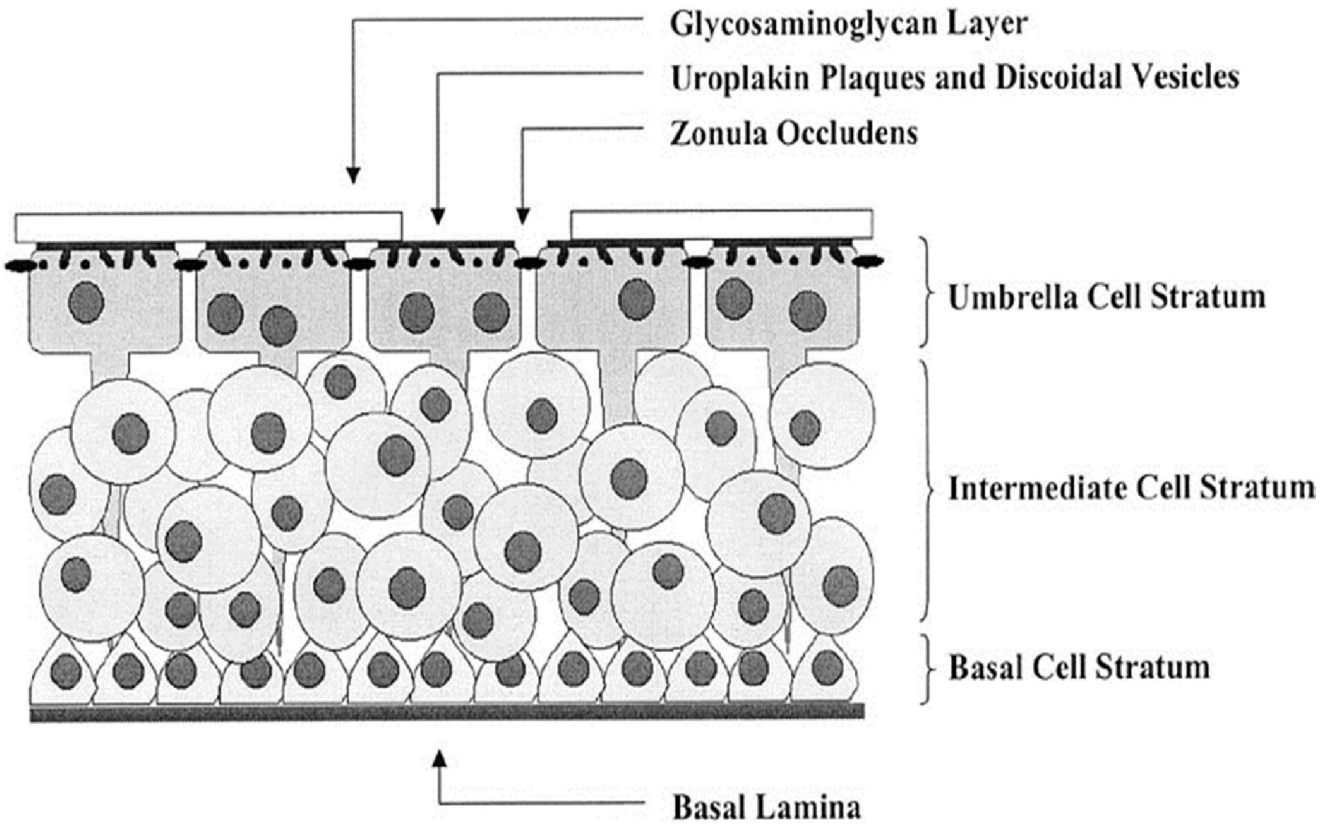
- Body – above UO's
- Base – trigone, bladder neck

- Layers
  - Serosa
  - Smooth Muscle + ECM (~50/50)
    - Collagen, elastin in proteoglycans matrix
  - Lamina Propria
  - Urothelium

BLADDER ANATOMY






Glycosaminoglycan Layer
Uroplakin Plaques and Discoidal Vesicles
Zonula Occludens
Umbrella Cell Stratum
Intermediate Cell Stratum
Basal Cell Stratum
Basal Lamina

Nervous System

- Parasympathetic = peripheral nerves that exit craniosacral spinal cord
- Sympathetic = peripheral nerves that exit thoracolumbar spinal cord
- Preganglionic fibers are myelinated
- Postganglionic fibers are unmyelinated

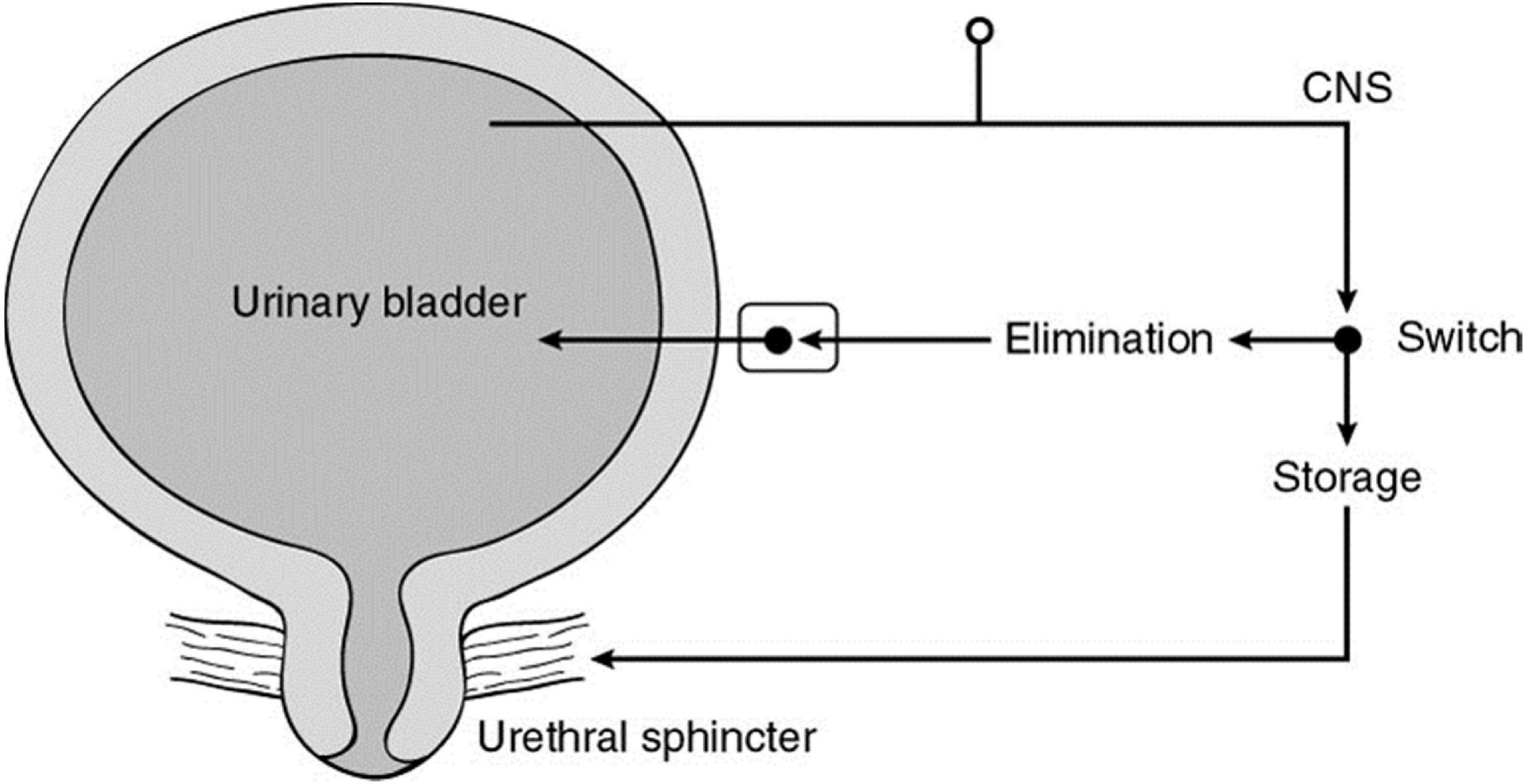
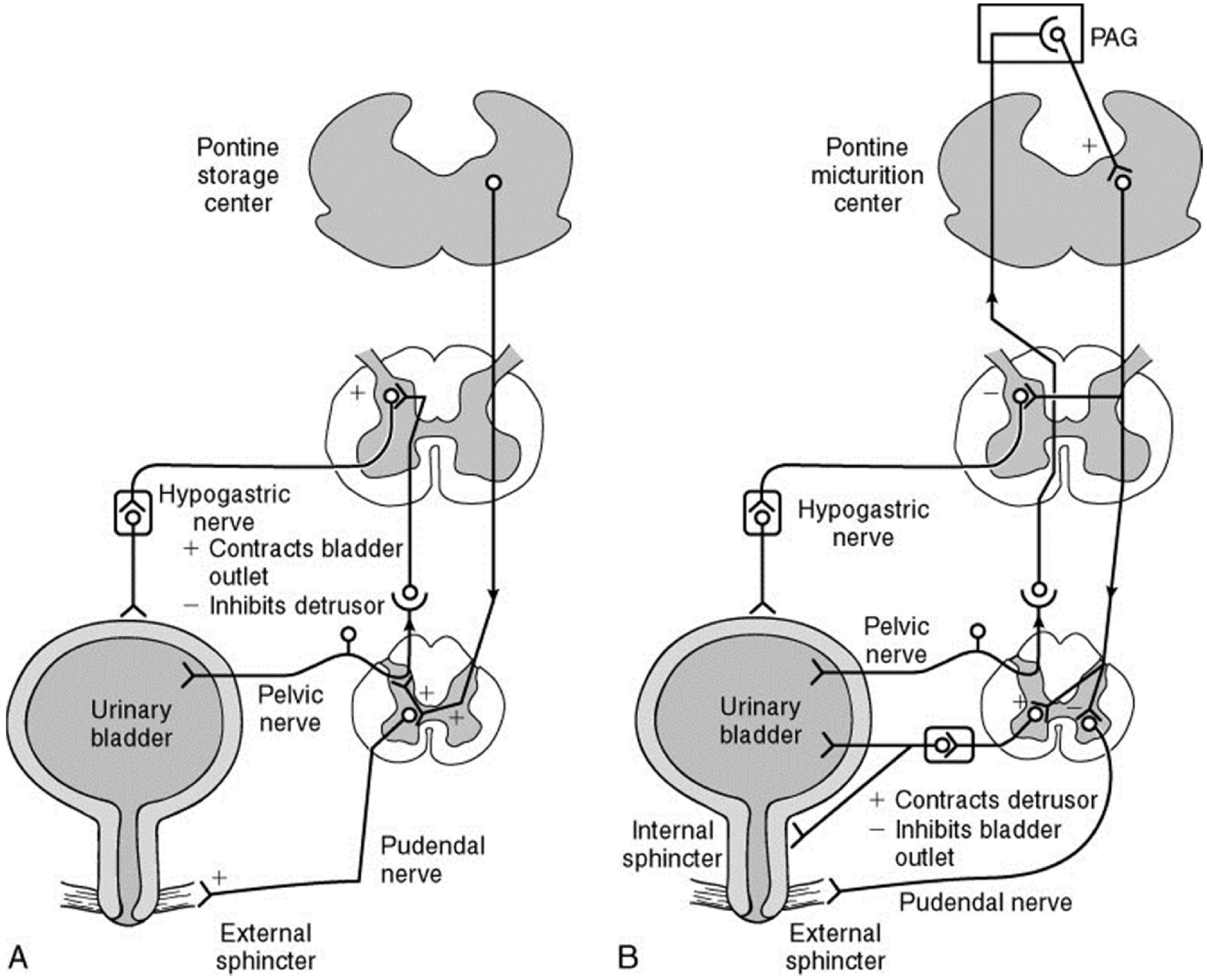

CNS
Urinary bladder
Elimination
Switch
Storage
Urethral sphincter

Table 23–4. REFLEXES TO THE LOWER URINARY TRACT

Afferent Pathway	Efferent Pathways	Central Pathway
Urine Storage	1. External sphincter contraction (somatic nerves)	Spinal reflexes
Low level vesical afferent activity (pelvic nerve)	2. Internal sphincter contraction (sympathetic nerves)	
	3. Detrusor inhibition (sympathetic nerves)	
	4. Ganglionic inhibition (sympathetic nerves)	
	5. Sacral parasympathetic outflow inactive	
Micturition	1. Inhibition of external sphincter activity	Spinobulbospinal
High level vesical afferent activity (pelvic nerve)	2. Inhibition of sympathetic outflow	
	3. Activation of parasympathetic outflow to the bladder	
	4. Activation of parasympathetic outflow to the urethra	


Pontine storage center
Hypogastric nerve
+ Contracts bladder outlet
– Inhibits detrusor
Urinary bladder
Pelvic nerve
Pudendal nerve
External sphincter
A
PAG
Pontine micturition center
Hypogastric nerve
Pelvic nerve
Urinary bladder
+ Contracts detrusor
– Inhibits bladder outlet
Internal sphincter
Pudendal nerve
External sphincter
B

Sympathetic Efferents (Motor From Cord)

- Preganglionic nerves exit T10-L2
- Variable ganglia locations
  - 'Paraganglia' – next to vertebrae
  - 'Preganglia' – between vertebra and organ
  - 'Peripheral ganglia' – with end organ
- Hypogastric Nerve
- Modulate contraction of urethral smooth muscle, bladder outlet
- Inhibit parasympathetics – indirectly inhibit bladder contractions

Parasympathetic Efferents (Motor From Cord)

- Preganglionic nerves exit S2-4
  - Nuclei in intermediolateral zone of sacral cord
- Nerves travel long distances to ganglia within or next to target organ
- Pelvic Nerve
- Modulate bladder contractions

Somatic Efferent (Motor From Cord)

- Preganglionic nerves exit S2-4
- Nerve bodies located on Onuf's nucleus
- Pudendal Nerve
- Modultaes striated (voluntary) urethral sphincter contracton

Afferent Innervation (Sensory to Cord)

- Afferent fibers contained in pelvic, hypogastric, pudendal nerves
- Enter via dorsal root ganglia
  - Sacral – pelvic, pudendal
  - Lumbar – hypogastric
- Two types
  - A-delta fibers
  - C fibers
- Neurotransmitters - numerous

Afferent Fibers

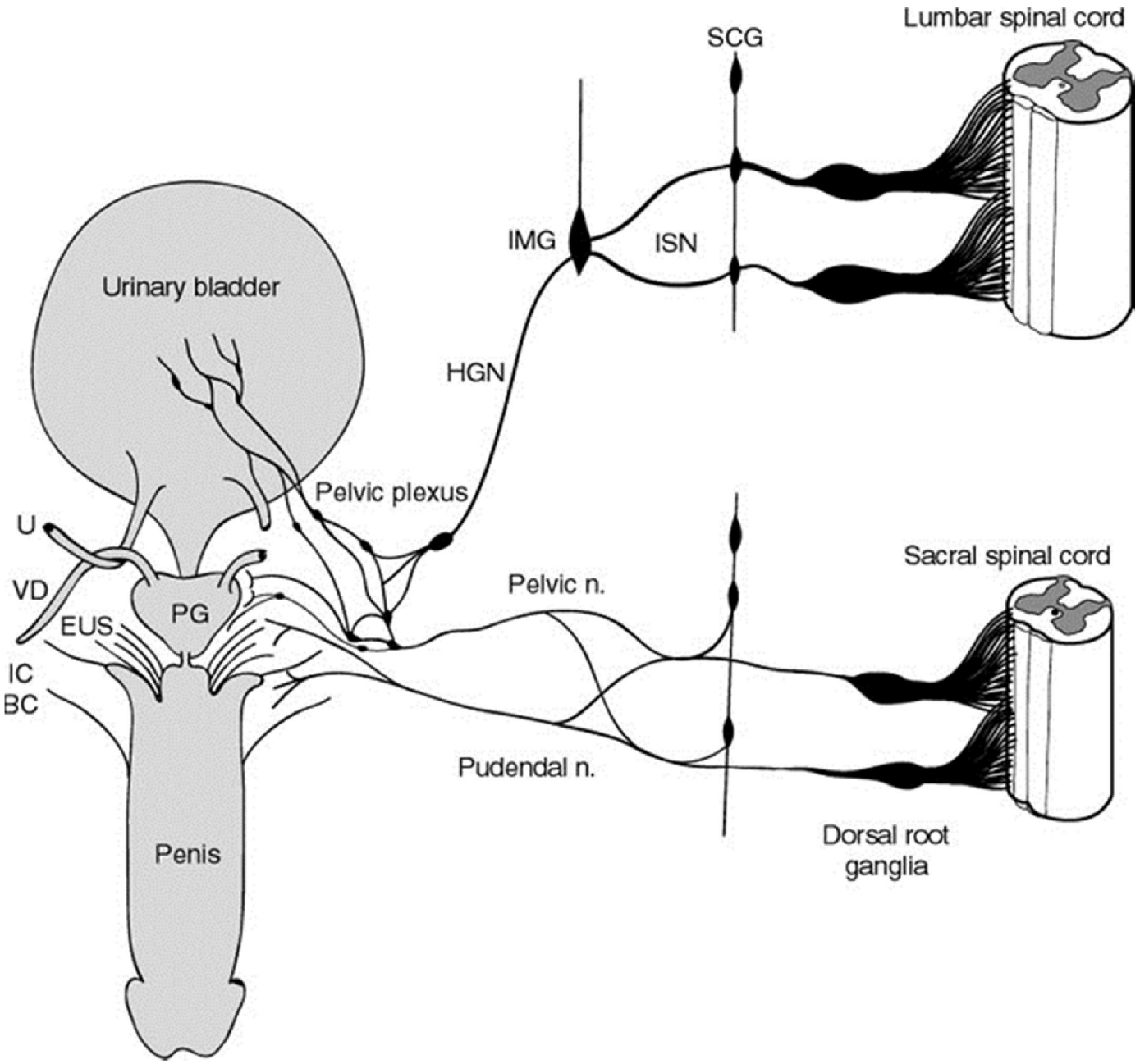
- A- delta (myelinated)
  - Sense bladder fullness, wall tension
  - Initiate normal voiding reflex

