

Urgency & Voiding Dysfunction Complicating Cystocele Repair or Incontinence Surgery

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Potential Effect of Prolapse Surgery on Lower Urinary Tract

1. **Straightening of UVJ**
2. **Denervation of Urethra and/or Bladder**
3. **Urethral Fibrosis and Narrowing**
4. **Change in Pressure Transmission Ratio**
5. **Loss of Compression or Obstruction of Urethra by Cystocele, Enterocele or Rectocele.**

Urodynamic Diagnosis - Cystocele

	0 n(%)	1 n(%)	2 n(%)	3 n(%)
USI	113 (18%)	246 (40%)	222 (36%)	32 (5%)
DO	55 (28%)	80 (41%)	48 (24%)	11 (6%)
Normal	30 (16%)	52 (42%)	31 (25%)	10 (8%)

Post Hysterectomy Vaginal Vault Prolapse

Symptoms (n= 693)

Vaginal Protrusion	94%
Stress Incontinence	33%
Urge Incontinence	26%
Voiding Difficulty	20%
Difficulty Defecation	20%

(Webb et al Obstet Gynecol 1998)

102 Continent Women Grade 2 or 3 cystoceles

Anterior
Repair+
Repair

52



4 USI (4%)
1 DO (2%)

Anterior

Kelly Plication

50



4 USI (8%)
1 DO (2%)

2 women required further Rx

Prospective RCTs of Sacrocolpopexy vs SSVVS

- Maher et al

Am J Obstet Gynecol 2004

- Benson et al

Am J Obstet Gynecol 1996

Comparison of Urinary Symptoms Preoperatively in the Abdominal (n=47 women) & Vaginal (n=48 women) Groups

Urodynamic diagnosis	Abdominal	Vaginal	P value *
Stress urinary incontinence	14 (30%)	15 (31%)	1.00
Overactive Bladder	13 (28%)	14 (29%)	1.00
Voiding Dysfunction	13 (28%)	9 (19%)	.34
Occult SI	5 (11%)	6 (13%)	.19

BLADDER FUNCTION

	Abdominal (36)%	Vaginal (39)%	p
De Novo SUI	7	22	
De Novo OAB	34	22	
De Novo Voiding Dysfunction	3	3	

Stress Urinary Incontinence

**Burch +
Sacrococpopexy**

**Burch +
SSVVS**

Cured

79% (11/14)

87% (13/15)

Repeat surgery

14% (2/14)

20% (3/15)

de novo SI

9% (2/22)

33% (8/24)

Overactive Bladder Syndrome

Sacrocolpopexy

SSVVS

Cured

27% (3/11)

37% (4/11)

de novo

34% (12/36)

22% (8/37)

Voiding Dysfunction

Sacrocolpopexy **SSVVS**

Cured

78% (7/9)

80% (4/5)

de novo

3% (1/38)

2% (1/43)

Outcomes from RCT *(Benson et al 1996)*

Outcome	Abdominal n=38	Vaginal n=42
Optimal	22 (58%)	12 (29%)
Satisfactory	10 (26%)	16 (38%)
Unsatisfactory (re-operation)	6 (16%)	14 (33%)
Post-op Incontinence	23%	44%
Dyspareunia	0%	58%
Follow-up	- 25 months -	

Summary Outcomes: Incidence of Occult Incontinence

Prospective Trials: Summary

- 36 - 80% incidence of Occult Incontinence in cases undergoing POP repair
- Incidence reporting confounded by techniques of POP reduction and observation of SUI sign
 - Pessary, swabs, speculum, packing, pad testing, urine dyes etc.

Incidence of SUI after POP Only Repair

3 Trials: Summary

Liang Trial: Vag POP repair & SUI (TVT) / control:

- 62% Occult Incontinence by UDS
- 53% developed SUI post "POP only" repair

CARE Trial: ASC/PV POP repair & SUI (Burch) / control:

- 35% Occult Incontinence by UDS, 19% by symptoms
- 44% developed SUI post "POP only" repair

Reena Trial: Vag "POP only" repairs, no SUI rx

- 68% Occult Incontinence – pad / dye test / pessary
- 44% developed SUI post "POP only" repair

