Interstitial Cystitis/Bladder Pain Syndrome

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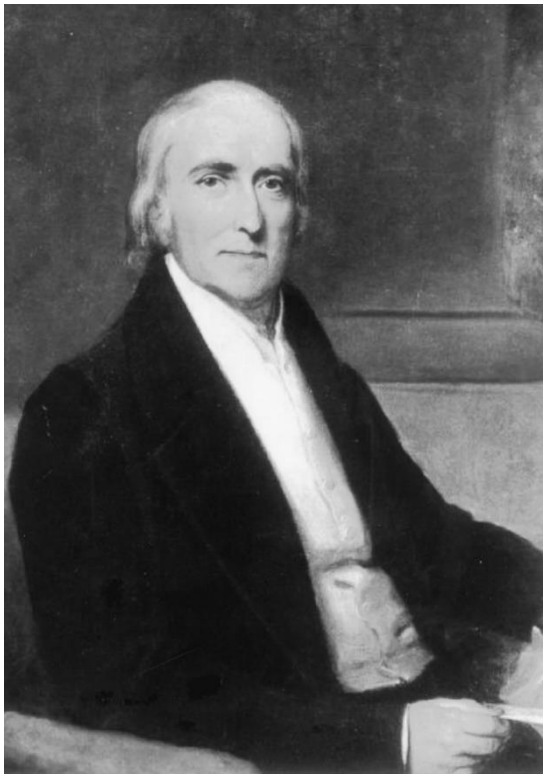
outline

- History of IC/BPS
- Dx of IC/BPS
- Terminology of IC/BPS
- Phenotyping of IC/BPS
- Pathogenesis of IC/BPS
- Tx of IC/BPS

Hx of IC/BPS



Philip Syng Physick:
Introducing an instrument called a **sound** through the urethra into the Bladder; it is called **sounding**. . .is never to be neglected when there is reason to suspect a stone in the bladder

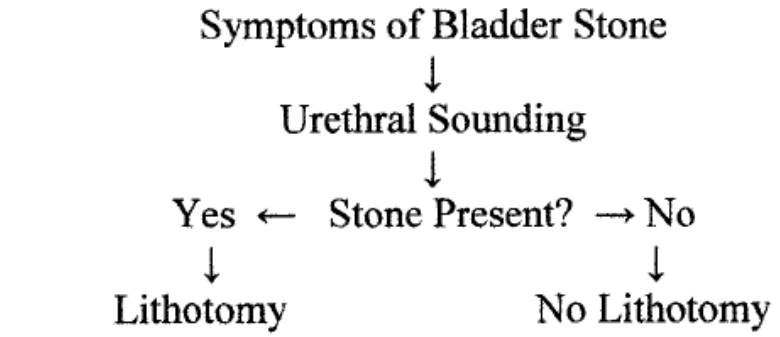
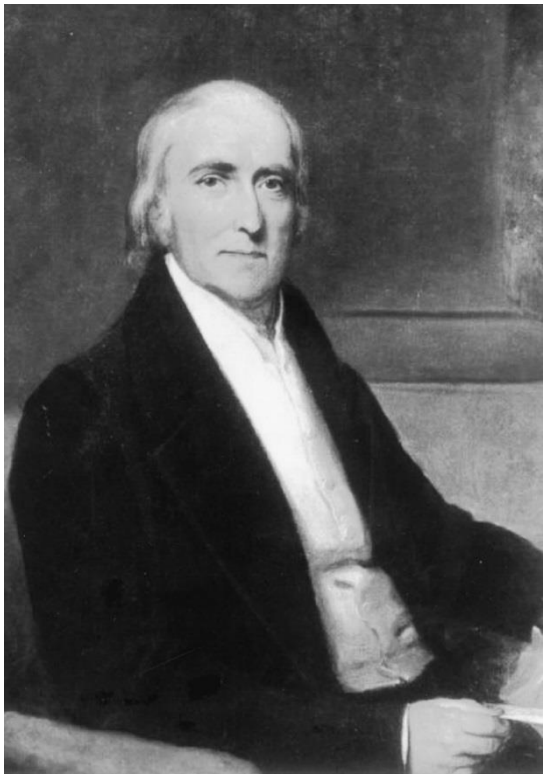


FIG. 1. Algorithm for diagnosis and treatment of bladder stones in early 19th century.

1808

J Urol. 2004 Jan;171(1):20-2.

Hx of IC/BPS



Philip Syng Physick:
Ulcers in the bladder sometimes occasion symptoms very much like those of the stone. . .great care should be taken not to mistake [an ulcer] for the stone

By 1836 he had expanded this concept to include a chronic frequency, urgency and pain syndrome occurring in the absence of demonstrable etiology which was called **tic doloureux** of the bladder.

1808

J Urol. 2004 Jan;171(1):20-2.

Hx of IC/BPS

Parrish in his book:
Paroxysmal frequency, urgency, dysuria and pelvic pain in 3 patients.
Unable to identify a specific etiology for the symptom

1836

Campbell Urology 10th edition, chapter 12

Hx of IC/BPS

Skene in his book:
First used the term **interstitial cystitis** to describe an inflammation that has “destroyed the mucous membrane and extended to the muscle

Campbell Urology 10th edition, chapter 12

Hx of IC/BPS

Guy Hunner:
reported on women with suprapubic pain, frequency, urgency lasting for long time. He found the red, bleeding areas in **cystoscopy** he described on the bladder wall came to have the Hunner ulcer

1915

Campbell Urology 10th edition, chapter 12

Hx of IC/BPS

Hand:

"I have frequently observed that what appeared to be a normal mucosa before and during the first bladder distention showed typical interstitial cystitis on subsequent distention"

and

"small, discrete, **submucosal hemorrhages**, showing variations in form … **dot-like bleeding points** … little or no restriction to bladder capacity."

1949

Campbell Urology 10th edition, chapter 12

Hx of IC/BPS

Walsh:
use the term **glomerulations** to describe
the petechial hemorrhages that Hand had described.

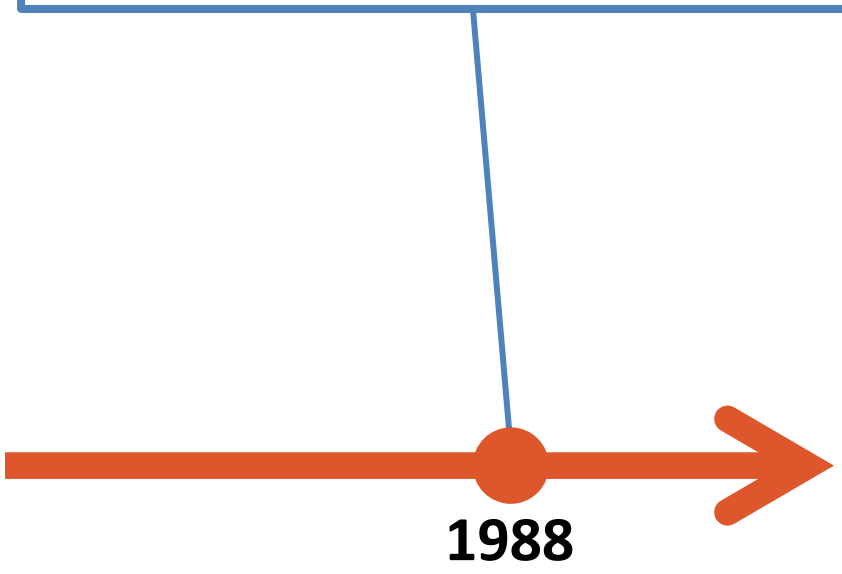
Campbell Urology 10th edition, chapter 12

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 H_2O 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:

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

To be diagnosed with interstitial cystitis, patients **must have** either **glomerulations** on cystoscopic examination **or a classic Hunner ulcer** …….