- C fibers (unmyelinated)
  - Detect noxious signals
  - Insensitive to normal distention
  - Become active (mechanosensitive) following inflammation, suprasacral SCI
  - Felt to initiate pathologic voiding reflex

Neurotransmitters

- Parasympathetic
  - Preganglionic neurotransmitter = Ach
  - Postganglionic neurotransmitter = Ach
  - Cholinergic Receptors

- Sympathetic
  - Preganglionic neurotransmitter = Ach
  - Postganglionic neurotransmitter = NE
  - Adrenergic Receptors


Lumbar spinal cord
SCG
IMG
ISN
Urinary bladder
HGN
Pelvic plexus
U
VD
EUS
PG
IC
BC
Sacral spinal cord
Pelvic n.
Pudendal n.
Penis
Dorsal root
ganglia

Receptor Distribution in LUT

- Cholinergic
  - Higher muscarinic receptor density in the bladder body than in the base
- Adrenergic
  - Alpha – predominate in bladder base, urethra
  - Beta – predominate in bladder body

Cholinergic Receptors

- Bind Ach released from
  - Postganglionic parasympathetic neurons
  - Preganglionic autonomic neurons
  - Somatic neurons
- Muscarinic
  - Found on all autonomic effector cells (bladder, sweat glands, bowel, CNS)
  - 5 known types (M, -M_5)
- Nicotinic
  - Found in skeletla muscle motor endplates, autonomic ganglia

Table 23–3. BLADDER AFFERENT PROPERTIES

Fiber Type	Location	Normal Function	Inflammation Effect
A-delta (finely myelinated axons)	Smooth muscle	Sense bladder fullness (wall tension)	Increase discharge at lower pressure threshold
C fiber (unmyelinated axons)	Mucosa	Respond to stretch (bladder volume sensors)	Increase discharge at lower threshold
C fiber (unmyelinated axons)	Mucosa muscle	Nociception to overdistention Silent afferent	Sensitive to irritants Becomes mechanosensitive and unmasks new afferent pathway during inflammation

Bladder Muscarinic Receptors

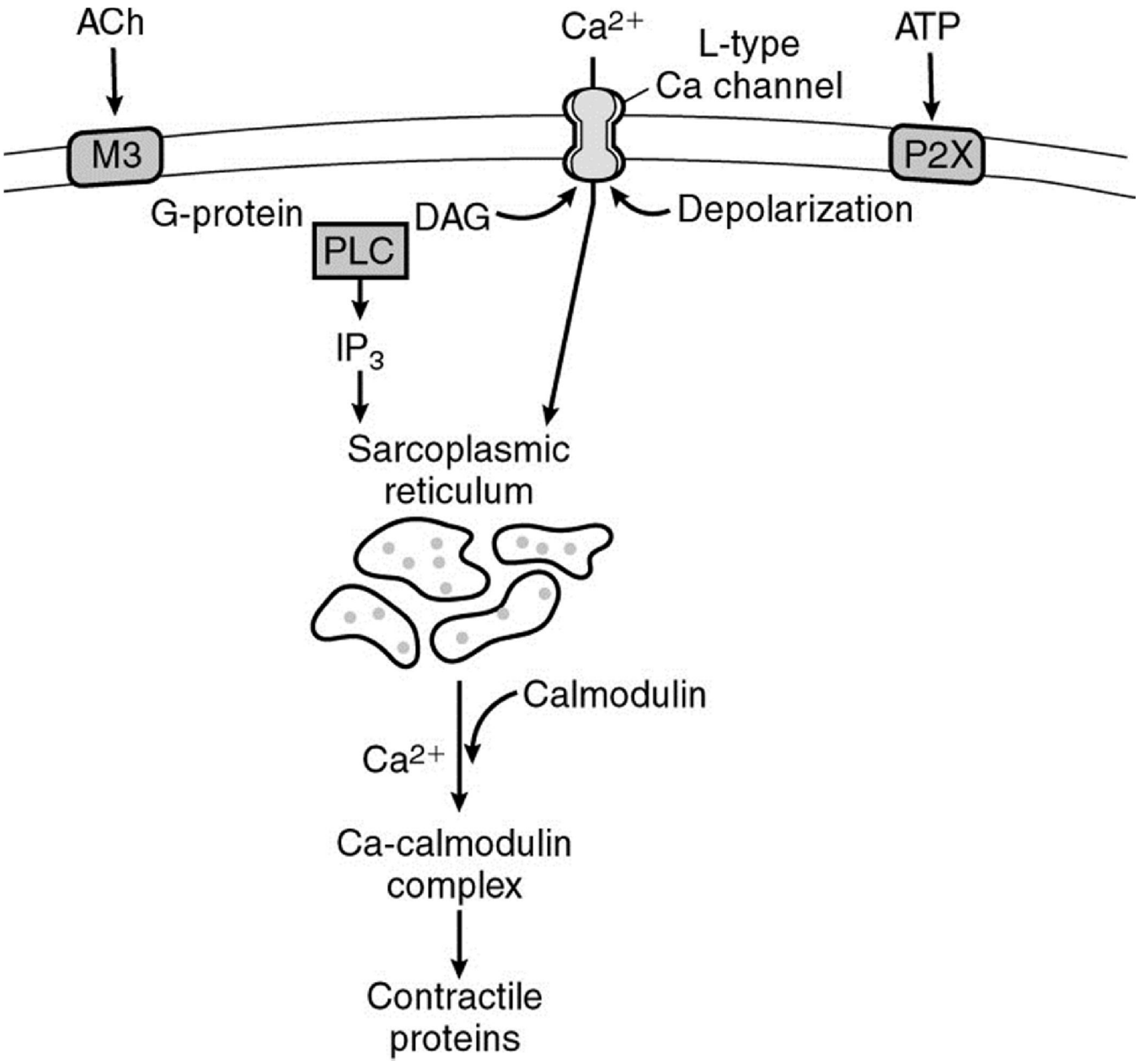
- M_3
  - 20%
  - Responsible for muscle contraction
    - Ach binding to M_3 elicits intracellular Ca++ release, etc.
- M_2
  - 80%
  - May enhance response to M_3 stimulation by inhibiting sympathetic suppression of detrusor muscle

Adrenergic Receptors

- Bind catecholamines released from postganglionic sympathetic neurons
  - NE, E
- Alpha receptors – vasoconstriction, smooth muscle contraction
- Beta receptors – increased myocardial contractility, smooth muscle relaxation

Contraction

- At rest, very low free Ca^{++} in cell
- Binding of ligand to receptor increases free Ca^{++}
  - Ca^{++} release from sacroplasmic reticulum – triggered by G-protein, IP_3
  - Ca^{++} influx via ion channels
  - Ca^{++} binds to calmodulin, which can then activate MLCK
  - MLCK phosphorylates myosin light chain
  - Myosin light chain changes shape, interacts with actin => contraction


ACh
Ca2+
L-type
Ca channel
ATP
M3
P2X
G-protein
PLC
DAG
Depolarization
IP3
Sarcoplasmic
reticulum
Calmodulin
Ca2+
Ca-calmodulin
complex
Contractile
proteins

Relaxation

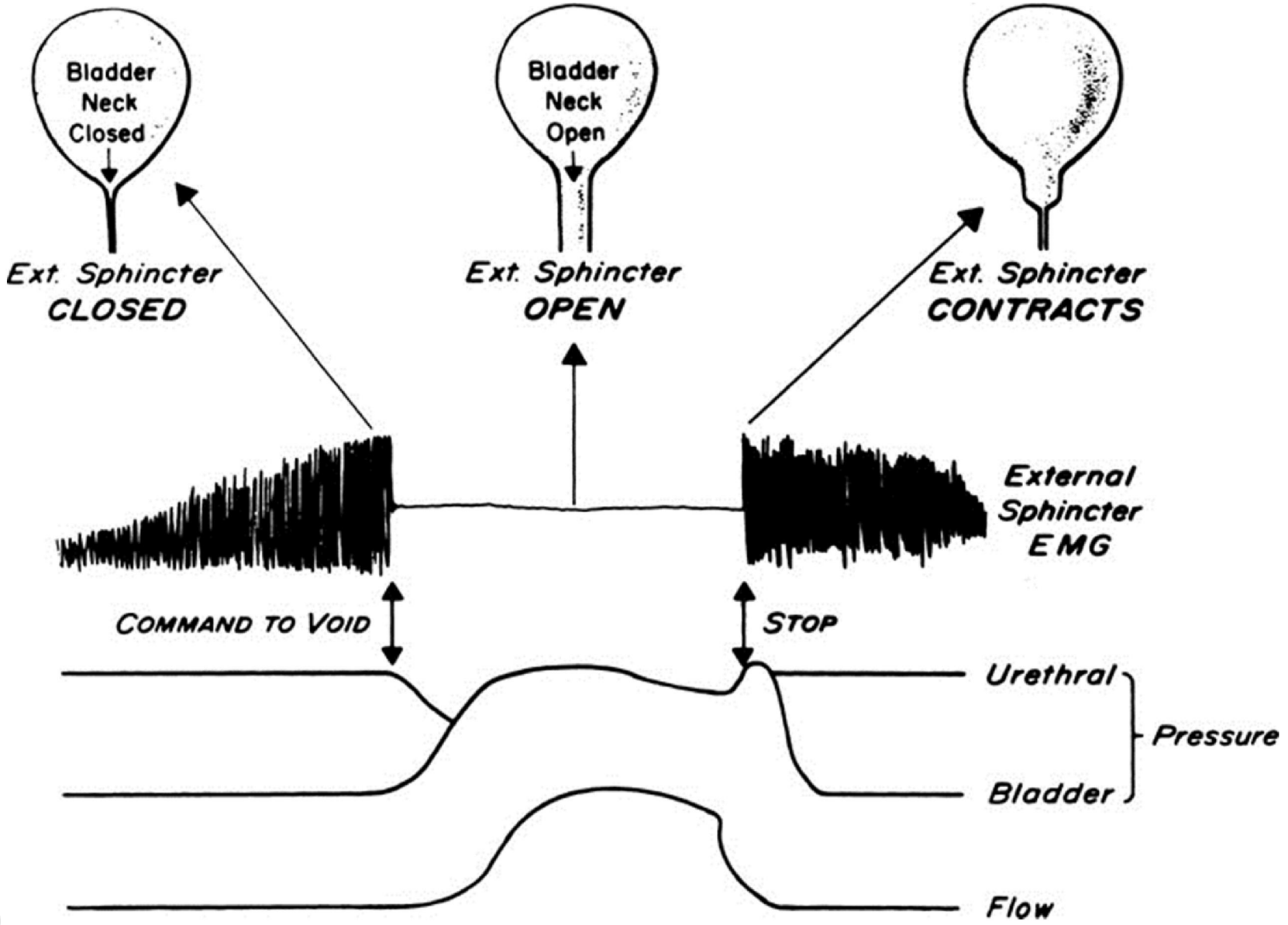
- Ca^{++} is pumped out against concentration gradient
  - Also activated by Ca^{++} – calmodulin complex
- Receptor-ligand complex is degraded
- Excess neurotransmitter outside of cell is degraded

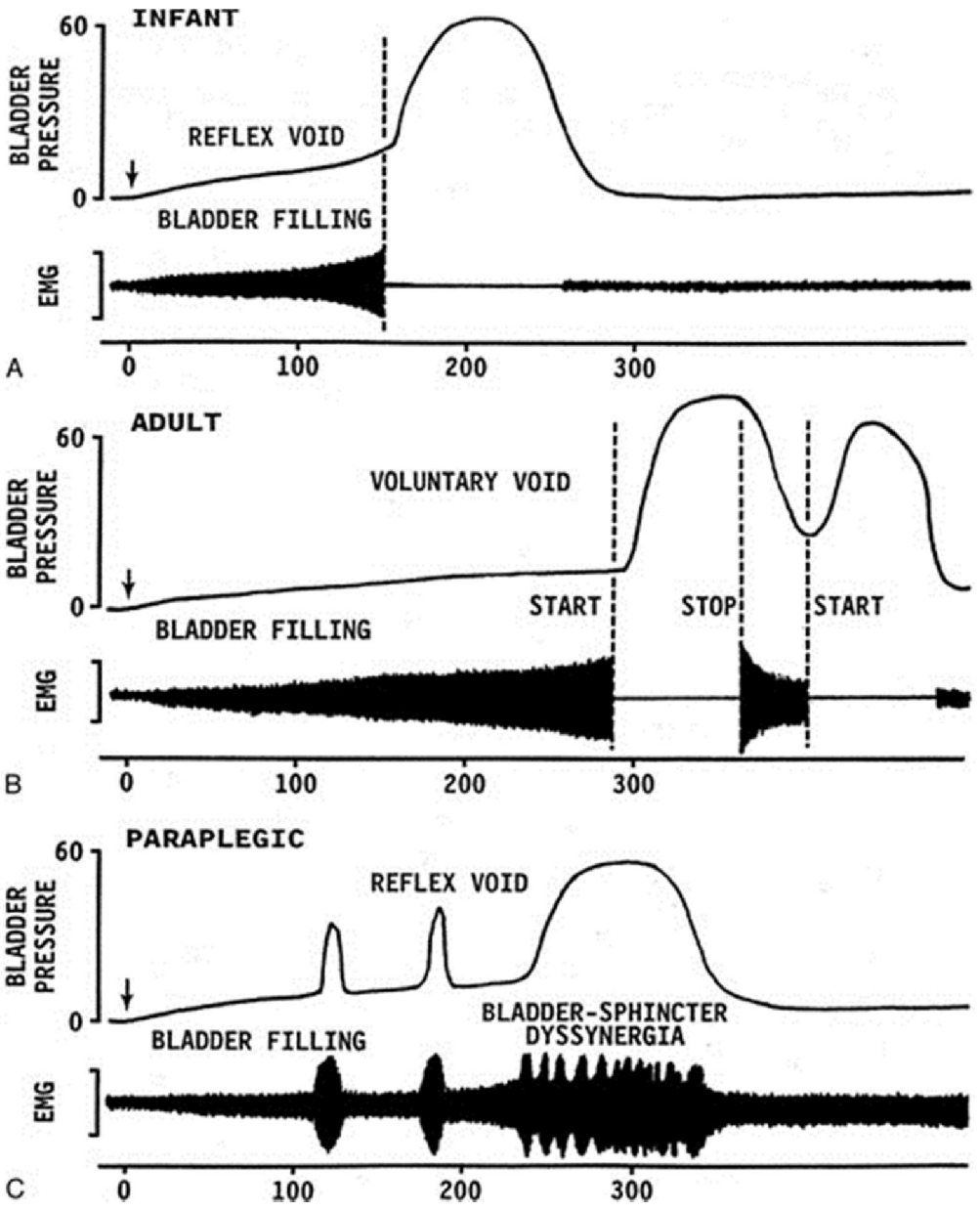
Storage

- Bladder fills, activates A-delta afferents
- Sympathetics stimulated
  - Internal sphincter contraction (bladder base and urthera) (Alpha)
  - Bladder relaxation (Beta)
- Increased somatic activity via pundendal nerve
  - Increased EUS tone
- Parasympathetics inactive
  - Sympathetic inhibition of parasympathetic transmission at ganglia level (Alpha)
- SPINAL 'GUARDING' REFLEXES

Voiding

- Increased bladder afferent activigy triggers ‘switch’ from storage to voiding
- Relaxation of EUS – intial event
  - Inhibition of somatic activity
- Activation of parasympathetic outflow to bladder, urethra
  - Bladder contraction (muscarinic receptors)
  - Urethral relaxation (NO)
- SUPRASPINAL REFLEX


Bladder Neck Closed
Ext. Sphincter CLOSED
Bladder Neck Open
Ext. Sphincter OPEN
Ext. Sphincter CONTRACTS
External Sphincter EMG
COMMAND TO VOID
STOP
Urethral Pressure
Bladder
Flow


