Interstitial Cystitis

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What Causes IC

- Auto Immune Disease
- Infection
- Glycosaminoglycan layer deficiency
- Reflex Sympathetic Dystrophy
- ? Hereditary

Are there different types of IC

Classification of Interstitial Cystitis

- Ulcerative
- Non Ulcerative
- Bladder Capacity under anaesthesia
- Presence or absence of Mast cells
- Treatment success or failure

NIDDK Inclusion Criterion

- **Glomerulations or Hunner's ulcer on cystoscopic examination, and**

- **Pain associated with the bladder or urinary urgency**

NIDDK Exclusion Criterion

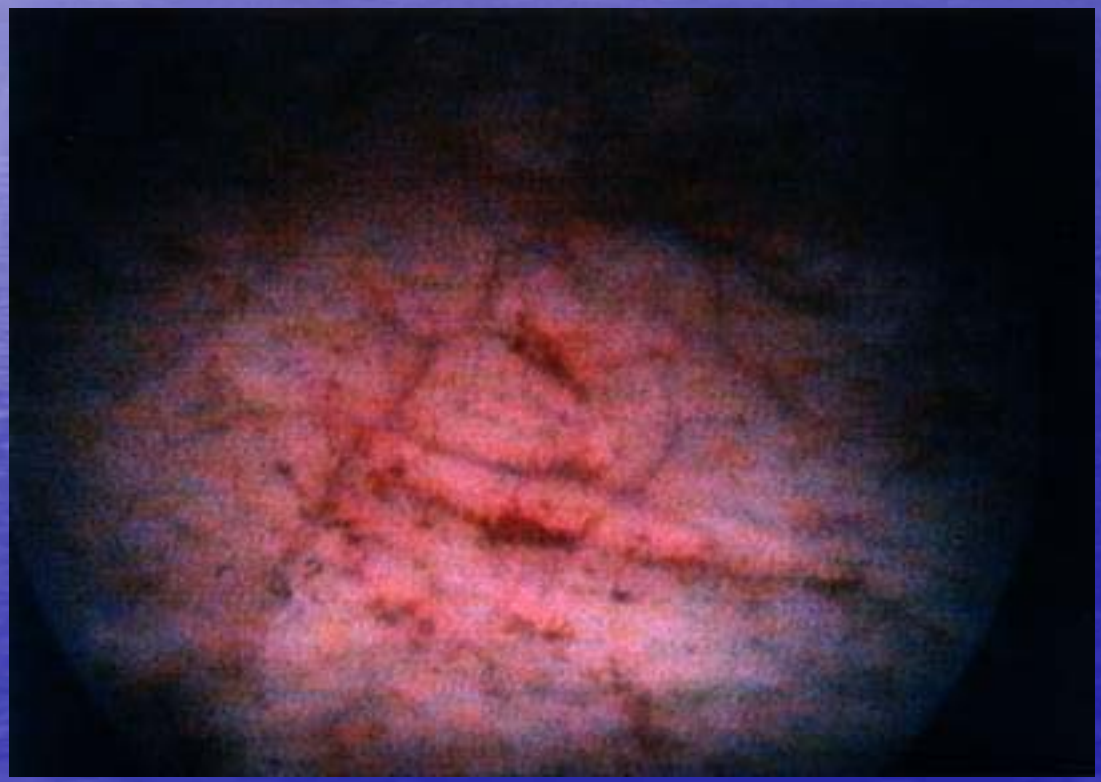
1. Bladder capacity >350 mL on awake cystometry using either gas or liquid as filling medium
2. Absence of intense urge to void with bladder filled to 100 mL of gas or 150 mL of water during cystometry, using a fill rate of 30-100 mL/min
3. Demonstration of phasic involuntary bladder contractions during cystometry using fill rate described above
4. Duration of symptoms less than 9 months and age <18
5. Absence of nocturia
6. Symptoms relieved by antimicrobials, urinary antiseptics, anticholinergics, or antispasmodics (muscle relaxants)
7. Frequency of urination while awake <8 times per day