Campbell Urology 10th edition, chapter 12

Diagnosis of IC/BPS

- The unexpected use of the **NIDDK research criteria** by the medical community as a definition of IC led to concerns that many patients with this syndrome might be **misdiagnosed**.
- **60%** of patients deemed to have IC by these experienced clinicians would not have met NIDDK research criteria.
- 2008 ESSIC: The diagnosis of BPS is thus made on the basis of exclusion of confusable diseases and confirmation by the recognition of the presence of the specific combination of symptoms and signs of BPS

Campbell Urology 11th edition, chapter 14

Confusable disease

Table 1 – Confusable diseases for bladder pain syndrome

Confusable disease	Excluded or diagnosed by[a]
Carcinoma and carcinoma in situ	Cystoscopy and biopsy
Infection with	
Common intestinal bacteria	Routine bacterial culture
Chlamydia trachomatis, Ureaplasma urealyticum	Special cultures
Mycoplasma hominis, Mycoplasma genitalium	
Corynebacterium urealyticum, Candida species	
Mycobacterium tuberculosis	Dipstick; if "sterile" pyuria culture for *M. tuberculosis*
Herpes simplex and human papilloma virus	Physical examination
Radiation	Medical history
Chemotherapy, including immunotherapy with cyclophosphamide	Medical history
Anti-inflammatory therapy with tiaprofenic acid	Medical history
Bladder-neck obstruction and neurogenic outlet obstruction	Uroflowmetry and ultrasound
Bladder stone	Imaging or cystoscopy
Lower ureteric stone	Medical history and/or hematuria: upper urinary tract imaging such CT or IVP
Urethral diverticulum	Medical history and physical examination
Urogenital prolapse	Medical history and physical examination
Endometriosis	Medical history and physical examination
Vaginal candidiasis	Medical history and physical examination
Cervical, uterine, and ovarian cancer	Physical examination
Incomplete bladder emptying (retention)	Postvoid residual urine volume measured by ultrasound scanning
Overactive bladder	Medical history and urodynamics
Prostate cancer	Physical examination and PSA
Benign prostatic obstruction	Uroflowmetry and pressure-flow studies
Chronic bacterial prostatitis	Medical history, physical examination, culture
Chronic non-bacterial prostatitis	Medical history, physical examination, culture
Pudendal nerve entrapment	Medical history, physical examination, nerve block may prove diagnosis
Pelvic floor muscle-related pain	Medical history, physical examination

CT = computed tomography; IVP = intravenous pyelogram; PSA = prostate-specific antigen.

[a] The diagnosis of a confusable disease does not necessarily exclude a diagnosis of BPS.

Diagnosis of IC/BPS nowdays

- The ICS defined the term ‘‘painful bladder syndrome’’ (PBS) as ‘‘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 **(>6mo)**
- The name IC is reserved for PBS with typical cystoscopic and histologic features

EAU guideline for chronic pelvic pain 2016
european urology 53 (2 0 0 8) 60–67

Diagnosis of IC/BPS nowdays

- The Panel used the IC/BPS definition agreed upon by the Society for Urodynamics and Female Urology (SUFU): "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

AUA guideline for IC/BPS

Diagnosis of IC/BPS

- BPS/IC can be considered a functional pain disorder and one of the chronic visceral pain syndromes affecting the urogenital and rectal area.
- These include vulvodynia, orchalgia, penile pain, perineal pain, and rectal pain

Campbell Urology 11th edition, chapter 14

Type of BPS

Table 2 – Classification of types of bladder pain syndrome on the basis of findings at cystoscopy with hydrodistention and of biopsies

	Cystoscopy with hydrodistention			
	Not done	Normal	Glomerulations[a]	Hunner's lesion[b]
Biopsy				
Not done	XX	1X	2X	3X
Normal	XA	1A	2A	3A
Inconclusive	XB	1B	2B	3B
Positive[c]	XC	1C	2C	3C

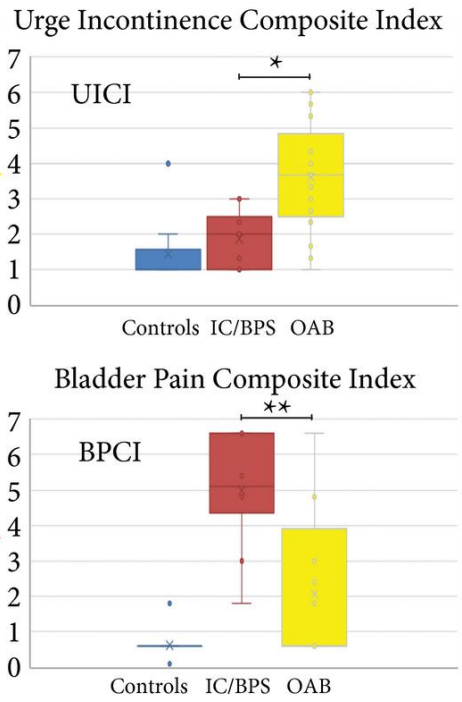
[a] Cystoscopy: glomerulations grade 2–3.
[b] With or without glomerulations.
[c] Histology showing inflammatory infiltrates and/or detrusor mastocytosis and/or granulation tissue and/or intrafascicular fibrosis.

CLASSIFICATION OF BPS
cystoscopy with hydrodistension[1] and biopsy if indicated

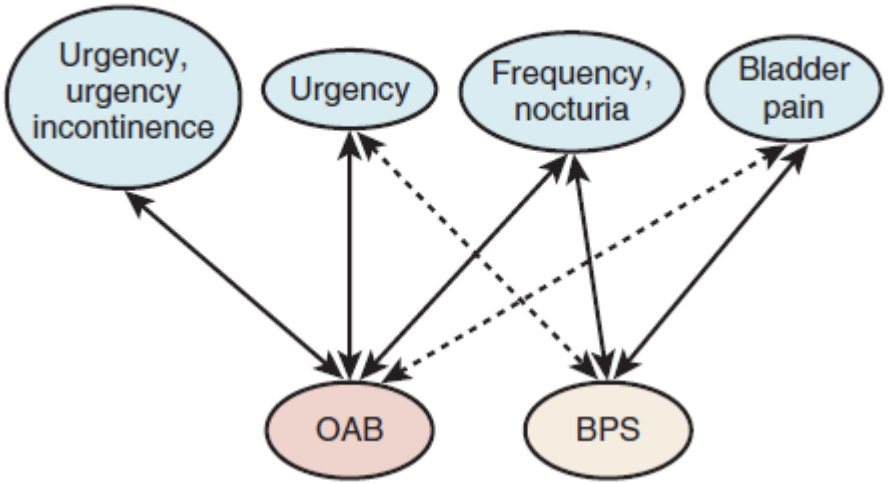
symbol 1: cystoscopy findings	symbol 2: biopsy findings
X: not done 1: normal 2: glomerulations grade II or III 3: Hunner's lesion (with or without glomerulations)	X: not done A: normal B: inconclusive C: inflammatory infiltrates, granulation tissue, detrusor mastocytosis or intra-fascicular fibrosis

IC/OAB ?

Instruments	Number	Question	Significance
OAB-q	OAB-q4	"During the past 4 weeks, how bothered were you by accidental loss of small amounts of urine?"	P=0.0002
	OAB-q8	"During the past 4 weeks, how bothered were you by urine loss associated with a strong desire to urinate?"	P=0.0001
	OAB-q25	"During the past 4 weeks, how often have your bladder symptoms made you worry about odor or hygiene?"	$P=3.5\times10^{-6}$
ICSI	ICSI4	"During the past month, have you experienced pain or burning in your bladder?"	$P=3.9\times10^{-7}$
ICPI	ICPI4	"During the past month: How much has each of the following been a problem for you: Burning, pain, discomfort, or pressure in your bladder?"	$P=1.7\times10^{-5}$
fGUPI	fGUPI2a	"In the last week, have you experienced: pain or burning during urination?"	$P=8.0\times10^{-6}$
	fGUPI2c	"In the last week, have you experienced: pain or discomfort as your bladder fills?"	$P=6.1\times10^{-7}$
	fGUPI4	"Which number best describes your AVERAGE pain or discomfort on the days you had it, over the last week?"	$P=1.6\times10^{-5}$



BJU Int. 2018 Sep 25. doi: 10.1111/bju.14568



significant bladder pain (35%) in OAB patients and
presence of urge incontinence (25%) in IC/BPS patients