INFANT
60
BLADDER PRESSURE
0
REFLEX VOID
BLADDER FILLING
EMG
A
0
100
200
300
ADULT
60
BLADDER PRESSURE
0
VOLUNTARY VOID
START
STOP
START
BLADDER FILLING
EMG
B
0
100
200
300
PARAPLEGIC
60
BLADDER PRESSURE
0
REFLEX VOID
BLADDER-SPHINCTER DYSSYNERGIA
BLADDER FILLING
EMG
C
0
100
200
300

PATHOLOGY

- Brain Lesion
  - Shy-Drager
  - Hydrocephalus
  - Parkinson's
- Above Pons
  - Urgency Incontinence
  - Retrusor Hyperreflexia Overactivity
  - No EUS Dyssynergia

Suprasacral Spinal Cord Injury

- Initial spinal shock
- Emergence of sacral reflex
- Mediated by 'silent' C-fiber afferents that become active
- ? Similar mechanism in other conditions ?
  - OAB
- These C-fibers can be deactivated by vanilloids (capsaicin, Rtx)
  - Rationale for trials of these agents

Spinal Cord Lesion

- Between Pons & Sacral Spinal Cord
  - e.g. MVA, MS, Myelomeningocele
- Spinal Shock
  - 6-12 Weeks
- Overactive Bladder
  - Urgency Incontinence
  - EUS Dyssynergia(DSD)

Sacral Cord Injury (Nerve injury)

- Sensory Nerve Bladder
  - Full Bladder
- Motor Nerve Bladder
  - Full Bladder (i.e. Detrusor Areflexia)
- Both Lead To Overflow Incontinence
  - e.g. Sacral Cord Tumor, Herniated disc, Crushed Pelvis, P. Lumbar Laminectomy, Radical Hysterectomy, or AP Resection

Peripheral Nerve Injury

- Identical To a Sacral Cord Injury
  - e.g. DM, AIDS, Poliomyelitis, Guillan-Barre, Severe Herpes, Neurophilitis (Tabes Dorsalis), Pernicious Anemia

Urinary Incontinence

- Conditions of urinary incontinence: failure to store and/or empty
  - Stress
  - Urge
  - Overflow ⇑ PVR
  - Transient
  - Functional
  - Mixed

Table 27–1. PROPERTIES OF THE BLADDER AND SPHINCTER THAT PROMOTE CONTINENCE

Bladder

Accommodation
Compliance
Capacity
Neural control

Sphincter

Coaptation
- Mucosal seal
- Inner wall softness

Compression
- Extracellular matrix
- Collagen
- Elastin
- Urethral smooth muscle
- Urethral striated muscle

Anatomic support
- Transmission of Pabd

Neural control

Table 27–2. CONDITIONS CAUSING URETHRAL INCONTINENCE

Bladder Abnormalities
Detrusor overactivity
Detrusor instability
Detrusor hyperreflexia
Low bladder compliance
Sphincter Abnormalities
Urethral hypermobility
Intrinsic sphincter deficiency

Table 27–4. CAUSES OF INTRINSIC SPHINCTER DEFICIENCY

Previous Pelvic Surgery

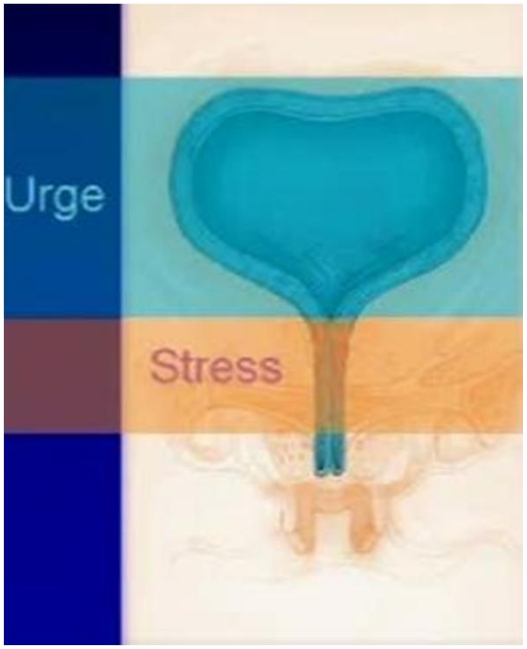
Anti-incontinence surgery
Urethral diverticulectomy
Radical hysterectomy
Abdominoperineal resection of the rectum
Urethrotomy
Resection or incision of the vesical neck

Neurologic Conditions

Myelodysplasia
Anterior spinal artery syndrome
Lumbosacral neurologic conditions
Shy-Drager syndrome

Aging versus Hypoestrogenic States

Primary (End-Organ) Causes of Voiding Dysfunction



- Urgency/OAB
  - Detrusor overactivity
  - With or without leakage
- Stress Incontinence
  - Diminished urethral sphincter funtion and/or
  - Support a.k.a urethra hyerpmobility

Neurogenic Bladder/Incontinence

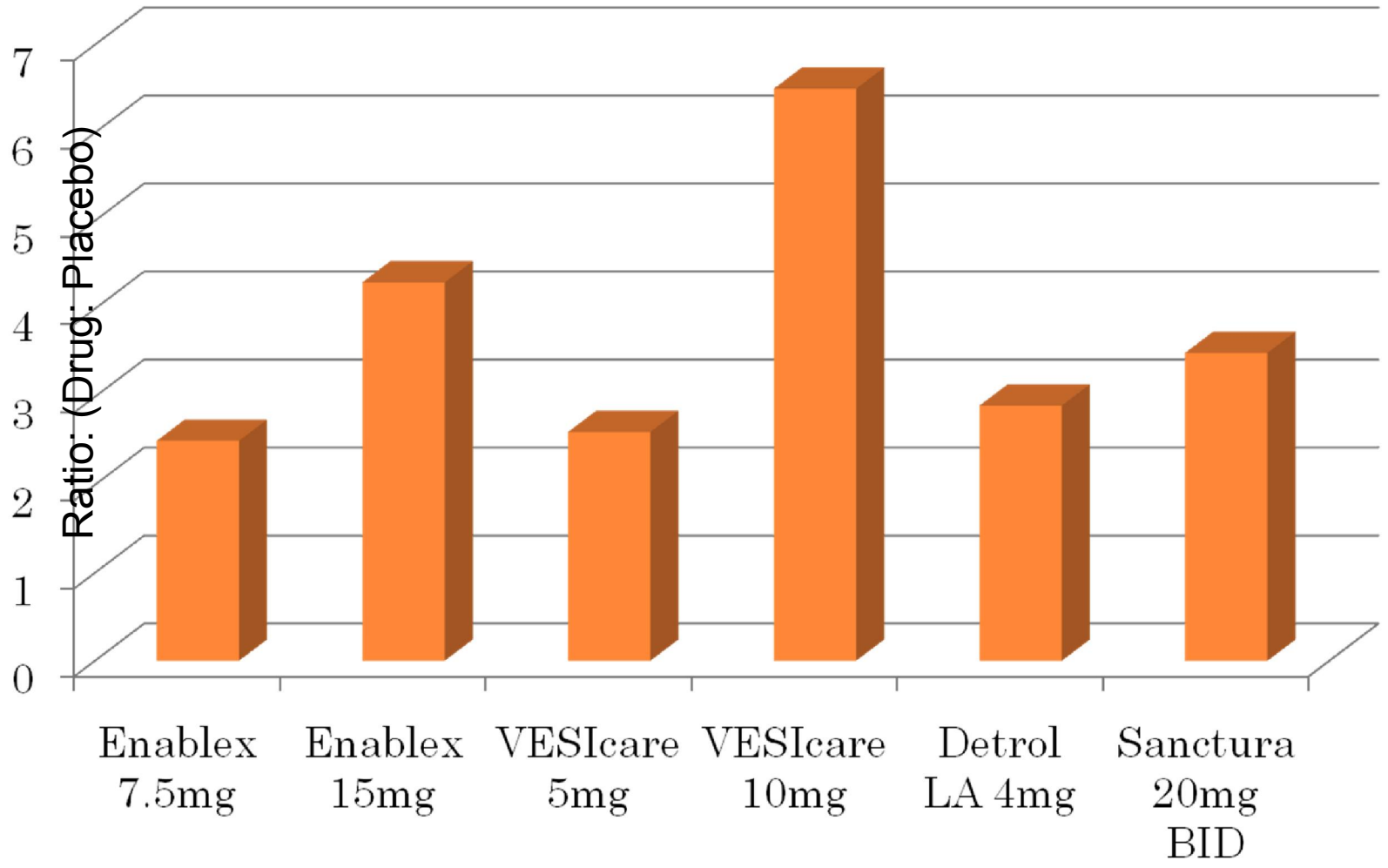
- management

- H & P
- Labs
- Medical treatment
- Surgical Treatment

Table 27–8. TREATMENT GUIDELINES

Condition	Treatment
Detrusor overactivity	Treat underlying condition (e.g., urethral obstruction, infection, bladder stones, bladder cancer, spinal cord tumors, spinal disc disease) Behavior modification Anticholinergics and/or musculotropic relaxants and/or tricyclic antidepressants (± intermittent catheterization) Electrical stimulation Biofeedback Neuromodulation Detrusor myectomy Augmentation enterocystoplasty (± intermittent catheterization) Continent urinary diversion
Low bladder compliance	Anticholinergics and/or musculotropic relaxants and/or tricyclic antidepressants (± intermittent catheterization) Neuromodulation Detrusor myectomy Augmentation enterocystoplasty (± intermittent catheterization) Continent urinary diversion
Sphincteric incontinence	
Intrinsic sphincter deficiency	Periurethral injections Pubovaginal sling Artificial urinary sphincter
Urethral hypermobility	Pelvic floor exercises (± biofeedback) Electrical stimulation Urethropexy or pubovaginal sling

(Drug: Placebo) Cross PI Comparison Dry Mouth Ratios



Muscarinic Receptor Profiles

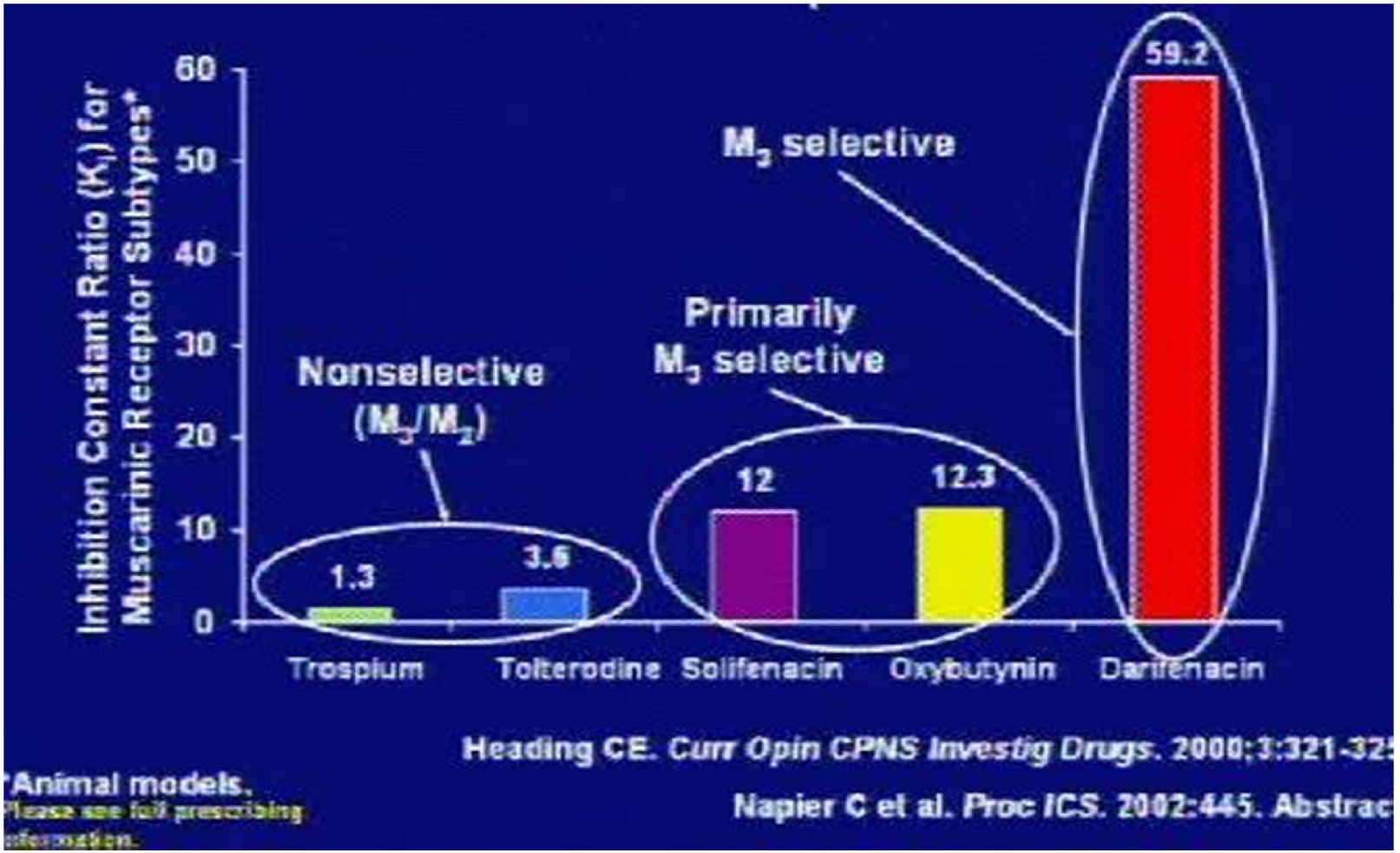


Table 27–7. CAUSES OF LOSS OF URETHRAL COMPRESSION AND SUPPORT

Loss of Urethral Compression	Loss of Urethral Support
Neurologic	Levator (hammock) weakness
Anterior spinal artery syndrome	Childbirth
Radical pelvic surgery	Trauma
Myelodysplasia	Pelvic surgery
Hypoestrogenic states	Hypoestrogenic states
Aging	Aging
Anatomic	
Scarring post urethral surgery	

Detrusor Leak Point Pressure vs. Valsalva Leak Point Pressure

- Detrusor LPP
  - Passive leakage as bladder fills up
  - 'Pop off valve'
  - Only applies to those with neurogenic bladder dsyfunction
  - DLCC >40cm H2O puts upper tracts at risk
- Valsalva LPP
  - Degree of strain that produces stress incontinence
  - Active
  - Assesses degree of urethral function/SUI

Labs

- U / A
- Urine Cytology (carcinoma-in-situ)
- Chem 7 - Renal function of DM
- Voiding Diary
- PVR

Labs: Urodynamics

- Uroflow
  - Obstruction
- CMG
  - Capacity of Compliance
  - Pressure Flow Study
    - Bladder Strength / Obstruction

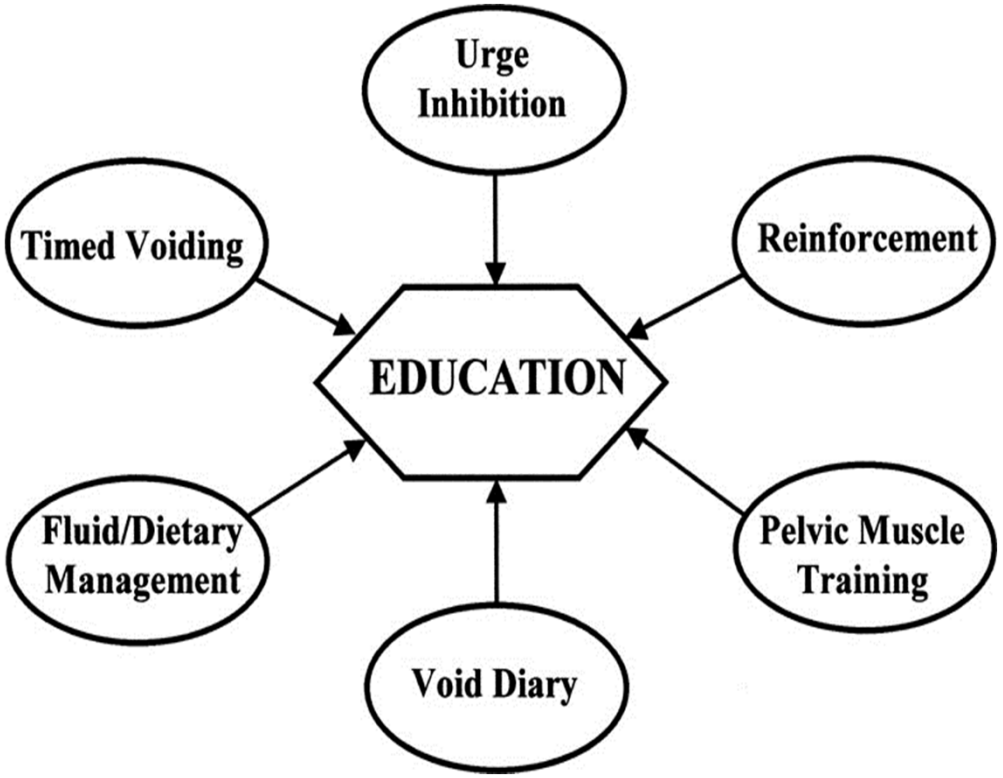
Labs: Urodynamics (2)