Reena et al., Int J Gyn OB April, 2007

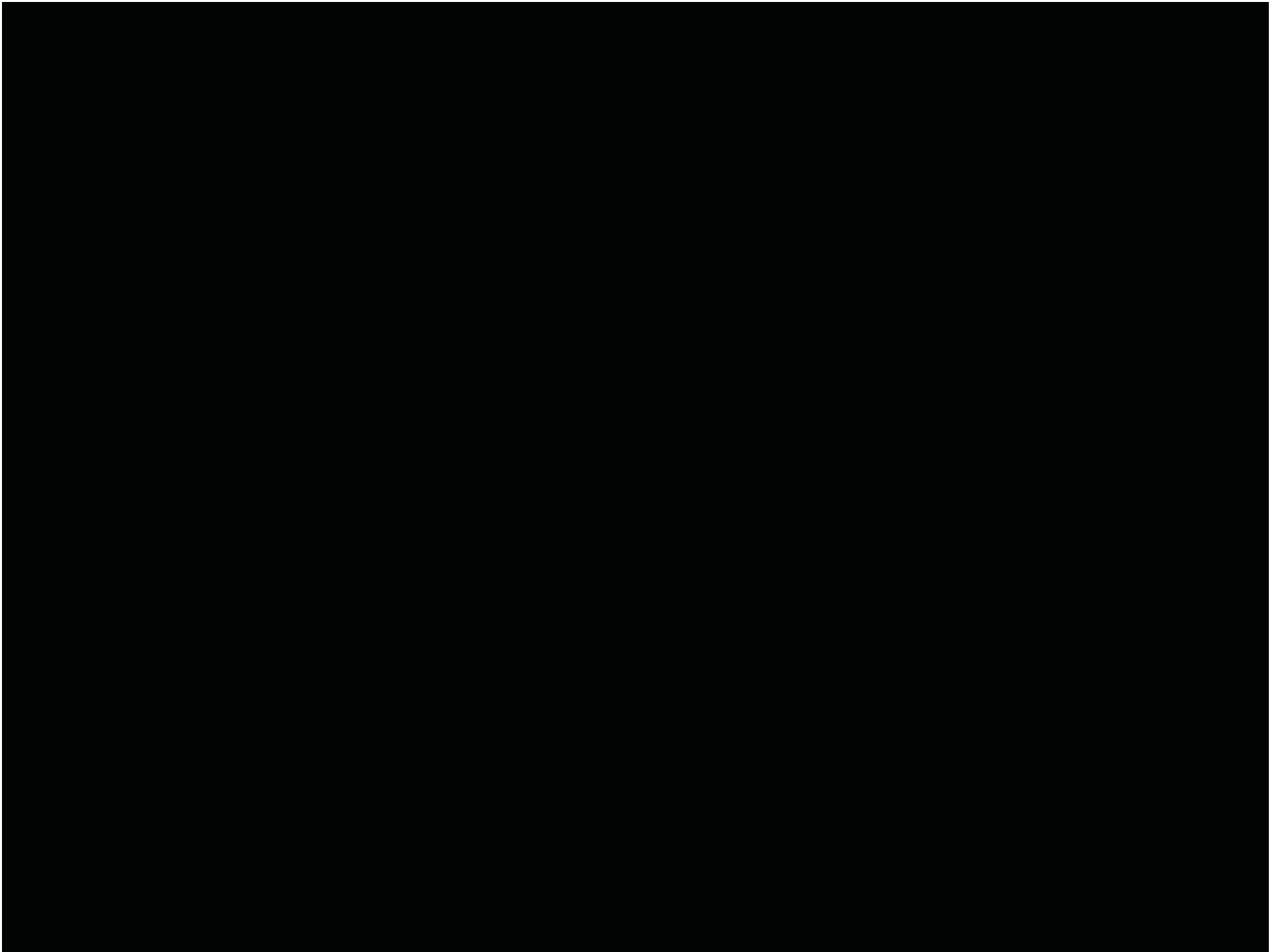
Summary Outcomes:

Stress Incontinence with POP Repairs

- In Severe (Stage 3-4) POP, there is ~ 50% (range 36 - 80%) incidence of Occult Incontinence
- If you only operate on the POP, you will find a ~50% (range 44 - 53%) incidence of SUI after your POP repair
- With Negative History and Negative Stress Test for USI with POP Reduction, the Chance for Developing USI after "POP only repair" is 0%.
- Performing a SUI procedure at the time of POP repairs carries a ~ 10% (range 0 - 37%) incidence De Novo Detrusor Overactivity and may be dependent on the procedure performed
- SUI repair outcomes (objective and subjective) with POP repairs appear to be similar to outcomes in SUI only repair cases

OAB: COPING MECHANISMS (ORIGINAL)







Nonpharmacological Therapy

Benefits and Limitations

Benefits

- ▶ **Scheduled or prompted voiding¹**
 - increase hold interval between voids
- ▶ **Physical therapy¹**
 - Kegel exercises, weighted vaginal cones (can help rehabilitate pelvic floor musculature)
 - Sacral cord feedback loop
- ▶ **Biofeedback¹**
 - Can help the patient isolate the correct muscles to exercise

Limitations

- ▶ **Long-term compliance²**
 - Proper execution is labor- and time-consuming, costly
 - Need for active patient participation, requires intact mental status
 - Gradual results, dry rate 25%-30%

1. Rosenberg MT, et al. *Cleve Clin J Med.* 2005;72:149-156.
2. Borello-France D, et al. *Clin Obstet Gynecol.* 2004;47:70-82.



