Interstitial Cystitis and Pelvic Pain: Looking Beyond the Bladder

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Disclosures

• Consultant
  – Medtronic
  – StimGuard
  – Uroplasty
  – Taris Biomedical
Symptoms and Diagnosis.—The symptoms are usually so clearcut and classic that the diagnosis can be suspected from the patient’s history.

The patient is usually a woman of the child-bearing age if the disease is of recent origin. If it is of many years’ standing, the woman may be older. She complains of pain in the bladder region. She will, if asked, point out the exact spots in the anterior abdominal wall, labia, urethra or other particular areas where the pain is referred. In a strikingly large number of cases, we have observed that this area corresponds to the location of the ulcer in the bladder. The patient will complain that her bladder is never free from an uncomfortable, dull, aching sensation and that pain is sharp and cutting and almost unbearable when the bladder becomes full. Emptying the bladder relieves the pain. The frequency of urination is marked both day and night. Often the nocturnal frequency is every 15-20 minutes. Nervousness, child-bearing, many diseases, automobile rides, train rides, constipation and fatigue aggravate the condition.

Nothing in the way of diet or antiseptics by mouth seems to do any good. On behalf of women who complain of bladder trouble for which the average physician can find no cause, we plead that they not be condemned as neurotics until Hunner’s ulcer has been ruled out.
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**)

Hunner’s Ulcer

A medical entity as confusing, poorly understood, baffling etiologically, and taking up as much space as it does in the text books on urology should merit a few words from the psychiatrist. The designation of the symptom of a ‘hunger urge’ which gives bladder discomfort? It makes a thoughtful physician wonder about the possibility of a mildly masochistic woman, i.e., destructive need in the female to suffer and “have trouble with” her genitourinary apparatus. Just
Non ulcerative IC/PBS as defined by the International Continence Society (ICS) is the complaint of suprapubic pain related to bladder filling accompanied by other symptoms, such as increased daytime and nighttime frequency in the absence of proven urinary infection or other obvious pathology.

syn·drome (sndrm) n. 1. A group of symptoms that collectively indicate or characterize a disease, psychological disorder, or other abnormal condition.
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
• Download at www.auanet.org

  ▪ Guidelines are based on a review of the medical literature (1983 to late in 2009) and expert opinion

  ▪ Expected to be updated as more research unfolds and understanding of condition expands

  ▪ Flexibility built into the guidelines to accommodate need to tailor treatment options to patient needs

  ▪ Recommend that healthcare providers consider patient preferences in designing treatment plans
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
PSYCHOSOCIAL FUNCTIONING ECONOMIC BURDEN

• Psychosocial/QOL impact
  – Affects worklife, psychological well being, personal relationships and general health
  – Higher rate of depression, anxiety, catastrophizing
  – Moderate to severe sexual dysfunction

• Economic Burden
  – 750 million dollars/year in health care costs
  – Lost wages/economic losses
AUA GUIDELINES—KCL TEST IS OUT

- Start with careful history, physical exam—rule out co-morbid conditions.
- Careful pelvic exam for PFD and vulvar diseases
- Order labs to rule other confusible conditions
- Take baseline voiding and pain measures
- Potassium sensitivity test is no longer recommended
  - Results not consistent
  - Can hurt patient and trigger IC flare
Assessment

• **Pain** is hallmark symptom, including pressure and discomfort
  – Especially pain that worsens with specific food or drink or as the bladder fills
  – Includes pain in bladder, urethra, vulva, vagina, rectum, lower abdomen and back
  – Frequency and urgency are common

• The PUF questionnaire & ICSI-PI may be helpful, but are not diagnostic.
AUA GUIDELINES—COMPLICATED CASES

- Complicated cases may require additional testing
  - Signs and symptoms of other problems: Incontinence, OAB, blood or pus in the urine, endometriosis, CP/CPPS, or GI conditions

- Urodynamic testing
  - No clinical standards for IC—Difficult for patients
  - ICA comment—Patients may need post-procedure rescue instillation

- Cystoscopy with hydrodistention under anesthesia
  - Find and treat Hunner's lesions
  - Rule out bladder cancer
  - **Glomerulations are no longer considered diagnostic**
  - No clinical standards for IC
  - May be therapeutic
TREATMENT STRATEGIES

