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THE PROSTATITIS SYNDROMES

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Disclosures 2021

• Farr Labs		consultant (inactive Dec 2020)
• Seikagaku Corp	Yes	consultant
• Redleaf Medical	Yes	scientific study/trial/consultant
• Urogen Pharma	Yes	consultant
• Kanglaite		consultant
• Alivio		consultant
• MicroGenDx		scientific study/trial/consultant
• Valensa Int		consultant
• Inmunotek		scientific study/consultant
• Japan TC Pharma		consultant
• OM Pharma		consultant
• HengRui USA		consultant
• UTIVA		meeting participant/lecturer
• Zambon SpA		consultant
• Shionogi		consultant

Prostatitis is an enigmatic medical problem

- Almost 9% of Canadian men experience some prostatitis symptoms over the course of a year
  - 6% of men are bothered by prostatitis symptoms
  - one-third usually experience remission within one year
- Clinically significant prostatitis symptoms account for ~3% of Canadian male outpatient visits to Urologists (~ 1% male visits to primary care physicians)
- < 10% of patients suffer from acute or chronic bacterial prostatitis, which is usually amenable to antimicrobial therapy
- Majority of men with chronic prostatitis have chronic pelvic pain syndrome (CPPS), characterized by pelvic pain, variable urinary symptoms, and sexual dysfunction – diagnosis and treatment is difficult

Nickel JC. Prostatitis. *Can Urol Assoc J* 2011;5:306-15.

Classification of the Prostatitis Syndromes

- **Category I:** Acute Bacterial Prostatitis (ABP)
- **Category II:** Chronic Bacterial Prostatitis (CBP)
- **Category III:** Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS)

Nickel JC. Prostatitis. *Can Urol Assoc J* 2011;5:306-15.

Classification of the Prostatitis Syndromes

Category I:

Acute Bacterial Prostatitis (ABP), associated with severe prostatitis symptoms, systemic infection, and acute bacterial urinary tract infection (UTI)

Classification of the Prostatitis Syndromes

Category II:

Chronic Bacterial Prostatitis (CBP), caused by chronic bacterial infection of the prostate, with or without prostatitis symptoms, and usually with recurrent UTIs caused by the same bacterial strain

Classification of the Prostatitis Syndromes

Category III:

Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS), characterized by chronic pelvic pain symptoms and possibly voiding symptoms in the absence of UTI

Bacterial Prostatitis vs Chronic Prostatitis/CPPS

- Prostatitis can be a source of frustration for the treating physician and the patient
- Diagnosis of acute or chronic bacterial prostatitis is based on history, physical, and urine culture
- CP/CPPS is more challenging to treat since etiology is poorly understood
  - a chronic neuromuscular pelvic pain syndrome
  - initiated by infection, trauma or other condition
  - propagated by genetic, anatomic, physiologic or neuroendocrine factors
  - development of peripheral and eventual central nervous system sensitization (neuropathic pain)
  - modulated by psychological parameters

Diagnosis of Cat 1 Acute Bacterial Prostatitis (ABP)

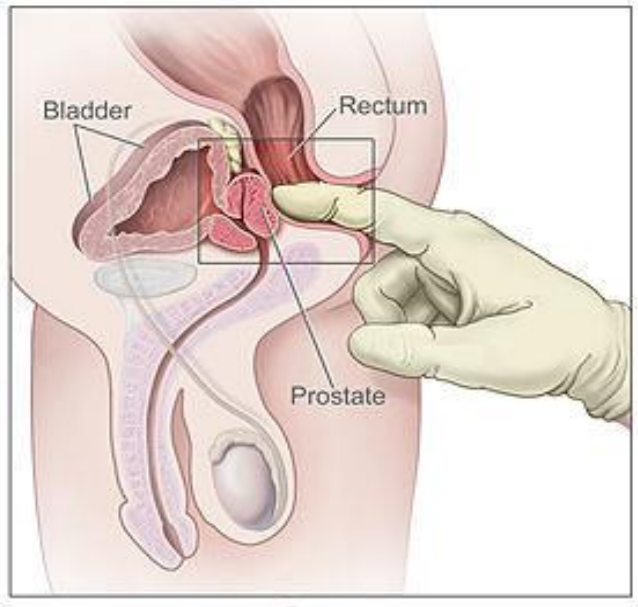
- **Pain** - suprapubic or perineal region, or in the external genitalia
    - dysuria
- **Urinary symptoms** - storage (irritative) – urgency, frequency and/or voiding (obstructive) – slow stream, intermittency, hesitancy, urinary retention
- **Systemic symptoms** - fever, chills, malaise, nausea, emesis, and signs of sepsis
- **Physical examination**
    - Prostate - tender, enlarged, and boggy; gently palpate not massaged
    - Abdominal - a palpable, distended bladder indicates urinary retention.
- **Tests** - Urine Culture, ultrasound (optional), no PSA

