INTERSTITIAL CYSTITIS/ PAINFUL BLADDER SYNDROME: Advances in Diagnosis and Management

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Outline

- Definition
- Epidemiology
- Etiology
- Diagnosis
- Evidence Based Management

Definition

- the complaint of suprapubic pain related to bladder filling, accompanied by other symptoms such as increased daytime and night time frequency, in the absence of proven urinary infection or other obvious pathology.

Abrams PH, Cardozo L, Fall M et al: The standardisation of terminology of lower urinary tract function: report from the standardisation subcommittee of the International Continence Society. Neurourol Urodynam 2002; **21**: 167,

Epidemiology

- Considerable variability among studies regarding incidence and prevalence
- First population based study in Helsinky (1975):
  - Prevalence in women 18.1 / 100,000
  - Both sexes 10.6 /100,000
  - Incidence in females 1.2 per 100,000

More recent studies suggest…

- Prevalence likely higher
- 197 women per 100,000 population (from physician-assigned diagnosis) (Clemens et al, 2005)
- 450 women per 100,000 population (from validated symptom questionnaire) (Roberts, 2003)
- 865 women per 100,000 population (from patient self-report)
- roughly 236,000 to > 1 million American women

EPIDEMIOLOGY

- Prevalence estimates per 100,000
  - United States: 35-24,000
  - Netherlands: 7
  - Finland: 10.6-450
  - Japan: 1.2
- Female to male ratio = 5:1
- Economic cost of disease ~ $427 million

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ETIOLOGY

- Likely multifactorial
- Many theories

Role of infection

- Little data to support the role of infectious etiology
- Bacterial cystitis may be the first step leading to a low level inflammatory response
- Unlikely that active infection is involved in the ongoing pathological process or that antibiotics have a role in treatment

Immune/neuroimmune mechanisms

- Excessive release of sensory nerve neurotransmitters and mast cell inflammatory mediators → propagation of symptoms
- Inflammation → altered nerve growth factor content →morphological changes in sensory and motor neurons →long-term symptoms after inflammation subsides.

Role of Mast Cells

- Histamine release in tissue causes pain, hyperemia and fibrosis
- a high number of activated mast cells have been seen in the bladder of patients with PBS/IC
- could contribute to failure of epithelialization of the bladder surface following injury by 2 potential mechanisms:
  1) inhibition of epithelial cell replication
  2) interference with epithelial cell spreading, thus resulting in the leaky epithelium found in some cases.

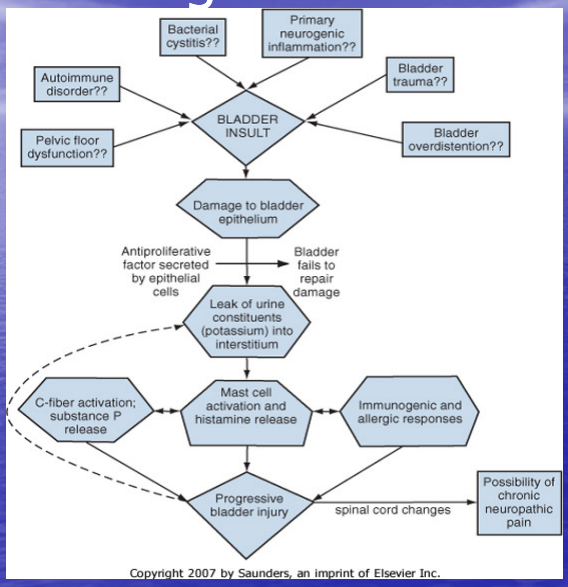
Leaky Epithelium

- GAG layer functions as a permeability and anti-adherence barrier
- Patients with IC have a lower excretion of urinary uronic acid and GAGS than normals, possibly due to a leaky transitional epithelium that might be absorbing these substances to surfaces.
- Increased mucosal permeability is non-specific and a consequence of bladder inflammation

Neurogenic inflammation

- Activation of sensory nerves →neuropeptides such as substance P, neurokinin A → neurogenic inflammation.

