Urinary Incontinence

PHYSIOLOGY OF MICTIONATION

Parasympathetic system
- Detrusor: stretchable smooth muscle innervated by parasympathetic system
- Cholinergics → GO
- Anticholinergics → STOP
- M₂ & M₃ receptors are more specific to bladder

Sympathetic system
- Internal sphincter: epinephrine controlled
- External sphincter: norepinephrine controlled
- α-adrenergic agonist: holds sphincter tight
  - α₁ stimulation → internal sphincter contracts
  - β₃ stimulation → bladder relaxes

Micturation reflex
- Urine fills bladder → bladder stretches → (+)parasympathetic → bladder contraction + internal sphincter opening → external sphincter relaxation & urge sensation → urination
- Normal post-void residual: 0-50mL
- Significant post-void residual: 100-250mL
  - Stagnant urine → ↑infection risk since urine is usually sterile

TYPES OF URINARY INCONTINENCE

- Functional UI
  - Inability to reach the toilet
  - Barriers: cognitive impairment, physical impairment, psychological unwillingness, environmental barriers
  - Etiology: physical disability, dementia, medications that cause drowsiness or affect balance
- Urge UI
  - Overstimulation of parasympathetic system → inability to delay voiding → leakage of urine
  - Most common type of urinary incontinence
  - Etiology: mostly idiopathic but also detrusor instability, CNS disorders (e.g. strokes), genitourinary conditions
- Stress UI
  - Cough, laugh, exercise → ↑intraabdominal pressure → involuntary loss of urine
  - Etiology: weak pelvic musculature, internal/external urethral sphincter weakness
- Overflow UI
  - Overly distended bladder → high post void residuals → ↑urination frequency → leakage of urine
  - Causes of high PVR: weak detrusor, undersignaling of detrusor, oversignaling of internal sphincter, urethral obstruction (BPH)
  - Etiology: BPH, acontractility, drugs (opiates, anticholinergics, antipsychotics, TCAs, allergy meds, etc.)
- Mixed UI: functional UI + urge UI + stress UI

TREATMENT

Nonpharmacologic therapy: 1st line for all UI types except in obstruction (e.g. BPH)
- More effective than medication
- Behavioral approaches: Kegel exercises, ↓fluid intake, avoid caffeine, avoid alcohol, ↓evening fluid intake, weight loss for overweight females with stress UI, diuretics earlier in the day
Pharmacologic treatment: when behavioral therapy alone has failed

Treatment of urge UI

- **Antimuscarinics**
  - Muscarinic receptor antagonists → ↓parasympathetic stimulation → detrusor relaxation → ↑volume of urine before urge to urinate
  - Older less preferred agents: propatheline, dicyclomine, imipramine, flavoxate
  - Preferred agents: oxybutynin, tolterodine, solifenacin, darifenacin, trospium, fesoterodine
    - Solifenacin & darifenacin: M3 receptor uroselective
    - Trospium: take on empty stomach, questionable clinical benefit
    - Fesoterodine: prodrug of tolterodine
  - Anticholinergic SE
    - Causes many patients to discontinue treatment (~80%)
    - Xerostomia, constipation, vision impairment, tachycardia, drowsiness
    - Consideration in elderly: worsens cognitive skills (e.g. patients with dementia)
    - Geriatric prescribing cascade: cholinesterase inhibitors prescribed for dementia → worsens or causes urge UI → antimuscarinics prescribed → worsens dementia & physical function
    - Tolterdine < oxybutynin
    - XL or ER < IR
  - Always start low and go slow → titrate slowly over 4-8 weeks
  - Drug interactions: CYP3A4 substrates
    - CYP3A4 inhibitors may ↑concentrations 4x
      - Fluoxetine, sertraline, fluvoxamine, erythromycin, clarithromycin, fluconazole, ketoconazole, grapefruit juice
    - Antacids cause rapid release of ER products → ↑peak levels by 150%
      - Separate administration by ≥4hrs

Treatment of stress UI

- **Topical estrogens**
  - Post-menopausal women
  - MOA: ↑# + ↑responsiveness of α-receptors
  - Topical has modest efficacy, PO does the opposite
- **Ephedrine, pseudoephedrine, phenylephrine**
  - MOA: α agonists → ↑internal sphincter pressure
  - Risks: ↑BP, stroke
- **Duloxetine**
  - MOA: ↑NE → contracts internal sphincter + relaxes detrusor
  - SE: nausea, headache, insomnia, ↑BP, withdrawal symptoms
- **Avoid α blockers:** doxazosin, terazosin

Treatment of overflow UI

- **Treatment of BPH** (most common cause of overflow UI)
- **Bethanechol:** if due to detrusor underactivity
- **Catheterization**
- **Treatment of constipation** which impedes outflow
- **Avoiding anticholinergic agents** which worsen overflow UI
  - Important to differentiate urge UI (anti-ACH treats) vs. overflow UI (anti-ACH exacerbates)