Overview of Today’s Lecture

- Review of normal urinary system anatomy & physiology
- Urinalysis review
- Obstructions, stones, and neoplasms
- Disorders of the lower urinary tract
- Disorders of the kidney

Urinary Tract Obstruction

- Urinary tract obstruction
  - interference with the flow of urine at any site along the urinary tract
  - Uni- or bilateral, partial/complete, sudden/insidious, anywhere, from inside urinary tract or elsewhere
  - Called Obstructive Uropathy when it causes kidney problems (hydronephrosis)

- Severity and sequellae based on:
  - Location
  - Completeness
  - Involvement of one or both upper urinary tracts
  - Duration
  - Cause
Urinary Tract Obstruction

- **Hydroureter**
  - Dilation of ureter

- **Hydronephrosis**
  - Obstructive uropathy
  - Enlargement of renal pelvis and calyces

- Compensatory hypertrophy and hyperfunction
  - When blockage is unilateral
  - Obligatory growth
  - Compensatory growth

- **Postobstructive diuresis**
  - Nephrogenic diabetes insipidus

Lower Urinary Tract Obstruction

- **Obstruction**
  - Urethral stricture, prostate enlargement, pelvic organ prolapse
  - Partial obstruction of bladder outlet or urethra
    - Low bladder wall compliance (high press. at low volumes)

- **Neurogenic bladder** (neurological origin)
  - Dyssynergia (loss of coordinated muscular contraction)
    - Detrusor hyperreflexia-overactive (upper NS)
    - Detrusor areflexia-underactive (below S1)

- **Overactive bladder syndrome** (OBS)
  - Frequency, urgency, nocturia
Urolithiasis (Kidney Stones)

• Kidney stones - Calculi or urinary stones
  • Urolithiasis – stones in the urinary tract
  • Masses of crystals, protein, or other substances that form within and may obstruct the urinary tract

  – Risk factors are varied:
    • Heredity, Gender, Race, Fluid intake, Diet

  – Kidney stones are classified according to the minerals that make up the stone
    • Calcium oxalate/phosphate – most common (70-80%)
    • Magnesium (struvite) (15-20%)
    • Uric acid (5-7%)
    • Cysteine (< 1%)

  – Signs/Symptoms
    • Hematuria
    • Flank pain (renal colic)

Kidney Stone Formation

• Conditions that encourage kidney stone (calculus) formation
  • Stasis, obstruction, infection
  • Salt in a higher concentration than the volume able to dissolve the salt
  • Dehydration/decreased urine volume
  • pH alteration (alkaline pH favors formation)

Tumors

• Renal tumors
  • Malignant, mature, male
  • Renal adenomas (oncocytomas; 10-15%; benign)
  • Renal cell carcinoma (RCC; renal adenocarcinoma)
    • About 90% of all primary renal malignancies
    • Renal tubular epithelium
    • Cigarette smoking, risk about 2x
    • Gross, painless hematuria

• Bladder tumors
  • Transitional (Urothelial) cell carcinoma is most common
  • Gross, painless hematuria
  • Most common in males older than 60 years and smokers

**Gross, painless hematuria should be considered a sign of urinary tract cancer unless proven otherwise.
Urothelial Carcinomas

- Occur in pelvis/collecting system
- Transitional epithelial tumors
- Few types
- Urothelial papilloma (benign)
- Malignant tumors here all have these two terms in their name: “papillary urothelial”
  - PUNLMP - “neoplasm of low malignant potential” (“only a ‘PUN’, nothing serious”)
  - Low grade (malignant - not invasive)
  - High grade (malignant - invasive)
- Carcinoma of the renal pelvis
  - About 10% of all renal malignancies
  - Tend to invade early (survival rate lower when this happens)

Gross, painless hematuria should be considered a sign of urinary tract cancer unless proven otherwise.

