Acute Renal Failure: Prerenal & Postrenal
Acute Renal Failure—Definitions

- Rapid ↑ in BUN or creatinine
- Can occur over several hours, days or weeks
- Some causes of ARF include:

<table>
<thead>
<tr>
<th>Several Hours</th>
<th>Several Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhabdomyolysis</td>
<td>Aminoglycosides</td>
</tr>
<tr>
<td>Contrast induced</td>
<td>Poststreptococcal glomerulonephritis</td>
</tr>
</tbody>
</table>
Acute Renal Failure—Definitions

- Renal insufficiency (azotemia)
  1. Renal failure that does not usually require dialysis
  2. Build-up of azole groups or nitrogens in the blood

- Uremia (end stage renal disease)
  1. Severe renal failure requiring dialysis
  2. Severe acidosis and fluid overload
  3. Altered mental status
  4. Hyperkalemia
  5. Anemia
  6. Hypocalcemia
  7. Pericarditis
Acute Renal Failure—Definitions

- Also defined by the *site of the defect*
  1. Pre-renal
     - Decreased perfusion
  2. Intra-renal
     - Tubular or glomerular defect
  3. Post-renal
     - Decreased drainage or flow
Acute Renal Failure—Diagnosis

- ↑ BUN regardless of cause
- May be falsely elevated with increased dietary protein or GI bleeding
  1. Derived from protein catabolism
  2. Increases with the severity of renal failure
- May be falsely decreased with liver disease, malnutrition or SIADH
Acute Renal Failure—Diagnosis

- Creatinine is the main measure of renal function.
- Creatinine clearance approximates the GFR:
  1. Slightly overestimates
  2. Always adjusted for weight
- May be falsely low with decreased muscle mass and increased in body builders
- Increases at maximum rate of 0.5 to 1.0/day
Prerenal Azotemia—Definitions

- Diminished perfusion
- Kidneys are intrinsically normal
- Causes include:
  1. Hypovolemia regardless of etiology
  2. Hypotension regardless of etiology
  3. Decreased cardiac output
  4. Third spacing
  5. Decreased albumin
Prerenal Azotemia— Diagnosis

- BUN to creatinine ratio of 20:1
- ↓ urine sodium
- ↓ fractional excretion of sodium
- ↑ urine osmolality (>500)
- SG >1.010
Pre

SUN: 20:1
CREAT

UNa Low
FeNa < 1%

Post

ATN: 10:1

High

> 4.0

> 1%

UOSM > 500
SP Grav TT
Prerenal Azotemia—Hepatorenal Syndrome

- Intense vasoconstriction of afferent arterioles → decreased renal perfusion
- Findings are consistent with prerenal azotemia
- Correct underlying liver disease
Prerenal Failure—The Effect of ACE Inhibitors

- Vasodilation of the efferent arteriole
- Transient decrease in GFR
- Effects are exaggerated in:
  1. The elderly
  2. Diabetics
  3. HTN
  4. Baseline renal disease
- Overall effect is decreasing the rate of progression to uremia and renal failure
Prerenal Failure—The Effect of ACE Inhibitors

- Vasodilation of the efferent arteriole
- Transient decrease in GFR
- Effects are exaggerated in
  1. The elderly
  2. Diabetics
  3. HTN
  4. Baseline renal disease
- Overall effect is decreasing the rate of progression to uremia and renal failure
Prerenal Failure—Hepatopulmonary Syndrome

- Similar to hepatorenal syndrome
- Renal failure is secondary to pulmonary disease
- Marked change in oxygen saturation with changes in position—*orthodeoxia*
Postrenal Azotemia—Etiology

- Bilateral obstruction to flow
  1. Bladder cancer
  2. Prostatic hypertrophy or cancer
  3. Bilateral ureteral disease
     - Retroperitoneal fibrosis
     - Neurogenic bladder
  4. Bilateral strictures
Pre
BUN/Creat: 20:1
UNa Low: 210
FeNa < 17
UOSM > 500
SP Grav TT

ATN
10:1

Post
High

BB
Postrenal Azotemia—Etiology

- Bilateral obstruction to flow
  1. Bladder cancer
  2. Prostatic hypertrophy or cancer
  3. Bilateral ureteral disease
     - Retroperitoneal fibrosis
     - Neurogenic bladder
  4. Bilateral strictures
Postrenal Azotemia—Etiology (Cont’d)

- Creatinine rises when 70-80% of renal function is lost
- Initial elevation of BUN:Cr ratio of 20:1 (as with prerenal azotemia)
- ↓ fractional excretion of sodium
- ↓ urine sodium
- With chronic damage, BUN:Cr ratio decreases to 10:1 (as seen in ATN)
Hydronephrosis—Left-Sided Ureteral Stone

This image was reproduced from Wikipedia, http://www.wikipedia.com
Acute Renal Failure: Tubulointerstitial Disease
Acute Tubular Necrosis—Etiology

- Damage is tubular or
- Decreased perfusion or
- Decreased drainage or
- Toxic injury or
- May be a combination of the above factors
Acute Tubular Necrosis—Phases

1. Prodromal
   - Time between acute injury and the onset of renal failure

2. Oliguric (<400 ml/24 h) or anuric (<100 ml/24 h)

3. Postoliguric
   - Diuretic phase when all fluids not previously excreted will leave the body in a vigorous polyuria
Acute Tubular Necrosis—Diagnosis

- BUN:Cr ratio of 10:1
- ↑ urine sodium (>40)
- ↑ fractional excretion of sodium (>1%)
- ↓ urine osmolality (<350)
<table>
<thead>
<tr>
<th></th>
<th>PRERENAL</th>
<th>ATN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine osmolarity</td>
<td>&gt;500</td>
<td>&lt;350</td>
</tr>
<tr>
<td>Urine Na+</td>
<td>&lt;20</td>
<td>&gt;40</td>
</tr>
<tr>
<td>FeNa+</td>
<td>&lt;1%</td>
<td>&gt;1%</td>
</tr>
<tr>
<td>Urine sediment</td>
<td>Scant</td>
<td>Full (brownish pigmented granular casts, epithelial casts)</td>
</tr>
</tbody>
</table>
Acute Tubular Necrosis—Treatment

