Naturopathic Management of:
Chronic Prostatitis and Pelvic Pain Syndrome

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DISCLOSURES

- President and part owner of Heron Botanicals
- CEO of Red Root Pharmaceuticals

NAME THAT SYNDROME

- Chronic pelvic pain syndrome (CPPS)
- Chronic abacterial prostatitis w/o inflammation
- Interstitial cystitis
- Urothelial syndrome
- Leaky urothelium

NIH CATEGORIES

Class	Prostatitis Type	Post-DRE UA	ICD-10
I	Acute bacterial	WBC, bacteria, RBC	N41.0
II	Chronic bacterial	WBC, bacteria	N41.1
IIIA	Chronic abacterial	WBC	N41.9 (?)
IIIB	Chronic pelvic pain	all negative	R10.2
IV	Asymptomatic inflammatory	WBC	N41.9 (?)

topics for today

If pre-DRE UA is WBC+: r/o urethritis, cystitis

CP/CPPS/IC OVERLAPS

- IC as a woman-only disease is simply wrong (Hassan 2007)
- It was just never investigated in men (CP was assumed)
- Overall IC is quite underdiagnosed conventionally (Clemens 2007)
- Many studies globally find IC is quite prevalent in men and women (Yarnell 2017)

Leaky Urothelium

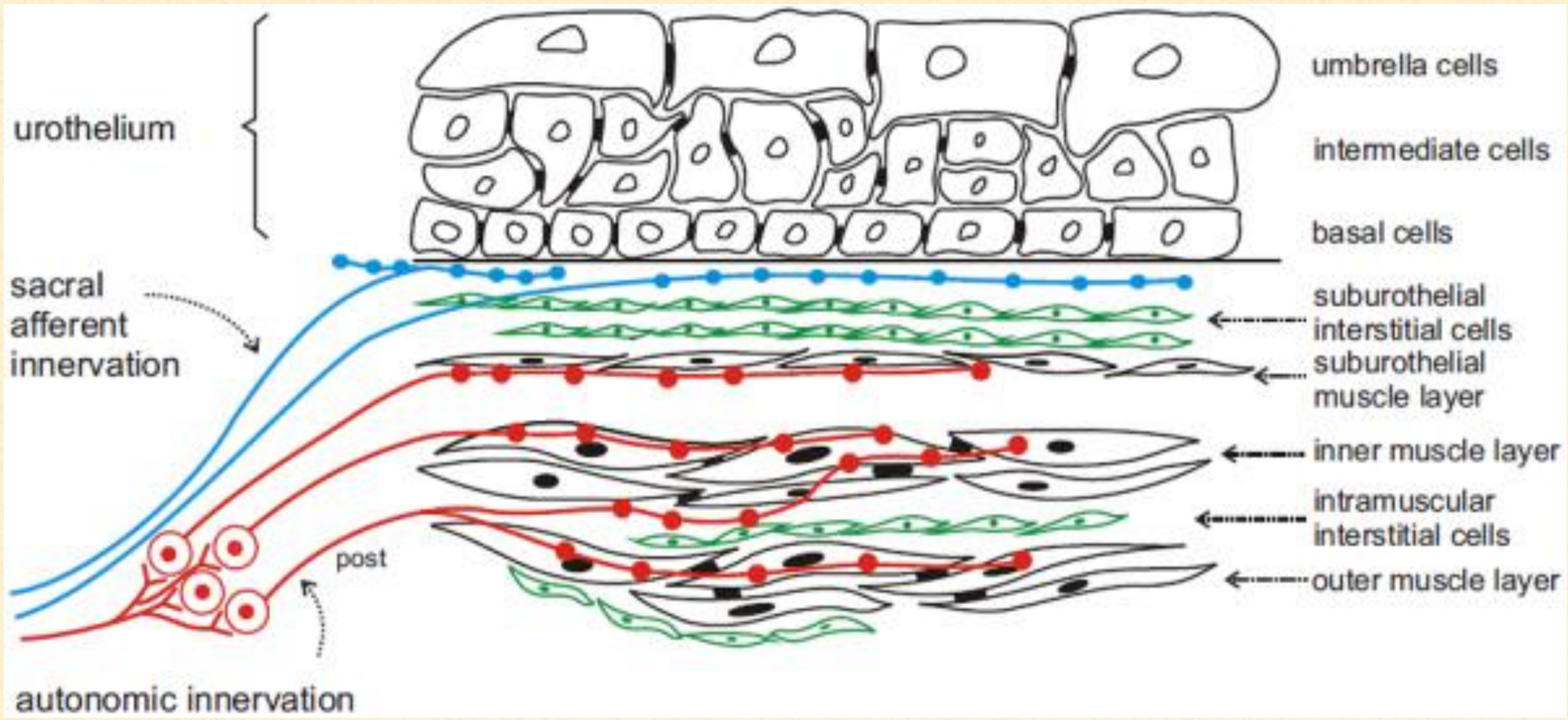
LEAKY UROTHELIAL SYNDROME

- Microscopic leaks in urothelium (thus doesn't only affect prostate but also bladder, urethra, possibly ureters)

- Lines of evidence:
  - Reflux of carbon particles into prostate tissue (Kirby 1982)
  - Potassium sensitivity test (Jiang 2016)
  - Bladder lactulose/rhamnose permeability (Erickson 2000)

NORMAL UROTHELIUM

Not shown: GAG layer



Ref: Birder 2014

PATHOLOGICAL FEATURES

Leaky urothelium

- Elevated bladder nitric oxide — Hosseini 2004
- Loss of tight junctions
- Umbrella cell loss
- Umbrella cell membrane alterations — Lewis 2000