- Begin with conservative therapies
- Initial treatment type and level should depend on severity, clinician judgment and patient preference
- 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
AUA GUIDELINES—First Line Therapies

- Heat or cold over bladder or perineum
- Dietary changes (refer to www.ichelp.org/diet)
- Nutrition/short-term pain relievers
  - Nutraceuticals (ie: quercitin, Prelief-like products)
  - Pyridium (phenazopyridine), antispasmodics
- Treat trigger points and hypersensitive areas
- Meditation and guided imagery
- Modify or stop Kegel’s, sexual intercourse, tight clothes
- Manage constipation
- Manage stress
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.
  – At this point, **NO** Kegel exercises

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

• Oral medicines (alphabetical)
  – Amitriptyline
  – Cimetidine (Tagamet)
  – Hydroxyzine (Vistaril, Altarax)
  – Pentosan Polysulfate* (Elmiron)

• Bladder instillations
  – DMSO*
  – heparin
  – Lidocaine/Bicarb

*Pearl:*
  If using DMSO, hold only for 15 or 20 minutes, longer can cause significant pain

*FDA Approved
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
AUA GUIDELINES—Fourth Line Therapy

- Neuromodulation
  - When other treatments haven’t helped enough
  - Helps with frequency and urgency
  - Not indicated for pain, but may help secondarily with pain
- **Immunosuppressant** (Cyclosporine)
  - Risk of side effects
  - Works best for Hunner’s Lesions

- **Botulinum toxin A**
  - Inject into bladder muscle
  - Side effects include painful urination and retention
  - May require long-term self-catheterization


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

AUA GUIDELINES—SIXTH LINE

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

- **Proper Selection**
  - Small anesthetic bladder capacities
  - Hunner’s Lesions

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**Scand J Urol.** 2014 Apr;48(2):210-5
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.

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Cystectomy for ulcerative interstitial cystitis: sequelae and patients’ perceptions of improvement.
Peters KM1, Jaeger C, Killinger KA, Rosenberg B, Boura JA.
Not effective or treatment carries an unacceptable risk
- Long-term oral antibiotics
- Bacillus Calmette-Guerin (BCG) instillation
- Resiniferatoxin instillation
- High-pressure, long-duration hydrodistention
- Long-term oral steroids

ICA also discourages use of the following treatments because of the severe pain they cause most patients
- Clorpactin WCS-90 (oxychlororosene sodium)
- Silver Nitrate
Chronic Pelvic Pain

• 1 out of 9 women in the U.S has CPP

• More than 1,000,000 of these women have been told they have IC
Challenge Treating IC/BPS

• “IC” may not be a disease of the bladder
• Rather the bladder is an innocent bystander is a larger pelvic/systemic process
• 20 years of clinical trials sponsored by industry and the NIH has shown no response over placebo when therapy is directed toward the bladder in IC/BPS
• To improve symptoms of IC you must be an astute clinician and think outside the bladder
Evidence for Central Up-Regulation

- Visceral pain syndrome (ie: IBS)
- The limbic system (modulates emotions and pain)
- Measured by Startle Blink Reflex (SBR)
- 6 IC pts and 19 controls were tested by actual or anticipated electrical bladder stimulation.
- IC pts had significantly greater SBRs during non-imminent threat periods than controls
- Similar findings seen in anxiety and PTSD pts
- On “High alert”.

University of Iowa studies demonstrated IC/PBS patients had increased urgency and bladder pain in response to stress.

IC/PBS patients exhibit abnormalities in their hypothalamic-pituitary-adrenal axis that alter their response to stress leading to neural upregulation and increased symptoms.

Basic Science Research

- In mice, cystitis induced pelvic pain
- Lidocaine instilled into the bladder or colon
- Resolved this pelvic pain
- This model supports the idea of neural cross-talk and also that the bladder is more vulnerable to this effect. One idea is that neuronal cross-talk is unidirectional.

