Evaluating Women with Bladder & Pelvic Floor Dysfunction

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Disclosures

- None (re: Industry, Pharmaceutical)
- Expert Witness
- Investor
Pelvic Organ Prolapse:

“What’s all this I hear about this ‘bad Mesh’”? 
Three walls

- Cystocele = anterior
- Apex = vault & enterocele
- Rectocele = posterior
Prolapse Presentation

“Bulge”, “Pressure”

- Anterior wall
  - Incontinence
    - SUI may be masked!
  - Obstructive voiding
    - Elevated PVR
    - UTI

- Apex
  - Bulging or mass

- Posterior wall
  - Stool trapping
  - Digital splinting
  - Beware of constipation!
Staging

- Baden-Walker
  - Grade 0-4
  - Uses introitus as border between grade 2 and 3
- Pelvic Organ Prolapse Quantification (POP-Q) grading
  - Introduced in 1996 as a ‘standardized’ approach
  - Best for application in research trials
  - Not widespread in use (Gyn > GU)
Staging through History

1963 Severity (Porges)
- Slight or 1st Degree
- Moderate or 2nd Degree
- Marked or 3rd Degree

1972 Vaginal Profile (Baden)
- Grade 1
- Grade 2
- Grade 3
- Grade 4

1980 Grading System (Beecham)
- Midplane of vagina
- Hymeneal ring
- Introitus
- 1st Degree
- 2nd Degree
- 3rd Degree

1996 Quantitative POP (ICS, AUGS, SGS)
- Stage I
- Stage II
- Stage III
- Stage IV

At Rest
- Complete eversion

 OU WB Beaumont Health System
What are the Treatment Options?

• Observation
  – Always an option if patient is asx’c and < Grade 4
  – 64 women monitored in one study for median 16 months
  – 78% no change in leading edge ≥ 2 cm
  – 19% progressed
  – 63% continued observation
Pelvic Floor PT / Strengthening

- Randomized, small n studies
  - Stage 1-2 prolapse

- Symptomatic improvement

- One-stage improvement in 18% vs 8% of placebo in one study

- Lifestyle changes to minimize increase in abdominal pressure
Pessary Reduction

- Hippocrates (5th cty BC)
  - Half a pomegranate dipped in wine
- Reasons to use
  - No desire for surgery
  - Unable to tolerate surgery
  - Postpone surgery
  - Child-bearing
  - Diagnostic tool
Pessary Use for POP

• Short-term satisfaction 63-90%,
  – Long-term studies vary (14% at 14 years vs 86% at 5 yrs)

• PESSRI study
  – Randomized study of ring vs Gellhorn
  – 12 week follow up
  – Improvement in questionnaire scores in both groups equally
How Are We Doing With Our Current Surgical Procedures?

• 11.1% lifetime risk of surgical intervention

• 29-40% of reconstructive procedures require surgical reintervention for failure within 3 years

• 60% of recurrences are at the same site

• 32.5% occur at a different site due to unmasking of an occult support defect

• Reoperation is the “tip of the iceberg”

1 Olson et al. Obstet and Gynecol 1997;89:501-506
3 Clark et al. Am J Obstet and Gynecol 2003;189:1261-1267
Surgical Repair
Native Tissue

- Anterior
  - Anterior colporrhaphy, anterior wall suspension
- Posterior
  - Posterior colporrhaphy, levator myorrhaphy
- Apical
  - Sacrospinous ligament fixation
  - Uterosacral ligament fixation
Prolapse History

• Anterior repair 30-60% failure @ 2 years
  – Anatomically not logical…
• Anterior compartment reinforced with “patch”
  – Biologic (1996)
  – Mesh (1999)
• Anterior / apical / posterior mesh “kits” (2005)
  – Novel anchoring = better / easier / faster
All Meshes are Not Created Equal

Erosion rates for materials

- Marlex
- Teflon
- Mersilene
- Goretex
- Polypropylene

Urogynecologic Surgical Mesh:
Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse

July 2011
October 2008: Public Health Notification
Followed the MAUDE database to 2010
– 2874 complications reported (1500+ for POP)
Mesh complications are NOT rare
Transvaginal mesh repairs does not conclusively improve clinical outcomes over traditional non-mesh repair
Transvaginal Mesh Lawsuit

Transvaginal Mesh Implant Lawsuit
Have you or a loved one suffered injuries from a vaginal mesh implant?

