Urinary System - Overview:

Major Functions:

1) Removal of organic waste products from fluids (excretion)
2) Discharge of waste products into the environment (elimination)
3) Regulation of the volume / [solute] / pH of blood plasma

HOWEVER, THE KIDNEY AIN'T JUST FOR PEE'IN...

- Regulation of blood volume / blood pressure (e.g., renin)
- Regulation of red blood cell formation (i.e., erythropoietin)
- Metabolization of vitamin D to active form (Ca++ uptake)
- Gluconeogenesis during prolonged fasting
Functional Anatomy - Kidney:

Located in the superior lumbar region

“Bar of soap”
12 cm x 6 cm x 3 cm
150 g / kidney

Layers of Supportive Tissue:

Renal fascia:
- Outer layer of dense fibrous connective tissue; anchors kidney in place

Perirenal fat capsule:
- Fatty mass surrounding kidney; cushions kidney against blows

Fibrous capsule:
- Transparent capsule on kidney; prevents infection of kidney from local tissues

Kidneys are located retroperitoneal

Renal ptosis:
- Kidneys drop to lower position due to loss of perirenal fat

Pyelonephritis:
- Inflammation of the kidney

Pyramids appear striped due to parallel arrangement of capillaries / collecting tubes

Renal cortex
Renal medulla
Renal pyramids
Renal papilla
Renal columns
Renal pelvis
Major calyx
Minor calyx

Renal hilum
- Entrance for blood vessels / nerves

Polycystic kidney disease
- (autosomal dominant condition)

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 25.2

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 25.3
Functional Anatomy - Kidney:

Blood Supply to Kidney:
- 1/4 of cardiac output delivered to kidneys
- 0.25 x 5 L / min = 1.25 L / min

Nerve supply to the kidney provided via the renal plexus (primarily sympathetic)

Nephron:
Functional unit of the kidney
(~ 1 million / kidney; urine formation)
- Filter ~ 180 L of blood plasma / day
- Produce ~ 1 - 1.5 L of urine / day
  99% of filtrate returned to blood

Nephron Anatomy:

1) Glomerulus
   - Network of capillaries
   - Tightly wound coil (~ surface area)

2) Renal tubule
   - Location of filtrate (plasma-derived fluid)
Urinary System

Functional Anatomy - Kidney:

Renal Corpuscle
(site of filtration)

- Glomerulus + Glomerular capsule
- Simple squamous epithelium
- Fenestrated capillaries
- Podocyte (‘foot cell’)
- Renal corpuscle
- Afferent arteriole
- Efferent arteriole
- Cortex
- Medulla

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.5 / 25.9

Filtration Membrane:

- Foot processes
- Podocyte cell body
- Fenestrated endothelium
- Basement membrane
- Podocytes (foot processes)
- Size selectivity (fenestrations / slits)
- Charge selectivity (basement membrane)

Glomerular mesangial cells:
Degrade macromolecules “hung up” in filtration membrane

~ 90 nm
~ 40 nm
Filtration slit

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.5 / 25.9

• Size selectivity (fenestrations / slits)
• Charge selectivity (basement membrane)
Urinary System

Functional Anatomy - Kidney:

**Proximal Convoluted Tubule (PCT)**

(major site of filtrate reabsorption)

- Simple cuboidal epithelium
  - Dense microvilli (↑ surface area)
  - ↑ mitochondria (↑ energy demands)
  - Infolded basal membrane (↑ surface area)

Convolutions increase length and enhance filtering ability
Loop of Henle
(site of filtrate concentration)

Thick Segment
• Similar in structure to the PCT

Thin Segment
• Simple squamous epithelium
• Freely permeable to water

Distal convoluted tubule (DCT) & Collecting Ducts
/site of secretion / selective reabsorption

• Simple cuboidal epithelium
• Intercalated cells (acid-base balance)
• Principal cells (water / Na+ balance)
• Smaller lumen; ↑ number of cells (compared to PCT)
Urinary System

Functional Anatomy - Kidney:

Juxtaglomerular Apparatus (JGA)
(Regulator of filtration rate / systemic blood pressure)
- Region where distal end of loop of Henle / DCT lies against afferent arteriole feeding glomerulus

Cell Types:
1) Juxtaglomerular (granular) cells
- Modified smooth muscle cells (afferent arteriole)
- Prominent secretory granules (renin)
- Mechanoreceptors; measure blood pressure

2) Macula densa cells
- Line loop of Henle / DCT near renal corpuscle
- Tall cells; nuclei clustered together
- Chemoreceptors; measure [osmotic] of filtrate

3) Extraglomerular mesangial cells
- Cluster between macula densa and JG cells
- Gap junctions; communication (?)