Disorders of the Lower Urinary Tract

- General Facts to keep in mind regarding lower urinary tract
  1. Sensitive to bacterial infection, especially ascending through urethra
  2. Urinary obstruction, stasis, and infection frequently occur together
  3. Most tumors of lower urinary tract are bladder tumors
     - High mitotic index of bladder epithelium
     - Character of chemicals/toxins to which bladder epithelium is constantly exposed
     - Urine (and toxins) tend to stay contact with bladder epithelium for a long time
  4. Disease typically presents with: urgency, dysuria, hematuria, urinary retention, and/or incontinence

Urinary Tract Infection (UTI)

- UTI is inflammation of the urinary epithelium caused by bacteria
- Can occur anywhere in urinary tract
  - Upper: Pyelonephritis (may be a complication of lower UTI)
  - Lower: Cystitis (bladder), urethritis, prostatitis
- Most common pathogens = coliform bacteria
  - Escherichia coli
- Factors normally protecting against infection/UTI
  - Washing out bacteria during micturition
  - Low pH/high osmolarity of urea
  - Tamm-Horsfall protein (antibacterial) and other bactericidal secretions from uroepithelium
  - Ureterovesical junction acts as valve
Urinary Tract Infection (UTI) (cont’d)

- **Bacterial (acute) cystitis**
  - Cystitis is an inflammation of the bladder
  - Most common form of UTI
  - Common manifestations of cystitis:
    - Frequency
    - Urgency
    - Dysuria
    - Lower abdominal and/or suprapubic pain

- **Urethritis (less common UTI)**
  - Inflammation of urethra
  - STIs most common cause

Urinary Tract Infection (UTI) (cont’d)

- **Non-bacterial cystitis (Painful Bladder Syndrome/Interstitial Cystitis)**
  - Not from infection; chronic
  - Interstitial cystitis involves all layers of bladder
  - Manifestations:
    - Most common in women 20 to 30 years old
    - Bladder fullness, frequency, small urine volume, chronic pelvic pain
    - Mucosal (Hunner) ulcers
  - Treatment
    - No single treatment effective, symptom relief
Voiding Disorders

- Think about the urination reflex. What can go wrong?
  - Urinary retention (> 100 ml after catheterization)
    - Neuromuscular, Coordination, Obstruction
  - Urinary incontinence
    - Can be temporary (transient) or persistent (established)
    - Embarrassing, elderly, erode skin
    - Types
      - Urge
      - Stress
      - Overflow
      - Functional

Disorders of the Kidney – General Terminology

- Azotemia
  - Renal failure manifested only by lab tests
  - Increased BUN and creatinine
  - No clinical symptoms
- Uremia (“urine in blood”)
  - Increased nitrogenous wastes PLUS clinical S&S
  - Manifestations (mnemonic: “BANE of HOPE”)
    - Bleeding/coagulation defects
    - Anemia (low erythropoietin)
    - Neuropathy
    - Edema (salt/water retention)
    - Hypertension (increased renin output)
    - Oliguria
    - Pericarditis
    - Encephalopathy

Acute Renal Failure (ARF)

- ARF (Uncommon)
  - Sudden decline in kidney function (trauma, rapidly progressive renal disease)
  - Decreased glomerular filtration & accumulation of nitrogenous waste in blood (azotemia) & oliguria (< 400 ml/day)
  - Anorexia, nausea, vomiting
  - Causes mnemonic: “Patient can’t VOID RIGHT” (see SG p 199)
- Classification of AKI
  - Prerenal – most common
    - Hypovolemia
    - Hypotension or hypoperfusion
  - Intrarenal (or intrinsic)
    - Glomerular and/or small vessel injury
    - Tubular epithelial injury (acute tubular necrosis)
    - Renal interstitial injury
  - Postrenal
    - Rare
    - Causes bilateral obstruction anywhere
**Oliguria in Acute Kidney Injury (AKI)**

- Schematic or representations
- Tubular injury (e.g., tubular damage)
- Decreased GFR (Glomerular Filtration Rate)
- Obstruction
- Tubular leak
- Increased intracellular pressure

**Chronic Renal Failure**

- Progressive loss of renal function that affects nearly all organ systems
- Causes and associations mnemonic: “DUG HIPPO” (see SG p. 200)
- There isn’t a system in the body that’s spared!

- Stages (NKF criteria):
  - (I) Normal (GFR > 90 mL/min)
  - (II) Mild (GFR 60-89 mL/min)
  - (III) Moderate (GFR 30-59 mL/min)
  - (IV) Severe (GFR 15-29 mL/min)
  - (V) End-stage (GFR less than 15 ml/min)

- Oliguria
  - Diminished renal reserve
    - GFR ~ 50%, no azotemia
  - Renal Insufficiency
    - GFR ~ 20-50% w/azotemia
  - Chronic Renal Failure
    - GFR < 20-25% w/mild uremia; dialysis
    - End-stage kidney
      - GFR < 5% w/frank uremia; dialysis or transplant

