Introduction to Renal Disease
MHD

Intro Objectives

• Define common terms used in discussion of renal disorders
• List characteristic signs and symptoms of renal dysfunction
• Define and describe common syndromes associated with renal disease
• List the renal syndromes used when evaluating a patient with a renal disorder

Review of Renal Basics

Major Anatomical Features of Urinary Tract

Kidney
• Glomeruli
• Tubules
• Interstitium
• Vasculature

Collecting system
• Calyces
• Ureters
• Bladder
• Urethra
Review of Renal Basics

Major Functions of the Kidney
• Glomerular filtration
• Excretion
  • Metabolic by-products, drugs, toxins
• Electrolyte and acid-base homeostasis
• Blood pressure regulation
• Volume homeostasis
• Endocrine regulation
  • Erythropoietin, vitamin D, renin

How do we know a patient has a “kidney problem”
• History
• Physical Exam
• Laboratory Evaluation
  – Serum electrolytes
  – Serum BUN, creatinine
  – Urinalysis
• Imaging
  – Ultrasound
  – CT scan
• Kidney Biopsy

Ways to categorize kidney dysfunction

<table>
<thead>
<tr>
<th>Site of lesion</th>
<th>Nature of factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glomeruli</td>
<td>Immunologic</td>
</tr>
<tr>
<td>Tubules</td>
<td>Metabolic</td>
</tr>
<tr>
<td>Interstitium</td>
<td>Infiltrative</td>
</tr>
<tr>
<td>Vasculature</td>
<td>Infectious</td>
</tr>
</tbody>
</table>

| Chronicity             | Hemodynamic                   |
|                        | Genetic                       |

Introduction to Laboratory Medicine
Common Laboratory Tests Module
Kidney Dysfunction - Chronicity

- **Acute**
  - Acute Kidney Injury (AKI)
    - Abrupt decrease in kidney function

- **Chronic**
  - Chronic Kidney Disease (CKD)
    - Evidence of kidney dysfunction/pathology >3 months

- **End Stage**
  - End Stage Renal Disease (ESRD)
    - Last stage of CKD
      - Need for chronic renal replacement therapy

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Do not memorize

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Approach to the Patient with Renal Disease
Features of Renal Dysfunction

- Too much or too little urine production
- Azotemia, uremia
- Proteinuria, hematuria, stone formation
- Abnormal urinary sediment
- Electrolyte and/or acid-base imbalance
- Hypertension, abnormal volume state
- Anemia, metabolic bone disease
- Fever, eosinophilia, rash, pain
- Toxicity from decreased renal clearance of drugs, endogenous substances (e.g. insulin)

Too Much or Too Little Urine

- Normal Urine Output
  - 1500ml/24 hour
- Oligura
  - <500cc/24 hours
- Anuria
  - Absence of urine output
- Polyuria
  - >3000ml/24 hours
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Azotemia and Uremia

- **Azotemia**: elevation in renal indices
  - BUN, technically
  - Usually reflects decrease in GFR

- **Uremia**: when azotemia gives rise to clinical manifestations and biochemical abnormalities
  - Clinical Syndrome
    - Fatigue, anorexia, nausea, mental status changes, itching
    - Serositis (pericarditis, pleural effusions)
    - Platelet dysfunction

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Proteinuria

- Normal Urinary Protein
  - Total protein: < 150mg/24 hours
  - Albumin: < 30mg/24 hours

- Nephrotic Range Proteinuria
  - "Nephrosis": > 3 – 3.5gm/24 hours

- Quantitation of Proteinuria
  - 24hr urinary collection
  - Random urine protein/creatinine ratio

Hematuria

- Gross vs. Microscopic (≥ 2 RBC/hpf)
- Glomerular vs. Nonglomerular
- Upper vs. Lower Urinary Tract

- Imposters
  - Free Hemoglobin
  - Myoglobin
  - Menstrual contamination

Nephrolithiasis

- Formation of stones in the collecting system
- Manifests clinically as renal colic and hematuria
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**Abnormal Urinary Sediment**

- Hematuria
- Dysmorphic RBC’s
- Pyuria
- Casts
  - RBC casts
    - Glomerulonephritis
  - WBC casts
    - Pyelonephritis
  - Tubular casts

**Types of Renal Tubular Casts**

- Hyaline casts
  - Do not imply overt “pathology”
  - Dehydration, exercise, diuretic therapy
  - Precipitation of Horsfall mucoprotein
- Epithelial casts (muddy brown casts)
  - Acute tubular necrosis
- Fatty casts
  - Lipiduria, usually seen in nephrotic syndrome
- Granular casts
  - Chronic kidney disease
  - Nonspecific finding otherwise
- Waxy casts
  - Advanced kidney disease
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Electrolyte/Acid-Base Imbalance

- Common imbalances in renal disease
  - Hyper/hyponatremia
  - Hyper/hypochloremia
  - Hyperkalemia
  - Hyperphosphatemia
  - Hypocalcemia
  - Anion gap metabolic acidosis
  - Non anion gap metabolic acidosis