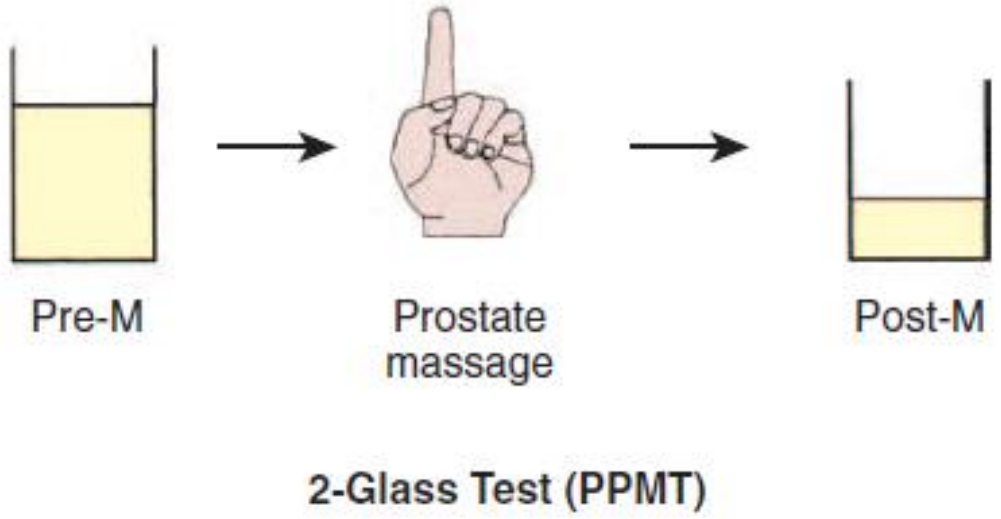
Diagnosis of Cat II Chronic Bacterial Prostatitis (CBP)

- **Presentation:**
  - recurrent or relapsing UTI, urethritis, or epididymitis with the same bacterial strain
- **Symptoms:**
  - Urinary: may have storage (irritative) or voiding (obstructive) symptoms
  - Pain: testicular, perineal, low back, ejaculatory, distal penile pain
- **Physical exam:**
  - usually afebrile; do not appear ill
  - Various pain areas – suprapubic, perineal, rarely external genitalia
  - Pelvic/DRE: the prostate may feel normal, tender, or boggy
- **Test:**
  - Cultures are important – 2 glass test (MSSU can be sterile between symptomatic episodes)

CAT II/III CP/CPPS Key Elements of Physical Examination

- **Abdominal, Pelvic and Prostate Examination**
  - Pain, spasm, trigger points, myofascial pain, prostate tenderness
  - 2-glass test





2-Glass Test (PPMT)

Treatment of Acute and Chronic Bacterial Prostatitis

ANTIBIOTICS

- Challenging
- Duration
  - Acute: 2-4* weeks
  - Chronic: 4-12* weeks
- Mainstays of treatment ~~are~~ were:
  - Trimethoprim with or without Sulfamethoxazole
  - Fluoroquinolones (e.g ciprofloxacin, levofloxacin)

* Based on antibiotic prescribed and patient response

Shoskes, Urol Update Series 2021

BUT the fluorquinolones are a problem

RAPID COMMUNICATION

Dangerous fluoroquinolones: The urologist's dilemma

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that tendonitis and serious te

Table 1. FDA safety warnings

Date	Warning – Fluoroquinolones are associated with:
July 2008	Tendonitis and tendon rupture
August 2013	Permanent peripheral neuropathy
July 2018	Serious mental disturbances
July 2018	Serious and significant decrease in blood sugar levels
December 2018	Increased risk of aortic dissection

The New Antibiotic Paradigm for Bacterial Prostatitis*

- Trimethoprim +/- sulfamethoxazole
  - 1 DS tab BID for 4 -12 weeks
- Fosfomycin – 3 gm q48 hours for 2-6 weeks
- Doxycline – 100 mg BID for 4 weeks
- Clarithromycin/Azithromycin – last choice

