This lecture will aim to…

- Review common urological contributors to pelvic pain
- Discuss the diagnosis and treatment of these conditions including: interstitial cystitis (IC)/painful bladder syndrome (PBS), chronic prostatitis, urinary tract infections (acute and chronic), and nephrolithiasis
- Review the concept of neuropathic pain and options for effective treatment
- Discuss treatment options and review appropriate workup and referral

The cause of pelvic pain, you ask?
As nebulous as the safe dose of happiness.
Visceral Sources of Pelvic Pain

- Gastrointestinal
- Urinary
- Reproductive
- Musculoskeletal/Other

Urinary causes of Pelvic Pain

- Interstitial Cystitis/Painful Bladder Syndrome (PBS)
- Chronic prostatitis, prostadynia
  - Epididymitis
  - Ochulalgia
  - Scrotalgia
- Recurrent urinary tract infections
- Urolithiasis
- Anatomical prolapse
- Chronic vaginitis/vaginosis

Gastrointestinal Causes of Pelvic Pain

- Constipation
- Irritable Bowel Syndrome/Disease
- Chronic Bowel Obstruction
- Diverticulitis
- Ulcerative Colitis
- Other Colitis
- Prostalgia
- Fissures
- Persistent maldigestion
- Hernia
Reproductive Cause of Pelvic Pain

- Prostatitis
- Testicular masses; hernia;
- Pelvic inflammatory disease
- Vaginal infections, vaginitis, vaginositis
- Vulvar pain syndromes
- Ovarian cyst
- Ectopic pregnancy
- Endometriosis
- Adenomyosis
- Adhesions
- Uterine fibroids
- Pelvic congestion syndrome

Musculoskeletal Dysfunction and CPP: cause or contributor?

- Levator ani syndrome
- Interstitial cystitis
- Piriformis syndrome
- Iliopsoas spasm
- Pelvic floor myalgia
- Vulvodynia
- Coccygodynia
- Pudendal neuralgia

Muscles of the pelvic floor - a wonderful woven web
Definition of Chronic Pelvic Pain

- Duration: 3 months or more
- Location:
  - Anatomic Pelvis; Abdominal wall below the umbilicus; Low back
- Functional impairment
  - Gastrointestinal, Urinary, Reproductive, Etc.
- Non-cyclic
  - ± dysmenorrhea
  - ± dyspareunia (men and women)
- Medical and/or surgical intervention is often indicated

How about those men?

Chronic Pelvic Pain Syndrome:

- Affects >15% of men
- Health impact equal to acute M.I., acute ulcerative colitis, and unstable angina
- 95% of men diagnosed as prostatitis have NO EVIDENCE of infection or prostatic inflammation

Complex Neurorological Network
**Definition of Painful Bladder Syndrome**

- The complaint of suprapubic pain related to bladder filling
  - May be accompanied by other symptoms such as increased urinary frequency and urinary urgency, in the absence of proven urinary tract infection or other obvious pathology
  - Also referred to as Interstitial Cystitis
  - Hunter vs non-Hunter type
  - Crossover with Chronic Prostatitis
  - Crossover with Endometriosis and Vulvodynia
    - 10-20% overlap with vulvodynia
    - Up to a 60-70% overlap with endometriosis

**Interstitial cystitis/Painful bladder syndrome: pathogenesis and Integrated pathophysiology**

- Urothelial dysfunction
- activation → upregulation
- nervous system

- Visceral organ hyperalgesia/allodynia
  - Gynecological
  - Urinary
  - Pelvic floor
  - Gastrointestinal

**Prostatitis...hand in hand with pelvic pain**

**Pitfalls in Diagnosis of Prostatitis**

- *Physician does not evaluate for WBC*
- Pudendal neuralgia has same symptoms
- detrusor-sphincter dyssynergia
- trigone infiltration by (prostate) carcinoma
- interstitial cystitis
  - Neurogenic inflammation of bladder
Testing for Anterior Abdominal Wall Tenderness

- Suprapubic tenderness
- Anterior vaginal wall/bladder base tenderness
- Levator muscle spasm
- Rectal spasm

Pathogenesis of PBS/IC: Defective Urothelial Barrier

Irritating Solutes → Irritated Urothelium → Inflammation

Lack of a clear, identifiable etiology of Chronic Pelvic Pain supports a heterogeneous, multi-systemic and multi-factorial disease

Transition from nociceptive to neuropathic pain is key…
In patients with chronic pain normal sensations are perceived as pain… enter the concept of neurological windup