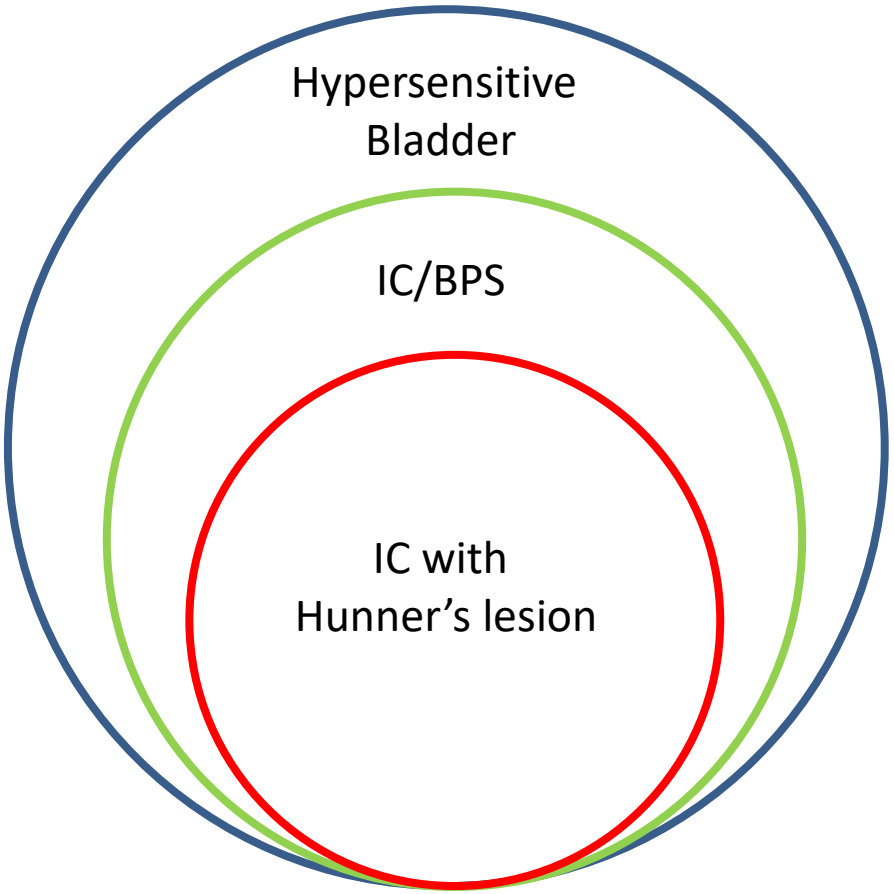
14% incidence of urodynamic detrusor overactivity in IC patients

BJU Int. 2018 Sep 25. doi: 10.1111/bju.14568

Terminology of IC/BPS

- ICS guideline:

A Standard for Terminology in Chronic Pelvic Pain Syndromes: A Report From the Chronic Pelvic Pain Working Group of the International Continence Society



Hypersensitive Bladder:
increased bladder sensation, usually associated with increased urinary frequency day and night, **with or without bladder pain** in the absence of pathology explaining the symptoms

IC/BPS:
Persistent or recurrent chronic **pelvic pain**, pressure or discomfort perceived to be related to the urinary bladder accompanied by at least one other urinary symptom such as an urgent need to void or urinary frequency

IC with Hunner's lesion:
same symptoms as IC/BPS.

Doggweiler R Neurourol Urodyn. 2017;36

Lower urinary tract evaluation

A. Questionnaires:
voiding diary,
Basic symptom severity Questionnaires: OSS
and IPSS
VAS pain score

B. Laboratory Testing:
U/A, U/C,
Investigations for Ureaplasma and Chlamydia (optional),
CT or cytology for patients with hematuria

C. Urodynamic Evaluation:
Flow metry and Post-void Residual, Filling Cystometry,
Pressure-Flow Study

*It is recommended to perform **filling cystometry and pressure flow study** if the flowmetry suggests **voiding dysfunction.***
*The demonstration of **pain** may identify the bladder and/or urethra as a pain generator*
*Males, **bladder outlet obstruction** might be a differential diagnosis*

Lower urinary tract evaluation

Chronic Pelvic Pa

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Phenotyping of IC/BPS

UPOINT phenotyping

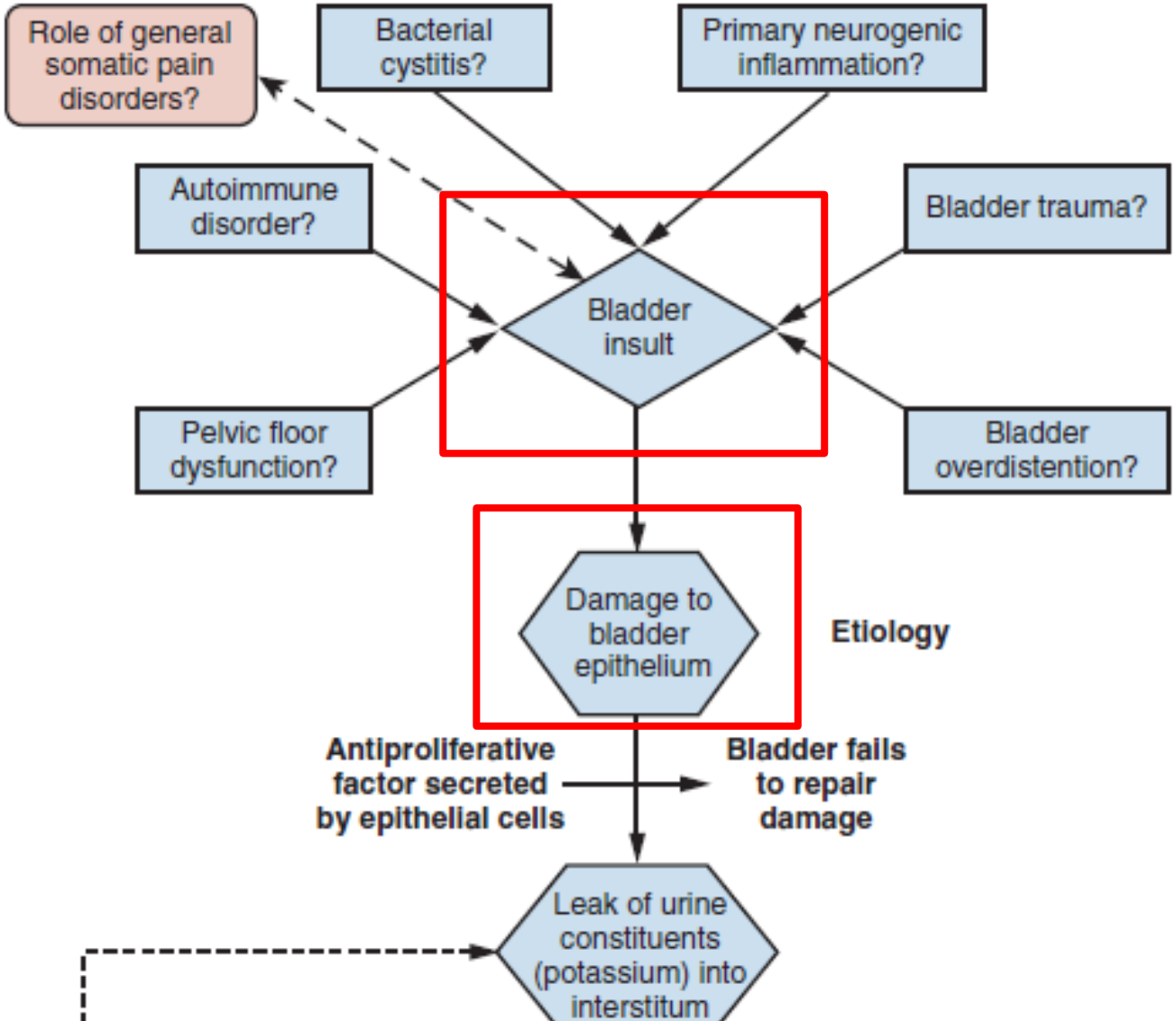
- ✓ 100% and 96% of the patients were included in the urinary and organ specific domains respectively.
- ✓ Psychosocial, infection, neurological and tenderness domains included 34, 38, 45 and 48 patients,
- ✓ Increased symptom duration leads to a greater number of domains.