- Voiding Cystogram
  - SUI (Urethral Motion / Cystocele)
  - ISD & Fistula
- EMG coordinated voiding
- Video Dynamics (Test All)
- Cysto , Bladder Cancer, Stones, etc

Treatment: Medical Biofeedback

- Pelvic Floor Exercises
- Behavioral Modification
- Bladder Relaxants
- Absorbent Products
- Food & Fluid Adjustements

Rx: behavioral modification

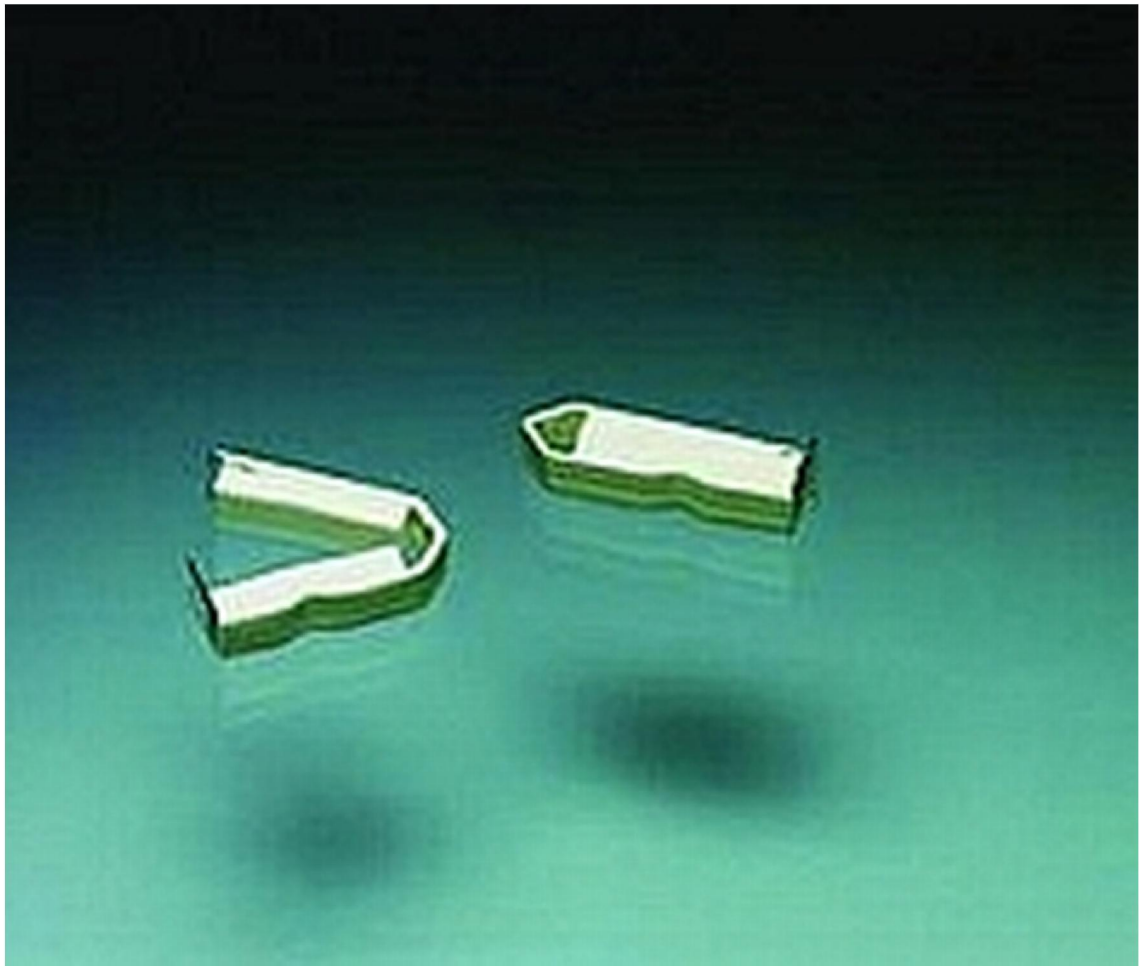


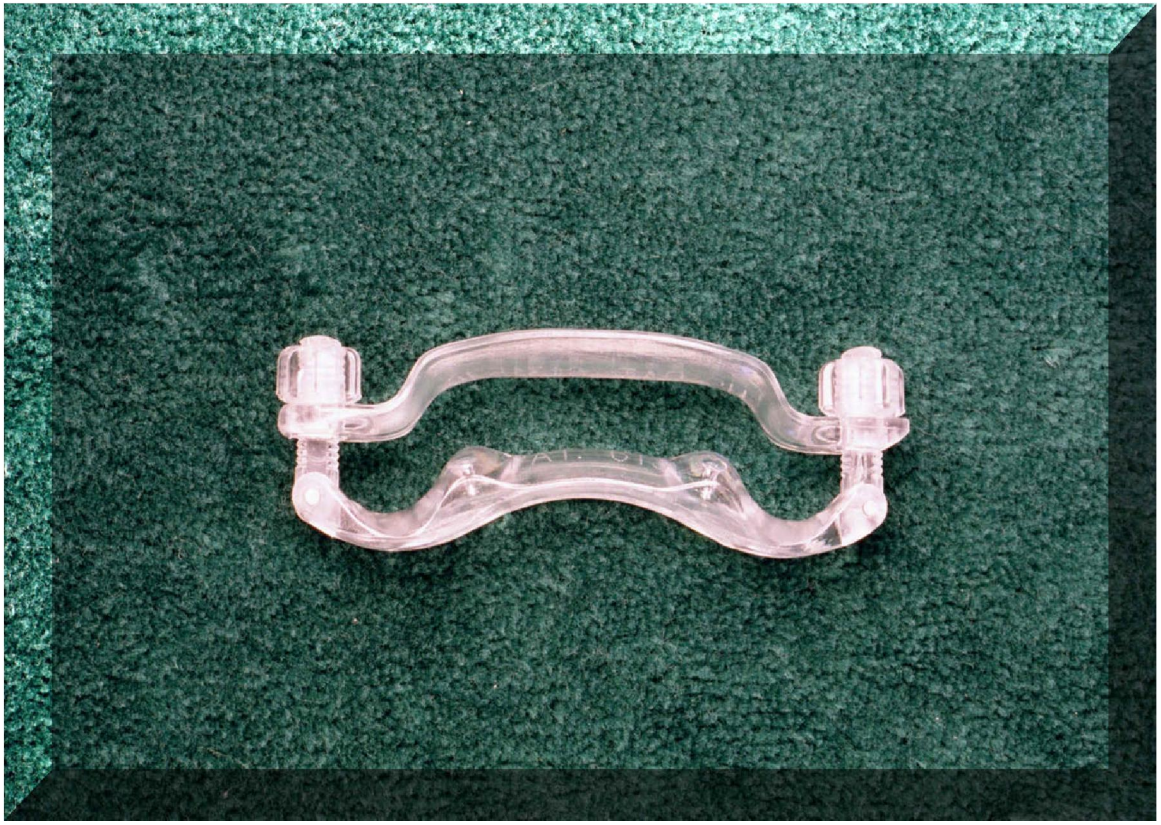
Rx: Medication

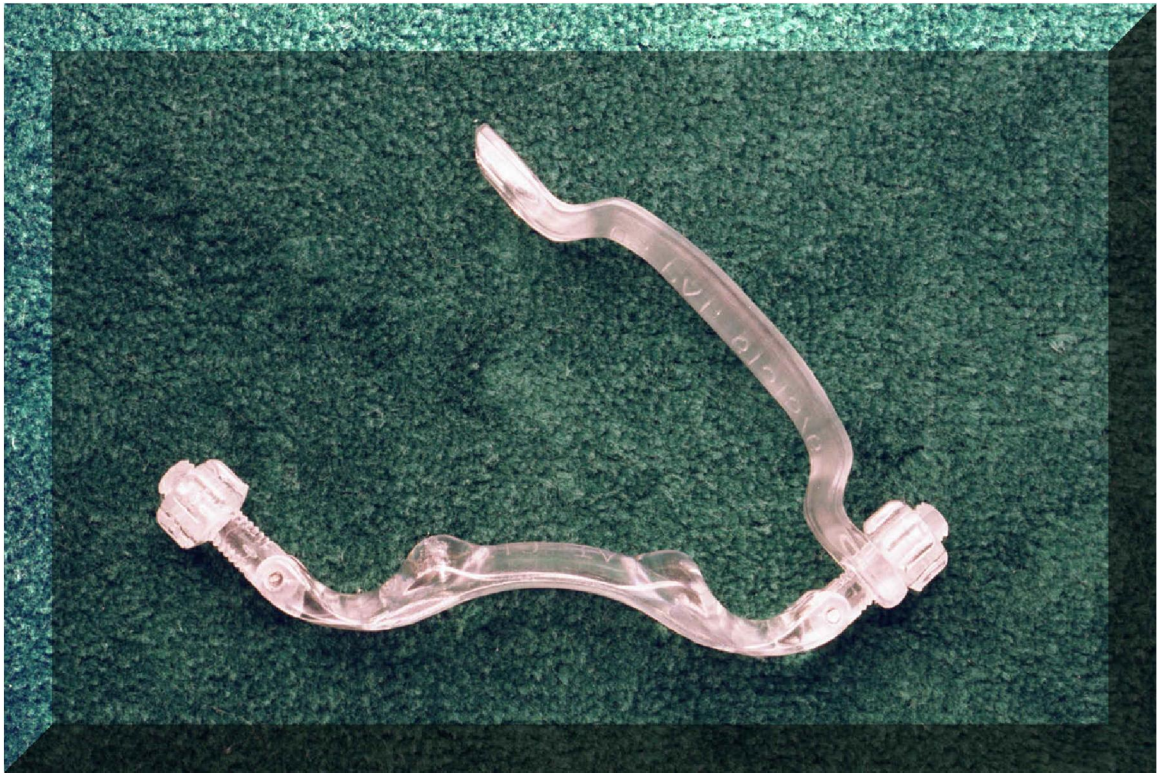
Table 23–5. DRUGS WITH BLADDER ACTION

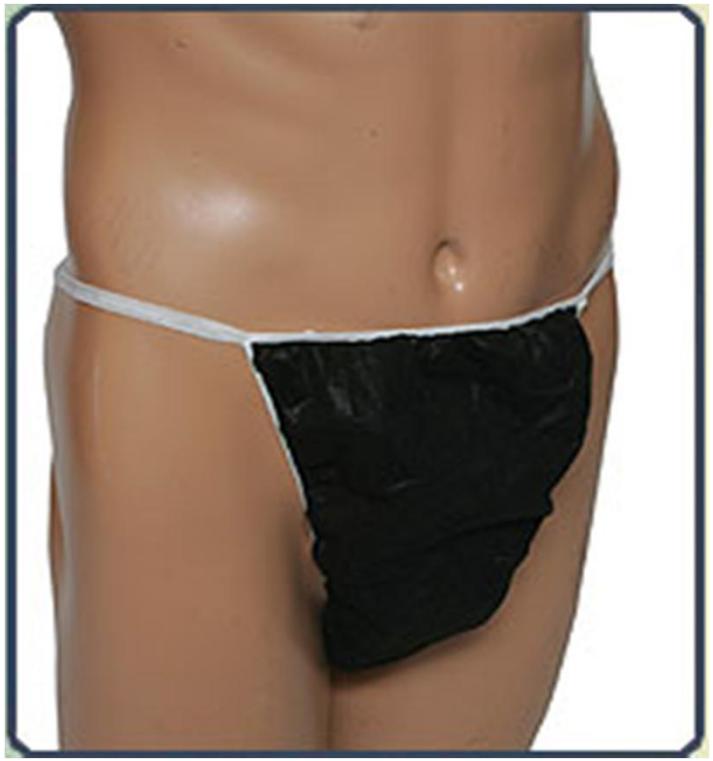
Classification	Examples	Pharmacologic Action
Anticholinergic agents	Atropine Glycopyrrolate Oxybutynin Propantheline Tolterodine	Inhibit muscarinic receptors, thus reducing the response to cholinergic stimulation. Used to reduce pressure during bladder filling and for the treatment of unstable bladder contractions.
Smooth muscle relaxants	Dicyclomine Flavoxata	Direct smooth muscle relaxation reduces intravesical pressure during filling and reduces severity and presence of unstable bladder contractions. Most of these agents have some degree of anticholinergic action.
Calcium antagonists	Diltiazem Nifedipine Verapamil	Used in the treatment of unstable bladder contractions to reduce the magnitude of the spikes by reducing the entrance of calcium during an action potential.
Potassium channel openers	Cromakalim Pinacidil	Act to increase the membrane potential and thus reduce the myogenic initiation of unstable bladder contractions.
Prostaglandin synthesis inhibitors	Flurbiprofen	Prostaglandins have been implicated in increased smooth muscle tone and in the induction of spontaneous activity. Inhibition of prostaglandin synthesis could promote relaxation of the bladder during filling and decrease spontaneous activity of the bladder.
β-Adrenergic agonists	Isoproterenol Terbutaline	Stimulation of β receptors induces relaxation of the bladder body, resulting in a decrease in intravesical pressure during filling.
Tricyclic antidepressants	Amitriptyline Imipramine	These agents have anticholinergic, direct smooth muscle relaxant, and norepinephrine-reuptake inhibition properties.
α-Adrenergic agonists	Ephedrine Phenylpropanolamine Midodrine Pseudoephedrine	Increase urethral tone and closure pressure by direct stimulation of α-adrenergic receptors.
Afferent nerve inhibitors	DMSO Capsaicin Resiniferatoxin	Reduce the sensory input from bladder and thereby increase bladder capacity and reduce bladder instability.
Estrogen	Estradiol	Direct application to the vagina or oral therapy may increase the thickness of the urothelial mucosa, making a better seal and reducing the incidence of incontinence. Other actions may include increasing adrenergic effects on the urethra and increasing blood flow.

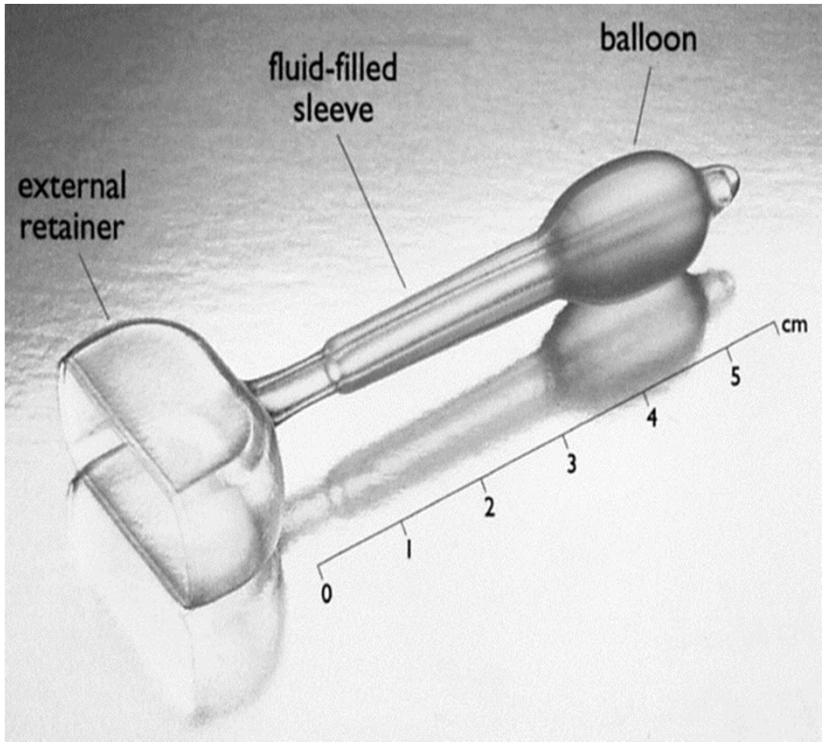
DMSO, dimethyl sulfoxide.