Pelvic Myoneuropathy

- A process seen in people of a particular genetic type and often with tense, anxious, and frequently atopic (allergy-prone) dispositions develop a chronic process in the pelvis that involves muscle, nerves and mast cells.
- Individuals tend to tense the muscles of their pelvic floors subconsciously and continuously
- Clenching of deep muscles can be provoked either by the individual’s tense disposition, or it can be the result of a “guarding” response to a previous trauma to the pelvic or spinal area
  - pelvic surgery, bicycling, childbirth, long periods of sitting and stress at work, and in some cases, urinary tract infections (prostatitis and cystitis)
  - Other common events that lead to injury are: chronic tense holding patterns that develop in childhood as a result of sexual abuse, traumatic toilet training, abnormal bowel patterns, guilt surrounding sexual feelings, dance training or stress
  - Repetitive minor trauma or strain, non-tissue or urinary obstruction
  - other inflammations of pelvic organs or referred pain from other attaching muscle groups or viscera or nerves
Chronic Pelvic Pain – an overlapping of diseases and conditions

- Endometriosis
- Adenomyosis
- Pelvic Infections
- Adhesions
- Interstitial Cystitis
- PBS
- Recurrent UTI
- Endometriosis
- Adenomyosis
- IBS
- Colitis
- Other GI Disorders
- Interstitial Cystitis
- PBS
- Recurrent UTI

Treating your patient with Pelvic Pain

- There is no sure-fire treatment approach that will work consistently with patients who live with CPP or PBS
- Identify the contributors
  - Work to optimize the function of the surrounding "asymptomatic" organs
- Determine how many "players" are needed in the initial as well as the ongoing treatment of the patient
  - If possible, develop a timeline that identifies where dysfunction began. What are the legs of the stool, so to speak.
- Educate the patient as to patho-physiology
- Develop a comprehensive treatment strategy
- Do not continue to utilize resources on ineffective therapies

Painful Bladder Syndrome

Treatment

- Pain Management
  - Antidepressants: Tricyclic (amitriptyline, nortriptyline), venlafaxine (Effexor) SNRI, duloxetine (Cymbalta) SNRI
  - Anticonvulsants: Gabapentin, Pregabalin
  - Botox, Neurontin, Elavil
  - Not Helpful: Narcotics, NSMIDS, antibiotics
- Anti-inflammatory therapies
  - Quercetin
  - Aloe Vera (whole leaf)
- Anti Histamine therapy
  - Hydroxyzine, Allegra, Claritin
- Urinary medications
  - Urinary analgesics: pyridium, uniflur, etc.
  - Urinary alkalizers: coffee timer, pretzel, pH control, etc.
  - Elmiron (pentosan polysulfate sodium) heparin like compound with structural similarity to a glycosaminoglycan
  - Anti cholinergics/Muscarinic Receptor Antagonists: Detrol (tolterodine), Sanctura (trospium chloride)
Neuromodulation
- Sacral
- Peripheral
  - PTNS – posterior tibial nerve stimulation
  - Especially helpful with urinary symptoms (urgency and frequency)
- Bladder installations
  - Heparin, alkalinized lidocaine, Elmiron, DMSO
- Physical therapy
- Psychotherapy
- Acupuncture – additional to the purpose of neuromodulation

Naturopathic Approach to Pelvic Pain
- If possible, identify the origin of the pelvic pain
- Work diligently to get the pain symptoms under control so that other therapies can work more effectively
- Understand the interplay of concomitant dysfunctions
- Begin the process of unwinding; stop and reassess as often as necessary
- Keep anxiety and pain as managed as possible

- Anti-inflammatory diet; consider testing for food sensitivities
- Quercetin or other anti-histamine therapies if appropriate
- GABA
- Support patient’s genetic predispositions
- Consider neurotransmitter testing
- Alkalinized or distilled water
- Cannabis (edible or vaporized)
- Use caution with supplements
Chronic Prostatitis

- Slow, indolent infection persisting more than 3 months
  - Associated factors
    - Recurrent Urinary Tract Infection
    - Asymptomatic bacteruria despite antibiotics
  - Causative organisms the same as in Acute Prostatitis
    - Enterobacteriaceae (80%), Enterococcus (15%), Pseudomonas aeruginosa