Nickel JC. J Urol. 2009;182(1):155-60

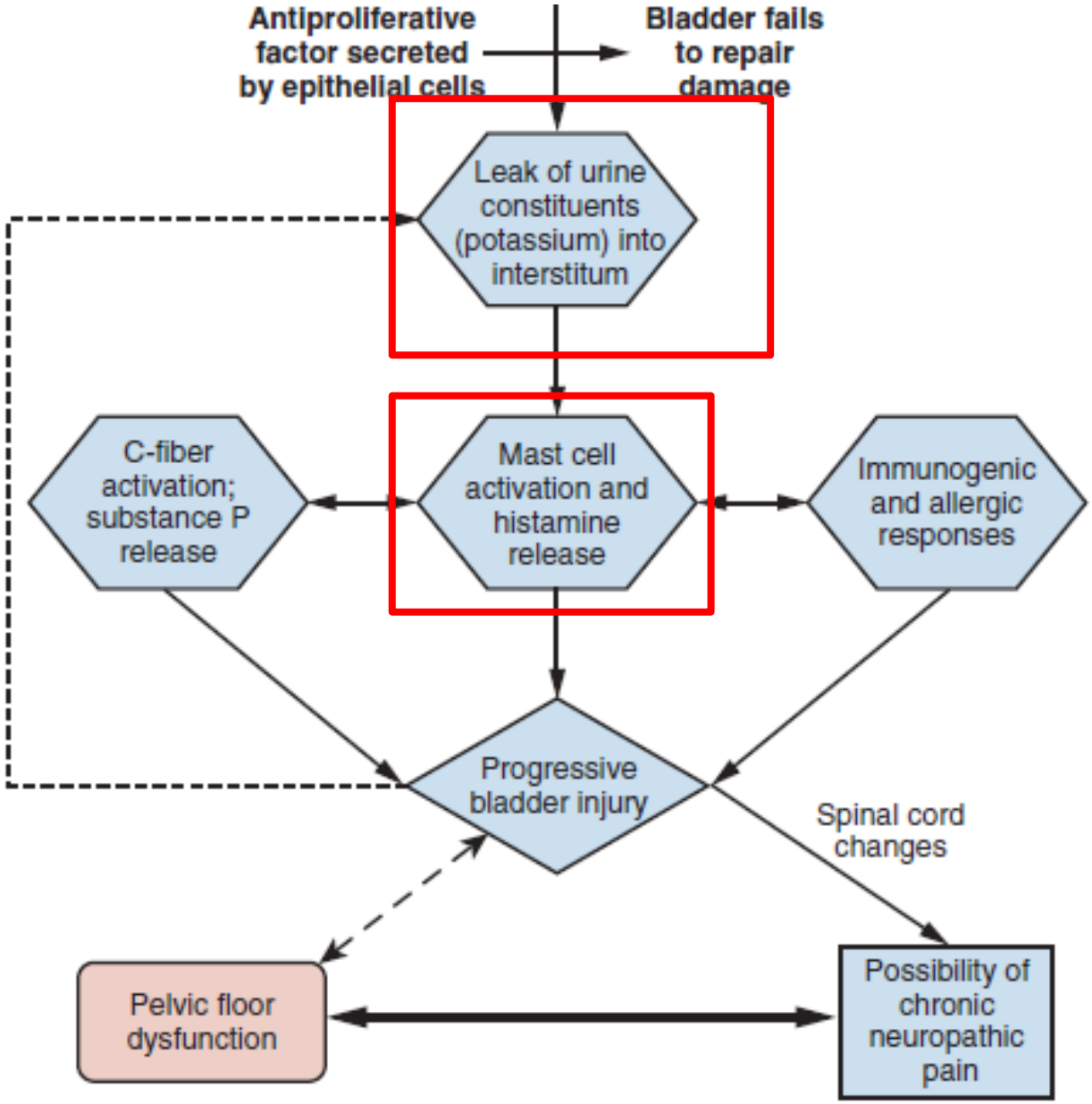
Pathogenesis of IC/BPS

- Bladder Glycosaminoglycan Layer and Epithelial Permeability
- Autoimmunity/Inflammation
- Mast Cell Involvement
- Inhibition of Uroepithelial Cell Proliferation: Antiproliferative Factor
- Neurobiology/ neurogenic inflammation
- Pelvic Organ Cross-Sensitization
- Nitric Oxide Metabolism

Pathogenesis of IC/BPS



Hanno P, Dinis P, Lin A, et al. International Consultation on Urological Diseases/European Association of Urology; 2013.



Hanno P, Dinis P, Lin A, et al. International Consultation on Urological Diseases/European Association of Urology; 2013.

Tx of IC/BPS

5.4.2. ***Management of BPS***

Summary of evidence	LE
There is insufficient data for the long-term use of corticosteroids.	3
Limited data exist on effectiveness of cimetidine in BPS.	2b
Amitriptyline is effective for pain and related symptoms of BPS.	1b
Oral pentosane polysulphate is effective for pain and related symptoms of BPS.	1a
Oral pentosane polysulphate plus subcutaneous heparin is effective for pain and related symptoms of BPS, especially in initially low responders to pentosane polysulphate alone.	1b
Intravesical lidocaine plus sodium bicarbonate is effective in the short term.	1b
Intravesical pentosane polysulphate is effective, based on limited data, and may enhance oral treatment.	1b
There are limited data on the effectiveness of intravesical heparin.	3
Intravesical chondroitin sulphate may be effective.	2b
There is insufficient data for the use of bladder distension as a therapeutic intervention.	3
Hydrodistension plus BTX-A is superior to hydrodistension alone.	1b
Intravesical BCG is not effective in BPS.	1b
Transurethral resection (coagulation and laser) may be effective in BPS type 3 C.	3
Sacral neuromodulation may be effective in BPS.	3
Pudendal nerve stimulation is superior to SNM for treatment of BPS.	1b
Avoidance of some food and drink may reduce symptoms.	3
Outcome of cystectomy for BPS is variable.	3

LE 1:

1. **Amitriptyline** is effective for pain
2. Oral **pentosanpolysulphate sodium** **(PPS)** is effective for pain
6. **Intravesical BTX-A injection** + HD are significantly superior to HD alone.
7. Intravesical **BCG** is **not effective** in BPS
8. Pudendal nerve stimulation superior to SNM

None of the present treatments affect all BPS subtypes or phenotypes.

EAU guideline for chronic pelvic pain 2016

Treatment	
Grade A recommended	Standard: Amitriptyline, Pentosanpolysulphate
	Intravesical: PPS, DMSO, onabotulinum toxin A plus hydrodistension
Grade B recommended	Oral: Cimetidine, cyclosporin A
	Intravesical: hyaluronic acid, chondroitin sulphate
	Electromotive drug administration for intravesical drugs
	Neuromodulation, bladder training, physical therapy
	Psychological therapy
Not recommended	Bacillus Calmette Guérin
	Intravesical Chlorpactin
	Hydroxyzine
Other comments	Data on surgical treatment are largely variable
	Coagulation and laser only for Hunner's lesions