- Correct the underlying cause
- Hydration
- Supportive care
Allergic Interstitial Nephritis—Etiology

- 70% of cases due to adverse effect to medications
  1. Penicillins
  2. Cephalosporins
  3. Sulfa drugs
  4. Allopurinol
  5. Rifampin
  6. Quinolones
Allergic Interstitial Nephritis—Etiology (Cont’d)

- Infections (viruses, bacteria or fungi). Most common causes includes
  1. Leptospirosis
  2. Legionella
  3. CMV
  4. Rickettsia
  5. Streptococci
- Autoimmune disease
  1. SLE
  2. Sjögren syndrome
  3. Sarcoidosis
  4. Cryoglobulinemia
Allergic Interstitial Nephritis—Diagnosis

- Characteristic findings include
  1. Rash
  2. Fever
  3. Joint pain
  4. Eosinophilia
  5. Increased serum IgE

- Best initial test—urinalysis
  1. Eosinophiluria (Wright or Giemsa stain)
  2. Hematuria
  3. Proteinuria (<2 g/24 hrs)
Allergic Interstitial Nephritis—Diagnosis (Cont’d)

- Most accurate test
  1. Biopsy
  2. Rarely performed

- Treatment
  1. Stop the offending agent
  2. +/- corticosteroids
Pigments—Etiology

- Myoglobinuria (rhabdomyolysis)
  1. Severe crush injury
  2. Seizures
  3. Severe exertion
  4. Less common: hypokalemia, hypophosphatemia, or meds (statins)

- Hemoglobinuria
  1. ABO incompatibility
Pigments—Etiology

- Directly toxic to renal tubules
- Precipitate in renal tubules
- Damage is directly proportional to duration of contact
- Worsened with dehydration
Pigments— Diagnosis

- Severe crush injury or seizure (potentially life threatening)
  1. EKG or serum potassium → peaked T-waves → IV calcium gluconate or calcium chloride
- Not potentially life threatening
  1. Urinalysis → Dipstick + for RBCs but none visualized on microscopy
- Confirmatory test
  1. Serum CPK → 10,000 – 100,000 (normal <500)
- Other findings: rapidly increased Cr, metabolic acidosis, decreased serum bicarb, hyperphosphatemia
Pigments—Management

- EKG abnormalities: IV calcium gluconate or IV calcium chloride stat
- Aggressive hydration
- Mannitol
- +/- Alkalization of the urine
Proteins— In Summary

- Associated with multiple myeloma
- Bence-Jones proteins cause tubular damage
- Also cause nephritic syndrome
Crystals—Etiology

- Oxalate
  1. Most common cause is ethylene glycol overdose
  2. Intoxicated person with increased anion gap metabolic acidosis
  3. Renal insufficiency
  4. Diagnosis is confirmed with envelope-shaped crystals seen on UA
  5. Treatment includes IV ethanol or fomepizole and dialysis
  6. Other causes include Crohn’s disease which results in chronic hyperoxaluria and stones
Crystals—Etiology

- Urate
  1. Most common cause is tumor lysis syndrome (acute) and gout (chronic)
  2. All patients undergoing chemo must receive vigorous hydration and allopurinol
  3. Stones and crystals precipitate in acidic urine
  4. Diagnosis by finding crystals in the urine
Hypercalcemia

- Results in:
  1. Stones
  2. Distal renal tubular acidosis
  3. Nephrogenic diabetes insipidus

- Most common cause:
  - Primary hyperparathyroidism

Surgical resection only done with symptomatic disease
5-mm Renal Stones—Passed Naturally without Intervention

These images were reproduced from Wikipedia, http://www.wikipedia.com
Large Stellate Urolith

This image was reproduced from Wikipedia, http://www.wikipedia.com
Staghorn Calculus and Scoliosis

This image was reproduced from Wikipedia, http://www.wikipedia.com
Ultrasound Ablation of a Large Renal Stone

This image was reproduced from Wikipedia, http://www.wikipedia.com
Toxins—Etiology

- Most common toxins implicated:
  1. NSAIDs
  2. Aminoglycosides
  3. Cephalosporins
  4. Contrast agents
  5. Amphotericin B
  6. Chemotherapy
  7. Radiation
  8. Heavy metals
  9. Cyclosporine
Toxins—Etiology

- Aminoglycosides: exacerbated by hypokalemia and hypomagnesemia, toxicity associated with trough level
- Amphotericin B: days-weeks (cumulative) of use results in $\uparrow$ Cr, $\downarrow$ K, $\downarrow$ HCO$_3$  
- Atheroembolic disease: renal failure several days after procedure. *Eosinophilia*, low complement, bluish discoloration of the extremities, livedo reticularis
- Contrast agents: 12–24 hours later. Poor function of renal parenchyma *prior to the procedure increases risk*. 
Analgesic Nephropathy—NSAIDs

- Several mechanisms are involved:
  1. Interstitial nephritis
  2. Direct toxicity
  3. Papillary necrosis
  4. Inhibition of prostaglandins
  5. Membranous glomerulonephritis

- Occurs in those with significant impairment: HTN, diabetes, and the elderly
- History of NSAID use with ↑ in BUN and Cr
- No specific treatment
Papillary Necrosis

- **Causes**
  1. Sickle cell disease
  2. Diabetes
  3. Urinary obstruction
  4. Chronic pyelonephritis
  5. NSAIDs
- **Presentation:** Acute onset of flank pain, hematuria, pyuria, negative urine cultures and fever
- **Most accurate test:** CT scan—“bumpy” contours of the renal pelvis
- **No specific treatment**
Preventing Contrast-Induced Renal Failure

- Vigorous hydration
- 1–2 L of 0.9% NS over 12 hours prior to procedure
- Bicarbonate and N-acetylcysteine have some protective effect
Glomerulonephritis: Nephritic Syndrome
Glomerulonephritis—An Overview

- Inflammation of the glomeruli due to
  1. Autoimmune events
  2. Circulating antibodies
  3. Vasculitis