Consolidating theories



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Nervous system and IC

- Repetitious activation of C fibers results in a progressive build-up of the magnitude of the electrical response recorded in the second order dorsal horn neurons.
- "wind-up" phenomenon
- persistent NMDA receptor activation cause spinal cord cells to undergo trophic changes, and the pain resulting from subsequent stimulation becomes exaggerated and prolonged.

DIAGNOSIS

- Diagnostic approaches vary widely
- No general agreement on a diagnostic algorithm
- Heavy reliance on other aspects of the NIDDK criteria

NIDDK criteria

- Based on consensus among a group of researchers who wanted to define strict, homogenous criteria for patient recruitment into research trials
- Not meant to define the disease, but rather to ensure comparability between that groups of patients research studies

NIDDK Criteria

To be diagnosed with interstitial cystitis, patients must have either glomerulations on cystoscopic examination or a classic Hunner ulcer, and they must have either pain associated with the bladder or urinary urgency. An examination for glomerulations should be undertaken after distention of the bladder under anesthesia to 80 to 100 cm H2O for 1 to 2 minutes. The bladder may be distended up to two times before evaluation. The glomerulations must be diffuse-present in at least three quadrants of the bladder-and there must be at least 10 glomerulations per quadrant. The glomerulations must not be along the path of the cystoscope (to eliminate artifact from contact instrumentation). The presence of any one of the following excludes a diagnosis of interstitial cystitis:

1. Bladder capacity of greater than 350 mL on awake cystometry using either a gas or liquid filling medium
2. Absence of an intense urge to void with the bladder filled to 100 mL of gas or 150 mL of liquid filling medium
3. The demonstration of phasic involuntary bladder contractions on cystometry using the fill rate just described
4. Duration of symptoms less than 9 months
5. Absence of nocturia
6. Symptoms relieved by antimicrobial agents, urinary antiseptic agents, anticholinergic agents, or antispasmodic agents
7. A frequency of urination while awake of less than 8 times per day
8. A diagnosis of bacterial cystitis or prostatitis within a 3-month period
9. Bladder or ureteral calculi
10. Active genital herpes
11. Uterine, cervical, vaginal, or urethral cancer
12. Urethral diverticulum
13. Cyclophosphamide® or any type of chemical cystitis
14. Tuberculous cystitis
15. Radiation cystitis
16. Benign or malignant bladder tumors
17. Vaginitis
18. Age younger than 18 years

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NIDDK Criteria - Criticisms

- ICDB study accumulated data on 424 pt with IC.
- Entry criteria were much more symptom driven than those promulgated for research studies
- Fully 90% of expert clinicians agreed that patients diagnosed with IC by those criteria in the ICDB indeed had the disorder.
- 60% of patients deemed to have IC by these experienced clinicians would not have met NIDDK research criteria.

NIDDK Criteria - Criticisms

- More recent studies challenge the need for cystoscopy for diagnosis
- 39-60% of patients have minimal reduction in capacity, minimal or scant glomerulations, and no consistent urine marker or bladder biopsy findings.
- 8.7% of patients in the IC database had normal cystoscopy
- Glomerulations are not specific for IC and may be just a response to distention after a prolonged period of under filling rather than a pathological process.
- Pts. with symptoms of less than 9 months duration could still have IC

Pathology

- Way to exclude other diagnoses
- No pathognomonic picture
- No consistent findings
- Great variation within the same patients
- pathologic findings

Associations among Pathologic Features and Patient Symptoms

Night-Time Frequency
Mast cell count in lamina propria on tryptase stain
Complete loss of urothelium
Granulation tissue in lamina propria
Vascular density in lamina propria
Urinary Urgency
Percentage of submucosal granulation tissue
Urinary Pain
Percentage of mucosa denuded of urothelium
Percentage of submucosal hemorrhage

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KCL Test

- **Comparing the sensory nerve provocative ability of sodium versus potassium using a 0.4 M KCl solution**
- **Pain and provocation of symptoms constitutes a positive test.**
- **Not valid for diagnosis of IC** (Chambers et al, 1999)
- A 36% false-positive rate in asymptomatic men (Yilmaz et al, 2004)

KCL test (continued)

- Up to 25% of patients meeting the NIDDK criteria will have a negative KCl test (Parsons et al, 1998)
- May be positive in overactive bladder, radiation cystitis and urinary tract infection

How does one make the diagnosis?