OAB

Pharmacologic Treatment Overview

- ▶ Oxybutynin IR 2.5 to 5 mg tid
- ▶ Oxybutynin ER 5 to 30 mg qd
- ▶ OxybutyninTDS 3.9 mg/ d
- ▶ Oxybutynin Gel 4mg/ d
- ▶ Tolterodine IR 1 or 2 mg bid
- ▶ Tolterodine ER 2 or 4 mg qd
- ▶ Fesoterodine 4 or 8 mg qd
- ▶ Hyoscyamine 0.125 to 0.375 mg qid/bid
- ▶ Imipramine 25 to 225mg qHS
- ▶ Trospium 20 mg qd/bid
- ▶ Trospium XR 60mg qAM
- ▶ Solefenacin 5 or 10 mg qd
- ▶ Darifenacin 7.5 or 15 mg qd



Behavioral therapy is important, but combined therapy works best

Behavioral
therapy

Combined
therapy

Drug
therapy

Combined
therapy

Mean
reduction
in UI (%)



$P = 0.034$



$P = 0.001$



ALTERNATIVES TO DRUG THERAPY





Acupuncture

- ▶ **Chang (1988) Prospective Sham-Controlled Trial of Posterior Tibial Acupuncture (SP-6)**
- ▶ **52 Women with OAB**
- ▶ **Bladder Capacity ↑88.5% vs. 23.1% of controls**
- ▶ **65% Dry vs. 23% of controls**

Chang PL. J Urol 1988; 140:563-66.



Acupuncture

- ▶ **Emmons & Otto: Prospective Randomized Sham-Controlled Trial in 85 Women with OAB**
- ▶ **87% Completed 4 Weeks of Acupuncture at SP-6 vs Sham**
- ▶ **59% Decrease in UUI vs. 40% in Sham Group**
- ▶ **Significant Reduction in Frequency (14%), Urgency (30%), Voided Volume (13%) and MCC (13%) (p=0.01)**
- ▶ **UDI: 54% vs. 34% Improvement in the Sham Group (p<0.001)**

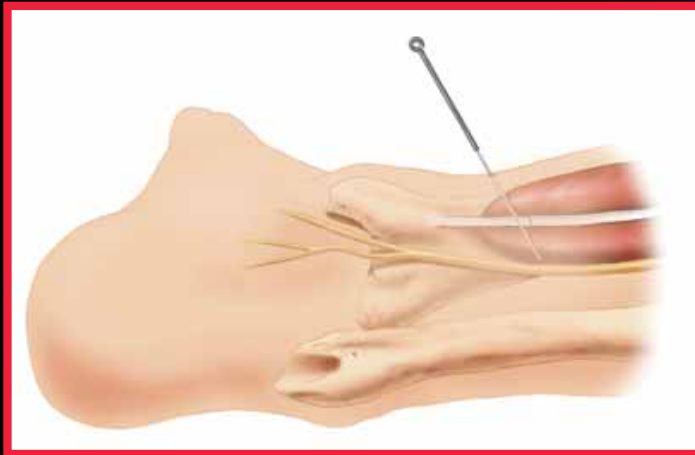


Neuromodulation - Electrical

- ▶ **Electrical stimulation of sacral or peripheral nerves**
- ▶ **Modulates :**
 - **Bladder**
 - **Sphincter**
 - **Pelvic floor muscles**