EAU guideline for chronic pelvic pain 2016

膀胱內肝素治療
用10000-25000單位泡在10毫升的生理鹽水中(有時候會再加上碳酸氫鈉)，
灌注到病患膀胱內，請病患忍住尿意至少兩個小時，每星期兩次至三次

膀胱內玻尿酸治療
一瓶的容量都是50毫升，可以直接灌注到病人的膀胱裡面。
通常使用方式是前四個禮拜每周灌注一次，接下來每個月灌注一次，持續四到五個月。

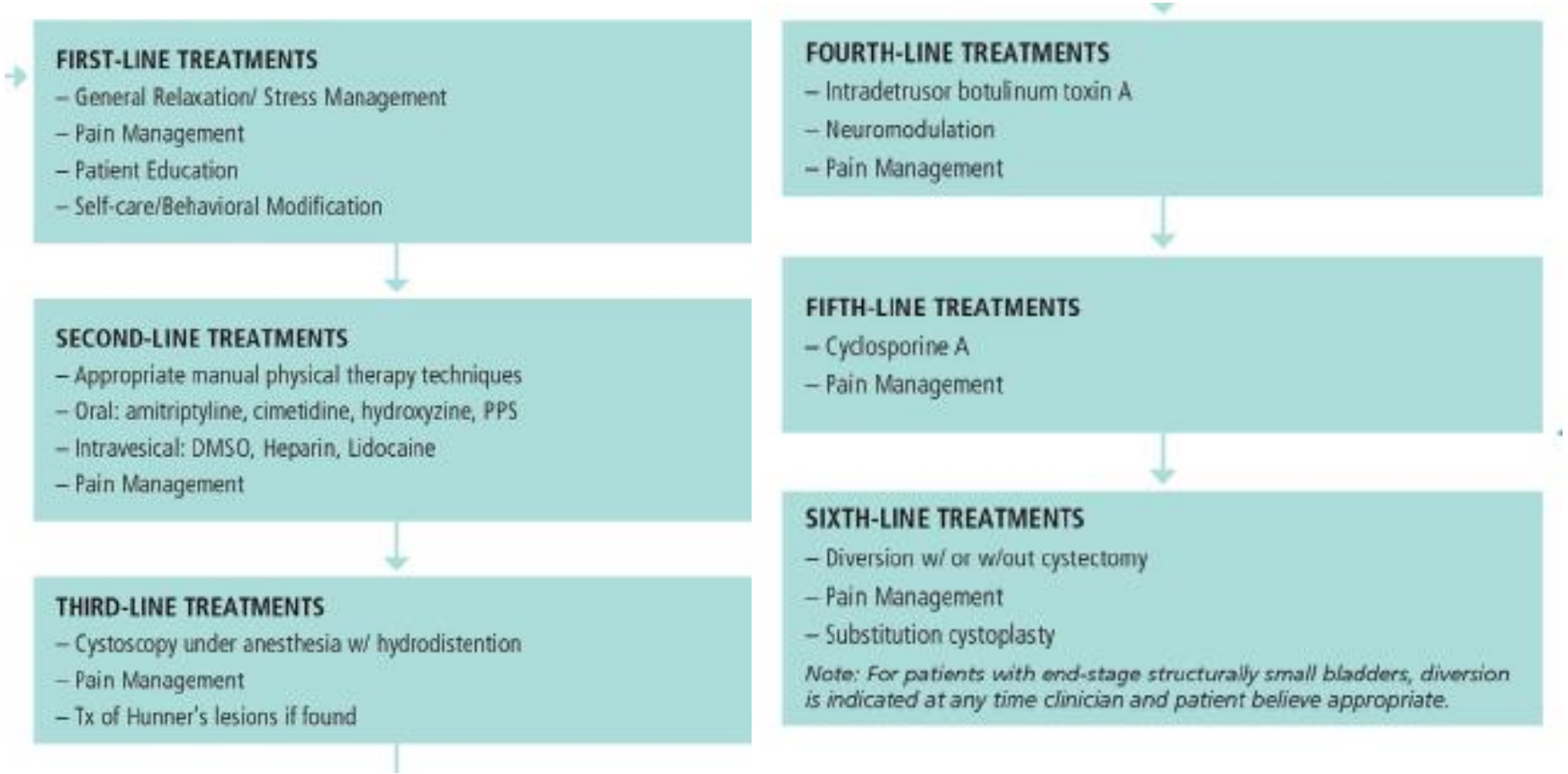
膀胱內DMSO療法 (二甲基亞碸，Dimethyl sulfoxide)
DMSO是一種有機硫的化合物，DMSO被認為作用在膀胱有減少膀胱發炎，
止痛以及幫助逼尿肌放鬆的作用

膀胱內Chondroitin Sulfate療法
Chondroitin sulfate，是膀胱表皮GAG層的成分之一。每週一次，
每次40毫升0.2%condroitin sulphate，總共治療四週，隨後每個月灌注一次，
總共12個月，病患在治療完成後整體改善率有76%。

表 58-1. 間質性膀胱炎之各種不同膀胱內治療方法之療效療程及缺點

	療 程	治療成效	缺 點
膀胱內肝素治療	每星期兩次至三次，總共療程為 12 星期	改善膀胱容量，減少膀胱過動	作用不能持續
膀胱內玻尿酸治療	四個禮拜每周灌注一次，接下來每個月灌注一次，持續四到五個月	約有 55%~85% 病患可以在治療完成後有顯著改善膀胱疼痛	價格昂貴，作用不能持續
膀胱內 Chondroitin Sulfate	每週一次，隨後每個月灌注一次，總共 12 個月。	整體改善率有 76%	雙盲試驗中效果不佳，可能需合併灌注碳酸氫鈉
膀胱內 DMSO 療法	一周兩次灌注持續四個禮拜，接下來每週灌注一次持續四週	改善膀胱疼痛	
膀胱內肉毒桿菌注射	單次注射即有療效，但可能半年後需要重複注射	改善膀胱疼痛及增加膀胱容量	較為侵入性，可能產生 UTI
膀胱鏡下以水擴張	單次擴張即有療效，但效果會隨時間遞減	改善膀胱疼痛及增加膀胱容量	較為侵入性，可能產生 UTI

Tx of IC/BPS



AUA guideline
J Urol. 2015 May;193(5):1545-53

BOX 14-7 Interstitial Cystitis Association Recommendations of Foods to Avoid

Milk and dairy products
- Aged cheeses
- Sour cream
- Yogurt
- Chocolate

Vegetables
- Fava beans
- Lima beans
- Onions
- Tofu
- Soybeans
- Tomatoes

Fruits
- Apples
- Apricots
- Avocados
- Bananas
- Cantaloupes
- Citrus fruits
- Cranberries
- Grapes
- Nectarines
- Peaches
- Pineapples
- Plums

Fruits—cont'd
- Pomegranates
- Rhubarb
- Strawberries
- Juices from above fruits

Carbohydrates and grains
- Rye bread
- Sourdough bread

Meats and fish
- Aged, canned, cured processed, smoked meats and fish

Nuts

Beverages
- Alcoholic beverages including beer and wine
- Carbonated drinks
- Coffee
- Tea
- Fruit juices

Seasonings
- Mayonnaise
- Ketchup
- Mustard
- Salsa

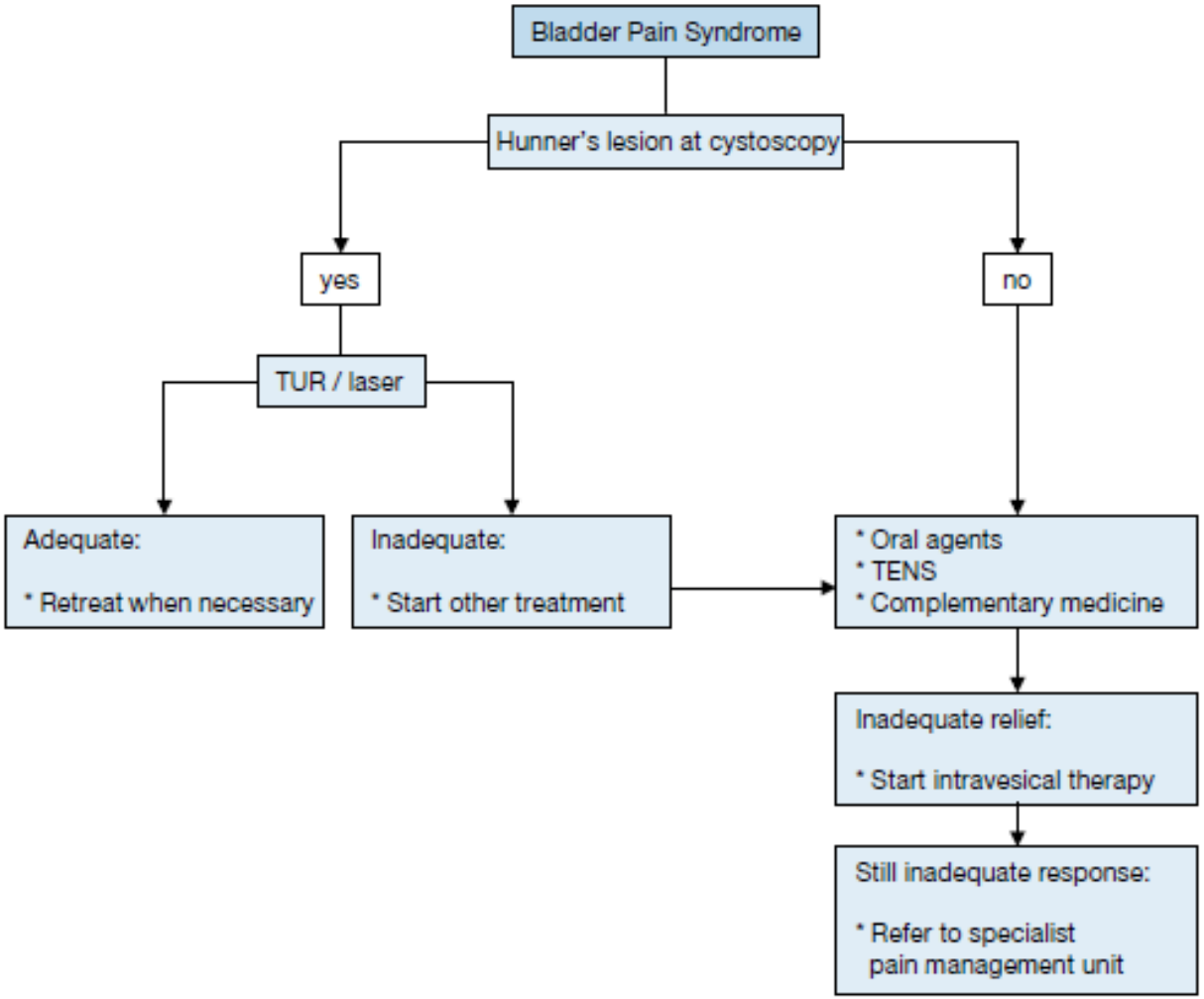
Seasonings—cont'd
- Spicy foods (Chinese, Mexican, Indian, Thai)
- Soy sauce
- Miso
- Salad dressing
- Vinegar