Three consensus panels concluded that the diagnosis is suspected on the basis of history, physical examination, and laboratory tests, including negative urinalysis, negative urine culture, negative cytology, and possibly cystoscopy findings.

Nickel JC: Interstitial cystitis: the paradigm shifts: international consultations on interstitial cystitis. Rev Urol 2004; 6: 200-202.

Antiproliferative Factor

- Frizzled-related peptide growth inhibitor
- Produced by the urothelium of patients with IC.
- Found in bladder urine but not in renal pelvic urine
- High APF has been linked to IC patients with many racial backgrounds

Zhang CO, Li ZL, Shoenfelt JL, Kong CZ, Chai TC, Erickson DR, Peters KM, Rovner ES, Keay S. Comparison of APF activity and epithelial growth factor levels in urine from Chinese, African-American, and white American patients with interstitial cystitis. Urology. 2003 May;61(5):897-901

Keay SK, Szekely Z, Conrads TP, Veenstra TD, Barchi JJ Jr, Zhang CO, Koch KR, Michejda CJ.An antiproliferative factor from interstitial cystitis patients is a frizzled 8 protein-related sialoglycopeptide. Proc Natl Acad Sci U S A. 2004 Aug 10;101(32):11803-8

Antiproliferative Factor

- APF seems to have role in increasing cell permeability
- induces reversible inhibition of HB-EGF production and normal bladder epithelial cell proliferation

Keay S, Zhang CO, Shoenfelt JL, Chai TC. Decreased in vitro proliferation of bladder epithelial cells from patients with interstitial cystitis. Urology. 2003 Jun;61(6):1278-84

Zhang CO, Wang JY, Koch KR, Keay S. Regulation of tight junction proteins and bladder epithelial paracellular permeability by an antiproliferative factor from patients with interstitial cystitis. J Urol. 2005 Dec;174(6):2382-7.

Antiproliferative Factor

- Sensitivity and specificity of increased APF activity in IC has been postulated to be 94 and 95%
- Could be used to gauge response to treatment – improvement in APF activity noted after hydrodistention and neuromodulation.

Erickson DRet al. Changes in urine markers and symptoms after bladder distention for interstitial cystitis. J Urol. 2007 Feb;177(2):556-60.
Chai TC, Zhang C, Warren JW, Keay S. Percutaneous sacral third nerve root neurostimulation improves symptoms and normalizes urinary HB-EGF levels and antiproliferative activity in patients with interstitial cystitis. Urology. 2000 May;55(5):643-6
Keay SK, Zhang CO, Shoenfelt J, Erickson DR, Whitmore K, Warren JW, Marvel R, Chai T. Sensitivity and specificity of antiproliferative factor, heparin-binding epidermal growth factor-like growth factor, and epidermal growth factor as urine markers for interstitial cystitis. Urology. 2001 Jun;57(6 Suppl 1):9-14

Prevalence of urine antiproliferative factor activity in interstitial cystitis patients and control groups **Groups No. Pos/Total No. (%)**
Pts: interstitial cystitis 206/219 **(94)**
Controls:
Asymptomatic 10/113 **(9)**
Overactive bladder 2/32 **(6)**
Bacterial cystitis 7/58 **(12)**
Microscopic hematuria 2/19 **(10)**
Stress incontinence 1/10 **(10)**
Neurogenic bladder 0/11 **(0)**
Benign prostatic hyperplasia 1/14 **(7)**
Nonbacterial prostatitis 1/16 **(6)**
Vulvovaginitis 0/12 **(0)**
Miscellaneous 1/16 **(6)**