NIDDK Exclusion Criterion

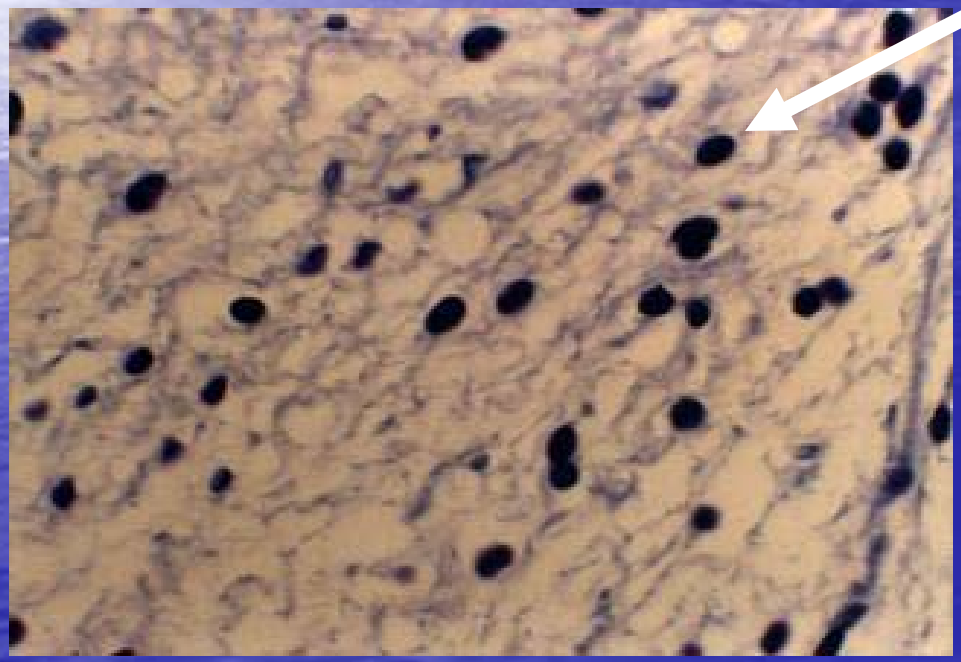
8. Diagnosis of bacterial cystitis or prostatitis within 3 month period
9. Bladder or lower ureteral calculi
10. Active genital herpes
11. Uterine, cervical, vaginal, or urethral cancer
12. Urethral diverticulum
13. Cyclophosphamide or any type of chemical cystitis
14. Tuberculous cystitis

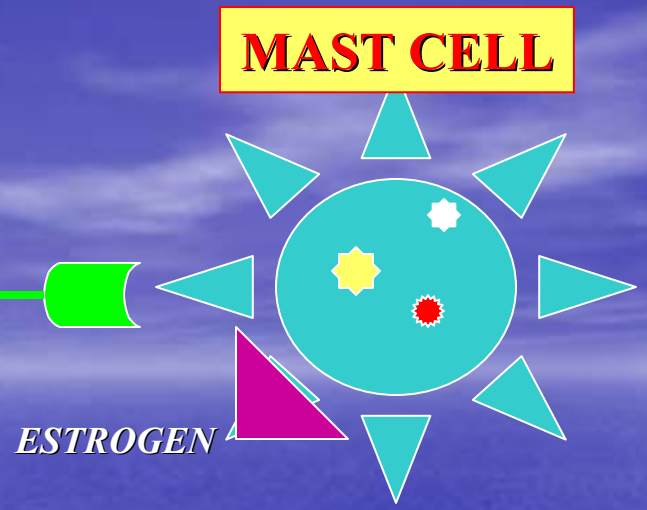
Diagnosis

Glomerulations



Biopsy





Histamine

Proteoglycans

Leukotrienes

Future Diagnostic Tools

URINARY MARKERS

- HISTAMINE

- CYTOKINES
  - Interleukin 1b
  - Interleukin 6

- KALLEKRINE
  - Correlates with bladder pain, frequency and successful hydrodistension

Special Concerns

- Cancer
- Pregnancy
- Coping

Current Management of Interstitial Cystitis

- Therapy exists in many forms
- Treatment largely empiric – only a few regimes evaluated as placebo controlled trials
- Multimodal therapy commonly used - no single treatment universally effective

Current Management of Interstitial Cystitis

- Conservative therapy
  - **Diet**
    - **53-63% can identify acidic fluids or foods incite flair**
      - **Mechanisms for this poorly understood not due to decreased urinary Ph from ingestion (Fisher et al)**
    - **Foods high in arylalkylamines**
      - **Mechanism tryptophan metabolites → Disruption of GAG layer (Kaufman et al)**
    - **Special diet remains a reasonable first line therapy for patients with irritative voiding symptoms**
    - **Tolerable food for IC patients include:-**
      - **Rice, pasta, potatoes, vegetables, chicken, meat, watermelons and grapefruit**

Current Management of Interstitial Cystitis

- Conservative therapy
  - Behavioural therapy
    - 50 – 75% reduction of symptoms in 50% of patient
    - Bladder training with deferment techniques → increase inter-void intervals
  - Treatment of Pelvic Floor Dysfunction
    - Lilius reported 81 % of his IC Patients to have spasm & tenderness of the levator ani musculature
    - Use of trans-rectal Thiele massage, biofeedback & electro-galvanic stimulation

