Voiding Dysfunction & BPH
Objectives Today

• 1. Anatomy of the lower urinary tract
  – A) Innervation of the bladder
  – B) Normal voiding

• 2. Classify Neurogenic Bladder

• 3. Classify Urinary Incontinence
  – A) Rx for different types of incontinence

• 4. BPH & LUTS
Disclaimer:

• This is a lot of information to cover and we are unlikely to cover it all today

• These slides are to be utilized for your reference to guide your self study
Disclaimer:

• These concepts were all addressed in Year 1 FERGU block: Normal and Dysfunctional Voiding
http://mcc.ca/examinations/objectives-overview/

For LMCC Part 1
Objectives applicable to this lecture:
  – Urinary Tract Obstruction
Male Anatomy

- ureteric orifice
- trigone of bladder
- bladder neck
- external urethral sphincter (striated sphincter)
Anatomy

• Bladder Innervation
  – Detrusor \(\rightarrow\) (parasympathetic S2,3,4)
  – Trigone \(\rightarrow\) (sympathetic L1,2)

• Urethra
  – Male
    – Internal/Involuntary Sphincter (Sympathetic L1,2)
  • Prostatic
    – External/Voluntary Sphincter (Pudental S2,3,4)
  • Membranous
  • Bulbar
  • Penile (spongy, pendulous etc)
Conceptual Neuro-anatomy

- Parasympathetic: PEE
- Sympathetic: STORE
Anatomy

- **Sympathetics (T11-L2) = Store**
  - From aortic and superior hypogastric plexis → hypogastric nerves → pelvic plexus cause detrusor relaxation and bladder neck contraction

- **Parasympathetics (S2,3,4) = Pee**
  - From pelvic splanchnic nerves cause detrusor to contract

- **Somatic (voluntary) control**
  - → Pudendal nerve (S2,3,4)
  - External Spincter
Anatomy

• Nerve Summary
  – Parasympathetic S2,3,4
    • + Bladder contraction, relax sphincters
    • Arise from sacral Cord
  – Sympathetic L1,2
    • + Tight trigone, + internal sphincter tone, relax detrusor
    • Arise from lumbar
  – Somatic S2,3,4
    • + External sphincter tone
Conceptual Neuro-anatomy

- Parasympathetic: PEE
- Sympathetic: STORE
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4. BPH & LUTS
Voiding

• Voiding
  – Filling
  – Emptying
Voiding

• Normal Filling Requires:
  – Accommodation of urine volume at low pressure (compliance)
  – Closed bladder outlet
  – No involuntary detrusor contractions
  – Normal sensation of bladder filling
How does filling work?

- As bladder fills → sympathetic reflex initiated to keep you dry!
  → Stimulation of alpha adrenergic receptors at bladder neck
  → Increase resistance of bladder neck
  → Activation of beta3 receptors in detrusor inhibiting contraction
  → Direct inhibition of detrusor motor neurons in sacral spinal cord
- Gradual increase in urethral pressure as bladder fills due to pudendal nerve → activation of external sphincter
- Formation of urethral mucousal seal
How does emptying work?

• Emptying Requires:
  – Coordinated detrusor contraction of adequate magnitude
  – Lowering of resistance at the level of the urinary sphincters (bladder outlet)
  – Absence of obstruction (either anatomical or functional)
How does emptying work?

- Emptying → Specifically:
  - Increased intravesical pressure produces the sensation of distension → I want to void!!

- Coordination of detrusor contraction and external sphincter relaxation
  - Brain (pontine micturition center) → inhibits the steady state spinal reflex of staying continent:
    - Stimulates Parasympathetics → contraction of detrusor
    - Inhibits sympathetics = internal sphincter relaxation
    - Inhibits pudendal = External Sphincter relaxation
Control of Micturition

1. PMC receives input from GU afferents as well as areas in the brain (e.g. cerebellum, cerebral cortex, basal ganglia)
2. It coordinates micturition, by turning off the sympathetic signals and turning on the parasympathetic signals
3. This allows the contraction of the detrusor and the relaxation of the bladder outlet
4. Simultaneously the PMC coordinates the relaxation of the external urethral sphincter
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Neurogenic Bladder

• Definition: dysfunction of the urinary bladder due to neurologic dysfunction or insult
Classifying Neurogenic Bladder

- Upper Motor Neuron  
  "spastic"