- Edema → salt and water retention → hypertension
- Hematuria with dysmorphic RBCs and RBC casts
- Proteinuria <2 grams/24 hours
- Fractional excretion of Na <1%
- Most important diagnostic test: renal biopsy
<table>
<thead>
<tr>
<th>Vascular Disease</th>
<th>Glomerular Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wegener’s granulomatosis</td>
<td>Goodpasture syndrome</td>
</tr>
<tr>
<td>Churg-Strauss syndrome</td>
<td>Postinfectious glomerulonephritis</td>
</tr>
<tr>
<td>Henoch-Schönlein Purpura</td>
<td>IgA Nephropathy (Berger disease)</td>
</tr>
<tr>
<td>Polyarteritis Nodosa</td>
<td>SLE</td>
</tr>
<tr>
<td>TTP</td>
<td>Idiopathic rapidly progressive glomerulonephritis</td>
</tr>
<tr>
<td>HUS</td>
<td>Alport syndrome</td>
</tr>
<tr>
<td>Cryoglobulinemia</td>
<td>Diabetes and HTN</td>
</tr>
<tr>
<td></td>
<td>Amyloid</td>
</tr>
</tbody>
</table>
Glomerulonephritis: Nephrotic Syndrome
Nephrotic Syndrome

- **Proteinuria** >3.5 grams per day
- **Hyperlipidemia** → unclear etiology
- **Edema** → secondary to increased salt and water retention and decreased oncotic pressure
- **Low serum albumin** → secondary to protein loss
Severe Generalized Edema

This image was reproduced from the Public Health Image Library, http://www.phil.cdc.gov
Nephrotic Syndrome (Cont’d)

- Associated with systemic illness
  1. Diabetes
  2. Hypertension
  3. Multiple myeloma
- Nephritic syndrome may progress to nephrotic syndrome
- Glomerular basement membrane loses its negative potential → protein loss
- Also associated with hyperlipidemia which gives the form of a Maltese cross in the urine
Maltese Cross

This image was reproduced from Wikipedia, http://www.wikipedia.com
Nephrotic Syndrome (Cont’d)

- Urinary loss of anticoagulant proteins, i.e., protein C, protein S, and antithrombin → hypercoagulable state
- Urinary loss of transport proteins → Iron, copper and zinc deficiency
Nephrotic Syndrome— Diagnosis

- Urinalysis shows >3.5 grams/24 hours
  1. Cumbersome test
  2. Most often used: single spot urine for albumin and creatinine
- Most accurate test to determine etiology is a renal biopsy
Nephrotic Syndrome—Diagnosis

- Urinalysis shows >3.5 grams/24 hours
  1. Cumbersome test
  2. Most often used: single spot urine for albumin and creatinine
- Most accurate test to determine etiology is a renal biopsy
Nephrotic Syndrome—Treatment

- Control underlying disease
- Steroids in all idiopathic primary renal disease
  1. Membranous type
  2. Nil lesion
  3. Membranoproliferative type
  4. Mesangial type
  5. Focal segmental disease
- Steroids ineffective?
  1. Add cyclophosphamide or mycophenolate (maybe azathioprine)
- ACE inhibitors or ARBs used in all patients but does not reverse disease
- Membranous
- Focal Segmental
- HIV
- Heroin

\[ \frac{1}{4} \text{ mg} \]

\[ 1+ \Rightarrow 25g \]
\[ 2+ \Rightarrow 50g \]
\[ 3+ \Rightarrow 75g \]
\[ 4+ \Rightarrow 100g \]
\[ 4+ \Rightarrow 150g \]
\[ 5+ \Rightarrow 200g \]
Membranous Glomerulonephritis

- Most common idiopathic disease in adults
- Also associated with cancer, infections, hepatitis, lupus, penicillamine, gold salts, and NSAIDs
Nil lesion—Minimal Change Disease

- Most common idiopathic cause in children
- NSAIDs
- Light microscopy is normal electron microscopy shows fusion of foot processes
- Responds very well to steroids
Membranoproliferative Glomerulonephritis

- Associated with chronic hepatitis and low serum complement
- Positive cryoglobulin?
  1. Interferon + ribavirin
- Dipyrimadole and aspirin are also used
Membranoproliferative Glomerulonephritis
Focal Segmental Glomerulonephritis

- Highly associated with **heroin and HIV**!
- Poor response to steroids
- Rapid progression to end-stage renal disease
Diagnostic Testing in Renal Disease
Diagnostic Testing in Renal Disease

- Urinalysis
- No recommendations for routine testing in the general population
- Screening in diabetes in HTN
Diagnostic Testing in Renal Disease

- Proteinuria
  - From either glomerular or tubal disease
  - Microalbuminuria $\rightarrow$ 30–300 mg/24 h
  - Mild proteinuria ($<1$ gm/day) in up to 10% of the population, usually resolves spontaneously
  - Proteinuria secondary to stress $\rightarrow$ fever, CHF, extreme exercise
  - Orthostatic proteinuria $\rightarrow$ prolonged standing $\rightarrow$ Benign
- Diagnosed by splitting 24 urine $\rightarrow$ First 8 hours, no protein; next 8 hours, positive protein
UA
HTN
x DM
10,000/Week
Trace 300-350
25m 1+
35m 3+
45m 4+
160m 4+
高血压
HTN
× DM
10,000/week
Trace 300-1g
15g
35g
45g
16g

Va Trac = Repeat = SOLR OR DIURSTIC
Benign
Diagnostic Testing in Renal Disease

- Hematuria
  - Bladder → intact RBCs
  - Kidney → dysmorphic RBCs
  - Etiology includes
    - Stones
    - Cancer
    - Bleeding disorders
    - Trauma
    - Cyclophosphamide
- VA
- HTN
- 30-300
- micro + ACE/ARB
- 300-1500
- 150
- 30
- 3+
- V/N
- V/N
- V/N
- 4+
- Stone
- Infection
- Tumor
- Trauma
- Trauma
Diagnostic Testing in Renal Disease