Treatment with Urgent[®] PC

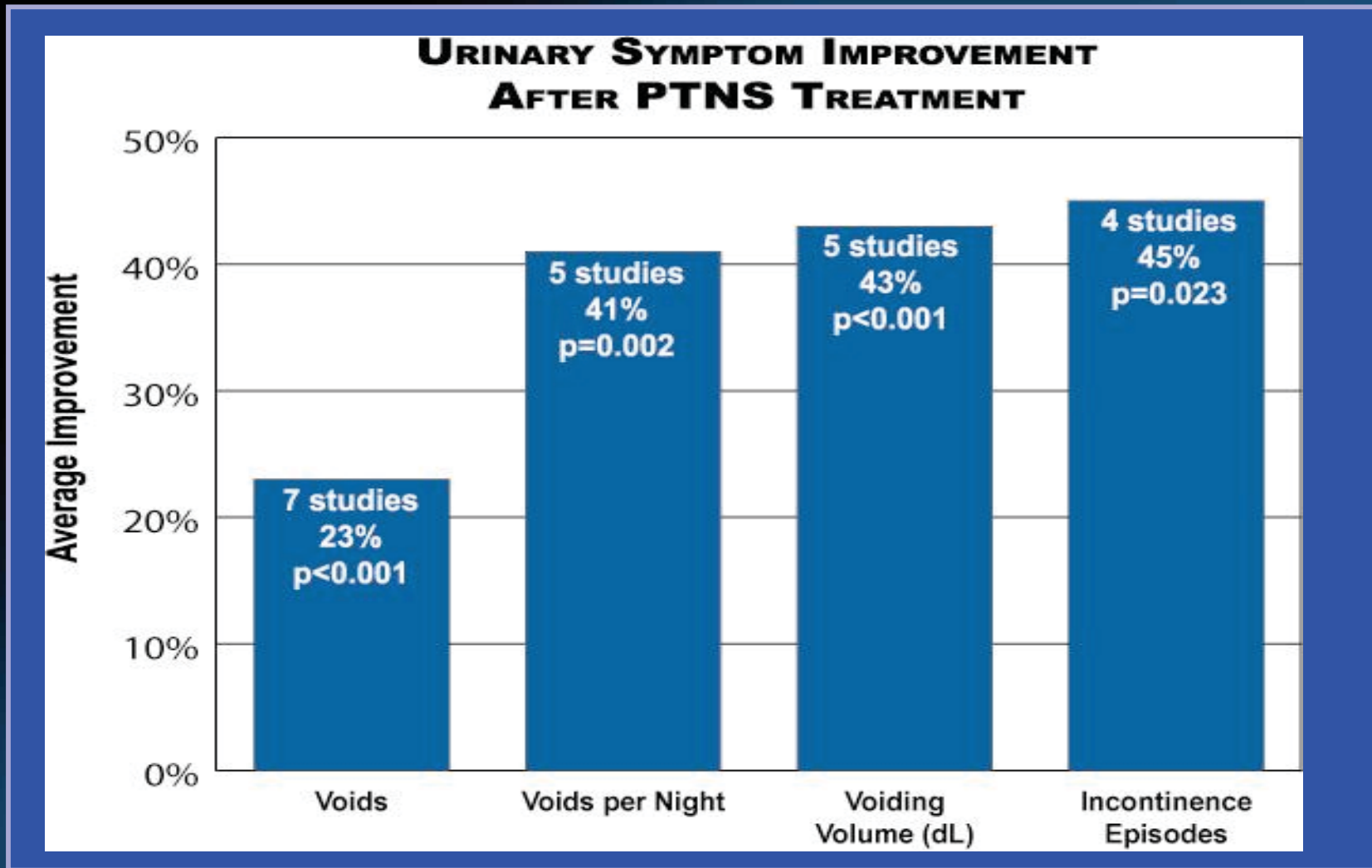


- Provides Percutaneous Tibial Nerve Stimulation (PTNS)

- ▶ Stimulation delivered via a 34 ga. needle electrode
- ▶ Needle electrode inserted above medial malleolus
- ▶ The needle electrode is connected to a battery-powered stimulator



Meta-Analysis of 7 PTNS Studies⁸



8. Martinson, M. (2008). Meta-Analysis of PTNS for Urinary Disorders. Sponsored by Uroplasty, Inc.



PTNS Long-Term Follow-up¹¹

- ▶ **Retrospective analysis of 256 patients (178 were treated for OAB symptoms)**
- ▶ **Sixty percent (107/178) of patients with OAB symptoms were responders**
- ▶ **Results stable at three-year mean follow-up when initial series was followed by maintenance therapy**
- ▶ **Only 10% of patients showed significant reduction of the obtained results**

11. Cappellano F., Finazzi Agro E., Giollo A., Petta F., Catanzaro M., Miano R., Germani S., Catanzaro F. (2006). Percutaneous tibial nerve stimulation (PTNS): results at long term follow-up. Abstract presented at the SIUD Congresso Nazionale 2006, 27-30 September, Rome, Italy.



What is InterStim Therapy?

- ▶ **Implantable, Programmable Sacral Neurostimulation System**
- ▶ **Therapy consists of 2 steps:**
 - 1. Test stimulation procedure – External Stimulator for 2-4 weeks**
 - 2. Implantation of neurostimulator (IPG)**



InterStim[®] Test Stimulation Procedure

- ▶ **done under local anesthetic**
- ▶ **outpatient procedure**



MULTINATIONAL CLINICAL RESULTS

- ▶ URGE INCONTINENCE:
 - 47% DRY
 - 28% WITH SIG IMPROVEMENT
- ▶ OAB: 76% WITH > 50% REDUCTION IN Frequency
- ▶ ADVERSE EVENTS: 15.3% (>50% due to lead migration)
- ▶ PATIENT SATISFACTION RATE: 84%



MULTINATIONAL CLINICAL RESULTS: 5 Year F/U

- ▶ URGE INCONTINENCE, OAB Dry & Retention (N=163)
- ▶ Leakage Decreased from 9.6 to 3.9/ day
- ▶ Frequency Decreased from 19.3 to 14.8/ day
- ▶ Voided Volume Increased from 92 to 165 ml
- ▶ 84% of UUI Patients & 71% with OAB Dry who were Successful at 1 year were Successful at 5 years