Preservatives and additives
- Benzyl alcohol
- Citric acid
- Monosodium glutamate
- Artificial sweeteners
- Preservatives
- Artificial ingredients
- Food coloring

Miscellaneous
- Tobacco
- Caffeine
- Diet pills
- Junk foods
- Recreational drugs
- Allergy medications with ephedrine or pseudoephedrine
- Certain vitamins

Tx for IC with Hunner's lesion

Algorithm 3: Treatment of BPS Type 3 C



EAU guideline for chronic pelvic pain 2016

Ketamine Cystitis

- ketamine has been used as a complete anesthetic agent since the 1960s
- Ketamine has been used as a recreational drug since the early 1990s in the USA
- In Taiwan, it has been classified as Schedule III controlled drug since 2002.
- The clinical symptoms of KC are recognized as painful hematuria, dysuria, frequency, urgency and postmicturition pain in Shahani's first report in 2007

Mechanisms of action

- N
- M
- N
- N

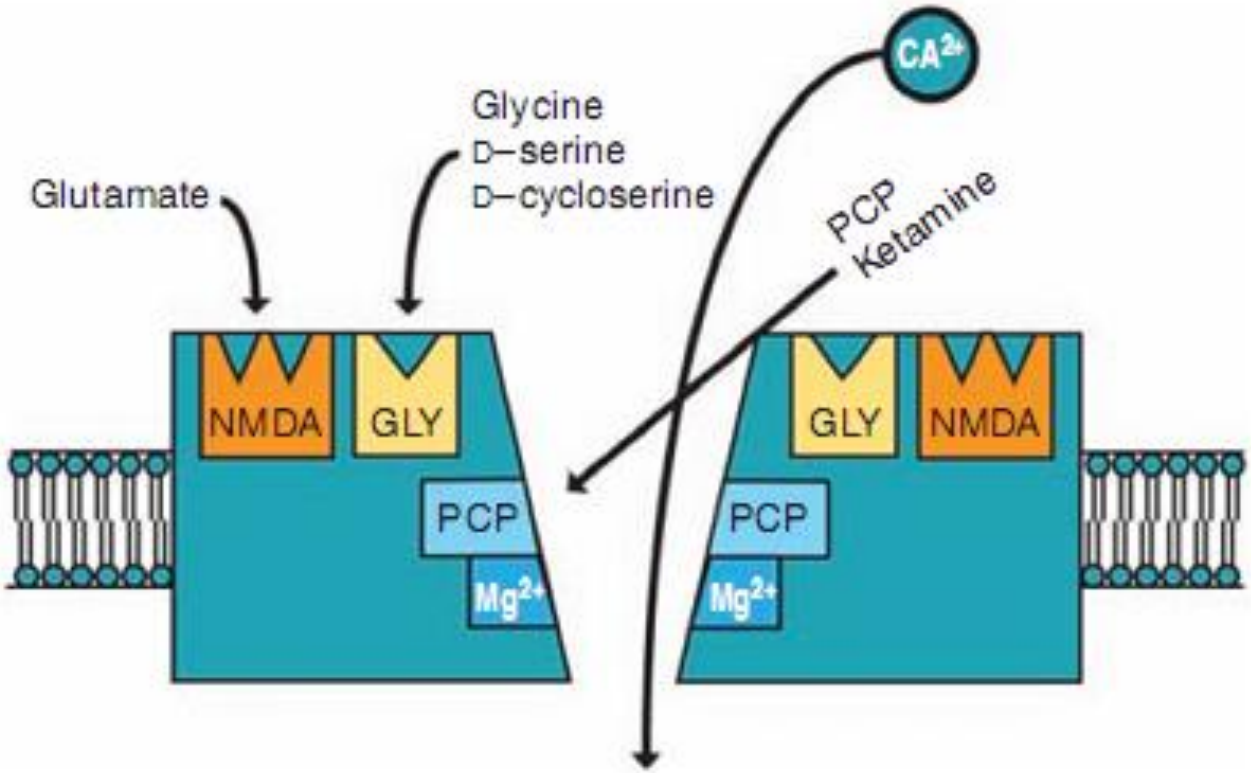


Figure 74-2 The properties of ketamine are primarily mediated by noncompetitive antagonism at NMDA receptors, which consist of five subunits surrounding a central ion channel that is permeable to Ca^{2+}, Na^{+}, and K^{+}. GLY, Glycine; NMDA, *N*-methyl-D-aspartic acid; PCP, phencyclidine.