- Lower Motor Neuron  
  "flaccid"
Neurogenic UMN

• Upper Motor Neuron
  – *Cerebral Injury* (stroke, tumour, brain injury)
    • Normal function to inhibit reflexive bladder emptying
    • Allows socially acceptable timing of voiding
    • Dysfunction leads to loss of voluntary control of micturition
    • Detrusor Overactivity
Neurogenic UMN

• Upper Motor Neuron Diseases
  – *Basal Ganglia disease* (Parkinson’s disease)
    • Detrusor overactivity
    • Contractions are short, relaxation of ext. sphincter is slowed → urgency, urge incontinence, slow flow
Neurogenic UMN

- Upper Motor Neuron Diseases
  - *Suprasacral spinal cord damage*
    - Above T6
      - → reflex micturition with detrusor-sphincter dyssynergia
    - Below T6
      - → reflex micturition with detrusor-sphincter synergia
Neurogenic UMN

• Upper Motor Neuron Diseases
  – *Cerebral Injury* (stroke, tumour, brain injury)
    • → detrusor overactivity
  – *Basal Ganglia disease* (Parkinson’s disease)
    • Detrusor overactivity
    • Contractions are short, relaxation of ext. sphincter is slowed → urgency, urge incontinence, slow flow
  – *Suprasacral spinal cord damage*
    • Above T6
      – → reflex micturition with detrusor-sphincter dyssynergia
    • Below T6
      – → reflex micturition with detrusor-sphincter synergia
Neurogenic LMN

• Lower Motor Neuron
  – Sacral Spinal cord damage
    • Pelvic fracture, cauda equina
    • Acontractile bladder, poor bladder sensation
  – Peripheral Nerve Damage.
    • Diabetes, pelvic surgery, XRT
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Voiding Dysfunction

Friendship is like peeing on yourself:

everyone can see it, but only you get the warm feeling it brings
Voiding Dysfunction

Etiology

- **Failure to Store (AKA Incontinence)**
  - Detrusor overactivity
  - Outlet incompetence

- **Failure to Empty (AKA Retaining)**
  - Detrusor underactivity
  - Outlet obstruction
Voiding Dysfunction

• Failure to Store
  – *Urge Incontinence* - involuntary loss of urine with a strong desire to void.
  – *Stress Incontinence* - loss of urine with increased intra-abdominal pressure (cough, laugh, jump, rise to standing etc).
  – *Overflow Incontinence* - loss of urine with bladder over-distension.
  – *Functional Incontinence* - loss of urine associated with cognitive or physical impairment.
  – *Mixed Incontinence* - combinations of above
Urge Incontinence

• Etiology
  – Stone, UTI, Tumor, Overactive Bladder

• Investigations
  – Hx, PE +/- urodynamics
Urge Incontinence

**Treatment**
- Treat underlying cause
- Timed voiding
- Bladder training – Biofeedback
- Pharmacologic
  - Anticholinergic – Oxybutinin
  - TCA’s – Imipramine
- Surgical
  - Bladder pacemaker
  - Bladder denervation (rare)
  - Bladder Augmentation – Mitrofanoff
  - Urinary Diversion
Stress Urinary Incontinence

• Etiology
  – Urinary retention + incr abdo pressure
  – Detrusor overactivity + incr abdo pressure
  – Intrinsic sphincter deficiency
  – Urethral hypermobility
    • Often related to weak pelvic floor muscles

• Risk Factors
  – Obesity, female, pregnancy, Vaginal deliveries, hysterectomy, prostatectomy, family Hx, caucasian, smoking, strenuous activity.
Stress Incontinence

• Treatment
  – Kegel exercises
  – Biofeedback
  – Pharmacologic
    • Alpha agonist (TCA, SSRI’s, pseudoephedrine) → incr sphincter tone and bladder outflow resistance
    • Estrogen cream/pill
  – Periurethral collagen injections
  – Pessaries
  – Surgery
    • Bladder neck suspension (Burch, MMK)
    • Urethral Slings (TVT, TOT)
    • Artificial sphincter
Stress Incontinence