(adapted from Keay S, Zhang CO, Marvel R et al: Antiproliferative factor, heparin-binding pidermal growth factor-like growth factor, and epidermal growth factor: sensitive and specific urine markers for interstitial cystitis. Urology 2001; **57:** 104)

Symptoms

- urinary urgency (57-98%),
- daytime frequency (84-97%),
- pain (66-94%)
- nocturia (44-90%)
- pain with voiding/dysuria (71-98%)
- suprapubic pain (39-71%)
- perineal pain (25-56%)
- patient sensation of bladder spasms (50-74%)
- pubic pressure (60-71%)
- dyspareunia (46-80%)
- Depression (55-67%)

Teichman JMH, Parsons CL: Contemporary clinical presentation interstitial cystitis. Urology 2007; 69 (supp 4A): 41-47.

Clinical Symptom Scales

- Three published PBS/IC symptom questionnaires:
  - University of Wisconsin IC Scale,
  - O'Leary-Sant IC Symptom Index and IC problem Index,
  - Pelvic Pain and Urgency/Frequency (PUF) Scale.

The University of Wisconsin IC Scale

- Includes seven PBS/IC symptom items
- captures severity of symptom expression
- IC patients do NOT score higher than controls (Porru et al, 2005)
- Addresses some QOL issues
- Easy to implement
- **Not validated for identification or diagnosis of PBS/IC**

O'Leary-Sant IC Symptom Index

- subjected to test-retest reliability analysis
- validated by administration to IC patients and asymptomatic controls
- centered on three questions related to urgency/frequency and one on bladder-associated pain

Pelvic Pain and Urgency/Frequency (PUF) Scale

- Includes questions that directly reflect a wide variety of the symptoms
- One third of the questions address pelvic pain
- A large study utilizing the PUF questionnaire has concluded that up to 23% of American females have PBS/IC (Parsons et al, 2002a)
- Face validity and utility in question.

THERAPY

THERAPY

- Conservative
- Hydrodistention
- Oral therapy
- Intravesicle therapy
- Neuromodulation
- Surgery

Conservative Approach

- A single trial with empirical course of antibiotics maybe warranted
- Doxycycline has been reported to have an efficacy of up to 70% in relieving / improving symptoms in a prospective cohort analysis (Burkhard et al, 2004)
- Repeat courses of antibiotics not recommended in absence of negative cultures.

Conservative Approach

- Patient education and empowerment
- Timed voiding and behavioral modification therapy
- Stress reduction, exercise, warm tub baths (No RCT evidence)

Dietary Modifications

- Elaborate dietary restrictions are unsupported by any literature.
- Anecdotal association of IC with many acidic foods.
- The only placebo-controlled dietary study, while small, failed to demonstrate a relationship between diet and symptoms (Fisher et al, 1993).

Hydrodistention

- Perform an initial cystoscopic examination
- Obtain urine for cytology
- Distend the bladder for 1 to 2 minutes at a pressure of 80 cm H2O.
- Bladder is emptied and then refilled
- A look for glomerulations or ulceration.
- A therapeutic hydraulic distension follows for another 8 minutes.

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Hydrodistention

- Therapeutic responses in patients with a bladder capacity under anesthesia of less than 600 cc were excellent in 26% and fair in 29% compared to 12% excellent and 43% fair in patients with larger bladder capacities.
- Most favorable responses were extremely brief, with the exceptional patient noting improvement for 6 months.

Hanno PM, Wein AJ: Conservative therapy of interstitial cystitis. Semin Urol 1991;9:143-147.

Hydrodistention

- Allows for "staging" of the disease, giving the clinician some idea of the capacity with which conservative therapies may work.
- A capacity with the patient under anaesthesia of less than 200 cc would not bode well for the likelihood of success of medical therapy
- Allows for identification of Hunner's ulcers.