**Signs and Symptoms of Kidney Failure**

- Proteinuria and proteinuria
- Uremic syndrome and proteinuria
- Nephrogenic diabetes (diabetes mellitus)
- Fluid and electrolyte balance
  - Sodium and water balance
    - Sodium retention in urine 
  - Potassium balance
    - Tubular secretion increases early
    - Once oliguria sets in, potassium retained
- Acid-base balance
  - Metabolic acidosis when GFR falls to 30-40%
- Calcium, phosphate, bone
  - Reduced renal phosphate excretion due to decreased renal synthesis of 1,25(OH)2 vitamin D3, and hypocalcemia
- Parathyroid dysfunction
  - Fractures
- Anemia
  - Lethargy, dizziness, and low hematocrit are common
- Alterations in trophic functions
  - Cardiovascular, pulmonary, hematopoietic, immune, neurologic, gastrointestinal, endocrine, and reproductive functions
Chronic Kidney Disease (CKD) (cont’d)

Two major factors thought to be important in advancing renal disease
- Proteinuria (PrU)
- ↑ angiotensin II

Common Pathogenic Processes observed in CKD
- Glomerular hypertension (angiotensin II) → PrU
- Glomerular hyperfiltration (angiotensin II) → PrU
- Glomerular hypertrophy (angiotensin II)
- Glomerulosclerosis (scarring of glomerular capillaries)
- Tubulointerstitial inflammation and fibrosis (PrU and angiotensin II)

Glomerular Disorders
- Glomerulonephritis (GN)
  - Inflammation of the glomerulus
    - *Almost all primary glomerular disease is autoimmune* (Type III)
    - Drugs or toxins (penicillamine, captopril, phenytoin and some antibiotics, including penicillins, sulphamides and rifampicin)
    - Viral causes (HIV)
    - Systemic diseases (secondary; SLE, DM, hypertension)

- Gomerulopathy – no inflammatory component

- Mechanisms of injury to glomerulus
  - Deposition of circulating soluble antigen-antibody complexes, often with complement fragments (Type III hypersensitivity – immune complex)
  - Antibodies reacting in situ against planted antigens within the glomerulus (Type II hypersensitivity – cytotoxic)
  - Nonimmune: due to drugs, toxins, ischemia

Four types of tissue reaction:
1. Thickening of basement membrane
2. Hypercellularity of glomerulus
3. Hyalinosis (proteinaceous material)
4. Sclerosis (collagen accumulation)

Results:
1. ↓ glomerular blood flow
2. ↓ glomerular hydrostatic pressure
3. ↓ GFR
4. Hypoxic injury
Mechanisms of Glomerular Injury

Mesangial Cells
- Extraglomerular
  - part of JG apparatus
- Intraglomerular
  - Filtration
  - Structural support
  - Phagocytosis
  **Contribute to extracellular matrix (Type IV collagen, laminin, fibronectin)**

Glomerulonephritis (GN)

- Manifestations:
  - Two major symptoms if severe
    - Hematuria with red blood cell casts
    - Proteinuria exceeding 3 to 5 g/day with albumin (macroalbuminuria) as the major protein
  - Oliguria (30 ml/hr or less)
  - Hypertension
  - Edema
  - Nephrotic sediment (primarily protein)
  - Nephritic sediment (primarily blood)

- Classification of GN can be based on a number of criteria:
  - Cause, e.g., diabetic nephropathy, lupus nephritis, IgA nephropathy
  - Pathologic lesions (proliferative, membranous, sclerosis + diffuse, focal, segmental-local)
  - Disease progression (acute, rapidly progressive, chronic)
  - Clinical presentation (nephrotic syndrome, nephritic syndrome, acute or chronic renal failure)

Glomerulonephritis: Nephritic Syndromes

- Nephritic syndrome
  - Usually acute and caused by autoimmune disease
  - Hematuria
  - Mild proteinuria and edema
  - Hypertension
  - Azotemia (increased BUN and blood creatinine)

Glomerular Inflammation

Nephritic Syndrome

- Hematuria
- RBC casts
- Proteinuria
- Azotemia
- Hypertension
- Edema

Autoimmune reaction (usual mechanism)

Glomerular damage

Oliguria
Glomerulonephritis: Nephritic Syndromes

There are two types of Nephritic syndromes

1. Acute Nephritic Syndrome (Acute proliferative GN)
   - Usually in children; 95% recover
   - Typical after streptococcal infection: Acute Poststreptococcal GN
     - α-strep ab deposits in glomerulus and begins damage