- Nitrites on dipstick
  - Bacteria reduce nitrate → nitrite
  - Marker of infection
- Bacteriuria
  - Isolated finding little significance
  - Except in pregnant women
  - Routine screening recommended
  - Treatment indicated if positive
  - 30% of pregnant women with bacteriuria progress to pyelonephritis
Nitrate → Nitrite

- Stone
- Tumor
- Infection
- Trauma

ULTRASOUND
Repeat? Self or Orthostatic
Benign
### Significance of Urinary Casts

<table>
<thead>
<tr>
<th>Type</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyaline</td>
<td>Dehydration. Accumulation of normal tubular protein. Does not always implicate disease</td>
</tr>
<tr>
<td>Red cell</td>
<td>Glomerulonephritis</td>
</tr>
<tr>
<td>Broad, waxy</td>
<td>Chronic renal failure</td>
</tr>
<tr>
<td>Granular</td>
<td>Also called “dirty” or “muddy”. Associated with ATN. Accumulated epithelial cells</td>
</tr>
<tr>
<td>White cell</td>
<td>Pyelonephritis, interstitial nephritis</td>
</tr>
</tbody>
</table>
Hyaline Urinary Cast—Dehydration

Reproduced with permission from Dr. Charles McWilliams, Nevis Rural Clinic, Sovereign Medical Order of the Knights Hospitaller, West Indies
EO → Allergic Interstitial

Protein Spot Alb/creas

Stone Infection Tumor Trauma

Time
End Stage Renal Disease/ Dialysis

• Overview
  1. Most common causes are diabetes and hypertension
  2. Glomerulonephritis
  3. Cystic disease
  4. Interstitial nephritis
End Stage Renal Disease/ Dialysis

- Indications for dialysis → life-threatening abnormalities
  1. Fluid overload
  2. Severe acidosis
  3. Pericarditis
  4. Encephalopathy and severe neurologic impairment
  5. Severe hyperkalemia
End Stage Renal Disease/ Dialysis

- Hemodialysis used in 85% of patients
- Peritoneal dialysis in 15%
  1. Most common complication is peritonitis
End Stage Renal Disease/ Dialysis

- Complications
  - Anemia → loss of erythropoietin
  - Hypocalcemia/ hyperphosphatemia → loss of 1,25 dihydroxy-vitamin D
- High phosphate: calcium carbonate, calcium acetate, Sevelamer, lanthanum, Cinacalcet
- Do not use aluminum-based binders!!
- Osteodystrophy (osteitis fibrosa cystica) → loss of 1,25 dihydroxy-vitamin D
\[ PD = H/D \]

\[ \text{Acid} \rightarrow H^+ \]

\[ \text{NH}_4^+ \rightarrow NH_3 \]

\[ \text{HPO}_4^2- \rightarrow HPO_4^- \]

\[ \text{OH}^- \rightarrow \sqrt{C} \]

\[ 1.25 \]

\[ \text{Amal/Day/Kg} \]
End Stage Renal Disease/ Dialysis

Peripheral smear of a patient with ESRD
End Stage Renal Disease/ Dialysis

- Complications (Cont’d)
  - Hypermagnesemia → decreased excretion
  - Hypertension and accelerated artherosclerosis → unclear etiology, most common cause of death, BP goal <130/80
  - Infection → uremia impairs WBC function
  - Bleeding → platelet dysfunction, treat with desmopressin
  - Dietary treatment → restrict sodium, potassium, magnesium, phosphate and protein
PD = HD

125 \rightarrow V_{Ca} \rightarrow \text{PTH} \rightarrow \text{Bone} \rightarrow \text{Ca}^{2+}

\text{Sevelamer} \rightarrow \text{CaCO}_{3}

99\% \rightarrow \text{Calcium}

BP 130/80

No Rx
## Survival Statistics

<table>
<thead>
<tr>
<th>Type</th>
<th>Survival Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live, related donor</td>
<td>95% at one year, 72% at 5 years</td>
</tr>
<tr>
<td>Cadaver donor</td>
<td>88% at one year, 58% at 5 years</td>
</tr>
<tr>
<td>Dialysis alone</td>
<td>30–40% at 5 years</td>
</tr>
<tr>
<td>Diabetics on dialysis alone</td>
<td>20% at 5 years</td>
</tr>
</tbody>
</table>
Renal Transplantation

- Average wait list is 2–4 years
- Post-transplantation graft rejection prevention
  1. Cyclosporine
  2. Tacrolimus
  3. Mycophenolate
Graft vs. Host Disease

© 2007 Kaplan Inc., Reproduced with permission from DxR Imaging
Severe Graft vs. Host Disease

Reproduced with permission from the European College for Hospital Teachers and Play Therapists by net, sponsored by the Program Minerva of the European Commission.
Tacrolimus
Cyclosporine
Mycophenolate
Need: Availability
4-5:1
Hyponatremia

- Serum sodium < 135 mEq/L
- Free water retention or urinary sodium loss
- Serum sodium largely determines serum osmolarity
  - Serum osmolarity = \(2 \times \text{sodium} + \frac{\text{BUN}}{2.8} + \frac{\text{glucose}}{18}\)
  - If serum glucose and BUN are normal, then serum osmolarity is \(2 \times \text{sodium} + 10\)
Hyponatremia

- Presentation
  1. Neurologic symptoms

- Treatment
  - Mild hyponatremia → fluid restriction
  - Moderate hyponatremia → 0.9% normal saline + loop diuretic
  - Severe hyponatremia → 3% hypertonic saline

- Complications of treatment
  - Rapid correction of serum sodium → central pontine myelinolysis!!
Hyponatremia— Specific Etiologies

- Pseudohyponatremia
  1. Total body sodium is normal
  2. Serum sodium is artificially low
  3. Treat the etiology:
     - Hyperglycemia ↓ serum sodium by 1.6 mEq/L per 100 mg/dL increase
     - Hyperlipidemia
     - Hypervolemia (↑ ECF)
- Hypovolemic
- CHF
- Cirrhosis
- Nephrosis