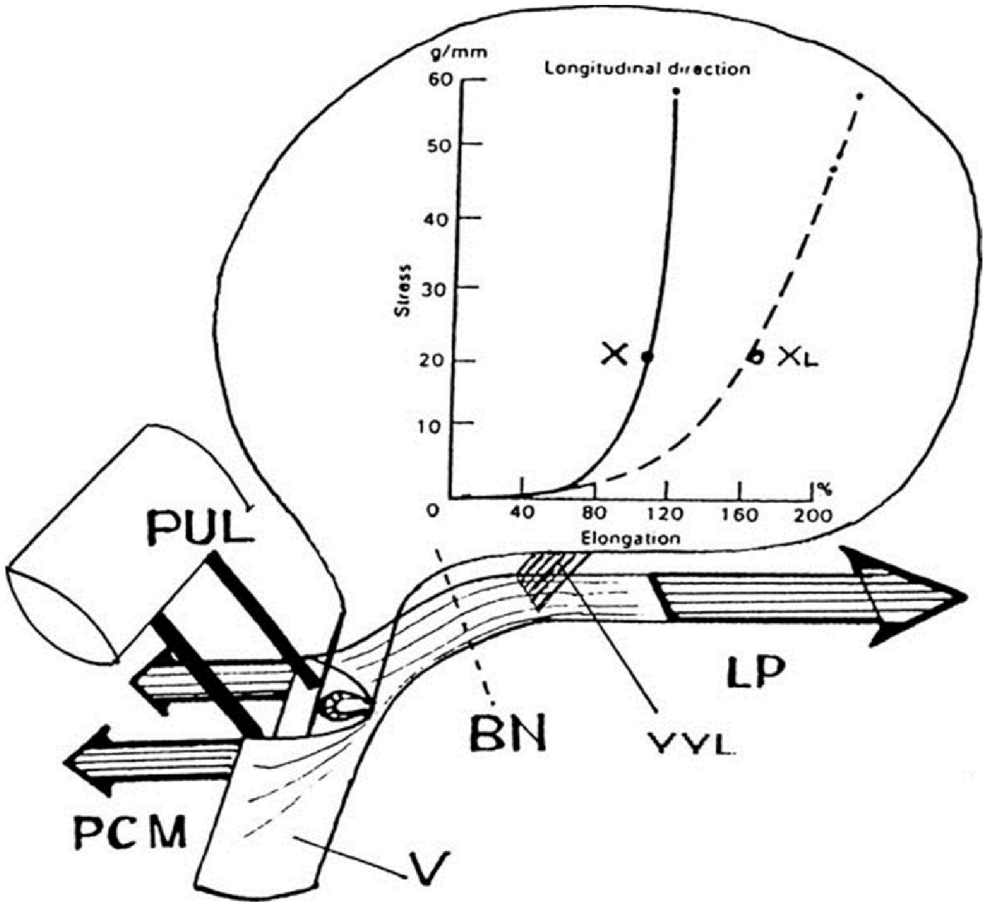




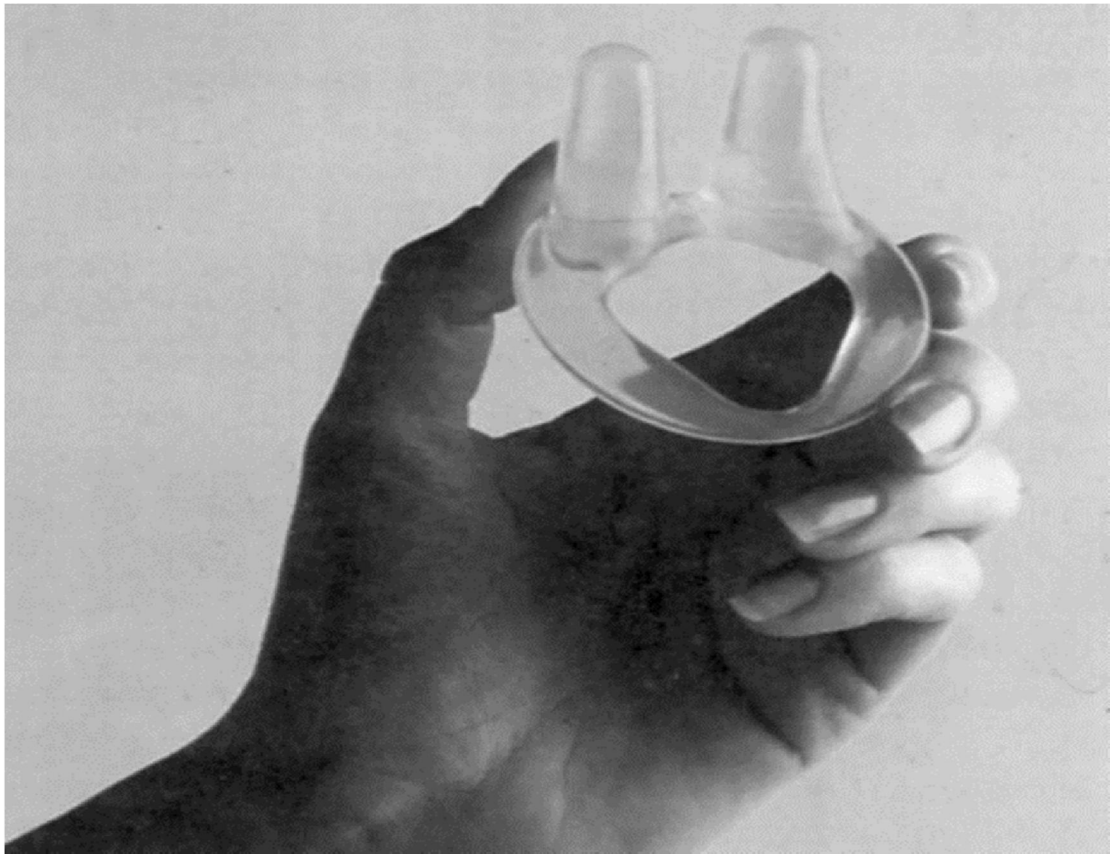




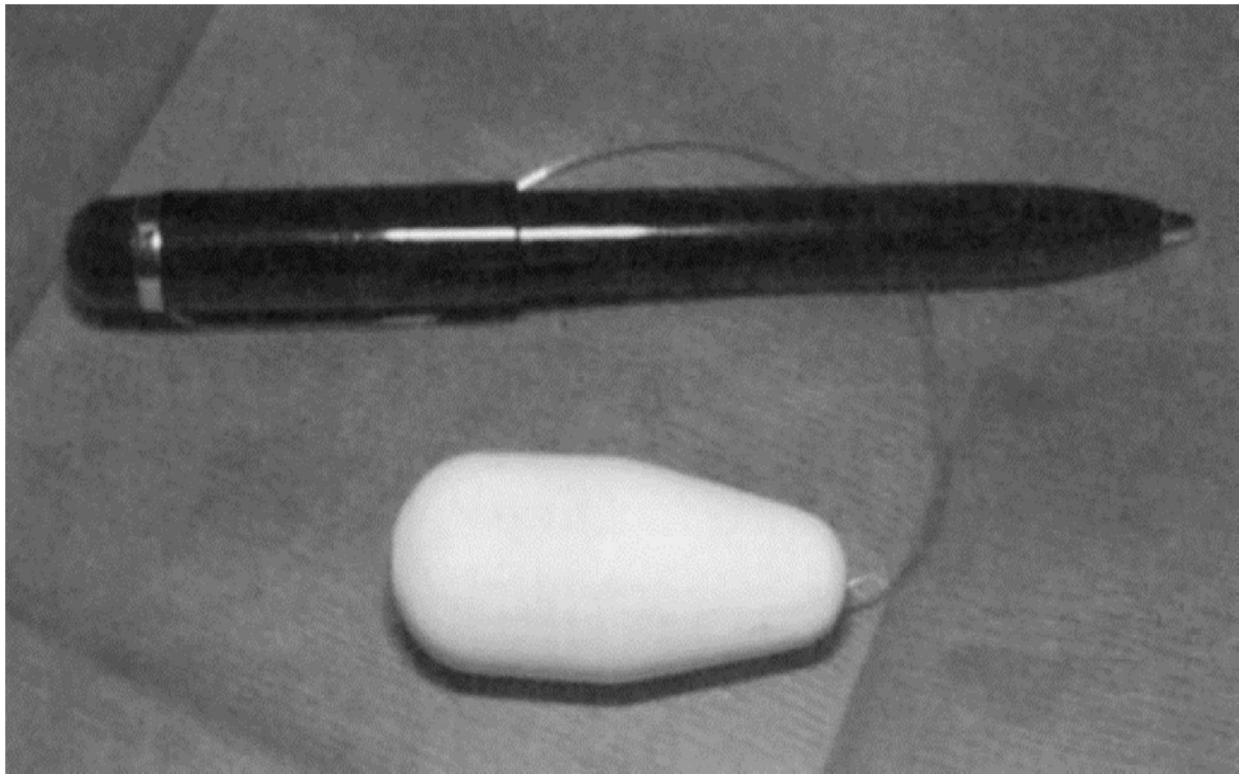

balloon
fluid-filled
sleeve
external
retainer
cm
5
4
3
2
1
0


g/mm
Longitudinal direction
60
50
40
30
20
10
0
Stress
X
XL
40
80
120
160
200
%
Elongation
PUL
LP
BN
VVL
PCM
V

Rx: Bladder neck support



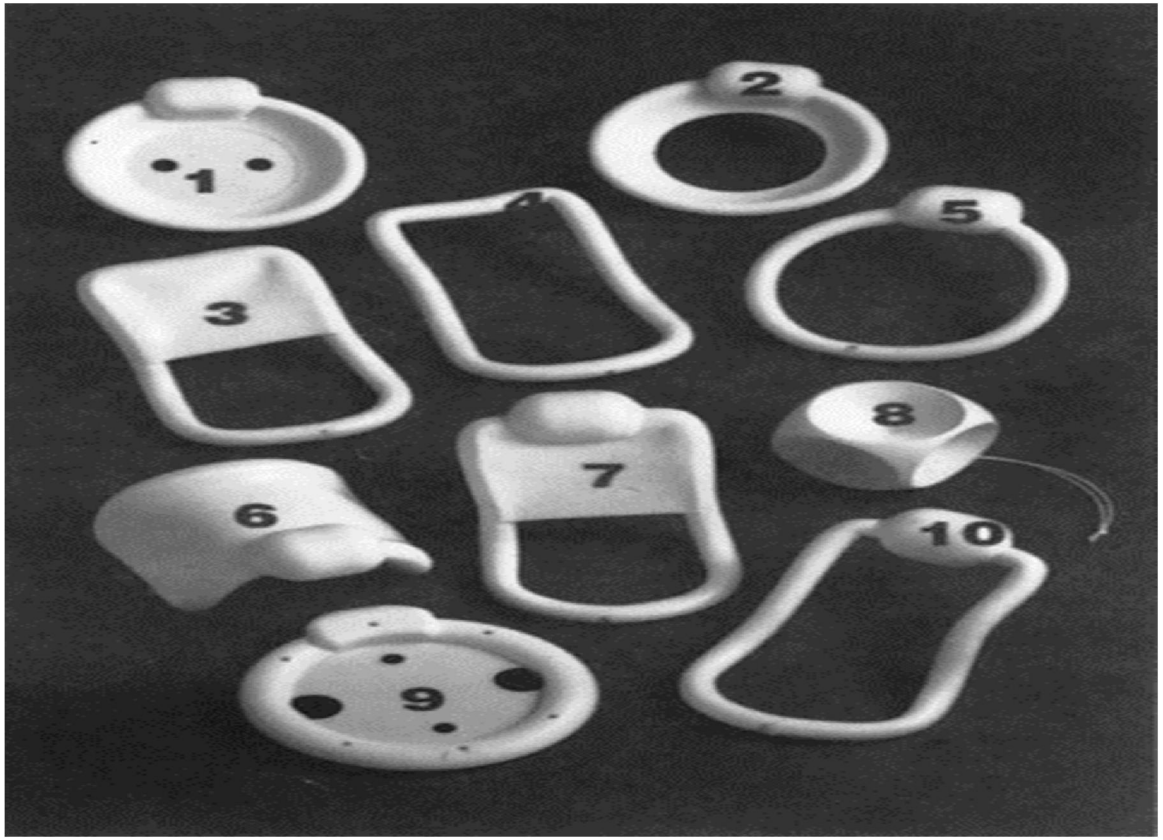
Rx: Vaginal cone



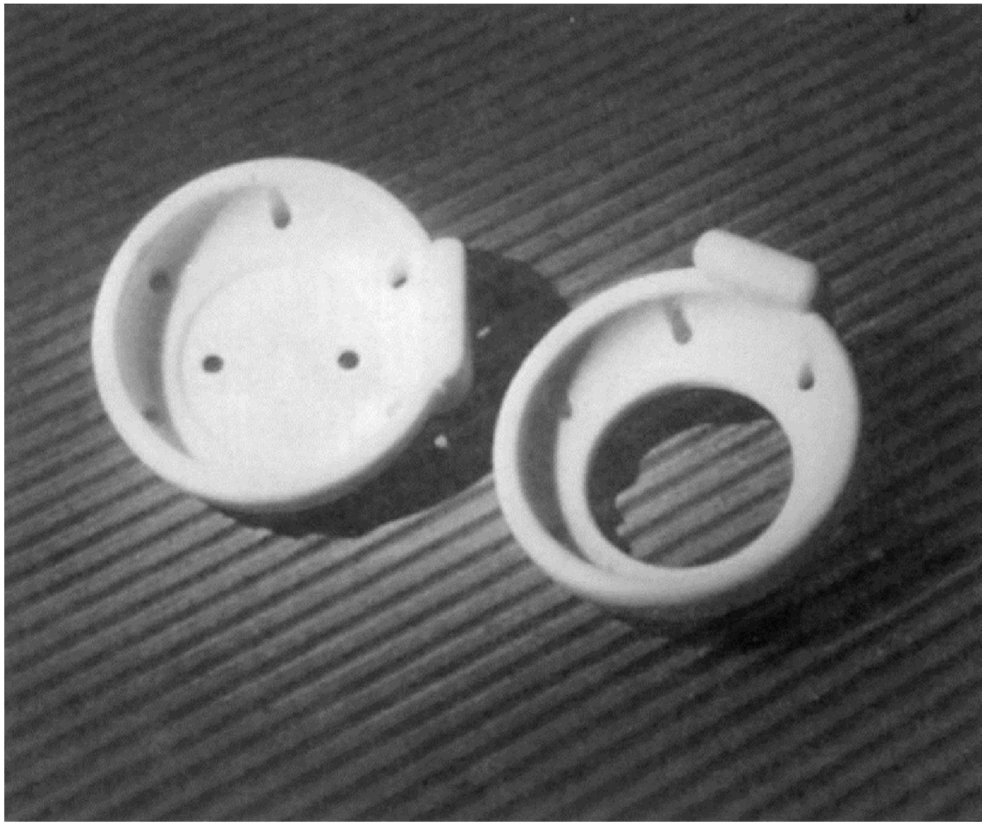
Innovations in Emptying

Chronic or Intermittent Catherization!

Rx: pessaries-dish, ring, knob



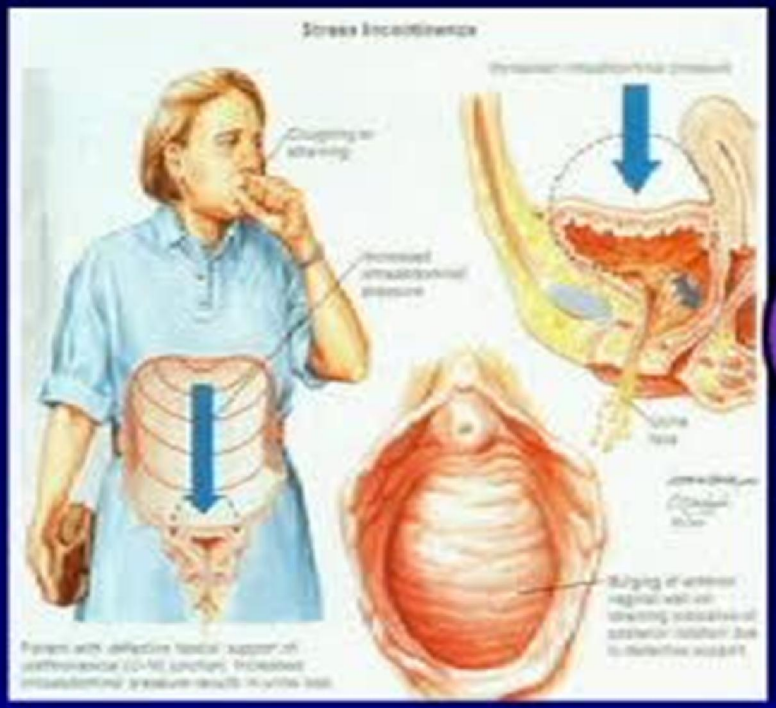
Rx: dish with & without support



Vaginal Urethral Compression and Increased Intrinsic Resistance:

Tampons and Injectables for Mixed Incontinence

" Tampon Test "