Symptoms (sudden onset)
- Irritative urinary symptoms (Mild to Moderate)
  - Dysuria, Urinary frequency, Urinary urgency, Ejaculatory pain, hematospermia
- Referred pain
  - Low pack, perineum, lower abdomen, scrotum, penis, inner thighs
- Absent Symptoms (in contrast to Acute Prostatitis)
  - Systemic symptoms rare
  - Obstructive urinary symptoms uncommon
- Signs: on DRE the prostate is often
  - Normal on exam, tender (TTP), boggy or indurated
  - Prostatic calculi may be present

Labs: Segmented Urine Culture

Differential Diagnosis
- Chronic non-infectious prostatitis, BPH, UT
  - Stone (prostate calculus, nephrolithiasis), bladder cancer, prostate abscess, enterovesical fistula

Management
- General
  - Antibiotics penetrate Chronic Prostatitis poorly
  - Prolonged antibiotic regimens are required
  - Treatment with antibiotics until urinalysis returns with no organisms
Prostatitis Treatment

Treat the symptoms that predominate and create the biggest barrier in optimizing ADL.

- Urinary frequency, urgency
  - Anti-cholinergics

Obstructive Voiding
- Alpha-blockers - Especially helpful to prevent urinary retention
  - Doxazosin (Cardura), tamsulosin (Flomax), terazosin (Hytrin), alftuzosin (Uroxatral)

Prostatic Tenderness/Pain/Enlargement
- Quercetin, Bee Pollen, Probiotics
- Inhibit DHT (Finasteride/Clotetaside)

Infection
- Antibiotic treatment (see following slide)

Psychosocial (depression, anxiety, catastrophic thinking)
- Counseling, EMDR, EFT, CBT
- Antidepressant therapy
- Exercise, stress management

Bowel Health
- Allergy Elimination
- Optimize bowel function

Pelvic Neuropathic Pain
- Tricyclic antidepressants
- Gabapentinoids

Muscle Spasm, tenderness, pelvic muscle tightness
- Physical therapy
- Muscle relaxants
  - Cyclobenzaprine
  - Botanical Formula (see above; might adjust antispasmodic herbs)
  - Magnesium citrate (for effects on bowel as well as on other muscle)
- Local heat therapy, hyperthermia (TUMP, etc.)
- High-frequency decontamination
- Prostate massage
- Donut cushion, seating disc
- Hydrotherapy
  - Sitz bath, suprapubic sit

Prostatitis Treatment: Antimicrobial Therapy

- Antimicrobials: 4-6 weeks of treatment (up to 12 weeks)
  - First Line: fluoroquinolones or sulfa
    - Ciprofloxacin 500 PO BID
    - Levofloxacin 500 mg PO QD
    - Norfloxacin 400 mg PO BID
    - TMP-SMX DS (160/800) PO BID
  - Second Line:
    - Doxycycline 100 mg PO BID
    - Azithromycin 500 mg PO QD
    - Clarithromycin 500 mg PO BID
  - DO NOT USE nitrofurantoin (Macrobid)
Cystitis

- Acute and Recurrent Cystitis (UTI)
  - Acute
  - Complicated vs. uncomplicated
  - Recurrent Urinary Tract Infection:
    - Incidence greater than 2-3 times per year
- Interstitial Cystitis (IC)/Painful Bladder Syndrome (PBS)
- Other Cystitis
  - Eosinophilic Cystitis

Recurrent Cystitis (UTI)

- Vast majority of recurrent UTI in women in from reinfection (99%)
  - Vaginal colonization is the most common cause
- Unresolved Bacteriuria (Refractory Infection)
  - Bacterial resistance to drug selected for treatment
    - Resistance developed by sensitive bacteria
    - Bacteriuria with 2 different species
    - Rapid reinfection with a second resistant organism
  - Analgesic abuse causing papillary necrosis
  - Azotemia
  - Giant staghorn calculi
  - Noncompliance

- Bacterial persistence (Same organism recurs)
  - Infected Renal Calculi, Chronic Bacterial Prostatitis, Unilateral infected atrophic Pyelonephritis, Infected Diverticulae, Polycystic Kidney Disease, Ureteral reflux, Medullary sponge Kidneys, Analgesic abuse causing infected papillary necrosis
- Reinfection (Urine cleared, but new infection occurs)
  - Colonization of vaginal introitus, Vesicovaginal fistulae, Vesicoureteral Reflux, Voiding dysfunction (seen with MS, neurogenic bladder, cystocele, rectocele), Immunosuppression, Chronic Renal Insufficiency, DM, Instrumentation (stent, nephrostomy tube, catheterization)
Risk Factors for recurrent UTI in women:
- Intercourse in the past month >9 times: Odds Ratio 10.3
- Intercourse in the past month 4-8 times: Odds Ratio 5.8
- Age at first UTI >15 years: Odds Ratio 3.9
- Mother with Recurrent UTI: Odds Ratio 2.3
- New sex partner in the last year: Odds Ratio 1.9
- Spermicide use in the last year: Odds Ratio 1.8