Oral Therapy

- Tricyclic antidepressants
- Antihistamines
- Sodium Pentosan Polysulfate
- Analgesics

Oral Therapy

Table 10-11. Some Oral Medications That Have Been Used for Treatment of PBS/IC

Drug	*Randomized Control Trial*	*% Success*
Amitriptyline	Yes	42%
Antibiotic regimens	Yes	48%
Anticholinergics and antispasmodics	No	Anecdotal
Azathioprine[Rx]	No	50%
Benzydamine	Yes	0%
Chloroquine[Rx] derivatives	No	50%
Cimetidine[Rx]	Yes	65%
Cortisone and other steroids	No	80%
Cyclosporine[Rx]	No	90%
Doxycycline[Rx]	No	71%
Gabapentin[Rx]	No	Anecdotal
Hormones	No	Anecdotal
Hydroxyzine[Rx]	Yes	31%
L-Arginine	Yes	Not effective
Methotrexate	No	50%
Misoprostol[Rx]	No	48%
Montelukast	No	90%
Nalmefene	Yes	Not effective
Narcotic analgesics	No	Anecdotal
Nifedipine[Rx]	No	87%
Phenazopyridine	No	Anecdotal
Quercetin	No	92%
Sodium pentosan polysulfate	Yes	33%
Suplatast tosylate	Yes	Pending publication
Vitamin E[Rx]	No	Anecdotal

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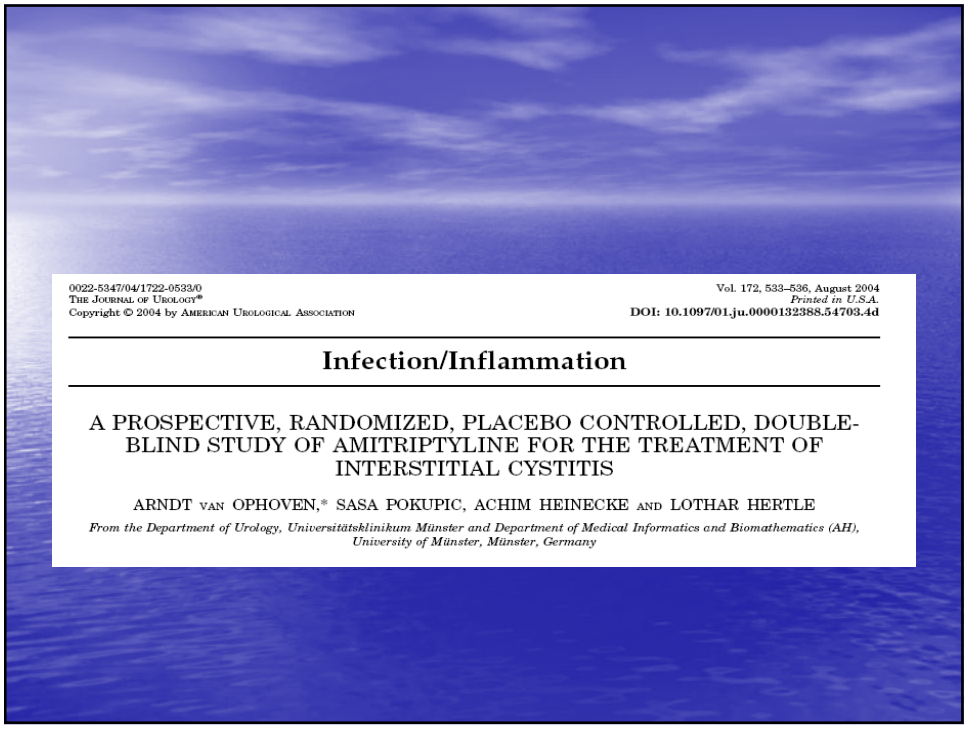
Tricyclic Antidepressants

- Amitriptyline has been the staple of oral therapy
- Mechanism of action:
  - central and peripheral anticholinergic actions
  - block the active transport system in the presynaptic nerve ending that is responsible for the reuptake of the released amine neurotransmitters serotonin and noradrenaline
  - sedatives, an action that occurs presumably on a central basis but perhaps is related to their antihistaminic properties