\+ Injectables

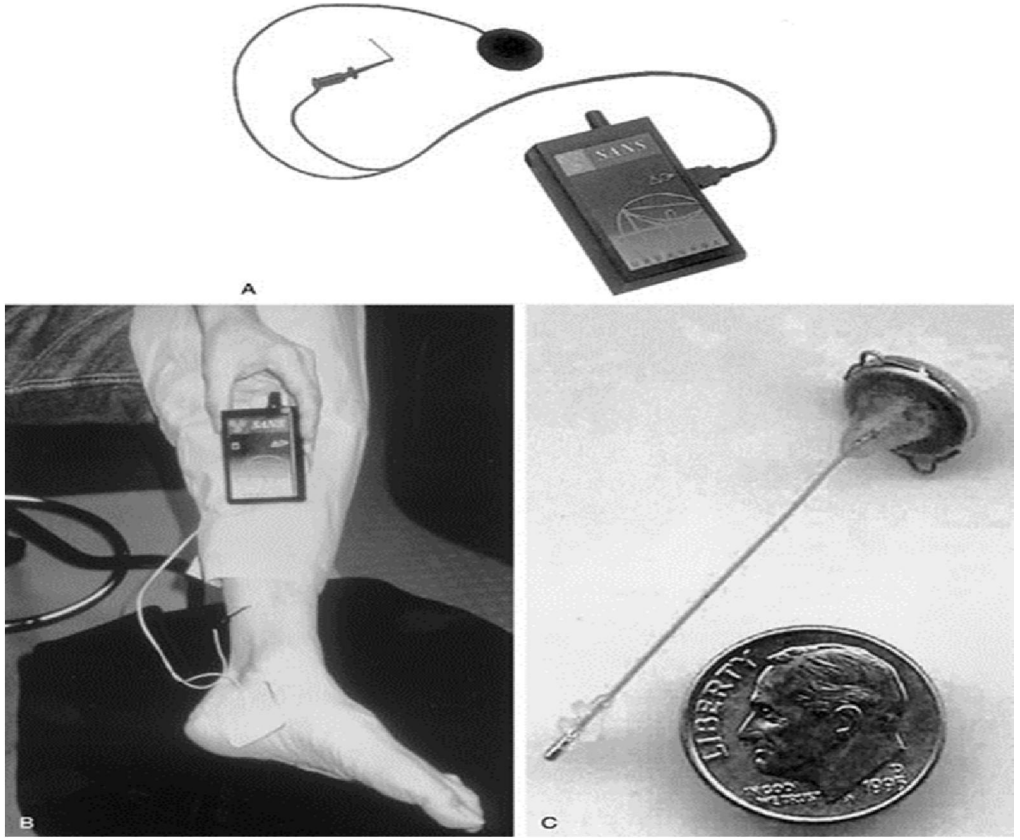
Neuromodulation with Neurotoxins

- Botulinum Toxin Injections
  - Cleveland Clinic Bladder Technique

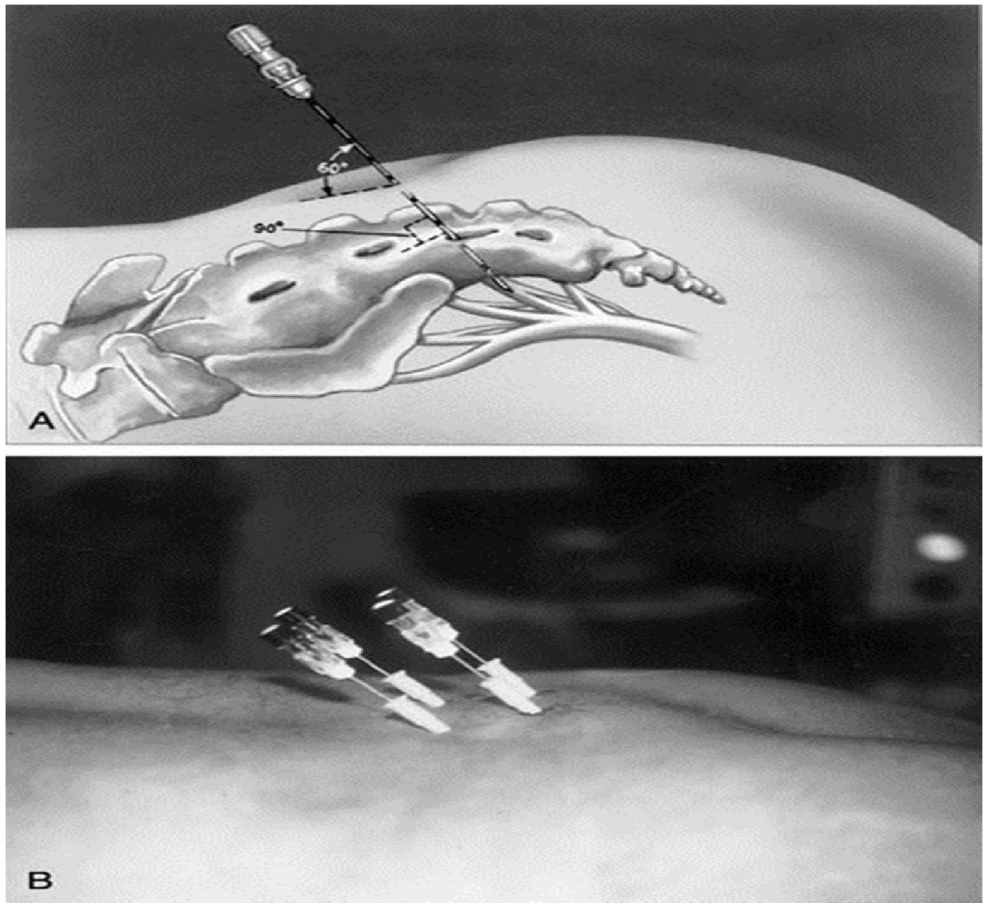
Treatment: Surgical Intermediate

- Neuromodulation
  - Ankle
- Urinary Diversion
  - Urethral Catheter
  - Suprapubic Catheter

Rx: Afferent nerve stimulator

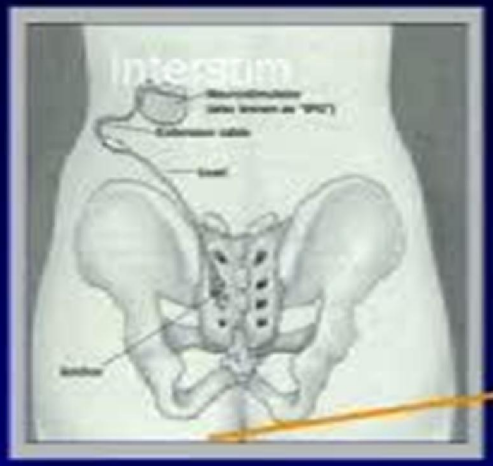


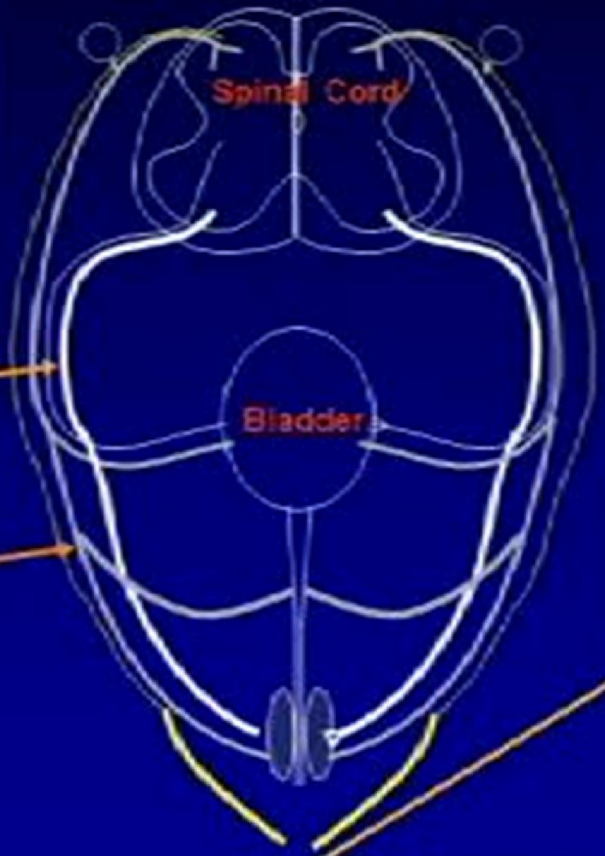
Rx: Interstim neuromadulator



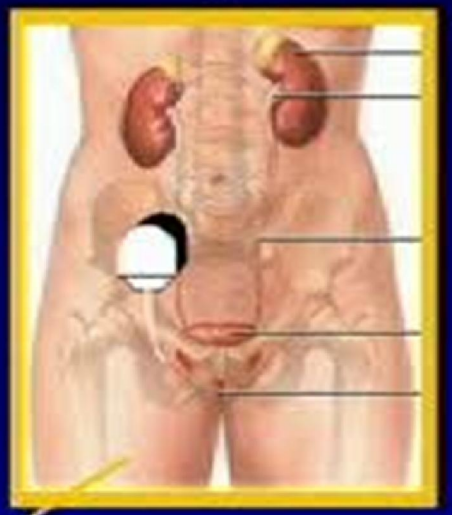
Pelvic Neuromodulation Approaches

Non-Selective, Unilateral





Selective, Bilateral



Tibial Nerve Stim

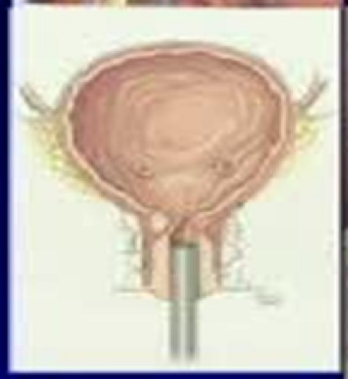
Dorsal Genital Nerves: DGN's

- Supraspinal Lesions (above pons)
  - CVA
  - Brain Tumor
  - Parkinson's & Shy Drager (Degeneration of ANS)

Injecting Techniques

Periurethral

"Bent Needle"



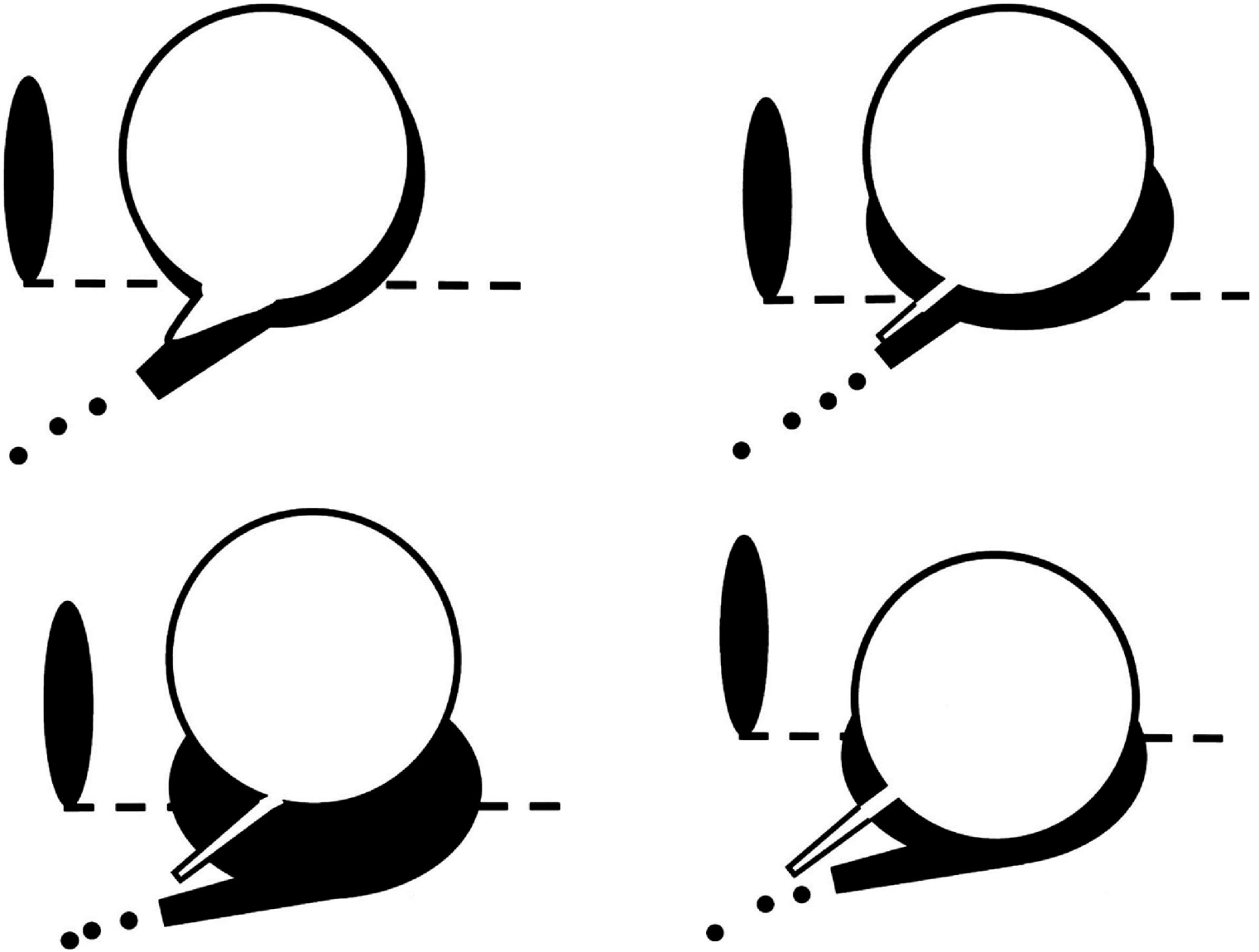
Transurethral

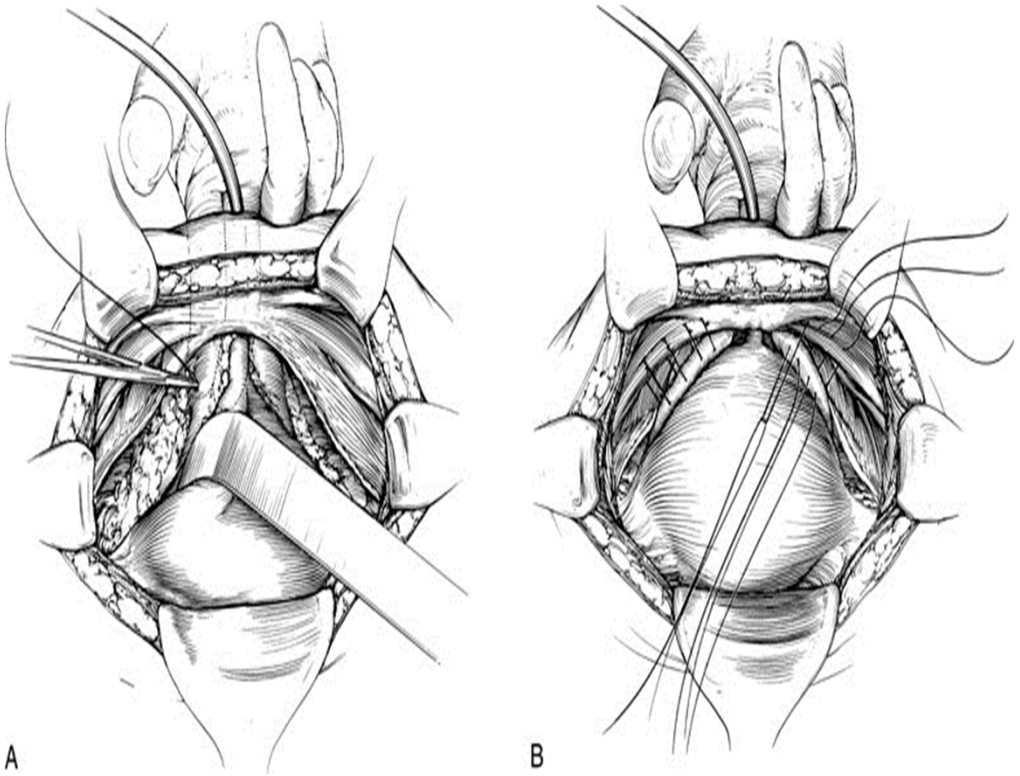
Injectables: Patient Driven Indications

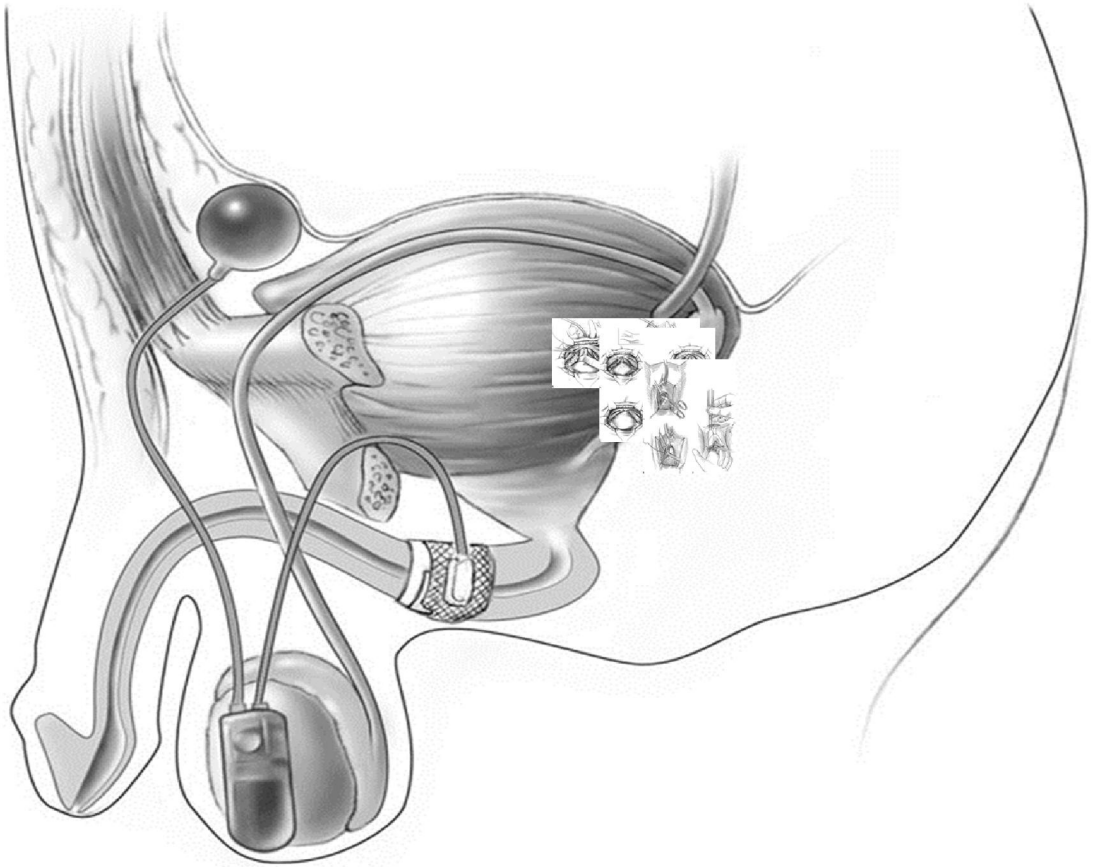
- Women with SUI whom wish to undergo a non-operative procedure for treatment
  - Non-surgical candidates: co-morbidity
  - Women on anti-coagulation therapy
  - No other vaginal pathology present
  - Adjuvent Treatment
    - Pessary/Tampon + Therapy
  - Plans for future vaginal childbearing
  - Wish to avoid a post-operative recovery period
  - Adjuvant treatment of SUI following surgical intervention