*as we phase out our use of fluoroquinolones for this indication

Rees et al. BJU Int 2015; 116: 509–525
Shoskes, Urol Update Series 2021

Special Treatment Considerations for Cat I ABP

- ABP can be a serious infection with fever, intense local pain, and general symptoms
- Septicemia and urosepsis are always a risk
- Considerations when treating ABP:
  - consider wide spectrum parenteral antibiotic for initial therapy*
  - determine need for urinary drainage (small caliber foley catheter)
  - hospitalization if justified by presentation and risk factors
  - auxiliary measures intended to improve outcome (systemic support, NSAIDS (e.g. ibuprofen), alpha blockers (e.g. tamsulosin 0.4 mg/daily) Imaging if no improvement (ultrasound, CT scan)

Special Treatment Considerations for Cat II CBP

- Treat voiding (obstructive) urinary symptoms
- Imaging if no improvement (ultrasound, CT scan) and/or cystoscopy
- Low-dose, long-term prophylaxis or suppression may be necessary for CBP (e.g. trimethoprim-sulfamethoxazole 1 tab BID for 3-4 months)

Cat III CP/CPPS: Key Elements of History

- A comprehensive systems review
  - past medical and surgical (particularly urologic) history
  - history of trauma, medications, and allergies
- No UTIs, no benefit with antibiotics
- The following presenting symptoms should be elicited:
  - pain location (severity, frequency, and duration)
  - Pain associated with ejaculation
  - lower urinary tract symptoms (obstructive/voiding and irritative/storage)
  - associated pain symptoms or syndromes
  - impact on activities/quality life.

Doiron, Nickel Can Urol Assoc J 2018; 12 (Suppl 3)

- The NIH Chronic Prostatitis Symptom Index from the Chronic Prostatitis Collaborative Research Network (CPCRN) is a validated questionnaire available at www.prostatitis.org/symptomindex.html.
- **NIH-CPSI - 9 simple questions** (total score 0-43)
  - **Pain** (0-21)
    - Location (0-6)
    - Frequency (0-5)
    - Severity (0-19)
  - **Urinary** (0-10)
    - Voiding/Obstructive (0-5))
    - Storage/Irritative (0-5))
  - **Impact/Quality of Life** (0-12)

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    - Voiding/Obstructive (0-5))
    - Storage/Irritative (0-5))
  - **Impact/Quality of Life** (0-12)

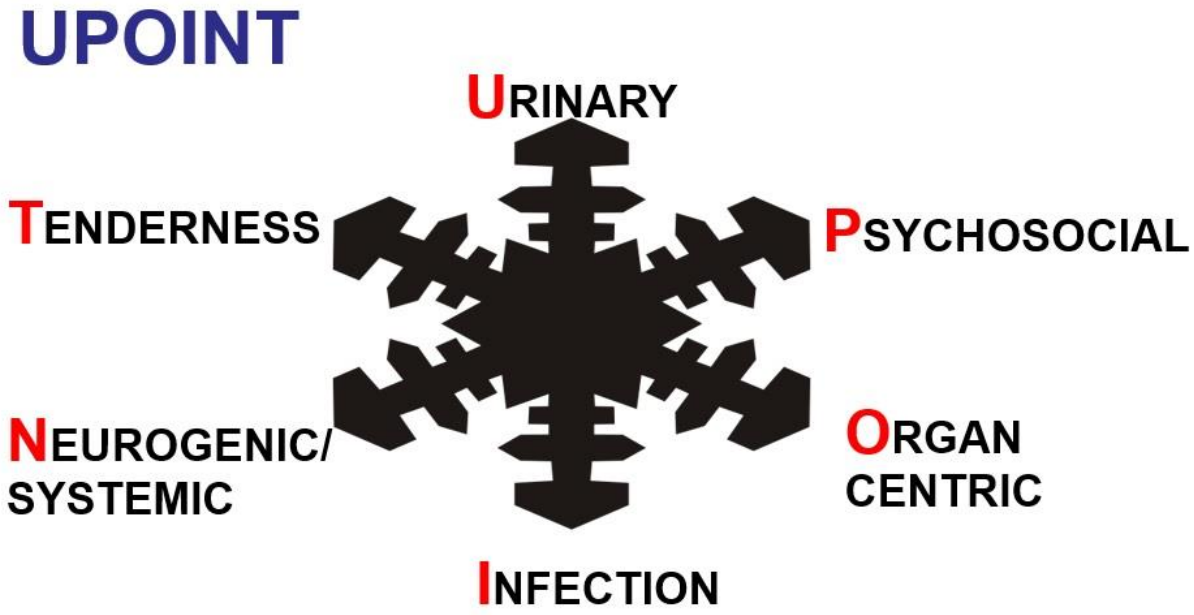
The score allow the physician to determine