- Retropubic Bladder Neck Suspension (BURCH)
Stress Incontinence

- Urethral Slings
Stress Incontinence

• Artificial Sphincter
Overflow Incontinence

• Etiology
  – Obstruction
    • Treatment
      – Treat underlying cause, eg BPH
  – Acontractile Bladder
    • Treatment
      – Timed Voiding
      – Double voiding
      – Clean intermittent Catheterization → Keep bladder volumes < 400ml and pt dry between catheterizations
      – Indwelling Catheter
      – Suprapubic Catheter
Transient Urinary Incontinence

- DIAPERS

D  Delirium – cognitive dysfunction can impair voiding
I  Infection – bladder irritation
A  Atrophic Vaginitis – post menopausal may cause, nocturia, freq, urgency
P  Pharmaceuticals/Polypharmacy
E  Excessive Urine production – diuretics, untreated DM
R  Restricted mobility
S  Stool Impaction/Constipation impairs bladder function and pelvic floor muscle function
Transient Urinary Incontinence

• Pharmaceuticals
  – Diuretics
  – Anticholinergics – impair bladder contraction
  – Sedatives- bzd’s – delirium
  – Narcotics – impair bladder contraction, constipate, delirium
  – Alpha agonist – increase sphincter tone – retention (nasal decongestants, imipramine)
  – Alpha blocker – lead to stress incontinence
  – CCB’s impair bladder contraction
Voiding Dysfunction Case

- So, you have this “friend” that has mentioned they occasionally have a case of wet undies...
Dx?
Dx?
Voiding

• Evaluation
  – History
    • Urgency, frequency, dysuria
    • Association with valsalva maneuver (sneeze, cough, lifting etc.)
    • Medications (diuretics, benzos, narcotics)
    • Fluid intake
    • Back or head injury
    • Parathesias, fecal incontinence
    • Diabetes
    • Other neurological disease (MS, Parkinson etc.)
Voiding

• **Physical**
  – mental status, mobility
  – abdominal and pelvic exam
  – neurological exam
  – anal tone, peri-anal sensation
  – Bulbocavernosus reflex (S2,3,4)

• **Investigations**
  – Urinalysis, serum creatinine
  – Voiding Diary
  – Post Void Residual (PVR; by U/S or catheterization)
  – Urine cytology- pts with irritative voiding symptoms
Voiding

• Special Urology Tests
  – Urodynamics
    • Uroflowmetry
    • Multichannel urodynamics
    • Video-urodynamics
  – Endoscopy (Cystoscopy)
  – Upper tract imaging (renal ultrasound)
Voiding

• Indications for Referral:
  – History or physical suggestive of neurologic disease
  – Hematuria, recurrent UTIs, bladder stones, renal insufficiency (post-renal) with incontinence
  – Elevated PVR, overflow incontinence
  – Incontinence in pts with prior lower GU surgery
  – Persistence of incontinence once reversible causes are corrected
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Lower Urinary Tract Symptoms (LUTS)

• “.. A constellation of obstructive and irritative voiding disturbances of the lower urinary tract”
LUTS

- LUTS
  - Storage symptoms/ irritative
    - Frequency, urgency, nocturia
  - Voiding symptoms/ obstructive
    - Hesitancy, slow stream, “stuttering” stream, straining to void, sense of incomplete emptying, “doub;e” voiding, post void dribble

- Dysuria and incontinence are not usually seen in uncomplicated BPH.
- Microhematuria is common
DDx of LUTS in Old Men

- **Prostate**: BPH, prostate cancer, prostatitis
- **Bladder**: cystitis, bladder tumour, bladder stone
- **Urethra**: urethral stricture, meatal stenosis, phimosis
- **Neurologic**: Parkinson’s disease, stroke, Alzheimer’s disease, spinal cord disease
- **Other**: Diabetes, sleep apnea, medication, diet, distal ureteral stone, pelvic mass
Evaluation of LUTS

- **Hx**
  - IPSS/AUA symptom score

- **PE**
  - General & GU exam, DRE, Focused Neurourologic Exam

- **UA/ UCx**
Evaluation of LUTS

+/- Serum Creatinine
+/- PSA
+/- Post void residual (PVR)
  • Measures amount of urine after voiding
  • Large volume may suggest blockage
  • Measured by bladder scanner (U/S) or Catheter
+/- Abdo Ultrasound
  • If hematuria, renal impairment, UTI’s, atypical symptoms
+/- Cystoscopy
+/- Urodynamics
  • If urinary retention, incontinence, atypical symptoms, neurological disease.
LUTS History