↑100: V1.6
Glucose: Na

↑Glucose ↑Glucose ↑Glucose
Hypovolemic
- CHF
- Cirrhosis
- Nephrotic

\[ \text{↑ 100: H}1.6 \text{ glucose: Na} \]

\[ \text{↑ glucose} \text{↑ glucose} \text{↑ Na} \text{↑ Na} \text{↑ H}_2\text{O} \]

Hypovolemia
Hyponatremia—Specific Etiologies

- *Hypovolemia (↓ ECF)*

<table>
<thead>
<tr>
<th>Urine Na &lt;10</th>
<th>Urine Na &gt;10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dehydration</td>
<td>Diuretics</td>
</tr>
<tr>
<td>Vomiting</td>
<td>ACE inhibitors</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Renal salt wasting</td>
</tr>
<tr>
<td>Sweating</td>
<td>Addison disease</td>
</tr>
<tr>
<td></td>
<td>Cerebral sodium wasting</td>
</tr>
</tbody>
</table>
Hyponatremia—Specific Etiologies

- Euvolemia
  1. Psychogenic polydipsia
  2. Hypothyroidism
  3. Diuretics
  4. ACE inhibitors
  5. Endurance exercise
  6. SIADH
VNa
EU

2807 Kx bipolar
on lithium
DrinK 18/7 Day
Urine: 18/7 Dpl
Na 140

Na:
Psycho
low

Uosm
low

Una
low

Nocturia:
+ + + + +
Hyponatremia— Specific Etiologies

- SIADH
  1. Etiology, organic: CNS disease, pulmonary disease, neoplastic disease
  2. Etiology, inorganic: SSRIs, TCAs, haloperidol, cyclophosphamide, vincristine, carbamazepine
  3. Diagnosis → Increased urine osmolarity and sodium (osmolarity of >100 is suggestive)
  4. Most accurate test: elevated ADH
  5. Treatment
     - Chronic SIADH: demeclocycline or lithium
\( U_{Na} : Low \) => \( U_{Osm} : Low \)

\( J_{Na} \) => Normal

\( S_{Osm} = 2 \cdot J_{Na} \) => \( U_{Na} : High \)

\( S_{JAD^+} \)

\( CNS : \text{ ANY} \)

\( Pulm : \text{ ANY} \)

\( SSRI \)

\( U_{Osm} : High \)
Hypernatremia—Etiology

- Insensible losses
- GI loss
- Transcellular shift
- Renal
  1. Nephrogenic diabetes insipidus
  2. Central diabetes insipidus
  3. Idiopathic (most common), trauma, infections, tumors, granulomas, hypoxic brain damage
  4. Osmotic diuresis
Hypernatremia—Etiology

- Presentation
  1. Primarily neurologic

- Diagnosis
  - Watching for a decrease in urine volume after administering ADH → central diabetes insipidus

- Treatment
  1. CDI → correct underlying cause, give vasopressin
  2. NDI → correct underlying cause, diuretic or NSAIDs
ING SKIN URINO - GI LOSS
DI U VOLUME
CDI \\
Glu ADH

NDI \\
↓H, ↑Ca++
Diarhetic
NSAIDS

DI NDI

SOSM

GIVE ADH

CDI NORMAL

KAPLAN MEDICAL
Insulin
Acidosis

K⁺ K⁺

Glucose

K⁺ K⁺

Insulin
Alkalosis

Beta-blocker
Dl oxin

Lysis

VAldo-Adson

Bz/Foliat replacement

VAldo
Hypokalemia

- Etiology
  1. GI loss
  2. Increased aldosterone states: Conn syndrome, licorice, Bartter syndrome, or Cushing disease
  3. Low magnesium
- Presentation
  1. Muscle and heart: weakness, arrhythmias
  2. Nephrogenic DI
- Diagnosis
  - EKG: T-wave flattening and U-wave
Hypokalemia

- **Treatment**
  1. Correct underlying cause
  2. Repletion
     - IV maximum of 10–20 mEq/hr
     - Oral: 200–400 mg/point of K decrease
     - GI tract slows absorption, dextrose ↑ K entry, use ½ NS or NS
     - Potential complication of rapid correction is **fatal arrhythmia**
     - Total body requirement is 4-5 mEq/kg/point decrease in K
     - **Do not use IV dextrose!**

[KAPLAN MEDICAL]
Hyperkalemia—Etiology

- Increased intake, usually with impaired excretion
- Cellular shift
  1. Pseudohyperkalemia
  2. Acidosis
  3. Insulin deficiency
  4. Tissue breakdown
  5. Periodic paralysis
- Decreased urinary excretion
  1. Renal failure
  2. Hypoaldosteronism
  3. Adrenal insufficiency or adrenalectomy
  4. Potassium-sparing diuretics
  5. NSAIDs
Hyperkalemia—Presentation and Diagnosis

• Presentation
  1. Muscle weakness with K > 6.5
  2. Abnormal cardiac conduction

• Diagnosis
  - EKG: peaked T-waves, wide QRS, short QT, or prolonged P-R
Hyperkalemia—Treatment

• Treatment
  1. Emergently (EKG changes): calcium chloride
  2. Sodium bicarbonate
  3. Glucose + insulin
  4. Diuretics, β-agonists
  5. Kayexalate ®
  6. Dialysis
Renal Tubular Acidosis
\[ \text{NH}_3 \rightarrow \text{NH}_4^+ \]

**Distal**

**Proximal**

Can't Excrete H^+

Using Basic
Renal Tubular Acidosis Type I (Distal)

- Etiology
  1. Usually sporadic, secondary to autoimmune disease, drugs, nephrocalcinosis, sickle cell, chronic infection, familial, chronic hepatitis

- Presentation
  1. Urine pH >5.4
  2. Hyperaldosteronism and hypokalemia
  3. Nephrocalcinosis and nephrolithiasis
NH₂ → NH₄⁺

Distal

Can’t Excrete H⁺

Urine Basic

Can’t Stone

Proximal

Absorbs Bicarb

Give Acid

Urine Basic

Give Bicarb
Renal Tubular Acidosis Type I (Distal)