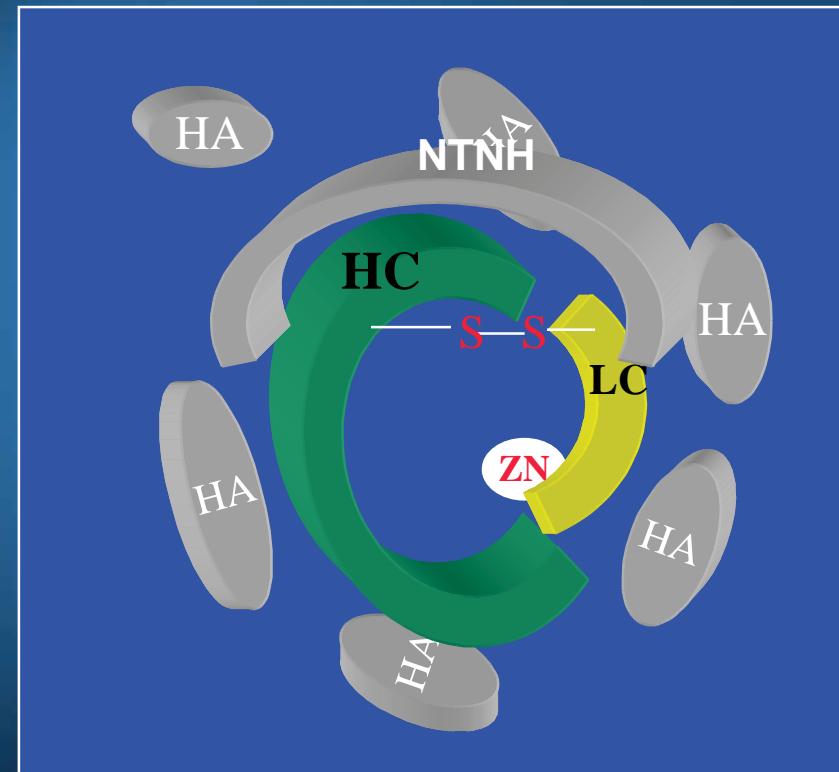
Botulinum Toxin

Structural Complex

Seven Serotypes A, B, C1, D, E, F, G

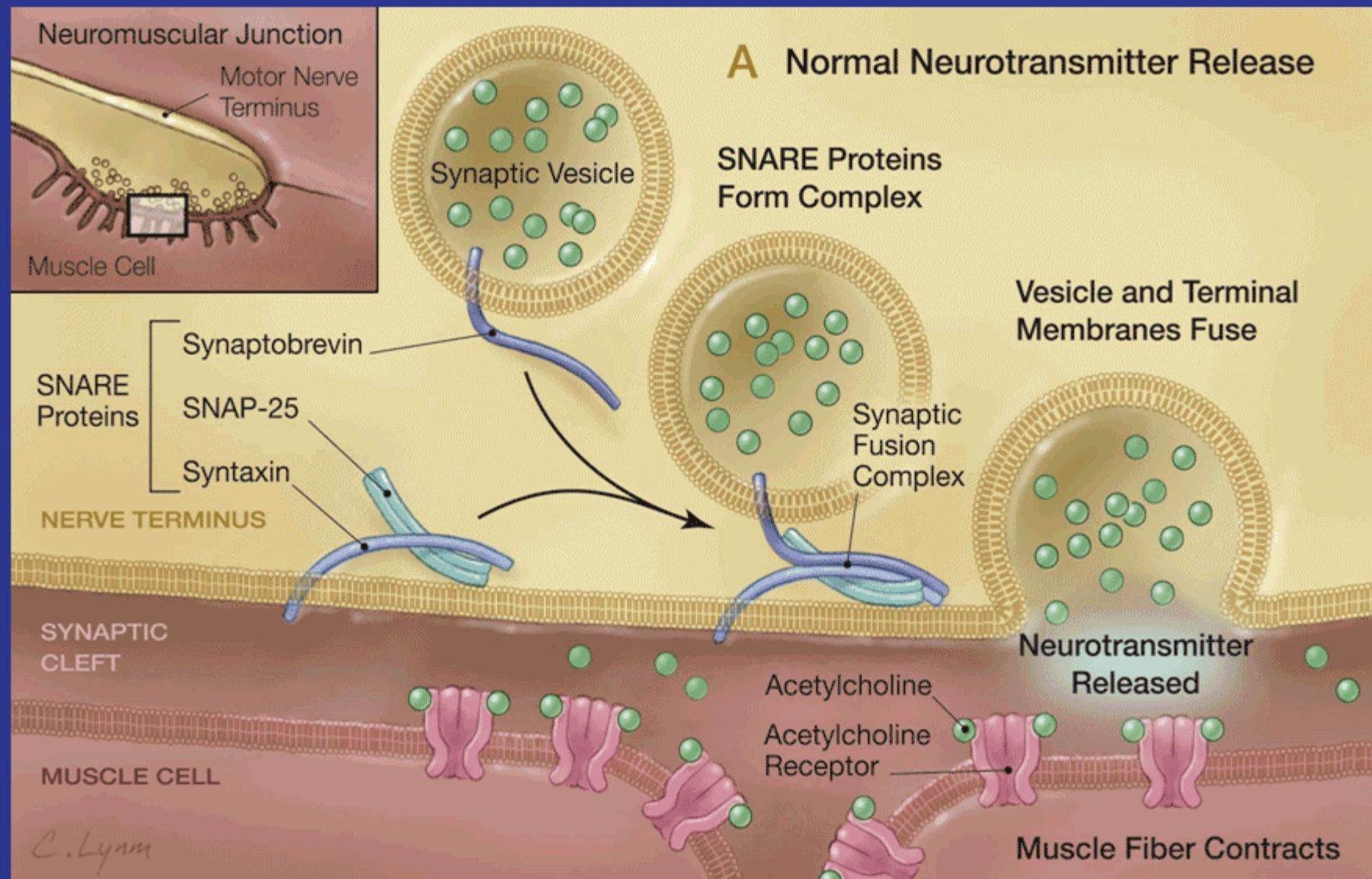
Neurotoxin Complex

- ▶ Di-chain 150kD neurotoxin component
- ▶ Di-sulfide bond
- ▶ Zn⁺ (metalloprotease)
- ▶ +/- non-hemagglutinin (NTNH) protein
- ▶ +/- hemagglutinin (HA) protein