Contact Us For A Free Case Evaluation
Speak Directly to an Attorney at (855)385-2529
or click here to contact us online

TO PAY $5.7M IN MESH LAWSUIT
Prospective Randomized Trials:

- **Finland** (Hiltunen R, Nieminen K, Takala T. et al. Low-Weight Polypropylene Mesh for Anterior Vaginal Wall Prolapse: A Randomized Controlled Trial. Am Col Ob Gyn, August 2007; n = 202)

- **USA** (Nguyen, et al. Outcome After Anterior Vaginal Prolapse Repair: A Randomized Controlled Trial OBST & GYN VOL. 111, 2008; n = 76)

- **Nordic group** (Altman D, Vayrynen T, Engh ME. Anterior colporrhaphy versus transvaginal mesh for pelvic-organ prolapse. NEJM 2011; 364(19):1826-1836) n = 389

Mesh Outcomes

• Prolapse repair
• All show improved objective outcomes
  – Anterior repair failure rate 30-60% → 4-8%
    • Leading edge at hymen (grade 3)

• But… Do patients feel better?
  – Newer data better “bulge” subjective symptoms
Risks of Prolapse Repair

• Any vaginal surgery (native tissue / mesh)
  – Surgical
  – Dyspareunia
  – Pelvic Pain
  – Re-operation rate

• Mesh specific
  – Mesh Exposure
  – Mesh Erosion
  – Mesh Contracture
Defining Terms

• Mesh Erosion = BAD
  – Mesh into adjacent organ
  – Bladder / urethra / bowel

• Mesh Exposure
  – Clinically less of a problem
  – Often asymptomatic
  – Usually easy to manage

Beaumont < 1%
Beaumont 8%
Erosion
Mesh Exposure

• Meta analysis = 10.3%
  – Risk Factors: young age, smoking, diabetes, inverted “T” incision, and increased sexual activity

• Beaumont experience = 8.1%
  – Risk Factors: ΔHgb and lower BMI

• Most are asx’c, ½ have excision

Sirls LT, McLennan GP, Killinger KM et al, FPMRS, 2013
Controversies

• Mesh was well studied
  – There was sufficient clinical data before release
  – There was adequate surgeon training available
  – Surgeons did know risks
But…
  – Inexperienced surgeons

We should police ourselves
What are the issues 2015?

• Dyspareunia
  – If native tissue
    • May relax as scar softens, tissue remodels
  – If mesh
    • May never improve, mesh does not change
    • Why it works better?
    • Exception
      – Palpable arms / pain / lyse
Cystocele Repair 2014

Are you wrong if you use native tissue
NO

Are you wrong if you use mesh
NO

Patient Selection and Counseling
Why Are Slings Included In The Controversy?

• Midurethral Mesh Slings = Gold Standard
  – Minimally invasive
  – Widely studied

• Same Mesh
  – Cast a wide net

• Mesh related complications
  – Erosion
  – Exposure
  – Dyspareunia
Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence

The polypropylene mesh midurethral sling is the recognized worldwide standard of care for the surgical treatment of stress urinary incontinence. The procedure is safe, effective, and has improved the quality of life for millions of women.


Introduction
The purpose of this position statement by the American Urogynecologic Society (AUGS) and the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU) is to support the use of the midurethral sling in the surgical management of stress urinary incontinence, the type of urine leakage generally associated with coughing, laughing and sneezing.
Chronic Pelvic Pain / IC:
What exactly is “IC”? 
DEFINITION OF IC/BPS

• SUFU Definition: “An unpleasant sensation (pain, pressure discomfort) perceived to be related to the bladder, associated with lower urinary tract symptoms of more than six weeks duration, in the absence of infection or other identifiable causes.