- **Diagnosis**
  1. Acid load test → urine pH remains elevated
  2. Hypokalemia

- **Treatment**
  1. Oral bicarbonate
  2. Potassium replacement
Renal Tubular Acidosis Type II (Proximal)

- Etiology
  1. Fanconi syndrome
  2. Wilson disease
  3. Amyloidosis
  4. Myeloma
  5. Acetazolamide
  6. Vitamin D deficiency, secondary hyperparathyroidism, chronic hypocalcemia
  7. Heavy metals
  8. Chronic hepatitis
  9. Autoimmune diseases
Renal Tubular Acidosis Type II (Proximal)

- Presentation
  1. Inability to absorb bicarbonate → urine pH < 5.4
  2. Hypokalemia, serum bicarbonate 18–20
  3. Malabsorption of glucose, phosphate, urate and amino acids
  4. Bone lesions (osteomalacia and rickets)
\[ \text{NH}_3 \rightarrow \text{NH}_4^+ \]

**Distal**

- Can't excrete H^+
- Urine basic
- Stones

**Proximal**

- Can't absorb bicarb
- Urine acidic
- No stone

**IV**

- Give bicarb
- Give bicarb

- K^+
\[ \text{D} + \text{H}^+ \rightarrow \text{NH}_4^+ \]

**Distal**
- Can't Excrete $\text{H}^+$
- Urine $\text{NH}_4^+$
- Basic
- Stones
- Give Acid
- Basic
- Bicarb
- Diamox

**Proximal**
- Can't Absorb Bicarb
- Urine $\text{NH}_4^+$
- Acid
- NO Stone
- Give Bicarb
- Urine Basic
- Diuretic
- $\text{K}^+$
Renal Tubular Acidosis Type II (Proximal)

- **Diagnosis**
  - Unable to absorb IV bicarbonate → acidemia and basic urine

- **Treatment**
  - Potassium replacement
  - Large amounts of bicarbonates + thiazide diuretic
Hyporeninemic/Hypoaldosteronism (Type IV)

- **Etiology**
  1. Aldosterone deficiency or adrenal insensitivity to angiotensin II
  2. Diabetes
  3. Addison disease
  4. Sickle cell disease
  5. Renal insufficiency

- **Presentation**
  1. Usually asymptomatic hyperkalemia
  2. Mild to moderate renal insufficiency
  3. Hyperchloremic metabolic acidosis (non-anion gap)
$NH_3 \rightarrow NH_4^+$

**Distal**
- Eliminate $H^+$

**Proximal**
- Can't absorb Bicarb
- Urinary Acid
- No Stone
- Give Bicarb
- Urinary Basic
- Diuretic

$IV DM VAIDO URENN$

$\uparrow K^+$
NH₃ ⇌ NH₄⁺
DISTAL
Proximal
Can't Excrete
URINE
Basic
+ DIPS
(Add)
Absorbs
Bicarb
URINE
Acid
No Stone
Bicarb
Basic
7.5°C

DM
 Aldosterone
FK⁺
K⁺
Rx Fludrocortisone
Metabolic Alkalosis

- \(\text{H}^+\) ion loss
- 1. Exogenous steroids
- 2. GI loss
- 3. Renal loss
- 4. Decreased chloride intake
- 5. Diuretics
- \(\text{HCO}_3^-\) + retention
  1. Bicarbonate administration
  2. Contraction alkalosis
  3. Milk-alkali syndrome
- \(\text{H}^+\) movement into cells
  - Hypokalemia
Respiratory Alkalosis

- Hyperventilation of any cause
  1. Anemia
  2. Pulmonary embolus
  3. Sarcoidosis
  4. Anxiety and pain
  5. Progesterone, catecholamines
  6. Salicylates
  7. Hypoxia
  8. Cirrhosis
Alkalosis

\[ \frac{\text{PCO}_2}{\text{Resp}} \rightarrow \text{HCO}_3^- \]

\[ \text{Mg}^2+ \rightarrow K^+ \]

\[ \text{K}^+ \rightarrow \text{Cl}^- \rightarrow \text{HCO}_3^- \]

\[ \text{Mg}^2+ \rightarrow \text{ATPase} \rightarrow \text{Aldo} \]
Acidosis

Anion Gap =
(Na+ + K+) – (HCO3− + Cl−)

Normal: 8 – 14
Metabolic Acidosis

- Low anion gap
  1. Myeloma
  2. Low albumin
  3. Lithium
- Normal anion gap
  1. Diarrhea
  2. Renal tubular acidosis
  3. Ureterosigmoidoscopy
Metabolic Acidosis (Cont’d)

- Increased anion gap (LA MUD PIE)
  - Lactate
  - Aspirin
  - Methanol
  - Uremia
  - Diabetic ketoacidosis
  - Paraldehyde, Propylene glycol
  - Isopropyl alcohol, INH
  - Ethylene glycol
Alkalosis

HCO₃⁻

Na⁺ - (Cl⁻ and Bicarb)

ACIDOSIS

Met

K⁺

Cl⁻ → HCO₃⁻

Lactate

UBP

Na⁺ (↑Cl⁻, ↑HCO₃⁻)

↑Lactate
Respiratory Acidosis

- Hypoventilation of any cause
  1. COPD
  2. Pickwickian syndrome
  3. Obesity
  4. Suffocations
  5. Opiates
  6. Sleep apnea
  7. Kyphoscoliosis
  8. Myopathies
  9. Neuropathy
  10. Effusion
Nephrolithiasis
Nephrolithiasis—Etiology

- Incidence: 1-5% of the population
  - Composition of stones includes
    - Calcium oxalate $\rightarrow$ 70%
    - Calcium phosphate $\rightarrow$ 10%
    - Mg/aluminum/phosphate (struvite) $\rightarrow$ 5-10%
    - Uric acid $\rightarrow$ 5%
    - Cysteine $\rightarrow$ 1%
    - Indinavir
CaOx
↑Calcium → Stones
Oxalates → Stones
Indinavir 4% → Stones