0022-5347/04/1722-0533/0
THE JOURNAL OF UROLOGY®

Vol. 172, 533–536, August 2004
Printed in U.S.A.
DOI: 10.1097/01.ju.0000132388.54703.4d

Infection/Inflammation

A PROSPECTIVE, RANDOMIZED, PLACEBO CONTROLLED, DOUBLE-BLIND STUDY OF AMITRIPTYLINE FOR THE TREATMENT OF INTERSTITIAL CYSTITIS

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Amitriptyline

- RCT, intent to treat
- N = 50 (44 women, 6 men)
- Methods:
  - randomized to amitriptyline (25) versus placebo (25)
  - prospectively treated for 4 months with a self-titration protocol that allowed them to escalate drug dosage in 25 mg increments in 1 week-intervals (maximum dosage 100 mg).
  - **primary outcome parameter.:** change from baseline in the O'Leary-Sant IC symptom and problem index
  - **secondary outcome parameters:** functional bladder capacity and frequency (48-hour voiding log), and intensity of pain and urgency (visual analog scales)

TABLE 2. *Changes in symptoms from baseline to 4 months*

Characteristic	Amitriptyline	Placebo	p Value
Mean score-sum ± SD	−3.4 ± 7.2	−3.5 ± 5.4	0.005
Mean pain intensity ± SD (mm on VAS)	−22.8 ± 26.1	1.0 ± 14.8	<0.001
Mean urgency intensity ± SD (mm on VAS)	−43.3 ± 23.5	−0.1 ± 3.2	<0.001
Mean 24-hr frequency ± SD	−4.0 ± 5.1	−0.6 ± 5.8	0.063
Mean functional bladder volume ± SD (ml)	19.0 ± 54.62	−7.7 ± 47.5	0.083

- statistically significant change in the symptom score
- statistically significant improvement of pain and urgency intensity compared with placebo

Amitriptyline…

- Anticholinergic side effects were reported by all except 2 patients in the amitriptyline group (92%) and by 5 patients in the placebo group (21%).
- Mouth dryness was the most frequent side effect reported in the amitriptyline group (79%).

Van Ophoven A, Hertle L. Long-term results of amitriptyline treatment for interstitial cystitis. J Urol. 2005 Nov;174(5):1837-40.

- Prospective cohort analysis
- N= 94
- Methods = patients stratified in 2 groups :
- IC with NIDDK
- IC without NIDDK (characteristic symptoms)
- Mean Follow up = 19 months
- Results: response rate = 64% (60 patients).
- mean dose = 55 mg (range 12.5 to 150)
- Side effects in 79 patients (84%) (dry mouth 79%, weight gain59%).
- therapeutic result was excellent or good in 43 (46%).
- dropout rate = 31% (29 patients)
- Non response to treatment was the primary reason for dropout in all cases, while side effects contributed to dropout in 25 (86%). Improvement in the various IC symptoms was statistically significant compared with baseline.

Antihistamines

- Stems from mast cell theory of IC
- In some uncontrolled studies, hydroxizine showed symptomatic improvement by up to 30%.
- No significant response to hydroxizine was found in an NIDDK placebo-controlled trial (Sant et al, 2003).
- Cimetidine, an H2 antagonist, showed efficacy in double blind, placebo controlled trial. (Thilagarajah et al, 2001)

Sodium Pentosan Polysulfate

- Its use stems from an attempt to correct a defect in the epithelial permeability barrier, the GAG layer, of the bladder
- a heparin analogue available in an oral formulation
- 3% to 6% excreted into the urine
- Contradictory reports of efficacy in literature.

Sodium Pentosan Polysulfate

- Two placebo controlled multicenter trials in the United States were published.
- In the initial study overall improvement of greater than 25% was reported by 28% of the PPS treated group versus 13% in the placebo group. (Mullholand et al, 1990)
- In the latter study the respective figures were 32% on drug versus 16% on placebo. (Parsons et al, 1993)

Mulholland SG, Hanno P, Parsons CL et al: Pentosan polysulfate sodium for therapy of interstitial cystitis. A double-blind placebo controlled clinical study. Urology 1990; **35**: 552.