• Often exists with other unexplained conditions
  – Chronic fatigue, Sjogren’s syndrome, fibromyalgia, IBS, vulvodynia, chronic headaches
Clinical Presentation

- Urinary Frequency
- Urinary Urgency
- Pelvic pain
  - Worse with bladder filling
  - Relieved with voiding
- Symptoms worse with stress
- Dyspareunia
- Vulvodynia
- Failed antibiotic therapy
- Failed anticholinergics
- Bowel dysfunction
- Fibromyalgia
- Allergies
- Chronic fatigue
- Autoimmune disorders
- Food sensitivities
- Migraine Headaches
Differential Diagnosis

• Recurrent UTI
• Urethral Stricture
• Bladder Cancer
• Urethral Diverticulum
• Neurogenic Bladder
• Psychological issues
• Vulvodynia
• Detrusor instability, OAB
• Pelvic Floor Dysfunction
• TB, Schistosomiasis
• Endometriosis
• Fibromyalgia
IC/BPS: An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than six weeks duration, in the absence of infection or other identifiable causes.

The evidence supporting the use of Neuromodulation, Cyclosporine A, and BTX for IC/BPS is limited by many factors including study quality, small sample sizes, and lack of durable follow up. None of these therapies have been approved by the U.S. Food and Drug Administration for this indication. The panel believes that none of these interventions can be recommended for generalized use for this disorder, but rather should be limited to practitioners with experience managing this syndrome and willingness to provide long term care of these patients post intervention.

**Basic Assessment**
- History
- Frequency/Volume Chart
- Post-void residual
- Physical examination
- Urinalysis, culture
- Cytology if smoking hx
- Symptom questionnaire
- Pain evaluation

**Dx Urinary Tract Infection**
- Signs/Symptoms of Complicated IC/BPS
  - Incontinence/OAB
  - GI signs/symptoms
  - Microscopic/gross hematuria/sterile pyuria
  - Gynecologic signs/symptoms

**TREAT & REASSESS**

**Consider:**
- Urine cytology
- Imaging
- Cystoscopy
- Urodynamics
- Laparoscopy
- Specialist referral (urologic or non-urologic as appropriate)

**Clinical Management Principles**
- Treatments are ordered from most to least conservative; surgical treatment is appropriate only after other treatment options have been found to be ineffective (except for treatment of Hunner’s lesions if detected)
- Initial treatment level depends on symptom severity, clinician judgment, and patient preferences
- Multiple, simultaneous treatments may be considered if in best interests of patient
- Ineffective treatments should be stopped
- Pain management should be considered throughout course of therapy with goal of maximizing function and minimizing pain and side effects
- Diagnosis should be reconsidered if no improvement w/in clinically-meaningful time-frame

**First-Line Treatments**
- General Relaxation/Stress Management
- Pain Management
- Patient Education
- Self-care/Behavioral Modification

**Second-Line Treatments**
- Appropriate manual physical therapy techniques
  - Oral: amitriptyline, cimetidine, hydroxyzine, PPS
  - Intravesical: DMSO, heparin, Lidocaine

**Third-Line Treatments**
- Cystoscopy under anesthesia w/ hydrodistension
- Pain Management
- Tx of Hunner’s lesions if found

**Fourth-Line Treatments**
- Neuromodulation
- Pain Management

**Fifth-Line Treatments**
- Cyclosporine A
- Intradetrusor BTX
- Pain Management

**Sixth-Line Treatments**
- Diversion w/ or w/out cystectomy
- Pain Management
- Substitution cystoplasty

**Research Trials**
- Patient enrollment as appropriate at any point in treatment process

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Diagnostic

- **Basic:** UA, culture, consider cytology if microhematuria present
- Potassium sensitivity test **not** recommended
- Cystoscopy **not** necessary in “uncomplicated cases”
TREATMENT STRATEGIES