Colon → Bladder
Uterus → Bladder

IC & Pelvic Floor Dysfunction

• Approximately 70%-90% of patients with IC have pelvic floor dysfunction¹

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

Pelvic Floor—Urinary Symptoms

- Shortened PFD/Trigger points
- Weak Pelvic Floor Muscles
- More Frequency, Urgency, Pain
- Increased PFD needed to suppress Urgency/Frequency
- Slow relaxation
  Hesitant Painful Voiding

Source: UPPCRN PT Protocol V 1.0 Sept 2006
Prevalence of Abuse

• General Population\(^1\)
  – 1 out of 6 women were either sexually or physically abused during their childhood

• Beaumont’s mailed survey study\(^2\)
  – 36.9% of women with IC reported being abused
  – 22.4% of the controls reported being abused
  – \( p = 0.001 \)

\(^1\) The Commonwealth Fund Survey-1998
\(^2\) J. Urol. 2007 Sep;178(3 Pt 1):891-5;

Fact or fiction—Is abuse prevalent in patients with interstitial cystitis? Results from a community survey and clinic population

Peters KM\(^1\), Kalinowski SE, Carrico DJ, Ibrahim IA, Diokno AC.
Results

Office Evaluation of Abuse: (n=87)

• 55% of these women had been abused physically, sexually or emotionally.

• Mean number of years from onset of abuse to IC diagnosis = 24.4 years.

• Abuse is more common in women with IC who have levator pain than those without levator pain (55% vs 36.9%).

• The pelvic floor may be a significant source of pain in women with IC.
Looking outside the Bladder

• The bladder may be an innocent bystander in a bigger process
• The pelvic floor is crucial in normal voiding and bowel function
• Pelvic floor dysfunction may be the cause of many of the symptoms of the IC syndrome
• Triggers for development of PFD may exist
  – Abuse, pelvic surgery, stress, untreated UTI, pelvic injury, nerve injury
Effect of Pelvic Floor on IC/PBS

Randomized Multicenter Pilot Trial Shows Benefit of Manual Physical Therapies in the Treatment of Chronic Pelvic Pain

MP FitzGerald,1 RU Anderson,2 CK Payne,2 JPotts,3 KM Peters,4 JQ Clemens,5 L Cen6 ,S Chuai6, JR Landis6

## Results

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<th></th>
<th>GTM</th>
<th>MPT</th>
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<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

Palpation of Pelvic Structures
Female Sexual Dysfunction

I wouldn’t say my love life is bad, but the last guy I turned on was Mr. Coffee.
Prevalence of Sexual Dysfunction

43%  31%

4 Laumann, et al. 1999
A Multidisciplinary Team Approach is Key to Success

Physical Therapists
Nutritionists
Rheumatologists
Pain Clinics
Urologists
NP/PA/Nurses
Psychologists
Integrative Med
Gynecologists/Primary Care

Patient
Vulvodynia

Definition: by the International Society for the Study of Vulvovaginal Disease (ISSVD):

- Vulvar discomfort, “burning pain”, in the absence of relevant clinical findings or neurologic disorder.
- Pain fiber proliferation, erythema and hypertonicity of the levator muscles are common.
- The vulvar pain must be present for at least three months.

Prevalence:

- Affects approximately 2.4 million women
Anatomy of the Vagina

- The vaginal vestibule originates from the same embryonic tissue as the urethra and bladder.
- This tissue has estrogen receptors.
- Anterior vaginal wall is more densely innervated than posterior vaginal wall.
- The nerve supply of the vulva is primarily by the pudendal nerve branches although there is a sacral component.

What Causes Vulvodynia?

- **Idiopathic/unknown**
- **Potential causes may be:**
  ~an injury to, or irritation of, the nerves that innervate the vulva
  ~an abnormal response of different cells in the vulva to environmental factors (such as infection or trauma)

**Trauma** (physical & psychological)
- Childbirth
- Surgery
- Sports injury
- Sexual abuse

**Psychological**

**Behavioral**

*Source: www.nva.org*
Other Potential Causes of Vulvodynia

- Genetic factors associated with susceptibility to chronic vestibular inflammation.
- More common in those having sex before age 16.
- A localized hypersensitivity to candida (yeast)—deep tissue samples, special staining.
- Spasms of the muscles that support the pelvic organs.