Diagnostic Workup
- Culture Culture Culture!
  - Antibiotic resistance is common and variable, especially in patients with recurrent cystitis
  - Consider a standing order for patients with recurrence
  - Consider more complete urological workup in patients with significant recurrence
  - Evaluation for urethral diverticulum, stones, issues from past surgical interventions (esp. related to mesh)
  - Other diagnostics to consider referring for OPVR (post-void residual), urodynamics, and other imaging may be indicated
**Treatment**

- **UTI Prophylaxis in women**
  - Indications: Recurrent Urinary Tract Infections occurring 3 or more times annually
  - Continuous UTI Prophylaxis (Average Course: Taken daily for 6 months)
    - Nitrofurantoin 50-100 mg PO QD
    - TMP-SMX 40/200 PO QD or 3x per week
    - Trimethoprim 100 mg daily
    - Cephalexin 125-250 mg PO QD
    - Ciprofloxacin 125 mg PO QD

- Postcoital Prophylaxis (one dose taken within 2 hours of intercourse)
  - Nitrofurantoin 50-100 mg once
  - TMP-SMX 40/200 to 80/400 once
  - Ciprofloxacin 125 mg once

- Self-starting regimen
  - Standing order for culture; patient education regarding importance and procedure
  - Emergency prescription available to start after onset of classic UTI symptoms
  - Choose a 3 day antibiotic course
  - Contact provider if symptoms last more than 48 hours despite antibiotics

- **Mannose**
  - D- Mannose has been shown to **BOTH** block bacterial adhesion on uroepithelial cells and antagonize invasion and biofilm formation
  - Dose: 1 gram TID-QID for acute management; 1 gram post coital for prophylaxis

- **Probiotics**
  - PV and PO probiotics have been shown to decrease UTI recurrence
  - Dose daily as well as post coital in patients with significant recurrence rates
**Cranberry**
- Daily cranberry prevents Recurrent UTI
- Contains proanthocyanidin compounds
- Inhibits E. coli from adhering to urinary tract
- Recommended daily dosing of cranberry juice
  - Cranberry extract 300-400 mg tablet bid or
  - Pure cranberry unsweetened juice 8 ounces tid

**Vitamin C**
- 500 mg TID-QID

**Behavior Modification and Urinary Hygiene**
- Educate patients about normal bladder function, fill volume, and general urinary hygiene
- Instruct women to void before and after intercourse. **Patients MUST need to void in order for good bacterial clearance**
- Consider contraceptive devices and spermicides to be potential risk factors
- Consider OCP to be contributory
- Address any atrophy
- Evaluate for use of sex toys/devices as well as use of hygiene products

**A few notes about referrals…**
- Referrals can be made for a consult (evaluation and treatment often with ongoing treatment and management being handed back to the referring physician OR for complete care (evaluation, treatment, and management)
- Difference is primarily a coding/billing issue, though for many specialists consults are handed back to the referring physician for management when appropriate
- You cannot refer for urological testing as you might for a radiological study
Nephrolithiasis

- Prevalence: 0.2% in U.S.
  - Life-time risk
    - Males: 10-12% vs. Females: 3-5%

- Recurrence of Nephrolithiasis
  - One recurrence in 50% of patients
  - More than 3 recurrences in 10% of patients

- Peak age: 20-50 years
- Overall Male: Female ratio 4:1
  - Males: Calcium oxalate
  - Females: Struvite
  - Both: Urate and Cystine Stones

Pathophysiology

- Stone formation is inhibited by Citrate
- Women have much higher levels of citrate than men
- Low citrate levels are related to most stone forms

Risk Factors

- General
  - Increases with advancing age up to 65 years
  - Male gender (men account for 66% of cases)
  - Geographic location (hot, arid climates)
    - Southeastern United States ("stone belt"), Mediterranean countries, Middle Eastern countries