- Begin with conservative therapies
  - Multiple concurrent treatments may be considered
- Ineffective treatments should be stopped once a clinically meaningful interval has elapsed
- Pain management should be continually assessed for effectiveness and engage other specialists
- Diagnosis of IC/BPS should be reconsidered if not improvement occurs after multiple treatments
  - “Look for something else!”
AUA GUIDELINES—Second Line Therapies

• **Physical therapy**
  – Resolve pelvic floor, abdominal, and/or hip muscle trigger points
  – Lengthen contracted muscles
  – Release scar tissue and connective tissue restrictions.
  – Beware of the therapist who offers “more Kegel exercises”

• **Pain management**
  – Drugs, stress management, manual therapy
  – Opioid painkillers
  – Complementary therapies

• **Oral medicines (alphabetical)**
  – Amitriptyline 10-25 mg qhs
  – Cimetidine (Tagamet)
  – Hydroxyzine (Vistaril, Altarax)
  – Pentosan Polysulfate* (Elmiron)

• **Bladder instillations**
A word about Elmiron

Pentosan Polysulfate Sodium for Treatment of Interstitial Cystitis/Bladder Pain Syndrome

- Randomized placebo controlled trial of 100 mg tid Elmiron to placebo
- Primary endpoint reduction in 30% of ICSI scores at 24 weeks
- No difference between two groups
Bladder Instillations

• DMSO (dimethyl sulfoxide)
  – May reduce inflammation, cause detrusor relaxation, or may ‘damage’ wall to allow meds to penetrate
  – Two randomized controlled trials (?unblinded by the scent)
  – 50 mL weekly or biweekly x 6-12 weeks, 15 minute retention

• Heparin sulfate
  – Exogenous GAG layer, anti-inflammatory, anti-proliferative effect
  – 10,000-20,000 U with cocktail
  – Alternatives: hyaluronic acid, polypentosan sulfate (Elmiron)
Bladder Instillations

• Lidocaine
  – Must alkanilize with 8.4% sodium bicarbonate
  – Bupivacaine (Marcaine) does not need alkaninization
  – Useful as a ‘rescue’ agent or as a diagnostic tool
  – Short term efficacy

New studies show promise for the lidocaine “pretzel”
Liposomes

- Concentric phospholipid bilayers
- Replace GAG layer
- Animal model studies show promise
- Enrolling patients for this study at William Beaumont Urology Research Center
  – 248-551-3565
- Cystoscopy & Hydrodistension under anesthesia
  - General or regional anesthesia needed
  - Look for Hunner’s lesions, stones, or tumors
  - See if bladder has become small and contracted
  - Keep time short (less than 10 minutes)
  - Keep pressure low (60 to 80 cm of water)

- Plan to ease post-op pain
  - Instillation of anesthetic during the procedure or other pain management techniques can reduce post-op pain

- Treat Hunner’s lesions
  - Electrocautery or laser surgery
  - Steroid triamcinolone (Kenalog) injection
Hunner’s Ulcer

- **Ulcerative IC** is defined as symptoms of urinary frequency and/or urgency and pelvic pain with documentation of an ulcerative lesion in the bladder on cystoscopic evaluation.
- (only in **5-10% of the IC cases**)

AUA GUIDELINES—Fourth Line Therapy

- Neuromodulation / InterStim (Medtronic)
  - Indicated for urinary frequency and urgency

- Not indicated or FDA-approved for pain, but may help secondarily with pain
AUA GUIDELINES—Fourth Line of Therapy

- **Botulinum toxin A**
  - Injected into bladder muscle
  - May have some benefit in IC/BPS pts with trigonal, bladder neck injections
  - May require temporary self-catheterization


*Cyclosporine A for refractory interstitial cystitis/bladder pain syndrome: experience of 3 tertiary centers.*

- **Immunosuppressant (Cyclosporine)**
  - Risk of side effects
  - Works best for Hunner’s Lesions

- **Exenterative Surgery**
  - Ileal loop diversion
  - Cystectomy
    - Ileal neobladder
    - Continent catheterizable stoma

- **Meticulous Patient Selection**
  - Small anesthetic bladder capacities
  - Multiple Hunner’s ulcers

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Ileal conduit without cystectomy may be an appropriate option in the treatment of intractable bladder pain syndrome/interstitial cystitis.
Norus T¹, Fode M, Nordling J.