- Some specific questions to ask
  - Hematuria
  - Dysuria
  - Incontinence
  - Abdo/flank pain
  - Previous transurethral surgery
  - CNS, neurologic diseases (parkinson’s, stroke)
  - Meds (oral decongestants, antidepressants)
  - DM
  - Previous STD’s or perineal trauma
• **Risk Factors**

  Increasing age

  Weight gain and abdominal adiposity in adulthood may contribute to LUTS

  Excessive alcohol drinking (>75 g/day) was associated with LUTS and BP

  Smoking – Nicotine increases sympathetic nervous system activity exacerbating LUTS
### INTERNATIONAL PROSTATE SYMPTOM SCORE (I-PSS)

<table>
<thead>
<tr>
<th>Question</th>
<th>Not at all</th>
<th>Less than 1 time in 5</th>
<th>Less than half the time</th>
<th>About half the time</th>
<th>More than half the time</th>
<th>Almost always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>2. Over the past month, how often have you had to urinate again less than two hours after you finished urinating?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>3. Over the past month, how often have you found you stopped and started again several times when you urinated?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>4. Over the past month, how often have you found it difficult to postpone urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>5. Over the past month, how often have you had a weak urinary stream?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>6. Over the past month, how often have you had to push or strain to begin urination?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

#### Total I-PSS Score = 

### QUALITY OF LIFE DUE TO URINARY SYMPTOMS

<table>
<thead>
<tr>
<th>1. If you were to spend the rest of your life with your urinary condition just the way it is now, how would you feel about that?</th>
<th>Delighted</th>
<th>Pleased</th>
<th>Mostly satisfied</th>
<th>Mixed about equally satisfied and dissatisfied</th>
<th>Mostly Dissatisfied</th>
<th>Unhappy</th>
<th>Terrible</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

#### Quality of Life assessment index QOL=
LUTS

• **DRE**
  – Healthy
    • Symmetric
    • Soft
    • Size – walnut/20g
      at 20 years of age
  – Unhealthy
    • Hard
    • Assymetrical
    • Nodule
    • Enlarged
LUTS

- Size of gland **NOT** = LUTS severity
Benign Prostatic Hyperplasia

• BPH is prevalent and relevant
  – Don’t forget it.
BPH Anatomy

• Prostate has 2 main types of tissue
  – Stroma
    • Smooth muscle
    • Collagen
  – Epithelium

• BPH occurs in transitional zone
• Prostate Cancer typically occurs in peripheral zones
LUTS
BPH

• Prevalence
  – Increasing prevalence with age, 80% of 80yo’s

• Pathophysiology
  – Growth of stromal component of prostate
  – Increased alpha 1A receptors leading to increased smooth muscle tone
  – Size and degree of BOO (bladder outlet obstruction) do not fully correlate with degree of symptoms
Complications of BPH

- Urinary retention (acute or chronic)
- Renal failure
- Recurrent UTIs
- Bladder stones
- Hematuria
Current practice

The therapeutic cascade (step-up):

- lifestyle measures,
- phytotherapy
- alpha blockade
- 5 ARIs
- combination med therapy
- anticholinergics (occasionally)
- intermediate therapies (MIS)
- intervention under GA (TUR, etc)
Lifestyle Modification

- decrease fluids
- caffeine
- alcohol
- time diuretics
- decongestants
- exercise
- weight loss
- sleep apnea
- diet
BPH Pharmacotherapy

- **Alpha Blockers**
  - Tamsulosin (Flomax): $\alpha_1$-subtype A selective; 0.4 mg daily; similar effectiveness but significantly fewer side effects compared to other $\alpha$-blockers; retrograde ejaculation prevalent
  - Silodosin (Rapaflo): $\alpha_1$-subtype A selective; 8 mg daily. SE: retrograde ejaculation. Rapid onset action
  - Terazosin (Hytrin): $\alpha_1$ selective; 2 mg – 10 mg daily; approximately 70% of men experience “satisfactory” improvement in symptoms; common side effects include dizziness, fatigue and rhinorrhea
  - Doxazosin (Cardura): $\alpha_1$ selective; 4 mg – 8 mg daily; side effects similar to terazosin; effectiveness similar to terazosin
  - Alfuzosin (Xatral): $\alpha_1$-subtype A selective; 10 mg daily; similar to flomax but less retrograde ejaculation
BPH Pharmacotherapy