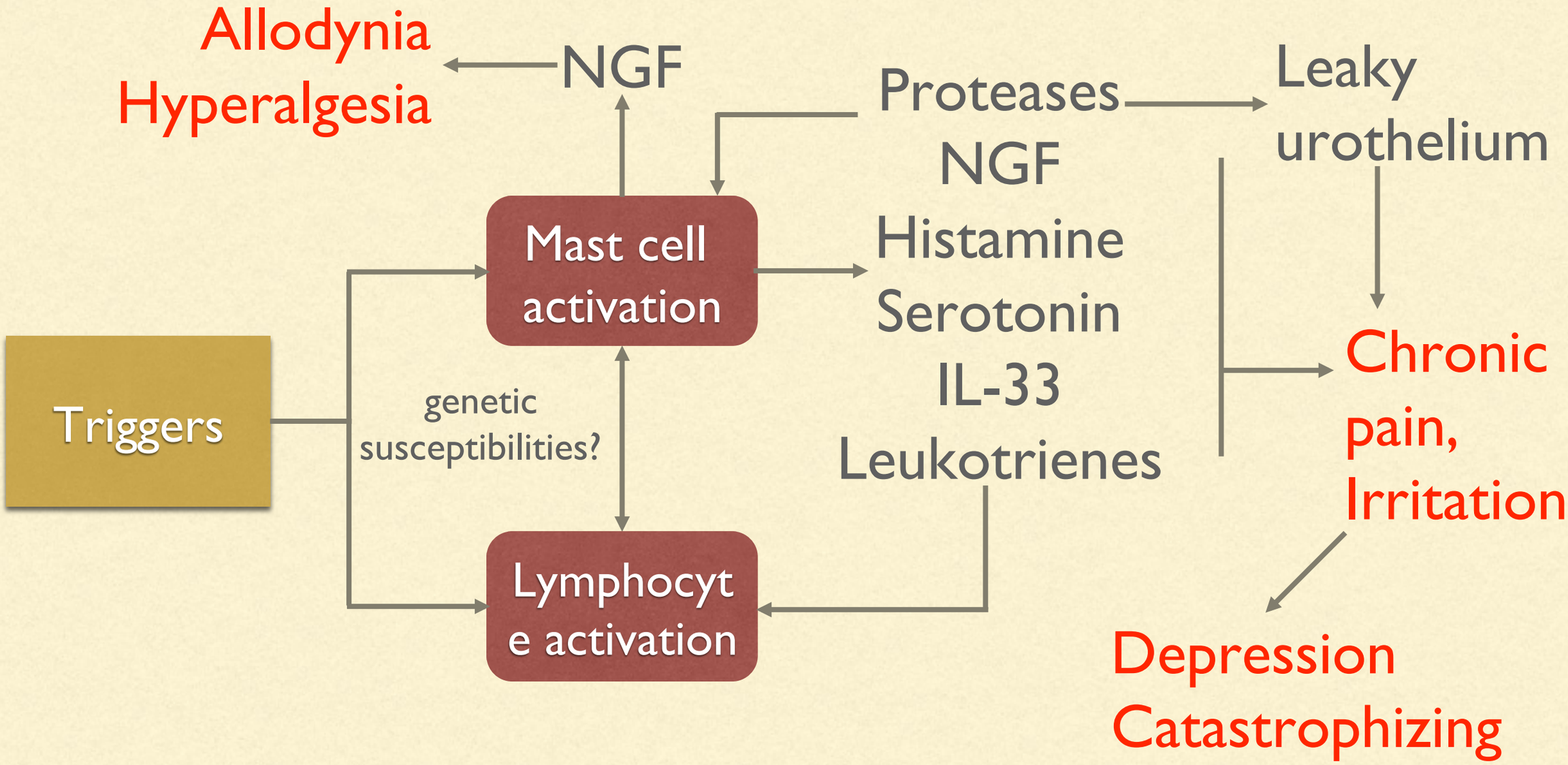
Inflammation

- Mast cell infiltration — Chaieb 2018; Done 2012; non-specific (Gamper 2015)
- IL-33 increased — Kochiashvili 2014
- NGF increased — Done 2012

Other

- Bladder fibrosis — Kim 2017
- Prostate fibrosis from chronic ischemic — Kogan 2018
- Low gut flora diversity — Shoskes 2016

INFLAMMATORY MODEL



LEAKY GUT —> LEAKY UROTHELIUM

- 90+% of IC patients have reactions to food; 48% of CPPS patients (Herati 2013; Friedlander 2012; Bassaly 2011)
  - Not all studies support this, but methodologies are a problem (Sutcliffe 2018)
- Clear case of food-induced eosinophilic IC (Sánchez Palacios, et al. 1984). Other cases of eosinophilic cystitis (Yamada 1985).
- Lack of research: gut permeability, leaky gut, zonulin + pelvic pain, prostatitis searches all yielded no hits in PubMed

"SIBO" AND CPPS/IC

- n=14 of 16 CPPS patients had positive lactulose breath test, IBS common in this group, rifaximin 550 mg tid x 10 d helpful IBS and CPPS sx (Weinstock 2011)

- n=95 w/ infertility, CP and IBS-D, randomized to rifaximin (400 mg bid 7 d/mon) + high-dose probiotics vs. no tx after post-antibiotic negative semen culture, some crossed over tx after 6 mon some stable for 12 mon, CP progression significantly reduced in all tx groups vs. no tx (Vicari 2014)

- n=17 of 18 IC patients have positive lactulose breath test, rifaximin (400–550 tid x 10 d) improved IC in 13 of these (Weinstock 2008)