Current Management of Interstitial Cystitis

- Oral Therapy
  - Pentosan Polysulphate (Elmiron)
    - **Hwang et al in 1997 performed a meta-analysis evaluating 488 patients and determined that elmiron was more efficacious than placebo in the treatment of frequency, urgency & pain in patients with interstitial cystitis**
    - **Dose 100 mg TDS 1 hr before or 2 hours after meals**
      - **Side effects 1-4 %**
        - **Alopecia, diarrhoea, nausea, headache, rash, dyspepsia, abdominal discomfort, liver function abnormalities & dizziness**
    - **Should be taken for at least 3 months as symptom improvement may not be immediate**
    - **Dose Escalation has recently been evaluated to 300 mg TDS decreased time to improvement with no serious adverse events but increase in minor side effects**

Current Management of Interstitial Cystitis

- Oral Therapy
  - Hydroxyzine
    - Antagonist of Substance P induced mast cell activation
    - Clinical benefit described by Theoharides
    - Average reduction of symptom score of 40% over 3 months
      - In IC patients with allergic problems mean reduction of symptom score of 55%
    - Also has anticholinergic, sedative and analgesic properties
    - Start at 10 mg Nocte with increases to 25, 50 & 75 mg on a weekly basis
    - Sedation may limit dose but there is a tachyphylaxis (sedation will abate after a few days)

Current Management of Interstitial Cystitis

- Oral Therapy
  - Amitriptyline
    - Central & peripheral anticholinergic properties
    - Central or antihistaminic sedation
    - Inhibition of serotonin and noradrenalin reuptake
    - Initial dose 10 mg Nocte. Increase to 25, 50 and 75 mg at 2-3 week intervals
    - Dry mouth and sedation typically the most common side effects

Current Management of Interstitial Cystitis

- Oral Therapy
  - Gabapentin (Neurontin)
    - Anticonculsant with proven effectiveness in neuropathic pain syndrome
    - Mode of action uncertain
    - At doses of 1200mg daily (range 300 – 2100mg daily) 48% IC patients reported improvement in pain
    - Dosing begins 100 mg Nocte with increments of 100 mg every 3 to 7 days added next in the morning then at midday

Current Management of Interstitial Cystitis

- Oral Therapy
  - Narcotics – both long and short acting are used
  - Opioids may be used in conjunction with other oral IC agents with hydroyzine and amitriptyline exhibiting the ability to potentiate narcotic pain relief
  - Opioids can be tapered as other IC treatments begin to take effect

Current Management of Interstitial Cystitis

- Intravesical Therapies

  Hydrodistension

Mechanisms of action:-

(1) Mechanical damage or ischaemia to the submucoal bladder plexus

(2) Widespread mast-cell degranulation with exhaustion of nociceptive and inflammatory mediators

Current Management of Interstitial Cystitis

- Intravesical Therapies

  Dimethyl sulfoxide (DMSO)

  Modes of possible action:-

  (1) antiinflammatory effect

  (2) desensitisation or blockade of afferent nociceptive pathways

Current Management of Interstitial Cystitis

- Intravesical Therapies

  Bacillus Calmette-Guerin

  - Attenuated Strain of Mycobacterium bovis
  - Found by serendipity IC misdiagnosed as CIS
  - BCG response rate 60% vs 27% placebo - persistence of response 89% of responders
  - A large multi-centre phase 3 clinical trial evaluating the efficacy of BCG in patients with IC is currently underway

Current Management of Interstitial Cystitis

- Intravesical Therapies

  Hyaluronic acid

  - component of the GAG layer
  - predominant concentration in the subepithelial connective tissue
  - patients refractory to previous medical therapy

    Morales et al
  - Response was reported in 71% at 12 weeks

Current Management of Interstitial Cystitis

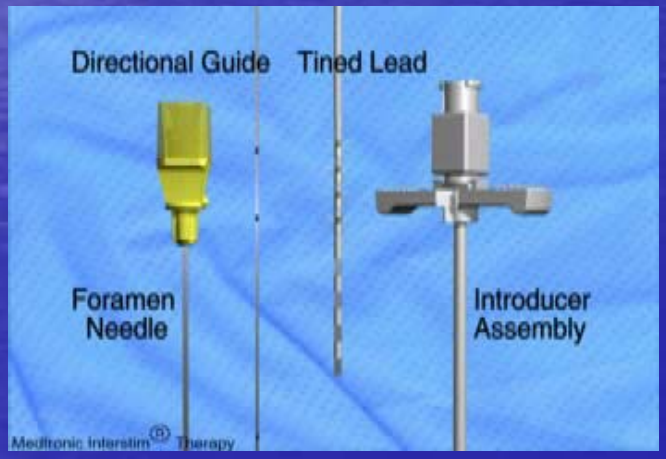
- Intravesical Therapies

  Resiniferatoxin

  - Ultrapotent vanilliod receptor agonist
  - Functions through desensitization of bladder afferents