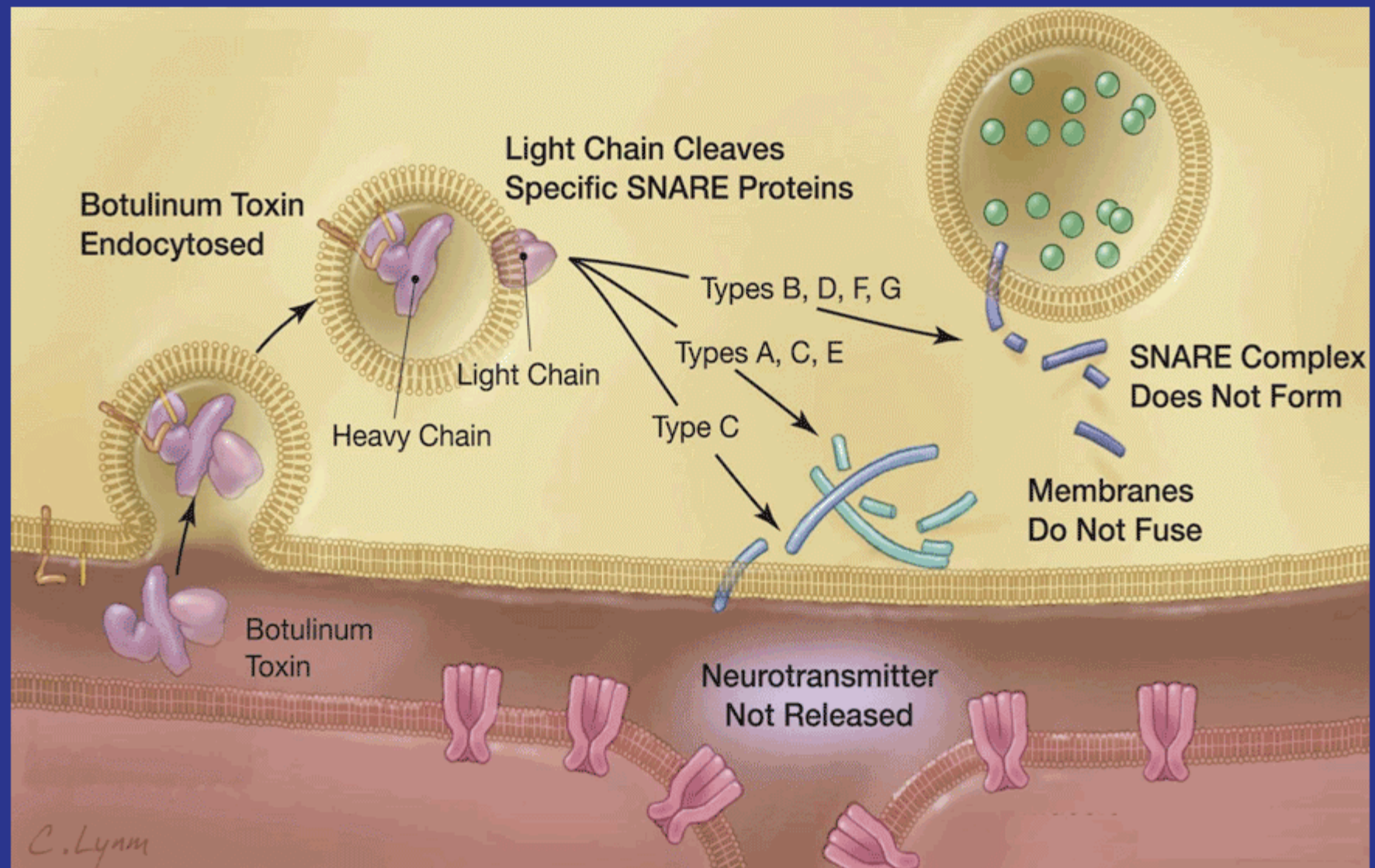


Example: 900 kD Complex (Type A)