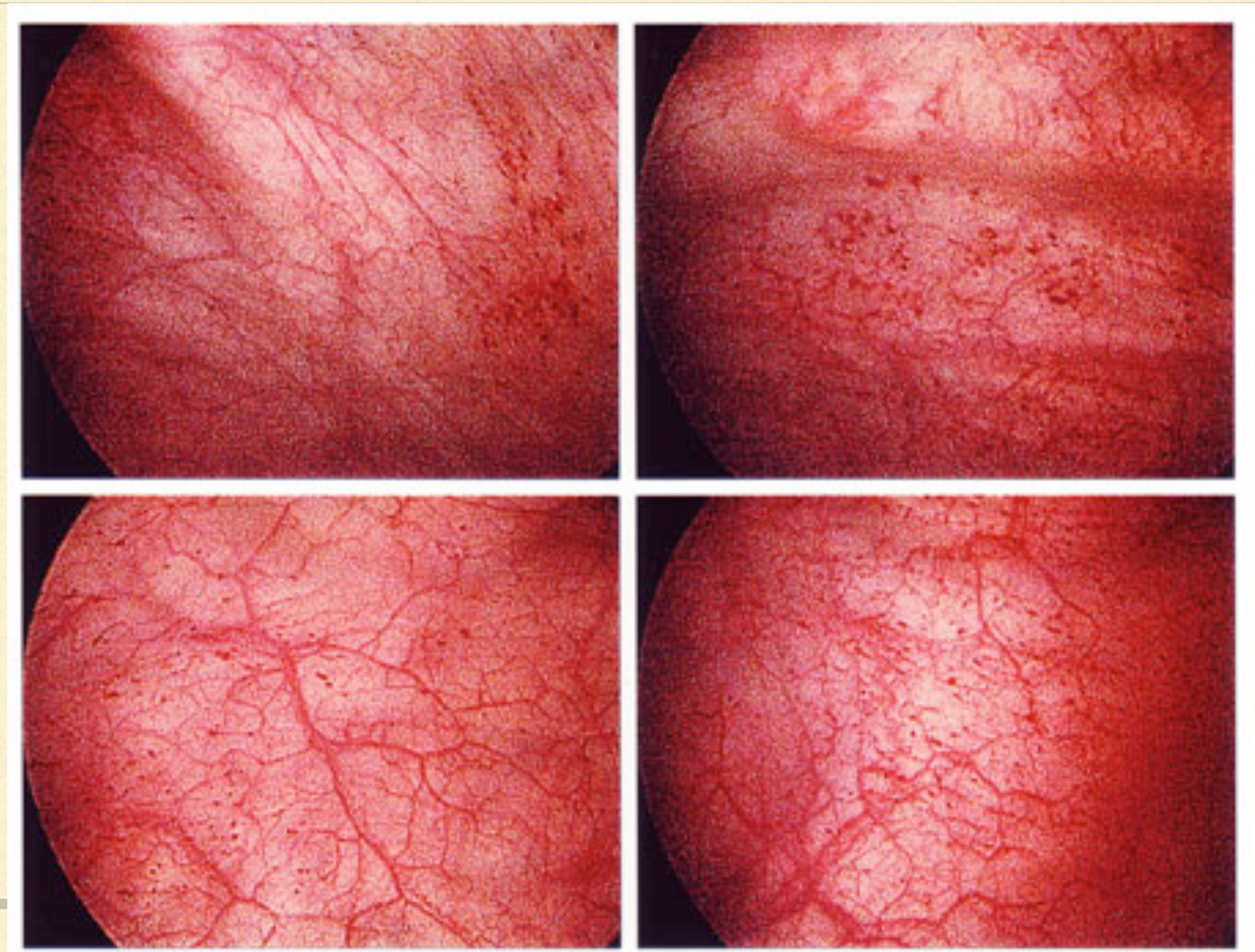
CLUES TO DIAGNOSIS

- History of food-associated symptoms
- Failure to resolve with prior treatments aimed at inflammation or killing bacteria
- Post-DRE leukocytes in urine (≥1+)
- Sudden larges flares in tPSA correlated with symptoms
- Tenderness of prostate on DRE (often absent)
- Calcification on TRUSP or other prostate imaging
- Bladder glomerulations and/or Hunner's ulcer on hydrodistention
- Inflammation seen on prostate biopsy (incidental finding)