Source: nva.org
Vulvar Pain—VVS
“Localized Provoked Vulvodynia”

- Based on Friedrich’s criteria: severe pain with touch at the vestibule; tenderness localized within the vulvar vestibule; vulvar erythema.
- Research does not support the idea that emotional/psych disorders cause VVS.
- Often, levator spasm is present—it is unclear which came first, the pain or the spasm.
- 80-90% of vulvodynia pts have a hypertonic pelvic floor.

(Butrick, 2009)
Evaluation

- History
- Screening neurologic exam
- Pelvic exam
  - Prolapse
  - Visual inspection
    - Atrophy
    - Dermatologic Process
  - Neurosensory Q-tip test
  - Levator Exam
Treatment Options

- Pelvic Floor Physical Therapy
- Local medications – vaginal/rectal suppositories
  - Muscle relaxants
  - Neuropathic pain agents
- Pelvic floor trigger point injections
- Pudendal blocks
  - Long-acting anesthetic +/- steroids
- Intra-muscular Botox – 100 to 300 units
Surgical Intervention:

- Vestibulectomy: excision of the inflamed vestibular epithelium. Success rates are reported to be up to 95%.* Sutures dissolve in 2 weeks. Post-op care involves topical estrogen, lidocaine, local massage and pelvic floor PT oftentimes.

- [http://www.cvvd.org](http://www.cvvd.org) Dr. Andrew Goldstein

Comfort

- **Topical**
  - 100% emu oil (contains Omega 3, 6,9)
  - Sesame oil with Vitamin E

- Vulvar hygiene—cotton underwear avoid constrictive garments

New topical OTC cream may be helpful. Studied in Switzerland. Research findings:
http://www.vulvodyniatreatment.com/about-the-study
Think Outside the Box

- Evaluate whole patient
- Identify pain triggers
- Prioritize problems
- Engage your colleagues
- Be open minded
- Mind-body connection
- Provide encouragement
- Provide support
Behavioral Therapy

- Guided Imagery
- Cognitive behavioral therapy
- Stress Reduction
- Increase water intake (dilute the urine)
- Dietary modifications
- Yoga/meditation
Pelvic Floor Dysfunction/Dyspareunia

Intravaginal Valium

Crystal Wand for Trigger Points

Vaginal Dilators

Injection of Marcaine and Kenalog into Trigger Points
Complementary Therapies

Vulvodynia

Guided Imagery

Reiki Therapy

Emu Oil

Sesame/Vitamin E Oil

Acupuncture
So, exactly what is IC?

PBS?

BPS?
71 years later.....
We still don’t know!!
Ponder this:

• What if the reason that 20 years of bladder directed therapy has not found an effective treatment is that the bladder is not the problem in most patients (ulcers excluded)?

• What if IC starts as PFD that is triggered from certain events such as abuse, pelvic surgery, UTI, stress etc. The inability to relax the pelvic floor results in voiding dysfunction, urgency, frequency, hesitation, dyspareunia, nerve upregulation, bowel dysfunction etc…?
Ponder this:

- What if we train our clinicians to evaluate the pelvic floor?
- What if PFD is found in 70-90% of patients with IC?
- What if we train physical therapists in directed myofascial release and make this treatment accessible to our patients?
- What if we add cognitive behavioral therapy, stress reduction, psychological support and coping skills?
- What if we use muscle relaxants rather than narcotics?
- What if we use neuromodulation techniques to treat the urgency/frequency/pain associated with IC?
- What if we inject botox in the levators rather than the bladder?
- What if we not ignore things such as sexual dysfunction?
- What if we engage our integrative medicine clinicians?
I believe that we will do more to advance the treatment of men and women with pelvic pain, urgency and frequency than we have in the past 20 years.

It is time to think outside of the bladder!
Where do we go from here?
Welcome to Beaumont’s Women’s Urology Center
At the Beaumont Women’s Urology Center one will find a multidisciplinary center with:

- Expert clinicians to address urologic symptoms, incontinence, pelvic and genital pain, bowel dysfunction and sexual function concerns
- Pelvic Floor Physical Therapists
- Psychological services
- Integrative medicine
- Innovative research