2. Hereditary Nephritis
   - Most common is Alport syndrome
     - X-linked recessive
     - Defect in Type IV collagen in glomerular BM
   - Thin BM Disease (TBMD)
     - Also called Benign Familial Hematuria
   - IgA Nephropathy (Berger Disease)
     - Autoimmune
     - Overproduction of ab from MALT

Rapidly Progressive GN (Crescentic GN)

Glomerulonephritis: Nephrotic Syndromes

Nephrotic syndrome (any glomerular disease can cause this)

- Excretion of 3.5 g or more of protein in the urine per day (proteinuria)
- In adults, usually a secondary disease

- Diabetes, amyloidosis, SLE

- Hypoalbuminemia
- Edema
- Hyperlipidemia
- Lipiduria

Proteinuria (albumin, Ig, anticoagulants)

Glomerular damage

Several common types of nephrotic syndromes

1. Membranous GN (MG)
   - Most common cause of nephrotic syndrome in adults
   - Autoimmune
     - 90% idiopathic, 10% from drugs, CA, SLE, other autoimmune disease
     - Thickening of glomerular BM from ab deposits with hypertension

2. Minimal Change Disease (MCD; lipoid nephrosis)
   - Most common cause of nephrotic syndrome in children (2-6 yrs)
   - Autoimmune (probably)
   - No hypertension

3. Focal Segmental Glomerulosclerosis (FSG)
   - Adolescents mainly
   - Idiopathic

4. Membranoproliferative GN (MPGN)
   - Children/young adults - autoimmune
   - Thickening and splitting of glomerular BM

All the syndromes beginning with "M" are autoimmune
Chronic Glomerulonephritis

- Diagnosis applied to:
  - Long-standing, end-stage, burned out, chronic glomerular disease
  - About half of patients have had a previous diagnosis of some type of GN; in the other half the cause is unknown.
  - Glomeruli are shriveled and scarred; TI network is obliterated making it difficult to discern the pathogenesis.
  - Tends to become self-perpetuating due to renal ablation glomerulopathy.
  - Result: shrunken, end-stage contracted kidney.
- Other secondary causes of glomerular disease
  - Diabetic glomerulosclerosis (#1 cause of renal failure in US)
  - Diabetic nephropathy = ischemic necrosis + bacterial pyelonephritis + glomerulosclerosis (Pee Glucose?)
  - Other causes: Lupus nephritis, Amyloidosis, Bacterial endocarditis, any disease with a vasculitis component.

Tubular and Interstitial Disorders

- Tubular and interstitial damage go together and are found in Tubulointerstitial nephritis (TIN).
- Toxic Injury
  - Acute (drug-induced; idiosyncratic, Type I or IV hypersensitivity)
  - Antibiotics, NSAIDs, Diuretics, Ibuprofen

Chronic Analgesic Nephropathy

- Induced by excessive use of analgesics in combination
  - Caffeine or Codeine
  - Aspirin or NSAIDS
  - Phenacetin or acetaminophen
- Other causes of tubulointerstitial injury
  - Urate (gout)
  - Bence-Jones proteins
Pyelonephritis

- Pyelonephritis (Upper UT)
  - Inflammatory disorder
  - Renal tubules, interstitium, calyces, and pelvis
  - Infection may be present
  - Combination of Chronic TIN, infection, stasis, obstruction, stone formation

- Acute pyelonephritis
  - Acute pyogenic infection of kidney
  - Usually E. Coli and other fecal flora

- Chronic pyelonephritis
  - Persistent or recurring episodes of acute pyelonephritis that lead to scarring
  - Reflux nephropathy (most frequent cause, especially in children)
  - Chronic Obstructive Pyelonephritis

Vascular Disorders of the Urinary System

- Vascular disorders may be a cause or a result of disease
- Benign Nephrosclerosis
  - Wear and tear pathologic changes
  - Advancing age and blood pressure
  - Sclerosis of small arteries and arterioles
    - Focal ischemia
    - Glomerular sclerosis
    - Tl inflammation

- Malignant Nephrosclerosis
  - Patients with malignant hypertension (BP > 160/100 mm Hg)
  - Malignant (Stage 2) hypertension is a medical emergency!
  - Fibrinoid (onionskin) necrosis of afferent arteriole (what will this lead to?)

- Extrarenal Disease
  - Atherosclerosis, fibromuscular diseaseae, emboli, sickle cell disease