Chapter 21

Diuretic Agents
Renal Structure and Function

- Kidneys at level of umbilicus
- Each weighs 160 to 175 g and is 10 to 12 cm long
- Most blood flow per gram of weight in body
  - 22% of cardiac output (CO)
- Active organ (not a passive filter)
Renal Structure and Function (cont’d)

- Nephron is functional unit (maintains homeostasis of internal volume/electrolytes)
  - Glomerulus
  - Proximal tubule
  - Loop of Henle
  - Distal tubule
  - Collecting duct
Glomerular filtration

- 20% of total blood flow through nephron
- 99% reabsorbed in tubules
- 1% excreted as urine
  - Adult output = 30 to 60 ml/hr
- Diuretics increase urine output by interfering with reabsorption in tubules
Renal Structure and Function (cont’d)

- Electrolyte filtration and reabsorption
  - Na: 70% is reabsorbed in proximal tubules, 20% in loops of Henle, 10% in distal tubules
    * Inhibition causes less H₂O retention
  - K: Reabsorbed mostly in proximal tubules
  - Cl and HCO₃⁻: Passively reabsorbed in tubules
  - Aldosterone: Increases Na and H₂O reabsorption in distal tubule
Renal Structure and Function (cont’d)

- Acid-base balance
  - May be caused by H₂O loss
  - Na reabsorption
    - With Cl to preserve neutrality
    - Exchange of Na for H or K
- Low Cl or K = metabolic alkalosis
- Loss of HCO₃⁻ buffer = metabolic acidosis
Diuretic Groups

- Osmotic diuretics
  - Impair proximal tubule and ascending limb of loop of Henle from reabsorbing NaCl
  - Glycerin, isosorbide, mannitol, and urea
  - Often used for cerebral edema
Diuretic Groups (cont’d)

- Carbonic anhydrase inhibitors
  - Work within proximal tubule
    - Decrease HCO$_3^-$ and NaCl reabsorption
    - Net result: Moderate NaCl increase plus water excretion
  - Weak action plus potential for metabolic acidosis
  - Hypokalemia is common adverse effect
Diuretic Groups (cont’d)

- Loop diuretics
  - Furosemide, bumetanide, torsemide
  - Inhibit NaCl reabsorption at ascending limb of loop of Henle
  - “High-ceiling” diuretics
    - Up to 20% of NaCl and H₂O lost
  - May cause acute vasodilation
  - Larger doses required with renal dysfunction
Diuretic Groups (cont’d)

- Thiazide diuretics
  - Block NaCl reabsorption at distal tubule
  - First-line treatment for mild hypertension (HTN)
  - Narrow therapeutic margin
  - May also decrease peripheral vascular resistance
Diuretic Groups (cont’d)

- Potassium-sparing diuretics
  - Block exchange of Na for K and H
    - Weak action
    - May cause hyperkalemia
  - Spironolactone
    - Competitive aldosterone antagonist
    - Common in cirrhosis and ascites
Diuretic Groups (cont’d)

- Potassium-sparing diuretics (cont’d)
  - Triamterene
    - Blocks Na channels in collecting ducts
    - Short-acting
    - Metabolized by liver
  - Amiloride
    - Blocks Na channels in collecting ducts
    - Moderately long half-life
Diuretic Combinations

- May produce additive or synergistic effect
- Most common is loop diuretic plus thiazide
## Drug Interactions

### TABLE 21-3

**Drug Interactions and Their Potential Side Effects Associated With Use of Diuretics**

<table>
<thead>
<tr>
<th>Interacting Drug</th>
<th>Potential Side Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiotensin-converting enzyme inhibitors <strong>AND</strong> K(^+)-sparing diuretics</td>
<td>Hyperkalemia and cardiac irritability</td>
</tr>
<tr>
<td>Aminoglycosides <strong>AND</strong> loop diuretics</td>
<td>Ototoxicity and nephrotoxicity</td>
</tr>
<tr>
<td>Digoxin <strong>AND</strong> thiazide and loop diuretics</td>
<td>Hypokalemia</td>
</tr>
<tr>
<td>(\beta) Blockers <strong>AND</strong> thiazide diuretics</td>
<td>Hyperglycemia, hyperlipidemia, hyperuricemia</td>
</tr>
<tr>
<td>Steroids <strong>AND</strong> thiazide and loop diuretics</td>
<td>Increased risk of hypokalemia</td>
</tr>
<tr>
<td>Carbamazepine or chlorpropamide <strong>AND</strong> thiazide diuretics</td>
<td>Increased risk of hyponatremia</td>
</tr>
</tbody>
</table>
Adverse Effects

- Hypovolemia
- Hypokalemia
- Acid-base disorders
- Glucose changes
- Ototoxicity
Other Considerations

- Not recommended during pregnancy/breastfeeding
- Side effects in children similar to adult
  - May require smaller doses
- Furosemide is effective/least toxic in pediatric practice
  - Loop diuretics may cause nephrocalcinosis