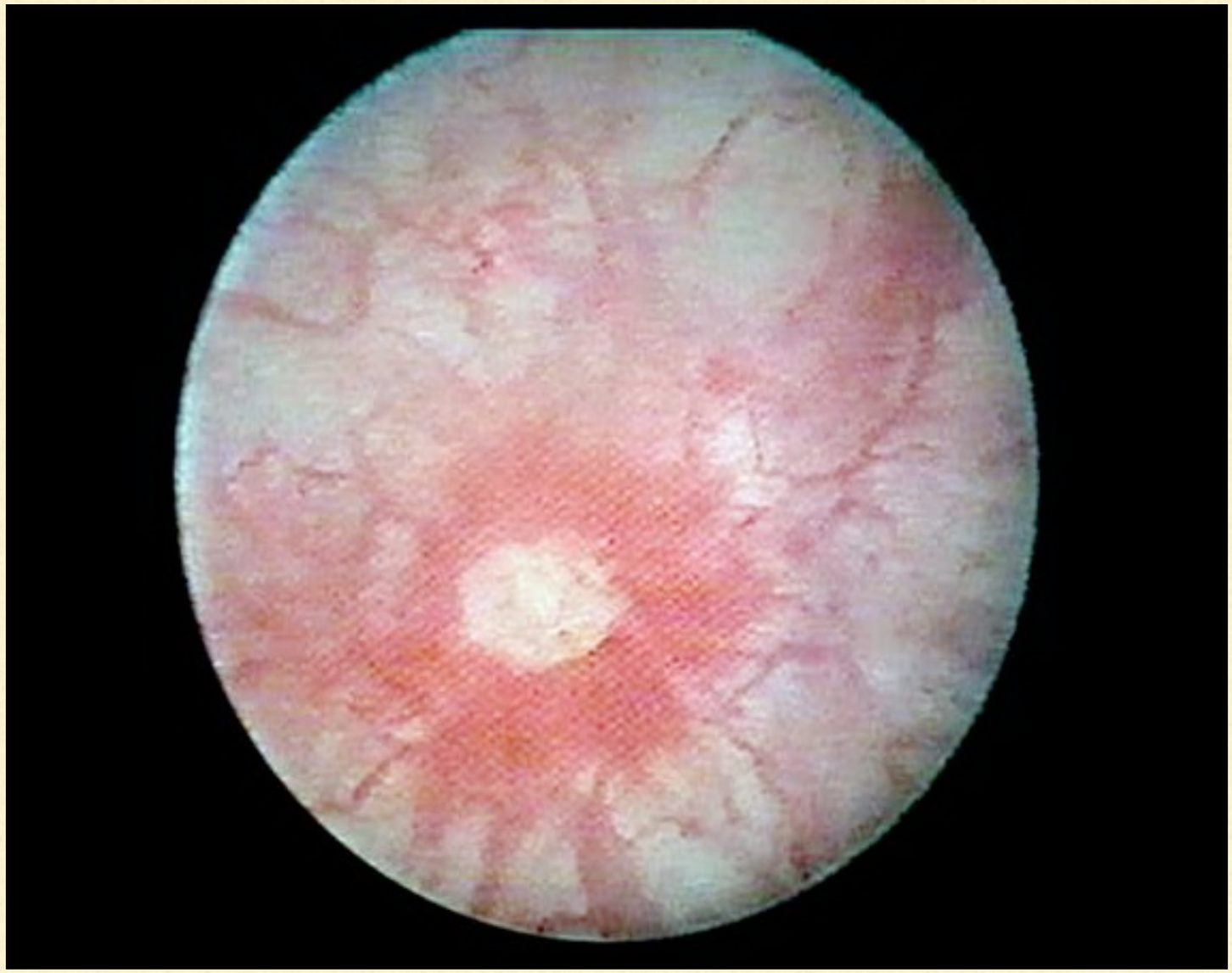
O'LEARY-SANT SYMPTOM SCORE

- Two scores: symptom index (0–20), problem index (0–16)
- Total score >6 = IC likely
- Total score >12 = IC almost guaranteed
- So order cystoscopy for sure if ≥12, possibly if ≥6
- Ref: O'Leary 1997