1. Cover all domains
2. The contribution of each domain on patient's experience
3. Change of symptoms and quality of life with treatment

The Key to Management of Cat III CP/CPPS

- Determine the Clinical Picture
- Consider each patient as a distinct individual
- Tailor a personalized phenotype directed therapy strategy
- Consider multimodal and/or multidisciplinary approach

The Snowflake Hypothesis



Primary Care Directed Therapies for CP/CPPS #1

Conservative

- Diagnosis
- Education
- Exercise
- Exercises
- Diet
- Avoidance
- Psychological support

Doiron, Nickel. Management of Chronic Prostatitis/Chronic Pelvic Pain Syndrome. Can Urol Assoc J 2018;12(Suppl3)

Primary Care Directed Therapies for CP/CPPS #1

Conservative

- Diagnosis → make a diagnosis
- Education → educate the patient
- Exercise → low impact
- Exercises → stretching, yoga
- Diet → elimination diet
- Avoidance → high impact, bicycle, etc.
- Psychological → pain psychologist

Primary Care Directed Therapies for CP/CPPS #2

TRADITIONAL

- Antibiotic therapy
- Alpha-blockers
- Anti-inflammatory therapy

VERY USEFUL

- Pelvic Floor Physiotherapy

USEFUL

- Muscle relaxants
- Five alpha-reductase inhibitors
- Neuromodulation agents
- Phytotherapies

Nickel JC, Shoskes DA, Wagenlehner FME. Management of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS): The studies, the evidence, and the impact. *World J Urol* 2013;31:747-53.
Doiron, Nickel. Management of Chronic Prostatitis/Chronic Pelvic Pain Syndrome. Can Urol Assoc J 2018;12(Suppl3)

Primary Care Directed Therapies for CP/CPPS #2

TRADITIONAL

- Antibiotic therapy → antibiotic naive
- Alpha-blockers → voiding (obstructive) symptoms
- Anti-inflammatory therapy → inflammation

VERY USEFUL

- Pelvic Floor Physiotherapy → pelvic floor dysfunctional pain

USEFUL

- Muscle relaxants → pelvic floor muscle spasm
- Five alpha-reductase inhibitors → older with benign prostatic hyperplasia
- Neuromodulation agents → neuropathic type pain
  - gabapentin, pregabalin, amitriptyline
- Phytotherapies → cause no harm and proven to help some
  - Quercetin
  - Rye grass pollen extract (Cernilton)

Rees et al. BJU Int 2015; 116: 509–525
Doiron, Nickel.. Can Urol Assoc J 2018;12(Suppl3)

Specialist Directed Therapies for CP/CPPS

- Pelvic Nerve Injection therapy
- Acupuncture
- Low intensity shock wave therapy
- Electromagnetic stimulation
- Pudendal nerve modulation
- Surgery

Doiron, Nickel. Management of Chronic Prostatitis/Chronic Pelvic Pain Syndrome. Can Urol Assoc J 2018;12(Suppl3)

When to refer to a Urologist

- **CAT I ABP**
  - Fails to respond to antibiotics within 24 hours
  - Unable to insert a foley to manage acute urinary retention
  - Symptoms continue after infection cleared
- **CAT II CBP**
  - Fails to respond to appropriate antibiotics
  - Symptoms persist even while on antibiotics
  - Bacterial infection recurs
- **Cat III CP/CPPS**
  - Fails primary care conservative management steps
  - Fails first line therapies
  - Unable to make a diagnosis
  - Other urology issues (e.g. urinary symptoms, hematuria)

The Key to Managing Men with Prostatitis Syndromes

- **Figure out what is going on (Make the Diagnosis!)**

  "The Clinical Picture"
- **Take care of the Patient** (education, diet, exercise)
- **Treat the Organ - Prostate** (medications, interventional treatments, surgery)
- **Identify and manage other pain generators** (pelvic floor, bowel, fibromyalgia)
- **Provide general psychological support "glass half full"**
- **Realistic goals**
- **Know when to refer**

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