Cystectomy for ulcerative interstitial cystitis: sequelae and patients’ perceptions of improvement.
Peters KM1, Jaeger C, Killinger KA, Rosenberg B, Boura JA.
AF-219

- P2X3 receptors – sensitization of afferent neurons in bladder
- A novel P2X3 antagonist Phase II study
- 74 women randomized to AF-219 or placebo
  - Dose escalation up to 200 mg bid
  - Reduction of NPRS 6.2-3.3 (6.4-4.5 in pcb)
  - Increased incidence of dysgeusia / ageusia

SUFU 2015, Podium #4
Challenge Treating IC/BPS

• “IC” may not be a disease of the bladder
  – The bladder is an innocent bystander is a larger pelvic/systemic process
  – A “disease of the lower urinary tract” or a disease that affects the lower urinary tract

• 20 years of clinical trials sponsored by industry and the NIH has shown no response over placebo with “bladder-centric” therapy in IC/BPS

• It is / has been time to “think outside the bladder”
IC & Pelvic Floor Dysfunction

- Approximately 70%–90% of patients with IC have pelvic floor dysfunction\(^1\)

- Levator ani muscle myalgia can be a source of chronic pelvic pain.

81 women with IC/BPS randomized at 11 centers to myofascial PT vs global massage
– 78 (96%) completed treatment
– Did not reach recruitment of 88 subjects

Symptom duration 3 mos - 3 years
GRA (mod or marked improvement) 59% in MPT vs 26% in massage group
## Results

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<th></th>
<th>GTM</th>
<th>MPT</th>
<th>Total</th>
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<tbody>
<tr>
<td>Number Randomized</td>
<td>24</td>
<td>23</td>
<td>47</td>
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<tr>
<td><strong>Total (p=0.03)</strong></td>
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<td>Responders</td>
<td>5 (21%)</td>
<td>13 (57%)</td>
<td>18 (38%)</td>
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Similar findings in f/u study of 81 women: 59% PT vs 26% massage


Randomized multicenter clinical trial of myofascial physical therapy in women with interstitial cystitis/painful bladder syndrome and pelvic floor tenderness.
Physical Therapy

- Should be performed by a physical therapist specially trained in pelvic floor dysfunction related to these symptoms.
- Involves internal and external therapy
- Biofeedback
- Very successful in improving symptoms pelvic pain, dyspareunia, urgency, frequency
Levator TPI with Curved Trumpet

- Discrete, identifiable nodular, hyperirritable focal area of muscle
- Inability to tolerate pelvic floor PT
- Refractory to muscle relaxants
  - Diazepam
  - Baclofen
A Multidisciplinary Team Approach is Key to Success
Behavioral Therapy

- Guided Imagery
- Cognitive behavioral therapy
- Stress Reduction
- Increase water intake (dilute the urine)
- Dietary modifications
- Yoga/meditation
“Neural-centric” Therapy
Electroceuticals

Pudendal neuromodulation for pelvic pain; Not just for OAB anymore?

Botox to the pelvic floor musculature instead of the bladder?

Tibial nerve stimulation: Are more “afferents” better?
What else for Pelvic Floor Dysfunction / Dyspareunia?

- Intravaginal Valium
  - 5-10 mg bid-tid
  - Pill, cream or suppository
  - In conjunction with PT or prn

- Crystal Wand for Trigger Points

- Vaginal Dilators

- Trigger Point Injections
Complementary Therapies

Vulvodynia

Guided Imagery

Reiki Therapy

Emu Oil

Sesame/Vitamin E Oil

Acupuncture
Welcome to Beaumont’s Women’s Urology Center
Thank You

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