GLOMERULATIONS



HUNNER'S ULCER



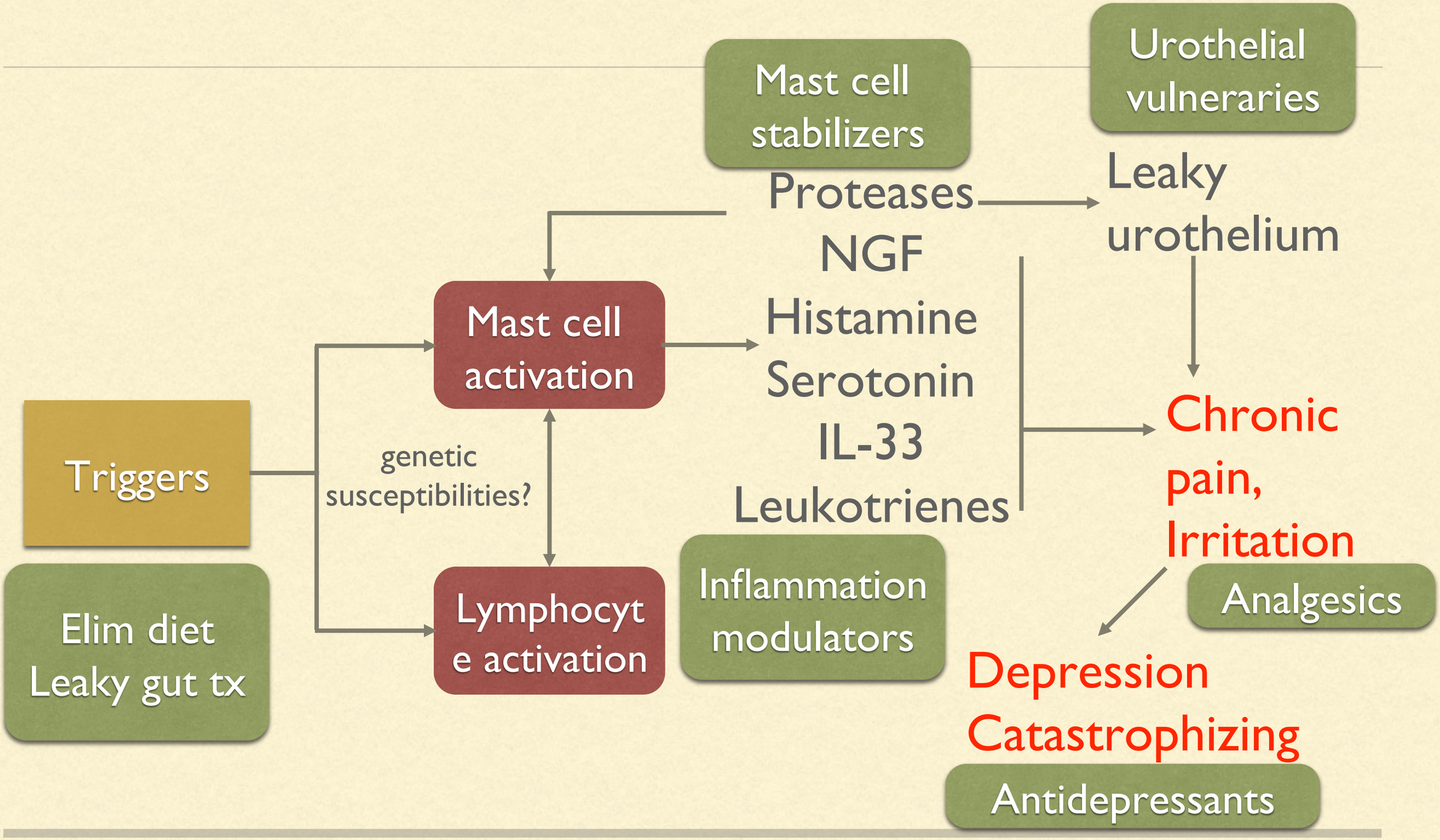
IC DIFFERENTIAL IN WOMEN

- Endometriosis, adenomyosis
- Vulvodynia
- Urethral syndrome
- Overactive bladder
- Diabetes mellitus

IC URINE DISEASE MARKERS

Marker (Abnormal Result)	TEST PARAMETERS	REFERENCES
Antiproliferative factor (APF) activity present	Sensitivity: 94% Specificity: 95%	Keay 1996; Keay 2001; Zhang 2005
Epidermal growth factor (EGF) >11.8 ng/ml	Sensitivity: 87% Specificity: 91%	Keay 2001; Zhang 2005
Heparin-binding EGF-like growth factor (HB-EGF) <3.7 ng/ml	Sensitivity: 93% Specificity: 89%	Keay 2001; Zhang 2005

TREATMENT CATEGORIES



INFLAMMATION MODULATORS: POLYPHENOLS

- Quercetin 500 mg tid (Shoskes 1999)
  - *Serenoa*, quercetin, ALA, β-sitosterol (Suardi 2014)
- Quercetin, rutin, glucosamine/chondroitin sulfate, hyaluronate effective in open trial in IC (Theoharides 2008)
- Cromolyn sodium

INFLAMMATION MODULATORS: FLOWER POLLEN

- Positive meta-analysis of 4 randomized trials (Cai 2017)
- Equally effective as Eviprostat formula (Iwamura 2015)
  - *Chimaphila umbellata*, *Populus tremula*, *Pulsatilla pratensis*, *Equisetum arvense*, *Triticum aestivum* germ oil
- Includes some evidence it is superior to quercetin and saw palmetto (Mauirizi 2019; Macchione 2019)