↑Calcium?
Fat + Ca++
FFA + Ca++
Hypercalciuria—Etiology

- Increased absorption
  1. Vitamin D intoxication
  2. ↑ Vitamin D with sarcoidosis and other granulomatous disease
  3. Familial

- Idiopathic renal hypercalciuria

- Resorptive
  1. Hyperparathyroidism (10-30% will present with stones)
  2. Multiple myeloma, metastasis, hypercalcemia of malignancy
Hyperoxaluria—Etiology

- Primarily familial
- Enteric

  Fat malabsorption

  →

  Fat binds calcium

  →

  Increased oxalate resorption
Hyperoxaluria— Findings

Reproduced with permission from Dr. Charles McWilliams, Nevis Rural Clinic, Sovereign Medical Order of the Knights Hospitaller, West Indies, Caribbean
CaOx
↑Calcium ⇒ Stones
Oxalates ⇒ Stones
Indium 4% =

↑Calcium
Fat + Ca+
FFA + Ca++

*Suicide
AG Acido
Other Stones to be Considered

- Hypocitruria
  - ↓ citrate leads to ↑ calcium absorption
  - Induced by acidosis
- Uric acid stones
  - Form in acidic urine
  - Causes include gout, leukemia, and Chron disease
  - Radiolucent
Other Stones to be Considered

- Cystinuria
  1. Genetic only
- Infection
  - Urease producing organisms → alkaline urine → struvite stones
  - *Proteus, Staphylococcus, Pseudomonas,* and *Klebsiella*
Stones—Clinical Findings

- Presentation
  1. Constant, flank pain radiating to the groin
  2. Hematuria

- Diagnosis
  1. Plain x-ray
  2. Ultrasound
  3. Strain the urine
  4. Serum and urine calcium
  5. IV pyelogram
  6. Helical CT without contrast
CaOx
↑Calcium → Stones
Oxalate
Indinavir
↑Calcium
Fat + Ca++
FFA + Ca++
Suicide
✉️
↑AG
Acidosis
Gastric Fluid Fast!
↑Ca++
Proteus
↑pH
420°ED
Pain → Groin hernia
4/20 ED
PAIN → Groin hemorrhage
PAIN Meds
Office
Sono
ED,
1st X-ray
CT → Best
Large Kidney Stone on Abdominal X-ray

This image was reproduced from Wikipedia, http://www.wikipedia.com
Stones—Management

- < 5 mm → pass spontaneously
- < 2 cm → shockwave lithotripsy
- Uretoscopy
- Percutaneous removal results in longer hospital stay
- Analgesia, hydration and bed rest are mainstays regardless of size
Shockwave Lithotripsy

This image was reproduced from Wikipedia, http://www.wikipedia.com
420 AED
Pain → Groin
hematuria
Ketorolac → Pain
Ickn 2cm
Wait
Small
Urine/CT
Wait
Small
Surgery
Office
Sonde
ED
1st XRay
CT-Best
Hereditary Cystic Disease
Adult Polycystic Kidney Disease
Adult Polycystic Kidney Disease

**Etiology**

1. Genetic
2. Pathogenesis is uncertain

**Presentation**

1. Flank pain, hematuria (microscopic or gross), infections and calculi
2. May be asymptomatic
3. Extra-renal manifestations includes
   - Hepatic cysts $\rightarrow$ 40-60%
   - Colonic diverticula
   - Hypertension $\rightarrow$ 50%
   - Mitral valve prolapse $\rightarrow$ 25%
   - Intracranial aneurysm $\rightarrow$ 10-20%
Adult Polycystic Kidney Disease

- Diagnosis
  1. Ultrasound and CT scan
- Treatment
  1. Nonspecific
  2. Manage complications
Simple Renal Cyst

- Very common
- Represent 65-70% of all renal masses
- Smooth-walled with no debris → expectant management
- Irregular-walls or debris → aspiration to exclude malignancy
Cystic
Stone
Infection
Dialysis
Simple
Smooth
No Debris
Essential Hypertension

- In the normal population (i.e. NO diabetes and NO renal disease)
  
  Systolic > 140
  
  or
  
  Diastolic > 90

- Discovered on multiple readings in the absence of a specific etiology
Avoid “White-Coat Hypertension”

- Allow the patient to sit quietly for 5 mins
- NEVER label a patient as hypertensive with one reading
- Repeat 3-6 times over several months before confirming the diagnosis and initiating therapy
Essential Hypertension

- In diabetics and those with renal disease
  
  Systolic > 130
  
  or
  
  Diastolic > 80

- In addition -> those with BP > 160/110 must receive two-drug therapy
Essential Hypertension

Presentation

1. Most common → asymptomatic patient with elevated BP found on routine screening

2. When symptoms are present
   - Acute → hypertensive emergency
   - Long-term → end-organ damage
   - Secondary HTN → concomitant symptoms
Essential Hypertension—Labs

- Focus → evaluate for end-organ damage and rule-out secondary causes
  1. Urinalysis
  2. Hematocrit
  3. Serum potassium
  4. Serum BUN and Cr
  5. ECG
  6. Blood glucose
  7. Plasma lipids
## Classification and Treatment Guidelines

<table>
<thead>
<tr>
<th>Class</th>
<th>Systolic</th>
<th>Diastolic</th>
<th>Lifestyle Mod.</th>
<th>Drug therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-HTN</td>
<td>120-139</td>
<td>80-89</td>
<td>Yes</td>
<td>Only if (+) end-organ damage</td>
</tr>
<tr>
<td>Stage 1 HTN</td>
<td>140-159</td>
<td>90-99</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Stage 2 HTN</td>
<td>&gt;160</td>
<td>&gt;100</td>
<td>Yes</td>
<td>Two-drug regimen</td>
</tr>
</tbody>
</table>
Drug of Choice?