Normal Neurotransmitter Exocytosis

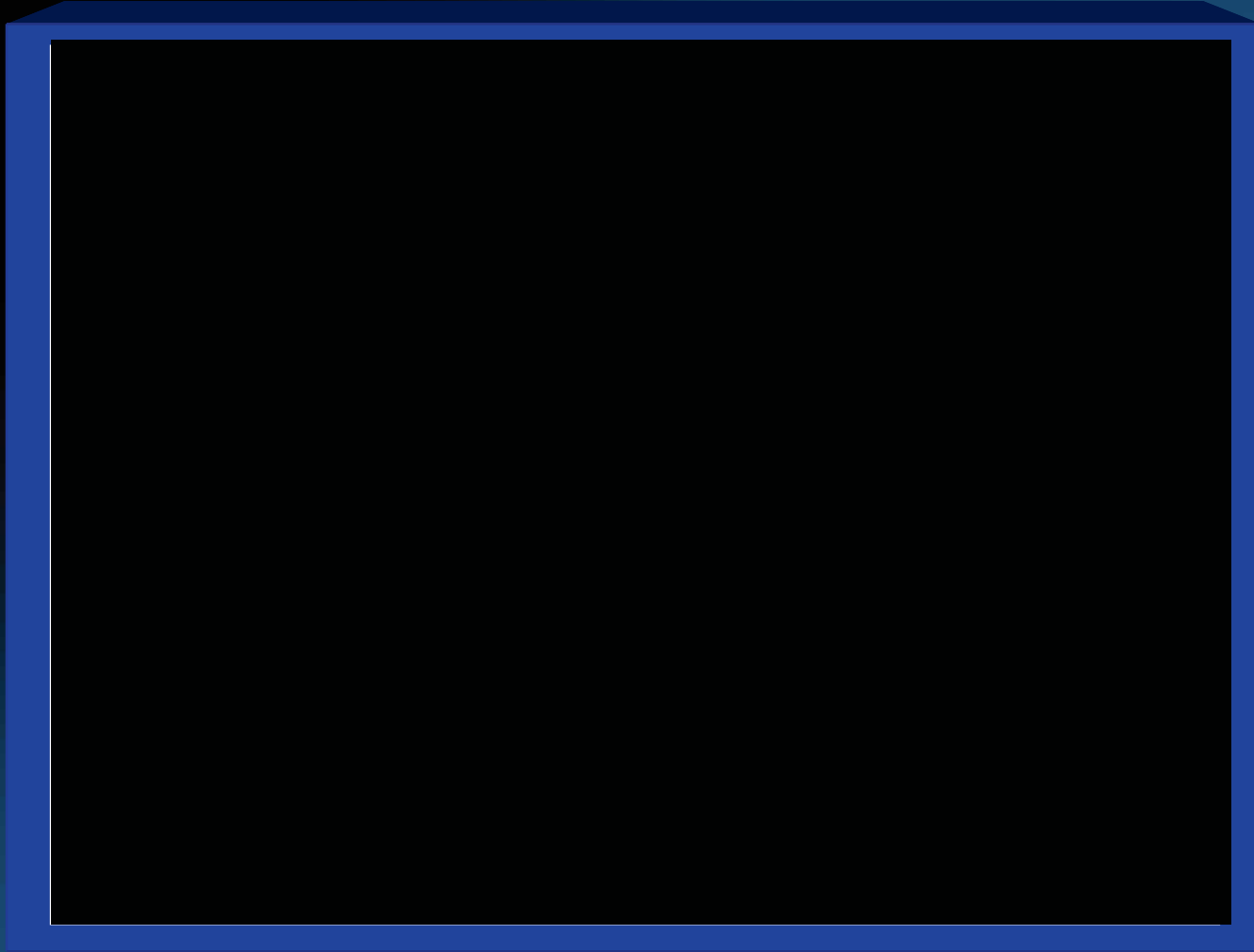


Neurotransmitter Exocytosis: Intracellular Inhibition with BoNT





Botulinum Toxin Bladder Injection Video





Botulinum Toxin

Neurogenic OAB

- ▶ **59 patients**
 - 53 spinal cord injury
 - 6 multiple sclerosis
- ▶ **Poorly responsive to medical therapy**
- ▶ **Prospectively randomized 1:1:1 to**
 - Placebo (21 patients)
 - 200 units BoNT-A (19 patients)
 - 300 units BoNT-A (19 patients)
- ▶ **Patients followed for 24 weeks**



Botulinum Toxin - Neurogenic OAB

Clinical Response

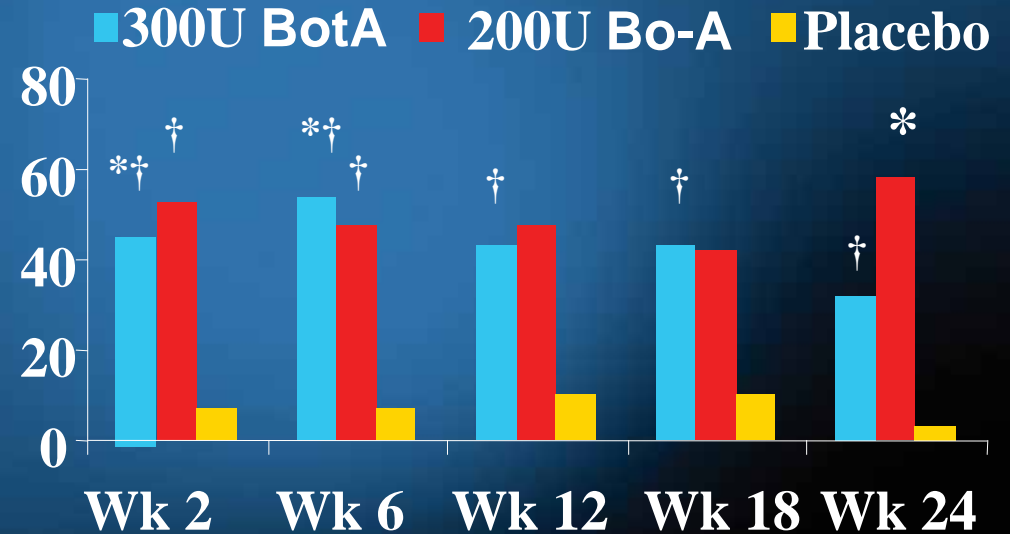
▶ Baseline incontinence episodes/day

- Placebo – 3.0
- 200 U – 1.9
- 300 U – 2.8

▶ Dry Rate

- Placebo – 24% (5/21)
- 200 U – 74% (14/19)
- 300 U – 53% (10/19)

Reduction in number of UI episodes compared to baseline (%)