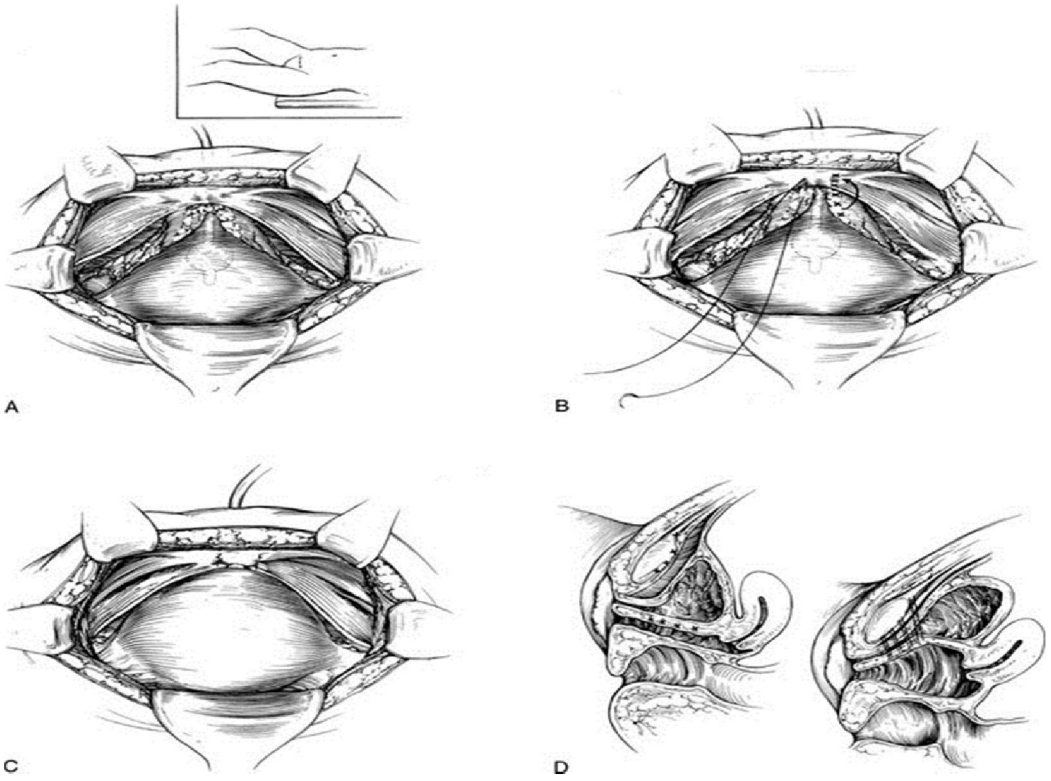
Treatment: Surgical

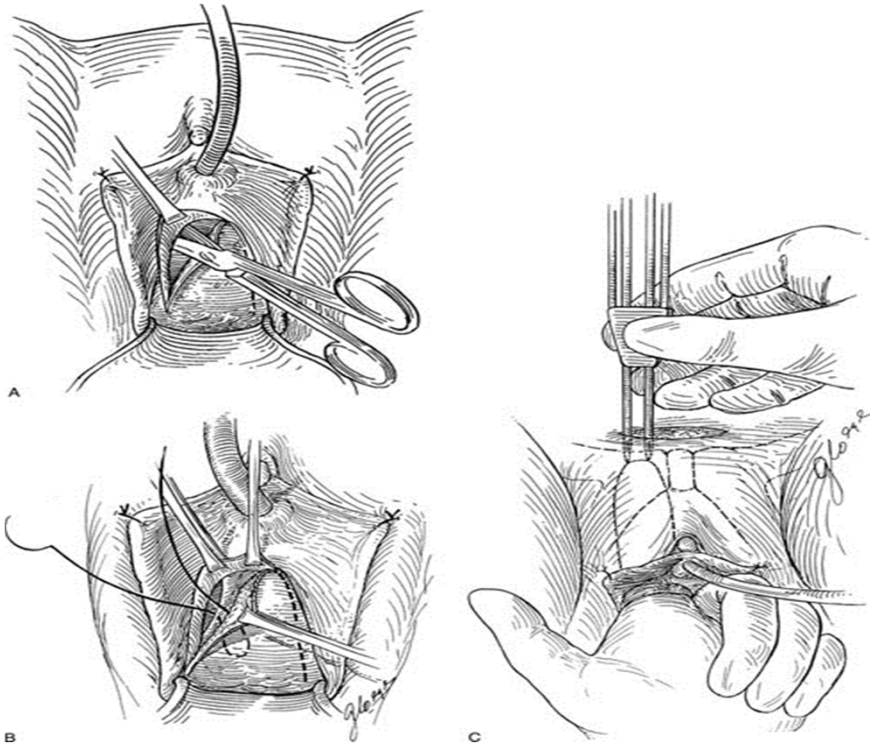
- Open Bladder Neck Suspension
  - Burch / MMK
- Needle Suspension: (Stamey)
- Needle Support: (TOT)
- Neuromodulation: (Surgery)




A
B




A
B
C
D


A
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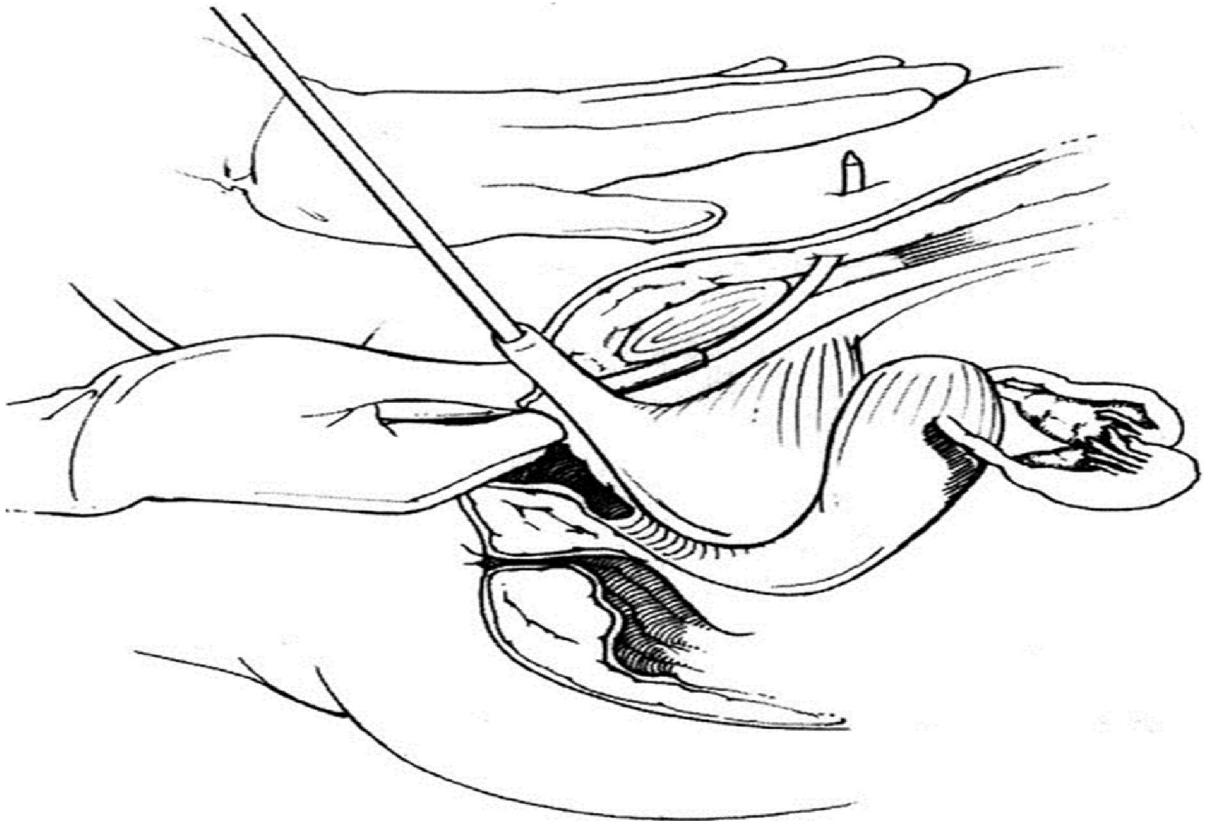
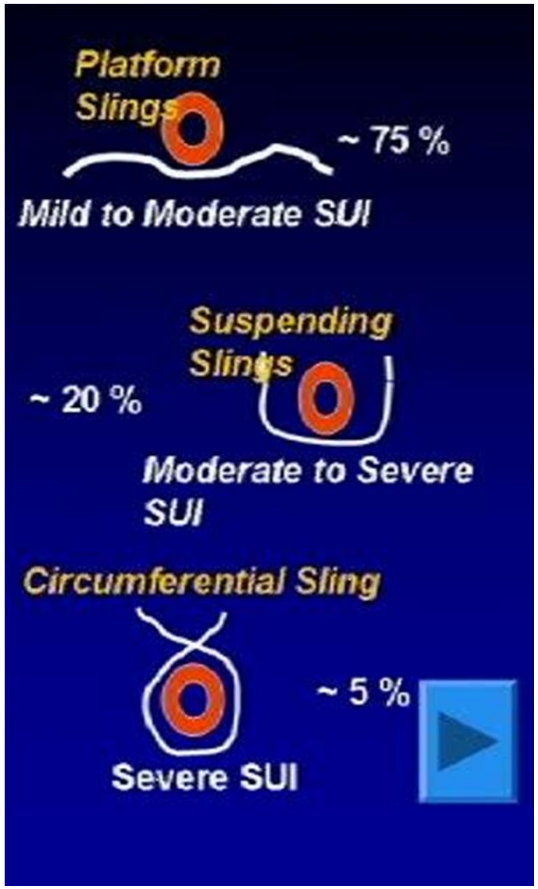
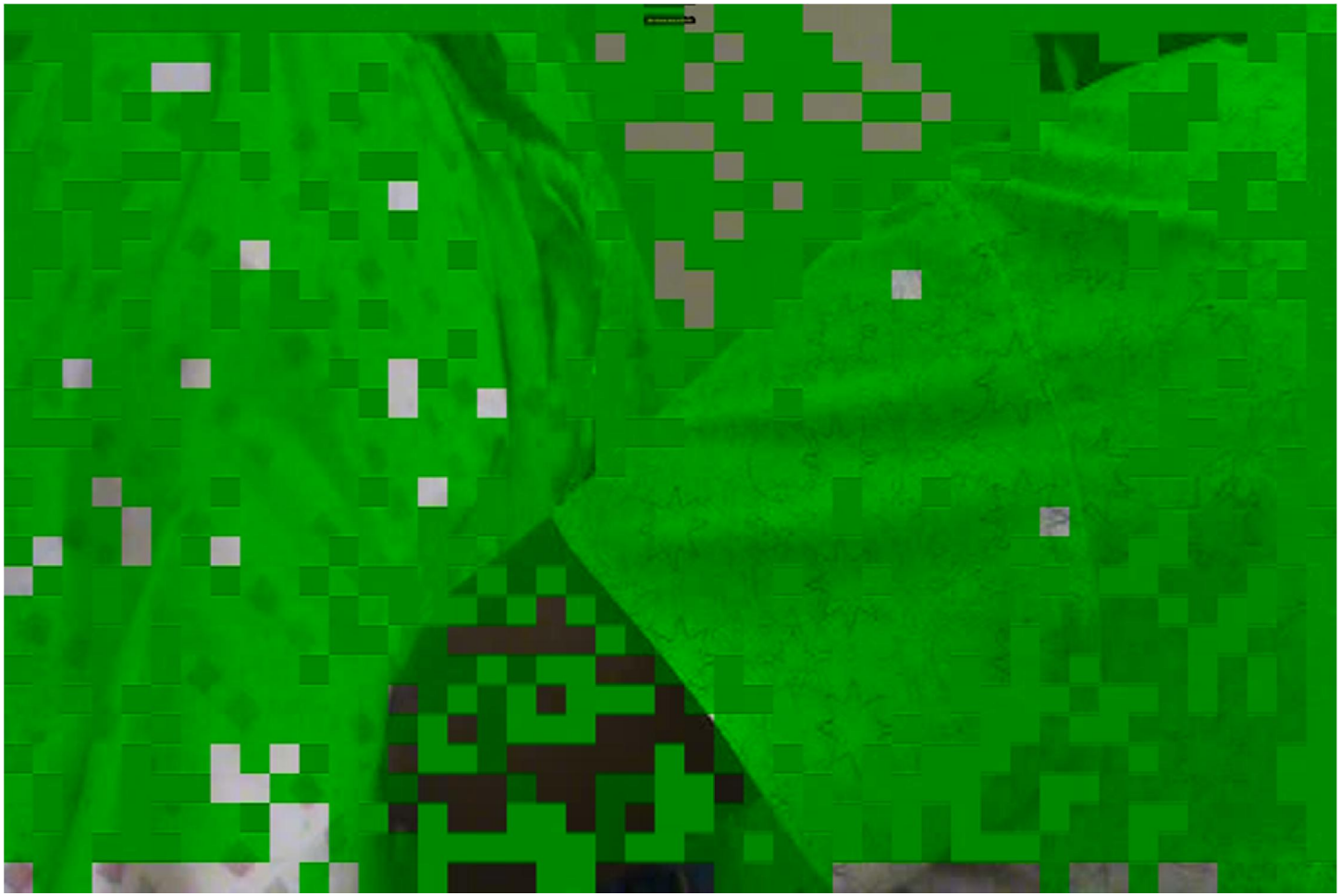
C