• **Alpha Blockers**
  – Side Effects
    • Dizziness
    • Asthenia (fatigue)
    • Nasal congestion
    • Retrograde ejaculation
    • Orthostatic hypotension (uncommon)
    • Syncope (rare)
BPH Pharmacotherapy

• 5 alpha reductase inhibitors...
  – Finasteride
  – Dutasteride

Let's look at physiology....
Regulation of Cell Growth in the Prostate in BPH

Serum testosterone (T) → T → 5AR (1 and 2) → DHT → DHT-androgen receptor complex → Prostate cell

Growth factors → Unbalanced → Increased Cell growth → Cell death
Two 5a-reductase (5-AR) Isoenzymes Convert Testosterone to DHT

Testosterone → Type II 5AR → DHT → Prostate enlargement
→ Type I 5AR → Testosterone

Different Type I and Type II 5-AR Isoenzyme Inhibition by Dutasteride and Finasteride

Testosterone

Dutasteride

Type II 5AR

Finasteride

Type I 5AR

Prostate volume reduced

DHT

BPH Pharmacotherapy

• 5 alpha reductase inhibitors:
  – Reduce rate of Acute Urinary Retention
  – Decrease rate of surgery over 6 years
  – Work best in larger prostates
  – Decrease size by 25%
  – Decrease PSA by 50%
  – Slower onset of action than alpha blockers
Incidence of Acute Urinary Retention at Year 4 by Baseline Prostate Volume Tertile

- Placebo (N=155)
- Finasteride (N=157)

14 to 41 (Low-Tertile): 8.9% Placebo, 5.1% Finasteride (50% reduction)

>41 to 57 (Mid-Tertile): 11.7% Placebo, 6.8% Finasteride (40% reduction)

58 to 150+ (High-Tertile): 22.0% Placebo, 5.6% Finasteride (74% reduction)

Reduction in risk over 4 years (Life Table Analysis)
Incidence of BPH-Related Surgery at Year 4 by Baseline PSA Tertile

- Placebo (N=1503)
- Finasteride (N=1513)

Percent of Patients

Baseline PSA (ng/mL)

- 0 to 1.3 (Low-Tertile)
  - Placebo: 7.8%
  - Finasteride: 4.4%

- 1.4 to 3.2 (Mid-Tertile)
  - Placebo: 43%
  - Finasteride: 46%

- 3.3 to 12 (High-Tertile)
  - Placebo: 12.6%
  - Finasteride: 8.3%

Reduction in risk over 4 years (Life Table Analysis)
BPH Pharmacology

• 5 Alpha reductase inhibitors
  – Side Effects
    • Erectile Dysfunction <5%
    • Decreased libido <4%
    • Decreased Volume Ejaculate < 3%
    • Gynecomastia <1%
BPH Pharmacotherapy

• Combination of Alpha Blockers and 5 Alpha reductase inhibitors
  – Long and short of it is:
    • IF prostate small and PSA low
      – Use alpha blocker
    • IF prostate large and PSA high
      – Use Combo
BPH and Surgery

• Surgical Options
  – “Minimally invasive therapy”
    • Injections – eg. Botox™, alcohol
    • Photodynamic therapy (PTD)
    • Microwave heat treatment
    • High Intensity Frequency Ultrasound (HIFU)
    • Needle ablation / radio-wave treatment
    • Electrovaporization of prostate
  – Green light Laser therapy
  – Transurethral resection (TURP)
  – Open prostatectomy
BPH and Surgery

• Indications for surgery
  – Symptoms refractory to medical therapy
  – Recurrent UTI
  – Urinary Retention
  – Recurrent Hematuria
  – Renal Impairment
  – Bladder Calculi
TURP – Gold Standard

• TURP – Transurethral Resection of prostate
  – Electrocautery resection of prostatic tissue
  – Endoscopic
  – Pt stay is usually 1 night
TURP
Before and After TURP

BEFORE

AFTER
TURP

• Complications
  – Bleeding
  – Perforation
  – TUR Syndrome
    • With prolonged procedure
    • Absorption of hypotonic solution leads to:
      – Hyponatremia, hypervolemia, hypertension, mental confusion, seizures, nausea, vomiting, visual disturbances
      – Occurs in < 2% of cases
Other Surgical Options

• Green light laser
Other Surgical Options

- Open Prostatectomy
  - For LARGE prostates
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