Parsons CL, Benson G, Childs SJ et al: A quantitatively controlled method to study prospectively interstitial cystitis and demonstrate the efficacy of pentosanpolysulfate. J Urol 1993; **150**: 845.

Sodium Pentosan Polysulfate

- A recent NIDDK study looking at PPS and hydroxyzine, alone and in combination, compared to placebo failed to show a statistically significant response to either medication.

Sant GR, Propert KJ, Hanno PM et al: A pilot clinical trial of oral pentosan polysulfate and oral hydroxyzine in patients with interstitial cystitis. J Urol 2003; **170**: 810.

Cyclosporine Versus Pentosan Polysulfate

- randomized comparative study
- N = of 64 IC patients diagnosed by NIDDK criteria
- Methods: randomized in a1:1 ratio to cyclosporine A (Sandimmun Neoral®) or to pentosan polysulfate sodium (bene-Arzneimittel GmbH, Munich, Germany) treatment for 6 months.
- endpoints : daily micturation frequeny, voided volume, number of nocturia episodes, O'Leary-Sant symptom and problem indexes, visual analogue scale for pain and subjective global response assessment.
- Results:
  - CyA was found to be superior on all parameters at 6 months.
  - more adverse events noted in the cyclosporine arm.

Sairanen J, **Tammela TL**, **Leppilahti M**, **Multanen M**, **Paananen I**, **Lehtoranta K**, **Ruutu M**.Cyclosporine A and pentosanpolysulfate sodium for the treatment of interstitial cystitis: a randomized comparative study. J Urol. 2005 Dec;174(6):2235-8.

Intravesicle Therapy

- **remains a mainstay of treatment in the therapeutic armamentarium of IC**

DMSO

- Mainstay of intravesicle treatment
- Pharmacologic properties:
  - membrane penetration
  - enhanced drug absorption
  - anti-inflammatory action
  - analgesic action
  - collagen dissolution
  - muscle relaxation
  - mast cell histamine release

DMSO

- Success rate of up to 70% noted in prospective studies done in 1970's
- most patients ultimately required re-treatment or further therapy with other modalities
- Patients with bladder instability do not respond

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Heparin

Mechanism of action:

- mimic the activity of the bladder's own mucopolysaccharide lining
- anti-inflammatory effects
- inhibit fibroblast proliferation, angiogenesis, and smooth muscle cell proliferation.

Heparin

- No systemic absorption
- Some SMALL case series showing symptomatic improvement (Parsons, 2000) (Kuo, 2001)
- Unproven by any placebo-controlled trial.

BCG

- Unclear mechanism of action
- immunologic and/or anti-inflammatory mechanisms have been postulated (Peters et al, 1999)
- Early small RCT showed high response rate of 60% compared with a 27% placebo response (Peters et al, 1997).
- Recent large RCT fails to show high response rate.

BCG

0022-5347/05/1734-1186/0
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Vol. 173, 1186–1191, April 2005
Printed in U.S.A.
DOI: 10.1097/01.ju.0000152337.82806.e8

A RANDOMIZED CONTROLLED TRIAL OF INTRAVESICAL BACILLUS CALMETTE-GUERIN FOR TREATMENT REFRACTORY INTERSTITIAL CYSTITIS

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- RCT
- N = 265
- Participants were randomized to intravesical BCG or intravesical placebo, and received up to 6 instillations within 6 to 10 weeks.
- F/U 24-28 WKS
- Primary outcome: patient reported global response assessment
- Secondary outcomes: 24-hour voiding diary, pain, urgency, validated IC symptom indexes and adverse events

RESULTS

- Response rates for the primary outcome were 12% for placebo and 21% for BCG (p 0.062). **No statistical significance reached.**
- Small improvements were observed for all secondary outcomes, some more so with BCG, but these differences were of borderline statistical significance.
- Although a large number of adverse events were reported in the BCG arm, there was no statistically significant difference between the treatment arms in overall adverse event rates

Conclusion

- Intravesical BCG therapy was reasonably well tolerated but not more effective than placebo in this population of patients with moderate to severe IC.