- Initial treatment
  1. **Diuretic** → mortality benefit
  2. If diuretics fail → add a second drug
      - Beta-blocker
      - Calcium-channel blocker
      - ACE inhibitor
      - Angiotensin-receptor blocker
Individualized Treatment

- Diabetics
  1. ACE inhibitors or angiotensin-receptor blockers

- Post-MI
  1. Beta-blocker

- Decreased left-ventricular systolic function
  1. ACE inhibitor and/or beta-blocker

- Pregnancy
  - α-methyldopa, labetalol, hydralazine or calcium-channel blockers
  - ACE-inhibitors and angiotensin receptor blockers are a NO-NO!!!!
  - Diuretics are relatively contraindicated
Long-term Complications

- Cardiac → Acute MI, CHF, left-ventricular hypertrophy, aortic aneurysm, and dissection
- Cerebrovascular → TIA or stroke
- Renal → proteinuria, microscopic hematuria, increased BUN/Cr, CRF
- Retinopathy → Hemorrhages, exudates, arteriolar narrowing, and papilledema
Hypertensive Emergency—An Overview

- Cardiac, neurologic, renal, and retinal involvement
- Diastolic typically > 120-130 mmHg
- Symptoms → headache, dizziness, chest pain, dyspnea, blurry vision, and palpitations
- Signs → Evidence of stroke, subarachnoid hemorrhage, encephalopathy, myocardial ischemia, papilledema
Hypertensive Emergency—Diagnosis

- White-coat syndrome is NOT a concern given clear-cut symptoms
- CT scan of the head → rule-out or rule-in hemorrhage
- ECG → rule-out or rule-in acute MI
Hypertensive Emergency—Treatment

- IV nitroprusside and labetalol are the two drugs of choice
- Nitroglycerin if (+) myocardial ischemia
- IV Enalaprilat, esmolol, diazoxide and trimethaphan are also used
- **DO NOT LOWER TOO FAR!!**

1. Stay above a diastolic of **95-100 mmHg**
Secondary Hypertension

• Who should be screened?
  1. Those who are very young or very old
  2. Those with key features of a particular cause
  3. Hypertension refractory to therapy
Renal Artery Stenosis

- **Etiology**
  1. Elderly → atherosclerotic disease
  2. Young → fibromuscular dysplasia

- **Findings**
  - Abdominal bruit that radiates laterally (50-70% of patients)
Renal Artery Stenosis

- **Diagnosis**

1. **Best initial test is an ultrasound**
2. Captopril renogram
3. **Arteriogram** is best to **confirm** the diagnosis
4. Duplex ultrasound (accuracy is operator dependant)
5. MRI angiography

- Best initial treatment is **percutaneous transluminal angioplasty** → If failure occurs → repeat stenting → failure stills occurs? → surgical correction → surgical correction fails? → ACE inhibitors
Renal Artery Stenosis

- **Diagnosis**
  1. Best initial test is an ultrasound
  2. Captopril renogram
  3. Arteriogram is best to confirm the diagnosis
  4. Duplex ultrasound (accuracy is operator dependant)
  5. MRI angiography

- Best initial treatment is **percutaneous transluminal angioplasty** → If failure occurs → repeat stenting → failure stills occurs? → surgical correction → surgical correction fails? → ACE inhibitors
Primary Hyperaldosteronism (Conn Syndrome)

- **Etiology**
  1. Most common cause → **unilateral adenoma** (sometimes bilateral)
  2. Remaining cases due to bilateral hyperplasia
- **Cancer is rare**

**Presentation**
- Hypertension (+) hypokalemia with or without symptoms
Primary Hyperaldosteronism (Conn Syndrome)

- **Diagnosis**
  1. Elevated serum and urine aldosterone

- **Treatment**
  - Adenoma → surgical resection
  - Hyperplasia → potassium-sparing diuretics
Pheochromocytoma

- **Etiology**
  1. Most common cause is a benign adrenal tumor.
  2. Rule of 10's: 10% bilateral, 10% malignant, 10% extra-adrenal

- **Presentation**
  - Episodic HTN with headache, sweating, palpitations and tachycardia
Pheochromocytoma

- **Etiology**
  1. Most common cause is a benign adrenal tumor.
  2. Rule of 10’s: 10% bilateral, 10% malignant, 10% extra-adrenal

- **Presentation**
  - Episodic HTN with headache, sweating, palpitations and tachycardia
Cushing Disease

- Etiology
  1. Most common cause is ACTH hypersecretion secondary to a pituitary adenoma

- Presentation
  - Hypertension with Cushingoid features
  - Truncal obesity, buffalo hump, menstrual abnormalities, striae, impaired healing
Other Causes of Secondary Hypertension

- Coarctation of the aorta
  1. Key feature is **BP > in the upper extremities versus the lower extremities**

- Other causes
  1. Oral contraceptives
  2. Acromegaly
  3. Congenital adrenal syndromes
  4. Chronic renal disease
## Antihypertensive Medications—Diuretics

<table>
<thead>
<tr>
<th>Thiazides</th>
<th>Loop Diuretics</th>
<th>Potassium Sparing</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCTA</td>
<td>Furosemide</td>
<td>Spironolactone</td>
</tr>
<tr>
<td>Chlorthalidone</td>
<td>Bumetanide</td>
<td>Amiloride</td>
</tr>
<tr>
<td>Metolazone</td>
<td>Torsemide</td>
<td>Triamterene</td>
</tr>
<tr>
<td>Indapamidide</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Antihypertensive Medications

- β-Blockers
- ACE-inhibitors
- Calcium-channel blockers
- Angiotensin receptor antagonists
- Central-acting sympatholytics
- Direct vasodilators
- α-adrenergic blockers
Complications—Left Ventricular Hypertrophy
Complications—Aortic Aneurysm

© 2007 Kaplan Inc., Reproduced with permission from DxR Imaging
Complications—Myocardial Infarction

© 2007 Kaplan Inc., Reproduced with permission from DxR Imaging
Complications—Peripheral Vascular Disease

© 2007 Kaplan Inc., Reproduced with permission from Dxr Imaging
Cushing Disease—Ecchymosis

Reproduced with permission from Endocrinologie, Universite Claude Bernard, Lyon, France

KAPLAN MEDICAL
Cushing Disease — Moon Facies

Reproduced with permission from Endocrinologie, Universite Claude Bernard, Lyon, France