Faust's Anesthesiology Review , 4th Edition, 2015

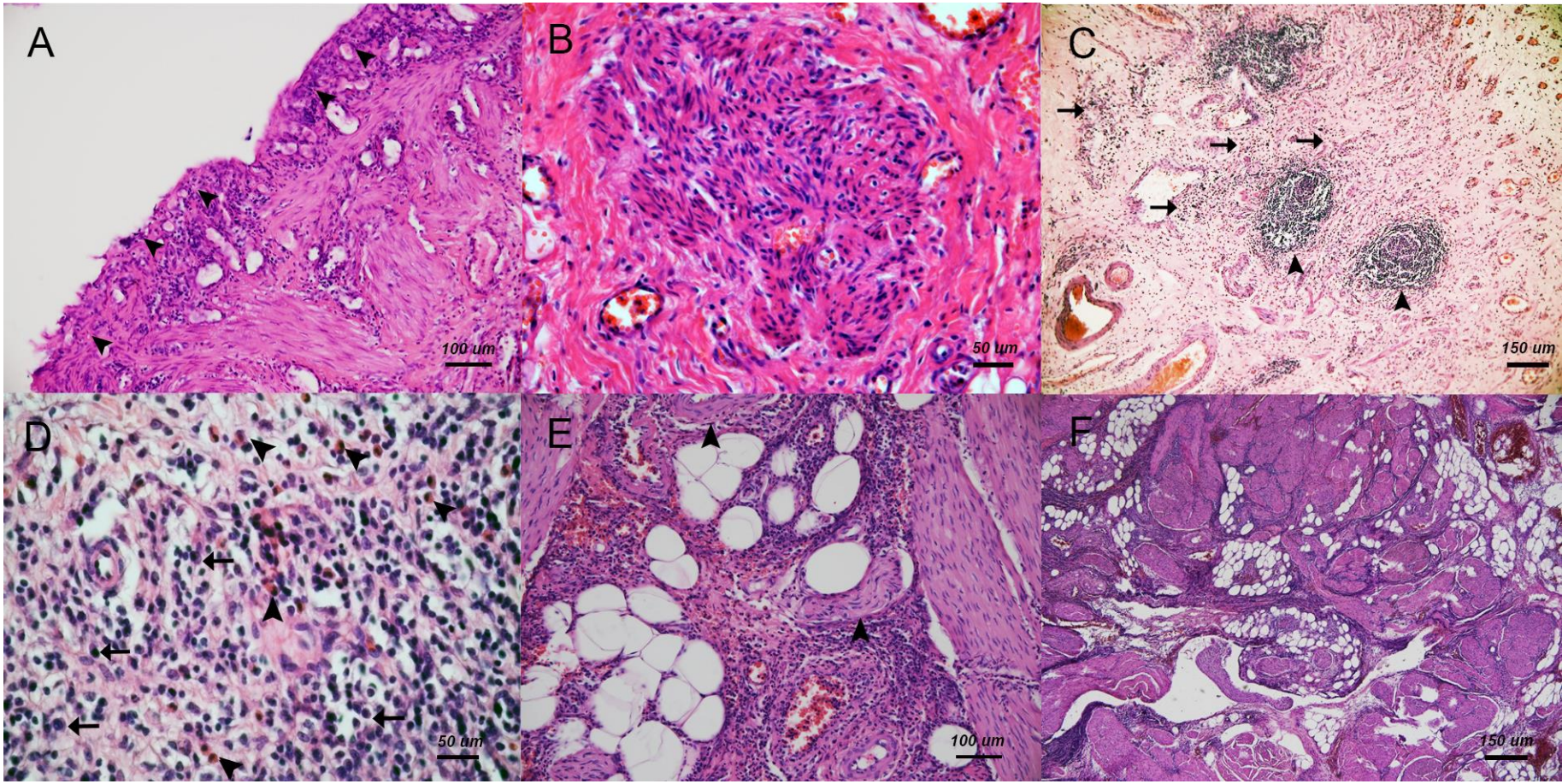
Pathogenesis of KC

Table 2 Possible pathogenesis pathways and associated treatment of KC

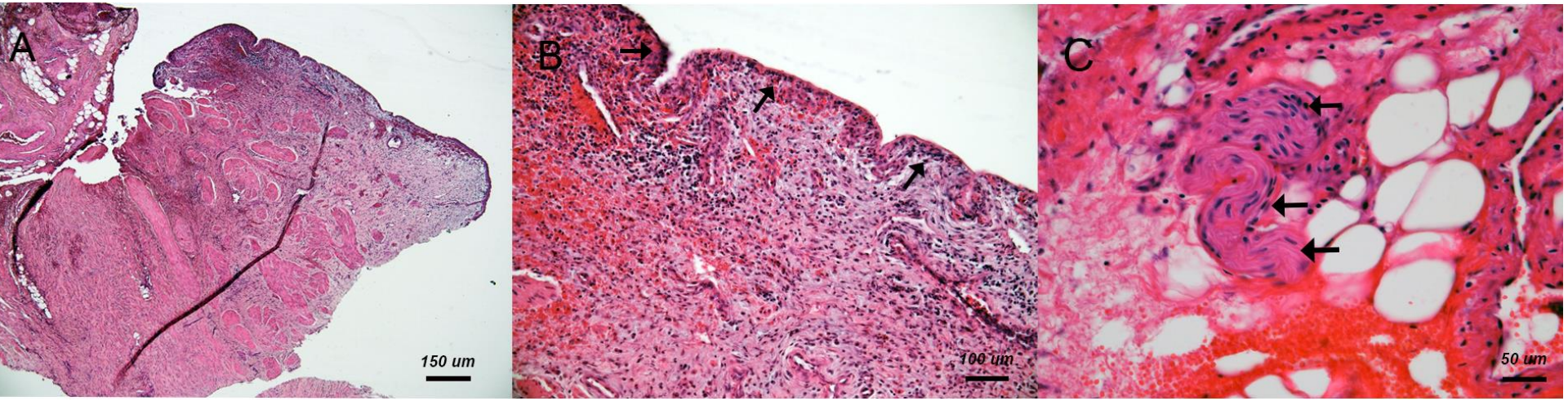
Possible pathogenesis pathways	Evidence in human study	Evidence in animal studies	Possible medical therapy base on pathogenesis
Direct toxic damage		Metabolite of ketamine which was a hydroquinone exerted toxicity and directly fragment DNA and abet chromosome in cells[21,22]	
Bladder barrier dysfunction	Decreased E-cadherin in urothelium of KC bladder[16]	Decreased ZO-1 and glycoprotein GP51 in KC bladder wall[29]	Intravesical instillation of hyaluronic acid, chondroitin sulphate or pentosan polysulfate[72–74]
Neurogenic inflammation	Increasing serum BDNF level[32] Nerve hyperplasia and increasing nerve growth factor receptor in KC bladder[36]	Increased P2X1 purinergic receptor expression in KC[37]	Intravesical BoNT-A injection[80]
IgE mediated inflammation and hypersensitivity	Increasing mast cell and eosinophil in urothelium of KC bladder[16,17] Elevated of serum IgE level[17]		Steroid or anti-IgE therapy
Carcinogenesis	Urothelial atypia and high level of expression of p53 and Ki-67 in KC bladder[42] Decreased E-cadherin in urothelium of KC bladder[16]	Increased expression of phosphorylated transgelin in bladder[46]	
Cell apoptosis	Increased expression of TUNEL staining in human KC bladder[16] Increased expression of Bax, decreased expression of Bcl-2 and pro-caspase-3 in cultured human uroepithelial cells[56]		
NOS-COX medicated inflammation		Increased expression of iNOS, eNOS and COX-2[60]	COX-1 and COX-2 inhibitor

IJU 2015

Pathological change of KC bladder



Pathological change of KC ureter



Goal to Ketamine Uropathy Management

Relief bladder pain

Decrease urgency or urge incontinence

Increase Bladder Volume

Prevent Upper Urinary Tract Injury

Tx of KC

- The only consensus on the effective management of KC is cessation of ketamine
- Mak et al. reported that the symptoms of KC, such as pain and urinary frequency, progressively improve with increased duration of abstinence
- However, In one study, 43% of patients with KC who had stopped using ketamine had the same symptoms
- 3.8% of patients even reported deterioration on stopping ketamine use

BJU Int. 2012; 110: 1762–6

First of all

- Quit ketamine

中止藥物的繼續影響

- Transfer patient to psychiatrist c
  ketamine cessation

請家人或伴侶嚴密監督，讓自己沒辦法再碰K他命；或者就乾脆住院

調整自己的生活

利用個別、團體、心理及行為治療、藥癮諮商等方式

NSAID

- Based on the increasing expression of COX-2 receptors, a COX-2 inhibitor should also be useful for relieving bladder pain.
- Tsai *et al*. reported that 11 patients with KC who received NSAIDs had inadequate responses to the therapy
- Saumya et al. NSAID no lasting benefit
- Chu *et al*. oral steroid also could not stop inflammation

Tsai, Int. J. Urol. 2009; **16**: 826-9
Chu PS, BJU Int. 2008; **102**: 1616-22
Saumya M. Scand J Urol. 2014; 48: 482–488

Anti-Cholinergics

- Chu PS: High-dose antimuscarinic agents were tried by these patients but none of them had any response. (0/59)
- Saumya et al. antimuscarinic no lasting benefit
- According to the study by Meng et al., the cholinergic muscarinic receptor M2 or M3 did not increase in the KC rat bladder, but the purinergic receptor P2X1 increased.

Chu PS, BJU Int. 2008;102((11)):1616–22
Meng E, J. Urol. 2011; 186: 1134–41

	N	NSAID	anticholinergics	2nd anti-inflammation or pain control
Lee in HK	319	effective	effective	effective
Chu in HK	59	N/A	none of them had any response	fail
Saumya in UK	34	no lasting benefit	no lasting benefit	no lasting benefit
Tsai in TW	11	inadequate responses	No response	N/A

Intravesical theraoy

- Chen et al.: 3 patients using intravesical hyaluronic acid (Cystistat®) ➔ Improvement of suprapubic pain for all three patients
- Lai et al: 3 patients using intravesical sodium hyaluronate solution ➔ some symptomatic relief.

Chen CH, J. Formos. Med. Assoc. 2011; 110: 787–91
Lai Y. Urol. Int. 2012; 89: 93–6.