- Inherited Conditions
  - Polycystic Kidney Disease, Renal Tubular Acidosis
  - Type I, Hyperparathyroidism, Cystinuria,
  - Hypocitruria, Hypercalcitria, Primary Hyperoxaluria,
● Medications
  ○ Allopurinol
  ○ Laxatives
  ○ Ephedra alkaloids
  ○ Carbonic anhydrase inhibitors (Diamox, Topamax)
  ○ Potassium channel blockers (Amiodarone, Sotalol, Dalfampridine)
  ○ Potassium sparing diuretics (Triamterene)
  ○ Protease Inhibitors (Indinavir)
  ○ Sulfonylureas (Glipizide, Glyburide)
  ○ Antibiotics (sulfonamides, fluoroquinolones, Ceftriaxone, Ampicillin, Amoxicillin)

● Dietary and Hydration Factors
  ○ Low urine volume
    ● Inadequate access to hydration or restrooms
    ● Athlete
    ● Heat exposure
    ● Bowel Disease
      • IBD, Bowel Surgery (e.g. Ileostomy), Chronic Diarrhea, PUD
  ○ Other dietary factors
    ● Animal protein intake
    ● High oxalate containing foods
    ● Excessive sodium intake
    ● Sugar intake/blood sugar levels
      • Type 2 Diabetics at increased risk

● Hypercalciuria (70% of stone formers)
  ○ Type 1: Increased PTH (resorptive hypercalciuria)
    ● Evaluate Vitamin D if low, normalize and retest for adequate evaluation of PTH
  ○ Type 2: Increased Calcium absorption from gut
  ○ Type 3: Increased Urinary Phosphorus loss
  ○ Type 4: Increased Urinary Calcium loss

● Hyperoxaluria
  ● Citrate deficiency vs. oxalate metabolism problem

● Hypocitraturia (as seen in Distal Renal Tubular Acidosis)

● Hyperuricosuria (can be seen in gout)

● Acidosis and aciduria (results in loss of citrate)
  ● Bowel disease, protein loading (especially with animal protein), Renal Tubular Acidosis, Acetazolamide (Diamox)
Prevention of Stones

- Hydration: more than just water
- Optimize calcium intake and utilization
- Weight bearing exercise, dietary evaluation of calcium sources and bioavailability
- Maintain adequate vitamin D levels
- Maintain fluid intake > 2.5 Liters per day
  - Most important single measure
  - Ingest 8 to 12 ounces fluid on awakening and at bedtime
  - Water and Citrus juice
- Maintain Urine volume > 2 Liters per day
  - Periodically measure urine output in a 2 liter bottle
  - Urine should be clear in appearance with minimal color
- Dietary restrictions
  - Limit animal protein to 8 ounces per day (or <1 gram/kg/day)
    - Animal protein increases urinary calcium and uric acid excretion
    - Animal protein decreases urinary pH and urinary citrate excretion
  - Limit sodium intake to less than 2-3 grams per day (less than 1.5 grams for some patients)
  - Limit high oxalate foods
  - Limit high sugar or fat content
  - Avoid excessive vitamin C
- Lifestyle
  - Move toward ideal weight for the patient
  - Encourage daily physical exercise
- Dietary increases or no restriction
  - Increase fiber from vegetable sources (being mindful of oxalates)
  - Maintain calcium intake at at least 1000 mg/day
    - No dietary calcium restriction for most stone formers (unless absorptive hypercalciuria)
    - Calcium binds oxalate in the intestine and decreases oxalate absorption
    - Take supplemental calcium citrate with meals
    - Aim for 50% daily calcium from diet and the rest from supplemental calcium citrate
    - Encourage calcium utilization through weight bearing exercise
    - Maintain adequate vitamin D levels
Imaging for Kidney Stones

- **Helical CT Urogram**
  - Sensitivity: 95 to 100%, Specificity: 94 to 96%
  - Preferred over IVP (intravenous pyelogram)
  - Will evaluate: renal morphology and ureteral stone localization
- **Abdominal US**
  - Sensitivity: 64-93%, Specificity: 97-100%
  - Will evaluate: renal stone and hydronephrosis
  - Indications: pregnant patients and children, suspected cholecystitis or gynecological condition
- **Abdominal XRay**
  - Sensitivity: 45-59%, Specificity: 71-77%
  - Will evaluate: radiopaque stones (calcium oxalate and struvite; some cystine stones)
- **Intravenous Pyelogram (IVP)**
  - Sensitivity: 64-87%, Specificity: 92-94%
  - Will evaluate: function or kidney and ureter

Lab evaluation for Kidney Stones

- **Urinalysis**
  - Acute
  - 24-Hour Urine Metabolites
    - Litholink
- **Blood Work**
  - Vitamin D
  - Really only helpful to evaluate contributing health conditions
    - Uric acid
    - Blood Sugar/HBA1C
    - WBC