Table 10-12. Some Intravesical Medications That Have Been Used for Treatment of PBS/IC

Drug	*Randomized Controlled Trial*	*% Success*
Silver nitrate℞	No	60%
Clorpactin WCS-90	No	60%
Dimethylsulfoxide	Yes	70%
Bacillus Calmette-Guérin	Yes	No proven efficacy
Resiniferatoxin	Yes	No proven efficacy
Hyaluronic acid	Yes	No proven efficacy
Heparin	No	60%
Chondroitin sulfate	No	33%
Lidocaine℞	No	65%
Capsaicin℞	No	No demonstrated efficacy
Oxybutynin℞	No	Efficacy suggested
Doxorubicin	No	Anecdotal efficacy
Pentosan polysulfate	Yes	40%

Neuromodulation

- relieves pain by stimulating myelinated afferents to activate segmental inhibitory circuits
- patients who do best with this treatment modality are those who have identifiable *pain and dysfunction in the pelvic muscles*

Neuromodulation – the process

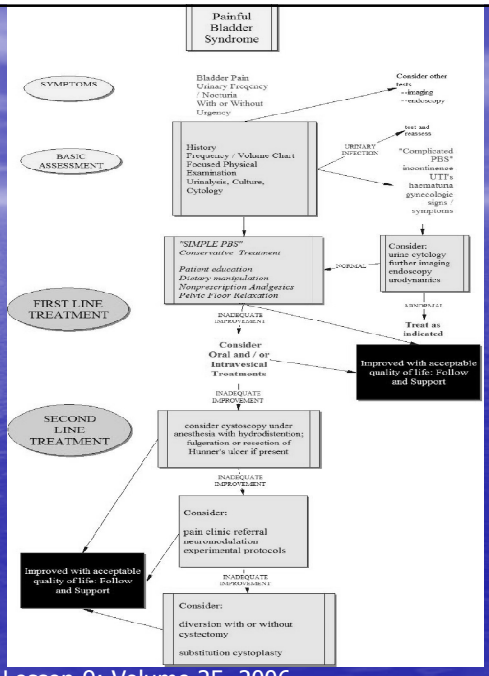
- Trial stimulation performed with a percutaneous temporary electrode for a 3 to 4-day temporary stimulation period to assess efficacy.
- S3 nerve is most frequently used.
- A wire electrode is inserted into the foramen and connected to an external pulse generator
- If the trial is successful, the patient would be considered for implantation of a permanent neural prosthesis.
- More recently, a staged procedure has supplanted the traditional percutaneous approach, as the response to stimulation can be better assessed with more accurate lead placement and stability than through the more hit or miss percutaneous lead placement

Neuromodulation – evidence

- No RCT evidence
- A decrease in antiproliferative factor activity and normalization of HB-EGF levels in patients with successful test stimulation (Chai et al, 2000a)
- In a prospective study of 27 refractory patients, implantation of sacral nerve root stimulator showed improvements in urinary frequency, voided volumes, nocturia and pain after a mean follow up of 14 months. (Commiter, 2003)
- Sacral neuromodulation can decrease narcotic requirements significantly in refractory PBS/IC (Peters et al, 2004)

Surgical therapy

- Reserved for motivated and well-informed patients in the category of extremely severe, unresponsive disease, a group which comprises fewer than 10%.
- Aimed at increasing the functional capacity of the bladder or diverting the urinary stream.
- Augmentation (substitution) cystoplasty and urinary diversion with or without cystectomy have been used as a last resort with good results in select patients.



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CONCLUSIONS

- Interstitial cystitis is much more common than what was initially thought
- Once confirmed by other centers, APF may prove to be a useful marker in diagnosis of IC
- Multiple effective treatment options are available.
- A step wise approach to management should be used.

Thank-you