Current Management of Interstitial Cystitis

Surgical Therapy

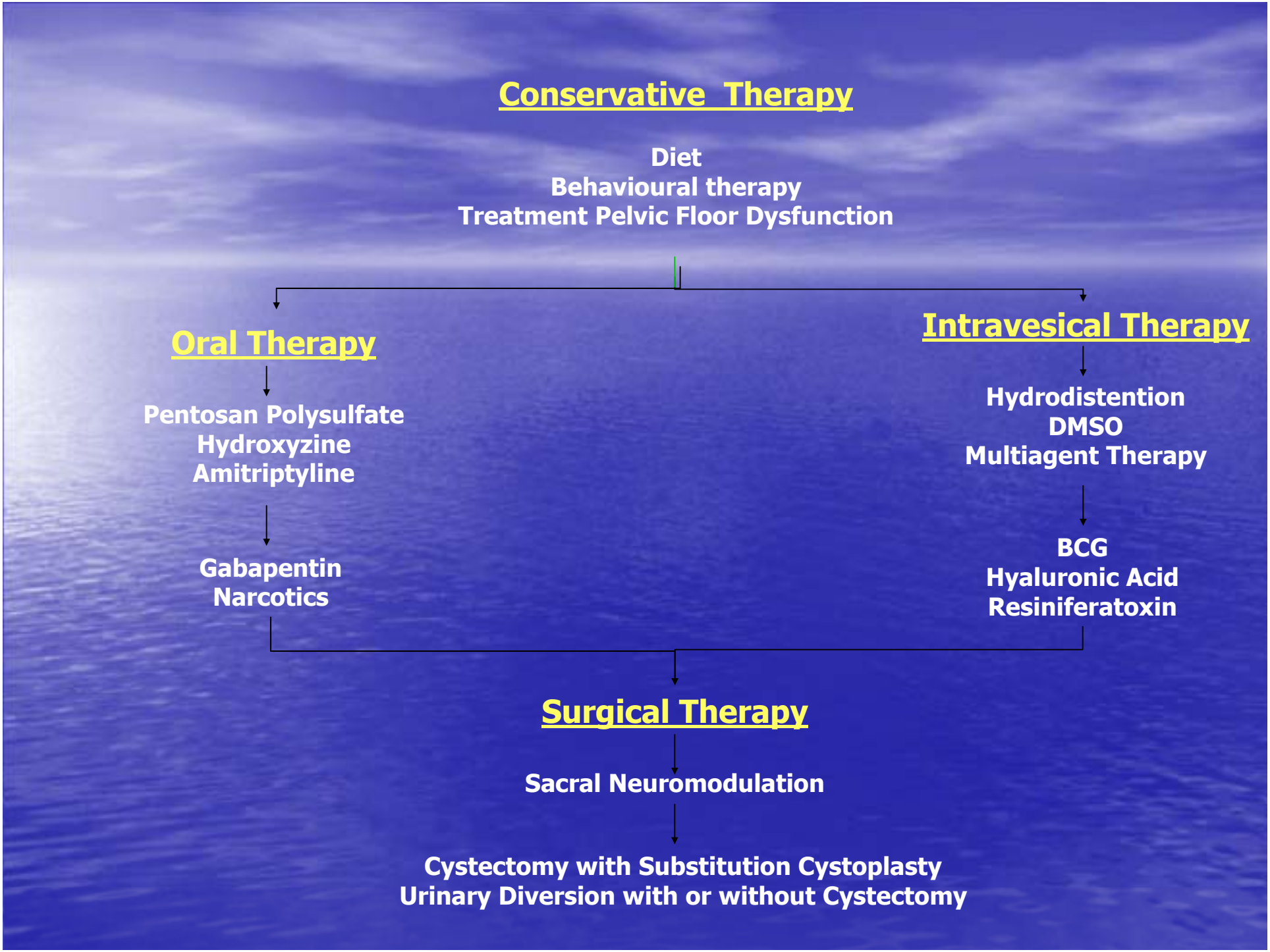


Sacral Neuromodulation

Current Management of Interstitial Cystitis

Surgical Therapy

- 10 % disease severe enough for major surgical intervention
- Surgical procedures include:
  - Subtrigonal or supratrigonal cystectomy and substitution cystoplasty
  - Cystectomy with urinary diversion (either ileal conduit, continent diversion or neobladder


Conservative Therapy
Diet
Behavioural therapy
Treatment Pelvic Floor Dysfunction
Oral Therapy
Pentosan Polysulfate
Hydroxyzine
Amitriptyline
Gabapentin
Narcotics
Intravesical Therapy
Hydrodistention
DMSO
Multiagent Therapy
BCG
Hyaluronic Acid
Resiniferatoxin
Surgical Therapy
Sacral Neuromodulation
Cystectomy with Substitution Cystoplasty
Urinary Diversion with or without Cystectomy

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