Intravesical theraov

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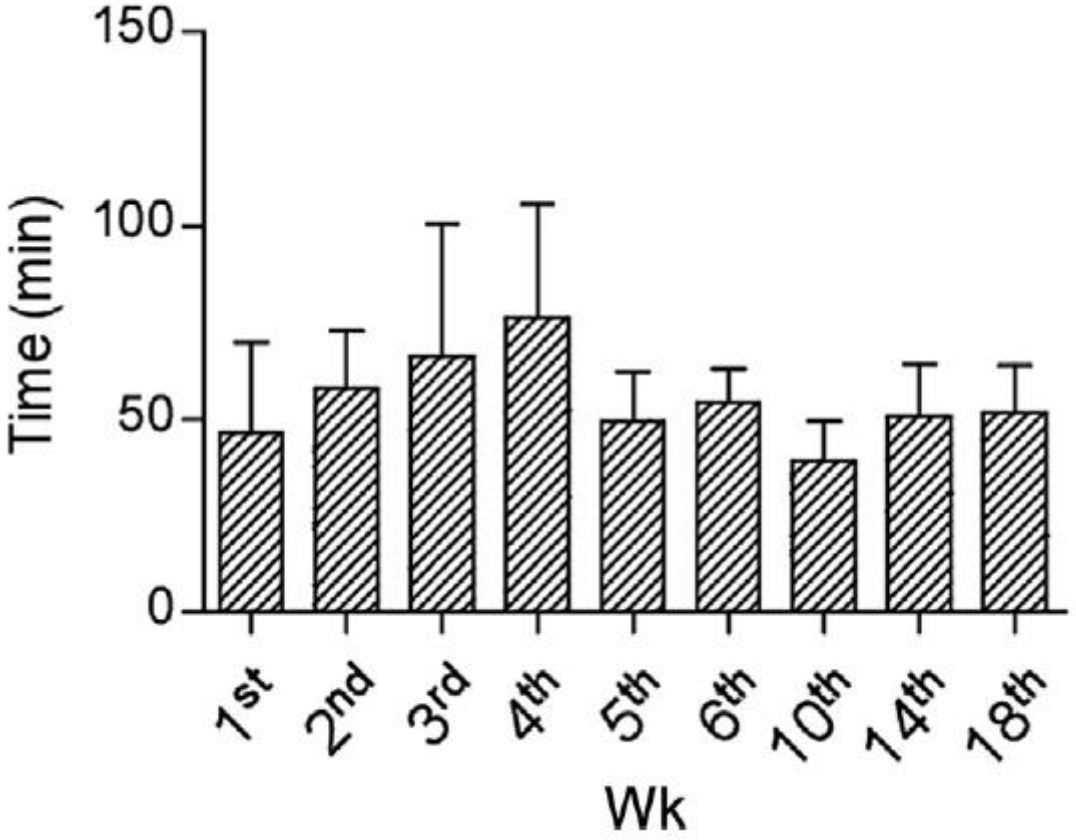

Table 1
Patient characteristics and ur

No.	Sex	MBC (mL)
1	Female	100
2	Female	120
3	Female	250
4	Female	500
5	Male	150

FBC = functional bladder cap

E. Meng et al. Urological Science, 2015: 176e179

Table 2
Change in scores of questionnaires after hyaluronic acid (HA) treatment (mean ± standard deviation).[a]

Time after HA treatment	0 (Baseline)	1 wk	2 wk	3 wk	4 wk	5 wk	6 wk	10 wk	14 wk	18 wk
VAS	7.0 ± 2.2	6.4 ± 2.7	5.4 ± 1.9	5.0 ± 2.2	4.4 ± 0.6	4.6 ± 1.9	3.6 ± 1.1	4.4 ± 3.6	3.8 ± 1.8	3.3 ± 2.1
Change from baseline		−0.60 ± 1.8	−1.6 ± 2.5	−2.0 ± 3.2	−2.6 ± 1.8*	−2.4 ± 3.5	−3.4 ± 2.7*	−2.6 ± 4.7	−3.2 ± 3.4	−4.2 ± 2.7
IPSS	28.8 ± 4.8	26.4 ± 3.1	26.2 ± 4.1	25.2 ± 5.3	22.4 ± 4.3	23.2 ± 4.6	22.8 ± 3.3	23.2 ± 3.1	22.6 ± 6.1	20.0 ± 6.0
Change from baseline		−2.4 ± 5.8	−2.6 ± 4.4	−3.6 ± 4.9	−6.4 ± 3.2	−5.6 ± 3.8	−6.0 ± 4.5	−5.6 ± 3.1	−6.2 ± 6.8	−7.8 ± 8.2
IPSS-V	16.2 ± 3.8	13.4 ± 1.8	14.0 ± 4.3	13.6 ± 4.7	11.6 ± 4.2	12.4 ± 4.7	12.0 ± 3.9	12.8 ± 4.4	11.8 ± 5.1	10.3 ± 3.2
Change from baseline		−2.8 ± 3.6	−2.2 ± 3.3	−2.6 ± 3.2	−4.6 ± 2.6*	−3.8 ± 2.9	−4.2 ± 3.0	−3.4 ± 3.2	−4.4 ± 4.3	−4.5 ± 4.5
IPSS-S	12.0 ± 2.4	11.6 ± 2.3	11.2 ± 1.9	10.8 ± 1.9	10.6 ± 1.7	10.0 ± 2.5	10.0 ± 1.9	8.8 ± 3.0	9.2 ± 3.6	9.7 ± 4.0
Change from baseline		0.40 ± 2.5	−0.40 ± 1.7	−1.0 ± 1.9	−1.8 ± 1.3	−1.8 ± 1.6	−1.8 ± 2.3	−2.2 ± 2.2	−1.8 ± 3.1	−2.0 ± 4.8
OABSS	11 ± 2.7	9.4 ± 2.8	10 ± 2.9	8.8 ± 2.5	9.2 ± 1.6	8.6 ± 2.7	8.4 ± 2.5	8.2 ± 3.3	7.2 ± 2.9	7.5 ± 2.4
Change from baseline		−1.8 ± 1.8	−0.80 ± 0.8	−2.4 ± 1.9	−2.0 ± 2.7	−2.6 ± 1.5	−2.8 ± 3.6	−3.0 ± 2.9	−4.0 ± 1.0	−3.0 ± 2.4
ICSI	16.4 ± 2.7	14.4 ± 2.1	14.8 ± 3.0	13.4 ± 2.3	13.6 ± 2.0	12.2 ± 2.2	12.6 ± 2.1	12.4 ± 3.4	11.8 ± 2.7	13.5 ± 1.3
Change from baseline		−2.0 ± 1.4	−1.6 ± 1.1	−3.0 ± 1.6*	−2.8 ± 1.5*	−4.2 ± 2.4*	−3.8 ± 2.2*	−4.0 ± 1.4**	−4.6 ± 3.4*	−1.5 ± 3.9
ICPI	14.2 ± 2.2	12.0 ± 2.6	13.0 ± 3.3	12.6 ± 4.0	11.8 ± 3.8	12.4 ± 3.6	12.4 ± 3.8	12.4 ± 3.5	11.4 ± 2.9	11.7 ± 4.5
Change from baseline		−2.2 ± 1.9	−1.2 ± 1.6	−1.6 ± 2.5	−2.4 ± 2.9	−1.8 ± 2.2	−1.8 ± 2.7	−1.8 ± 2.5	−2.8 ± 2.4	−2.8 ± 2.5

After 4 weeks, statistically significant mean decreases in VAS 7.0 to 4.4), IPSS voiding subscore (16.2 to 11.6), and ICSI (16.4 to 13.6).

However, only ICSI constantly reduced after 4 weeks of treatment.

Botulinum toxin injection

- Jiang et al in China: 6 KC patients underwent botulinum toxin 200U injection to 30 sites
- Frequency: 24.2±5.9 to 12.8±2.5*
  voided volume: 31.3±10.8 ml to 67.8±23.7 ml*
- Lieb et al in German: A KC patient received botulinum toxin injection twice (200U and 400U), no improve

Jiang. J Third Mil Med Univ,2012,34(11):1120-1122
Lieb M. Psychiatr. Prax. 2012; 39: 43–5

Surgical intervention

- Most paper recommend surgical intervention for KC with irreversible contracted bladder
- Partial cystectomy (supratrigone) + enterocystoplasty with/without ureteral reimplantation
- Total cystectomy + neobladder formation

TABLE I. Causes of Patient Selection for Conservative Treatment and Augmentation Enterocystoplasty

Conservative treatment	Augmentation enterocystoplasty
MBC >300 ml	MCB <100 ml with or without upper urinary tract damage
Normal upper urinary tract	MBC <300 ml with upper urinary tract damage
Improved bladder symptoms after treatment	Intractable bladder symptoms after treatment
Patients is afraid of surgery	Urge to change bladder condition
Doctor's opinion	Small functional bladder capacity persists

Thanks for your attention