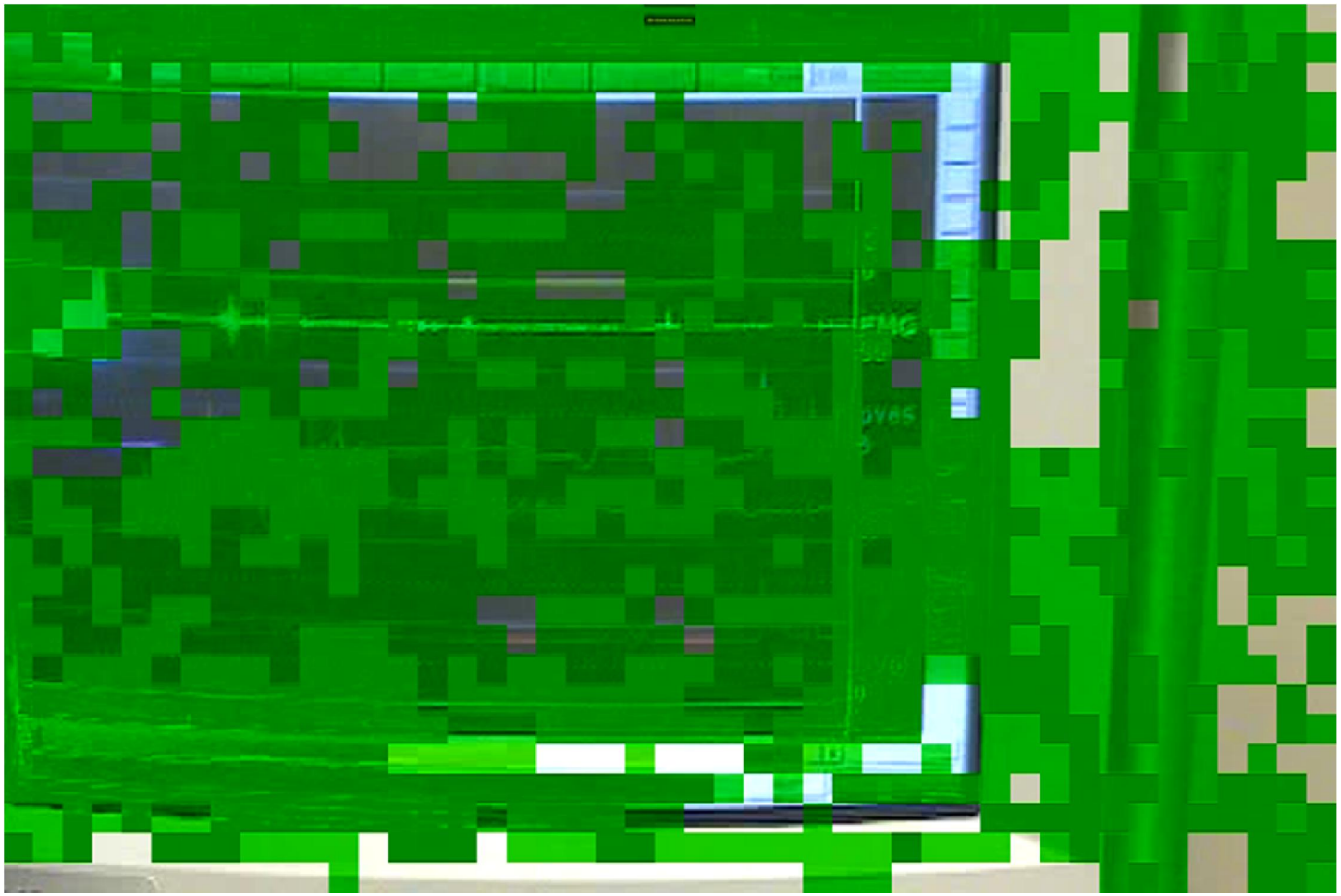


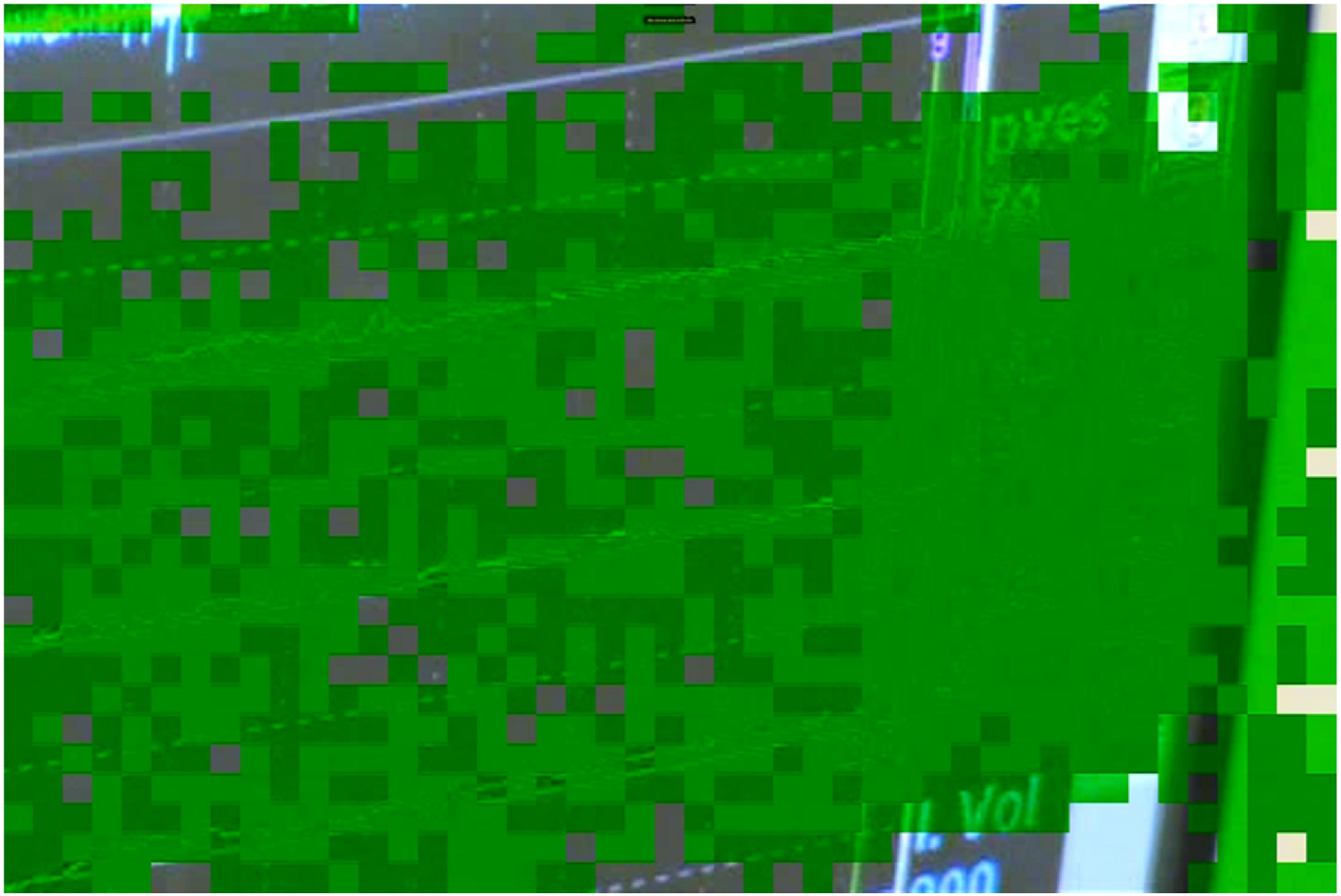
Innovations in Storage: Treatment of SUI

- Increasing uretrhal sphincter function and support using Sling Skill Set
  - Platform Slings
    - Mild to Moderate SUI
    - ~ 75%
  - Suspending Slings
    - Moderate to Severe SUI
    - ~ 20%
  - Circumferential Slings
    - Severe SUI
    - ~ 5%





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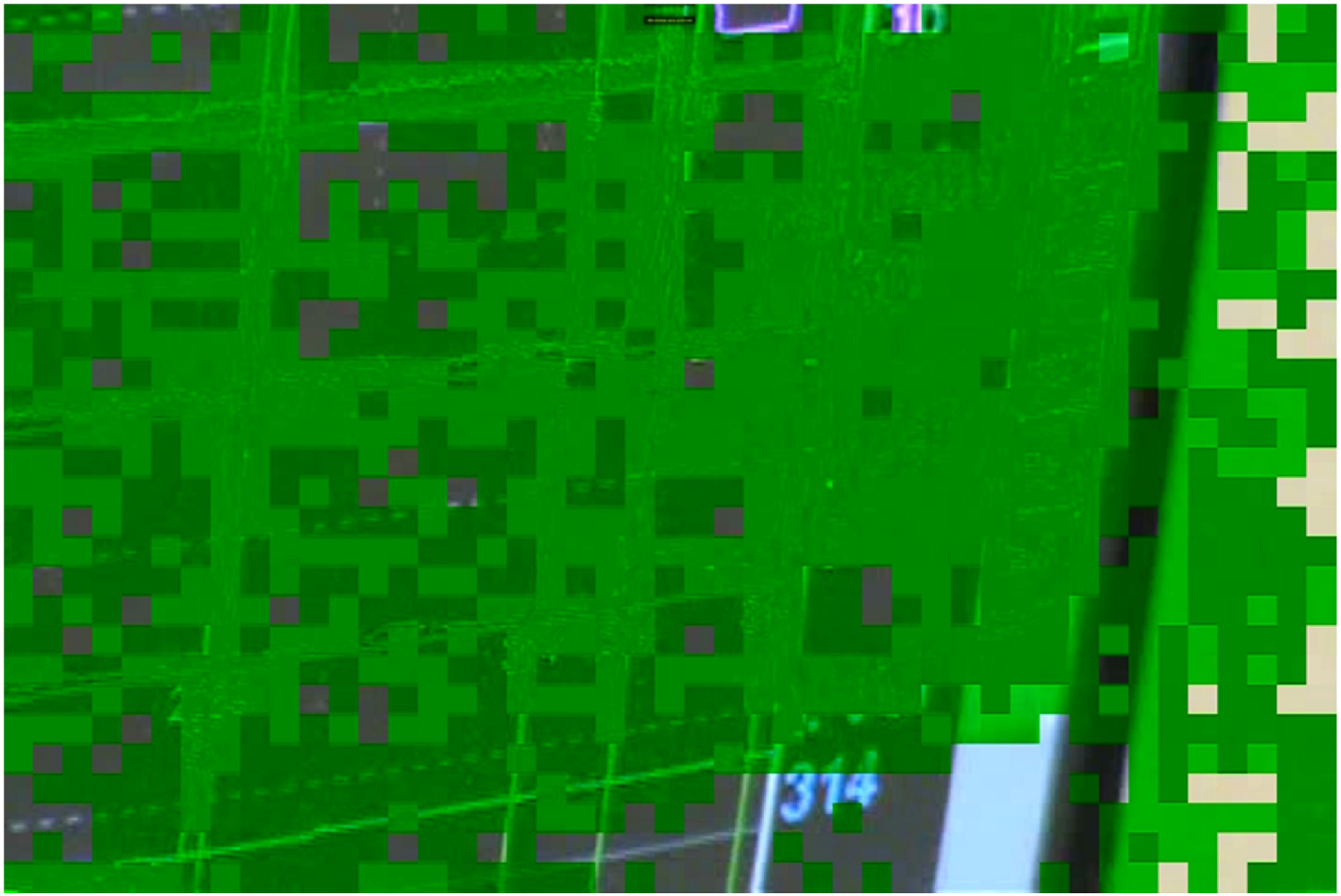
Vol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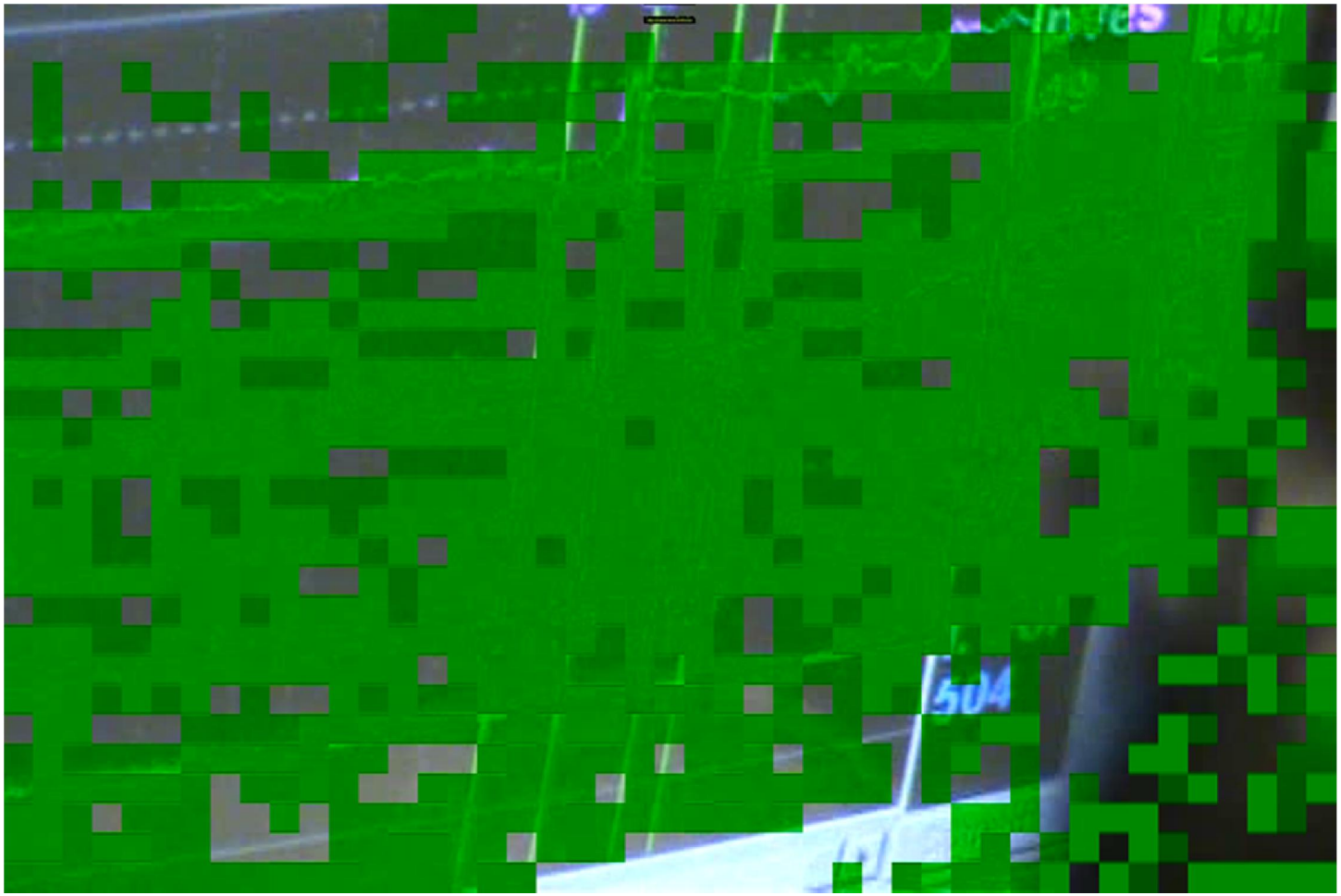

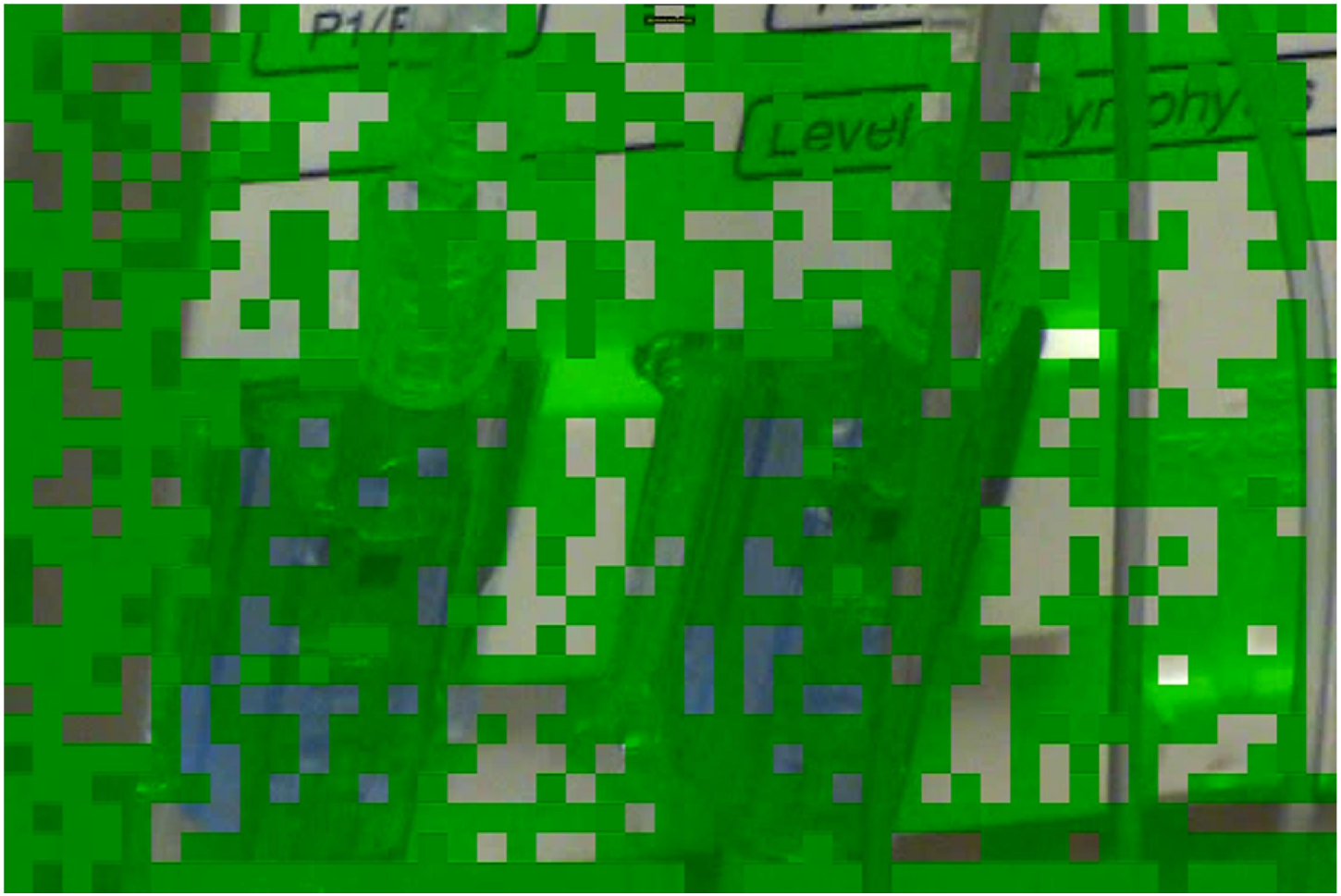
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