* $p < 0.05$ for differences between BoNT-A group and placebo

† $p < 0.05$ for difference within-group changes from baseline



Botulinum Toxin

Non-Neurogenic (Idiopathic) OAB

- ▶ 100 patients
- ▶ Refractory to anticholinergics
- ▶ Treated with 100 U BoNT-A (BOTOX™)
- ▶ Clinical results
 - Resolution of urgency – 82%
 - Resolution of incontinence – 86%
 - Frequency decreased from 14→7
 - Nocturia decreased from 4→1.5
- ▶ Mean duration of effect 9 months



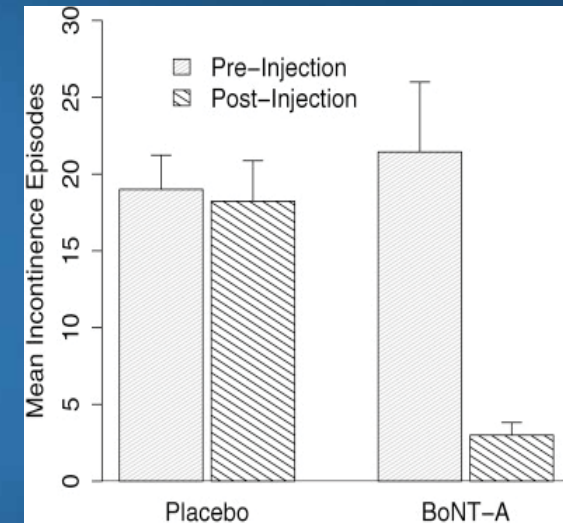
Botulinum Toxin

Non-Neurogenic (Idiopathic) OAB

Randomized controlled trial (UITN Trial)

200 U BoNT-A (Botox™)

- ▶ Randomization 2:1
 - 28 BoNT-A:15 to placebo
- ▶ BoNT-A significantly better than placebo
 - Mean PGI-I* score (2.7 vs. 4, $p=0.003$)
 - Number of incontinence episodes/day ($p<0.0001$)
 - Patient perception of symptom control ($p<0.0001$)
- ▶ Study placed on clinical hold secondary to higher than expected rates of elevated PVR and associated UTI





Botulinum Toxin

Idiopathic OAB

Randomized controlled trial - Sahai, et al

- ▶ 200 U BoNT-A (Botox™)
- ▶ 16 pts BoNT-A and 18 pts Placebo
- ▶ Significant QOL improvements at 4 & 12 wks
- ▶ Durable effects (10 Months)

	Baseline placebo/BTX	4 weeks placebo/BTX	12 weeks placebo/BTX
Urgency	3.91/4.98	3.17/1.9*	3.2/1.48**
MCC (ml)	198/182	169/313#	168/264+
Max detrusor pressure (cm H ₂ O)	79/85	75/35 #	79/44 #

*p=0.0284
 **p=0.0076
 #p<0.0001
 +p=0.0011



Botulinum Toxin

Non-Neurogenic (Idiopathic) OAB

Urinary Retention – idiopathic OAB studies

- ▶ 100 U Botox™: Temporary urinary retention in 4/100 pts¹
- ▶ 200 U Botox™: Symptomatic PVR (>150 ml) in 6/18 pts²
- ▶ 200 U Botox™: Increased PVR (>200 ml) in 12/28 pts³
- ▶ 300 U Botox™: Zero incidence of urinary retention⁴
- ▶ 500 U Dysport™: CIC/SP in 8/23 pts at 3 mos, 4/22 pts at 6 mos⁵

1. Schmid, et al, J Urol, 2006
2. Sahai, et al, J Urol, 2007
3. Brubaker et al, J Urol, 2007
4. Rapp, et al, Urolog, 2004
5. Jeffrey, et al, BJU Int, 2007



Botulinum Toxin

Non-Neurogenic (Idiopathic) OAB

Urodynamic identifiers of poor outcomes

- ▶ **Schmid, et al¹**
 - 100 units BoNT-A
 - Poor response in 8/100 pts → poor detrusor compliance

- ▶ **Sahai, et al²**
 - 200 units BoNT-A
 - Responders (25/33 pts) → average baseline max Pdet=74.4 cm H₂O
 - Poor responders (5/33 pts) → average baseline max Pdet=138 cm H₂O
 - Pretreatment max Pdet > 110 cm H₂O may predict poor response

1. Schmid, et al, J Urol, 2006
2. Sahai, et a, Urology, 2008



Botulinum Toxin

Duration/Repeat Injection

▶ Duration

- Neurogenic - therapy lasted an average of 9 months (range 6-14 months)¹
- Non-neurogenic - duration of clinical benefit average of 9 months²

▶ Repeat Injection³⁻⁵

- As effective as first injection
- No tolerance noted*
- No increase in adverse events noted

*Potential for antibodies does exist

1. Reitz, et al, Eur Urol, 2004
Urol, 2007

2. Schmid, et al, J Urol, 2006
Int, 2007

3. Grosse, et al, Eur Urol, 2005

4. Reitz, et al, Eur

5. Akbar, et al, BJU

UPDATE IN GYNECOLOGIC UROLOGY IN ST. JOHN

FEBRUARY 5-7, 2010