SERENOA + LYCOPENE + SELENIUM

- n=168 w/ biopsy-confirmed CP; most had BPH also (Morgia 2013)
- n=108 of these randomized to either SLS or no tx for 6 mon; n=60 randomized to SLS + alpha-blockers or not tx for 3 mon; then repeat biopsy
- Only SLS beat control for reducing inflammation
- Prior trial (n=102 with CPPS) found SLS beat *Serenoa* for improving symptoms, reducing inflam (Morgia 2010)

INFLAMMATION MODULATOR HERBS

Eryngium yuccifolium
(rattlesnake master)

Curcuma longa
(turmeric)

and other Zingiberaceae

Actaea racemosa
(black cohosh)

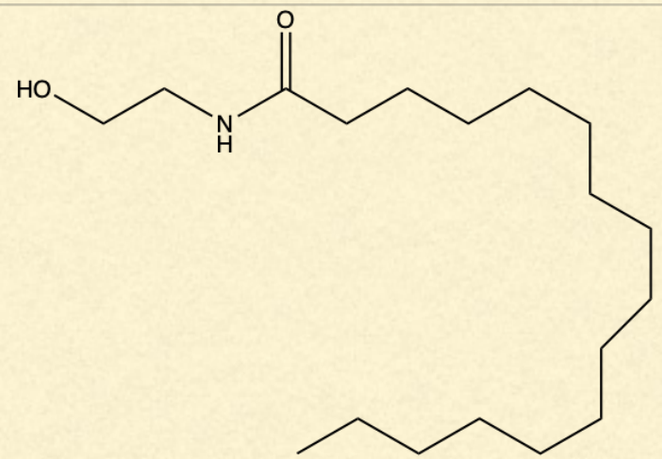
Echinacea angustifolia
(purple coneflower)

Fouquieria splendens
(ocotillo)

also pelvic lymphagogue

Chamaenerion angustifolium
(fireweed)

PALMITOYLETHANOLAMIDE (PEA)



PPARα
GRP55, GPR119

phosphatidylcholine
phosphatidylethanolamide

PEA → fatty acids + ethanol amide

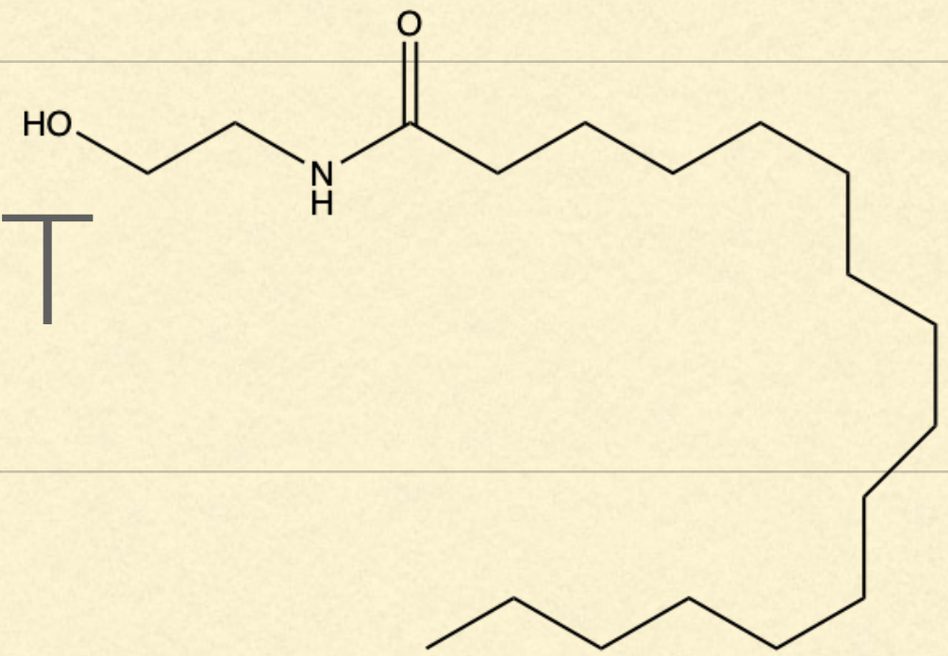
FAAH

AEA → fatty acids + ethanol amide

AEA → CB1, CB2

OEA → PPARα GPR119

PEA AS TREATMENT



- Single-blind, randomized trial (Giammusso 2017)
- n=44 CPPS patients
- Randomized to PEA 300 mg + α-lipoic acid 300 mg qd or saw palmetto extract 320 mg qd
- PEA + ALA significantly reduced symptoms vs. saw palmetto after 12 wk, no adverse effects in either group

DEMULCENTS; VULNERARIES

- *Aloe vera* gel 60 ml bid
- *Elymus repens* (couch grass) rhizome
- *Zea mays* (corn) *fresh* stigmata
- *Althaea officinalis* (marshmallow) root
- The latter 3 are best as cold infusions (5–10 g herb/cup of water) and have minimal/no utility as tinctures or glycerites (dose high or go home!)