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Causes of Hypertension

• Primary or “Essential” hypertension

• Secondary causes
  – Anatomic/vascular causes
  – Endocrinopathies
  – Renal diseases, volume overloaded states
  – Pregnancy related diseases
  – Medications

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Renal Hormone Regulation

• Erythropoietin: regulates HGB/HCT concentration
• Vitamin D: regulates calcium absorption, maintains normal levels of calcium and phosphorus
• Advanced kidney disease:
  • Chronic erythropoietin deficiency
  • Anemia of chronic disease, typically normocytic
  • Iron transport/storage dysregulation also contributes
  • Chronic hyperphosphatemia, decreased renal activation of vitamin D3 (1,25-OH form)
  • Hyperparathyroidism, renal osteodystrophy
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Fever/pain/rash/eosinophilia

- Nonspecific symptoms/signs
- Seen in many forms of renal dysfunction
  - Urinary tract infection
  - Nephrolithiasis
  - Renal infarction
  - Papillary necrosis
  - Acute interstitial nephritis
  - Renal cell carcinoma
  - Vasculitis (SLE, Wegener’s, e.g.)
  - Cholesterol atheroembolic disease

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Drug Toxicity from Renal Dysfunction

- Often unanticipated by clinicians when managing AKI/CKD
- May be presenting feature of AKI/CKD
- Management
  - Drug dosage adjustment
    - Decrease dose or increase interval or both
- Can happen with endogenous substances as well
  - Insulin: prolonged renal clearance, resultant hypoglycemia

Additional Definitions as you Begin this Block

Approach to the Patient with Renal Disease

Scientific American Medicine 2018
Glomerular Disease

- Diseases of the glomerulus can present as one of five clinical syndromes:
  - Acute glomerulonephritis
  - Rapidly progressive glomerulonephritis
  - Chronic glomerulonephritis
  - Nephrotic syndrome
  - Asymptomatic urinary abnormalities

Glomerulonephritis

- A number of disorders lead to glomerular injury
- Present with some combination of
  - hematuria, proteinuria, reduced GFR, and hypertension.
What is “Nephritic Syndrome”?  
- Diseases that cause active inflammation of the glomerulus associated with  
  - Hematuria (red cells and red cell casts)  
  - Azotemia  
  - Hypertension  
  - Oliguria  
  - Sub-nephrotic range proteinuria

What is “Nephrotic Syndrome”?  
- Diseases that cause massive leakage of protein across the glomerular basement membranes  
  - Criteria  
    - >3.5gm protein/24 hours  
    - Hypoalbuminemia  
    - Edema  
    - Hyperlipidemia  
    - Fat bodies in the urine/fatty casts

Approach to the Patient with Renal Disease

aka Acute Tubular Injury  
-Damage to tubular epithelial cells
Approach to the Patient with Renal Disease

- Decreased effective arterial flow
- Urine flow is obstructed: ureters, bladder, urethra

Some Renal Equations
How to Measure/Estimate GFR

- Creatinine Clearance from 24-hour urine
  \[ \text{GFR} = \frac{\text{U}_c \times \text{V}}{\text{P}_c} \]

- Cockcroft-Gault Formula
  \[ \text{GFR} = \frac{(140 - \text{Age}) \times \text{Weight (in kg)}}{72 \times \text{Serum Creatinine (in mg/dL)}} \]

  * Modification of Diet in Renal Disease (MDRD) Equation
    \[ \text{eGFR} = 186 \times \text{Serum Creatinine}^{-1.154} \times \text{Age}^{-0.203} \times [1.212 \text{ if male}] \times [0.742 \text{ if female}] \]

- Fractional Excretion of Sodium (FENa)
  \[ \text{FENa} = \frac{\text{uria} \times \text{serum Na}}{\text{urine Na}} \times 100 \]

- Fractional Excretion of Urea (FUREA)
  \[ \text{FUREA} = \frac{\text{uria} \times \text{serum urea}}{\text{urine urea}} \times 100 \]

- Can help determine cause of acute kidney injury
  - FENa < 1% or >2% helpful, 1-2% indeterminate
  - FUREA < 35% or >35% helpful

Fractional Excretion Sodium

- Prerenal azotemia
  - Reduction in the amount of glomerular filtrate entering each nephron increases the retention of salt and water, resulting in a lower fractional excretion of sodium (FENa)

- Acute Tubular Necrosis (ATN)
  - Nephrons excrete a large fraction of their filtered sodium and water, resulting in a higher FENa
Summary

• Summary of structure, work of kidneys
• Introduced ways to categorize kidney dysfunction
• Provided overview of features of renal dysfunction
• Introduced specific renal syndromes
  – Pre-renal, post-renal, intrinsic renal
• Defined nephritic, nephrotic syndrome
• Provided several formulas