ACUPUNCTURE

- Twice as likely as sham acupuncture to improve pelvic pain symptoms after 20 sessions in randomized trial (Lee 2008)

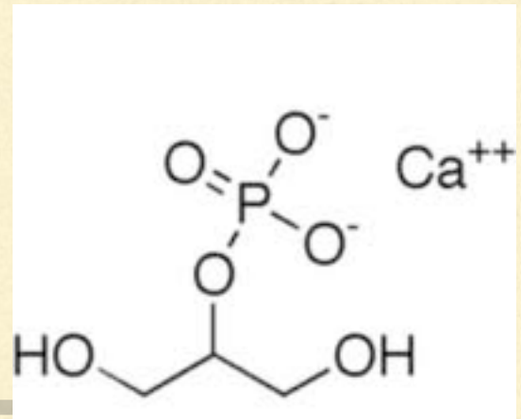
- In Chinese meta-analysis, moderately more effective than various comparative treatments to improve symptoms of CP (Wang 2008)

- Other clinical trials showing benefit (Chen 2003)

- Case series for IC in Japan, 3/8 responded after 3 mon, 2 w/ no recurrence for 48 mon (Katayama 2013)

CALCIUM GLYCEROPHOSPHATE

- Used to make “acidic foods” tolerable by patients
- Only very weak evidence supports it (Bologna 2001; Hill 2008)



CASE STUDY 1: LEAKY GUT

- 46-yr-old white male
- Frequent urination (including nocturia), small-volume voids; constant moderate pain; waxing-waning symptoms (in current flare x 5 mon)
- Previously responded to antibx but not currently
- DRE: saw MD four months ago and there was modest prostate tenderness
- Other notes: regular wine drinker, 16 pack-yr hx (stopped 19 yr ago), has small children (impact sleep)

Pelvic Floor Dysfunction

CLUES TO DIAGNOSIS

- Worse with chronic sitting
- History of bicycle, motorcycle, horse, etc. riding (not always)
- No inflammatory markers
- Failure to cure (or even help sometimes) with antibiotics or anti-inflammatories
- No obvious reactions to food
- Tenderness on palpation of pelvic floor
- Perineal trigger points

PELVIC FLOOR PT

- When in doubt, refer them out
- Not all physical therapists are knowledgeable about the pelvic floor: find one who is!
- In Seattle area I can recommend:
  - Kathe Wallace, Izette Swan, Holly Tanner, and Kathy Golic

HYDROTHERAPY

- Hot sitz baths
  - If they don’t like this or it aggravates, try contrast next
  - At least once hs for two weeks, more if helpful
- Contrast sitz baths more appropriate for inflammatory types

SPASMOLYTICS; ANALGESICS

- *Piper methysticum*(kava) root

start here

- *Pedicularis bracteosa* (lousewort) flowering top

- *Corydalis yanhusuo* (corydalis) prepared root

- *Gelsemium sempervirens* (yellow jessamine) root

low dose

- *Anemone occidentalis* (western pasqueflower) aerial parts

- *Hyoscyamus niger* (henbane) flower/leaf

* = Ecologically threatened

CASE STUDY 2: PELVIC FLOOR

- 43-yo white man
- Perineal/urethra pain since age 21 (little sleep, lots of beer, both still make him <), dizziness, very cold in the morning, anxiety (<grain, dairy elimination), waxing/waning, <sitting hard surface, tPSA 0.6 ng/ml, one post DRE UA positive, never since
- He has tried a wide range of supplements, antibx, phenazopyridine
- *Stachys* and *Pedicularis* both helpful; cold sitz helpful (<hot)
- Ultimately had pelvic floor PT and did mind-body medicine, had 99% improvement

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