Types of Nephrons:
1) **Cortical Nephrons** (85%):
   - Located in the upper cortex
   - Primarily involved in reabsorption

2) **Juxtamedullary Nephrons** (15%):
   - Bowman’s capsule in lower cortex; loop of Henle in medulla
   - Primarily involved in filtrate concentration

Nephron Capillary Beds:
1) **Peritubular Capillaries**:
   - Arise from efferent arterioles
   - Closely associate with PCT / DCT

2) **Vasa Recta**:
   - Arise from efferent arterioles
   - Closely associate with loop of Henle
Renal Physiology - Overview:

In a single day, the kidneys filter 60x the normal blood plasma volume present
- Consume 20 - 25% of all oxygen at rest

Major processes occurring in kidney:
1) **Glomerular filtration** (glomeruli)
   - Ultrafiltrate:
     All blood borne solutes except proteins that cross into the tubule system
2) **Tubular reabsorption** (Tubular network)
   - Materials reclaimed from filtrate back into the peritubular capillaries
3) **Tubular secretion** (Tubular network)
   - Materials moved from peritubular capillaries out into filtrate

Urine:
All metabolic waste and unneeded substances; descend collecting ducts to renal pelvis

Glomerular Filtration:
As in systemic capillaries, the pressures that drive fluid movement across the glomerular capillary wall are Starling pressures

**Starling equation:**
\[
GFR = K_f \left[ (P_{GC} - P_{BS}) - \pi_{GC} \right]
\]

- **GFR** = Glomerular filtration rate (mL/min)
- **K_f** = Hydraulic conductance (mL/min • mm Hg)
- **P_{GC}** = Glomerular capillary hydrostatic pressure (mm Hg)
- **P_{BS}** = Bowman's space hydrostatic pressure (mm Hg)
- **\pi_{GC}** = Glomerular capillary osmotic pressure (mm Hg)

**Net Filtration Pressure**

Since filtration of proteins is negligible, \( \pi_{BS} \) is removed from equation (= 0)

Average GFR = 120 – 125 mL/min
Glomerular Filtration:

Changes in the GFR can be brought about by changes in any of the Starling pressures

\[ \text{GFR} = K_f \left[ (P_{GC} - P_{BS}) - \pi_{GC} \right] \]

• Produced by changes in the resistance of the afferent and efferent arterioles

- Constriction of afferent arteriole

\[ \downarrow \text{RPF} = \downarrow P_{GC} = \downarrow \text{GFR} \]

- Constriction of efferent arteriole

\[ \downarrow \text{RPF} = \uparrow P_{GC} = \uparrow \text{GFR} \]

Changes in \( P_{BS} \) (e.g., kidney stones) and \( \pi_{GC} \) (e.g., nephronic syndrome) are often linked with pathologies.

Clinical Application:

Glomerular filtration rate is measured by the clearance of a glomerular marker

What makes a good marker?

1) It must be freely filtered across the glomerular capillaries (no size / charge restrictions)

2) It cannot be reabsorbed or secreted by the renal tubules

3) When infused, it cannot alter the GFR

\[ \text{GRF} = \frac{[\text{U}]_{\text{inulin}} \times \dot{V}}{[P]_{\text{inulin}}} \]

- \( \text{GFR} \) = Glomerular filtration rate (mL / min)
- \( [\text{U}]_{\text{inulin}} \) = Urine concentration of inulin (mg / mL)
- \( [P]_{\text{inulin}} \) = Plasma concentration of inulin (mg / mL)
- \( \dot{V} \) = Urine flow rate (mL / min)
Renal blood flow, and thus glomerular filtration rate, is autoregulated over a wide range of mean arterial pressures.

Glomerular Filtration:

\[
\text{GFR} = K_f \left( P_{GC} - P_{BS} - \pi_{GC} \right)
\]

Surface area (6 m^2)
Membrane permeability
Relatively fixed...

Recall:
\[ Q = \frac{\Delta P}{R} \]

Thus, changes in pressure must be countered with changes in resistance.

For renal autoregulation, it is believed that resistance is controlled primarily at the level of the afferent arteriole.

The major hypotheses explaining renal autoregulation are a myogenic mechanism and tubuloglomerular feedback.

- **Myogenic Hypothesis:**
  - Increased arterial pressure triggers contraction of vascular smooth muscle.
  - \( \uparrow \) renal arterial pressure
  - Walls of afferent arteriole stretch
  - Stretch-activated Ca^{2+} gates open
  - Afferent arteriole constricts; \( \uparrow \) resistance

- **Tubuloglomerular Feedback:**
  - Increased [solute] sensed in DCT; triggers contraction of vascular smooth muscle.
  - \( \uparrow \) renal arterial pressure
  - \( \uparrow \) GFR
  - \( \uparrow \) solute / water load in DCT
  - What is detected?
    - \( 1) \) Na^+ / Cl^-
    - \( 2) \) Ca^{2+}
    - \( 3) \) Total osmolarity
  - Macula densa cells detect change; send signal
  - What signal is sent?
    - \( 1) \) adenosine
    - \( 2) \) prostaglandins
    - \( 3) \) kinins
  - Afferent arteriole constricts; \( \uparrow \) resistance
In addition to autoregulation, extrinsic factors also contribute to renal blood flow regulation.

1) Sympathetic Nervous System (and circulating catecholamines)
   - Sympathetic nerve fibers innervate both afferent and efferent arterioles
     - Activate $\alpha_1$ receptors
     - Trigger vasoconstriction
   HOWEVER
   - More $\alpha_1$ receptors on afferent arterioles
   THUS
   $\uparrow$ Sympathetic input $\Rightarrow \downarrow$ RBF $\Rightarrow \downarrow$ GFR

2) Angiotensin II
   - Potent vasoconstrictor of both afferent and efferent arterioles
   HOWEVER
   - Efferent arteriole more susceptible than the afferent arteriole
   THUS
   Low levels of angiotensin II $\Rightarrow \downarrow$ RBF $\Rightarrow \uparrow$ GFR
   BUT
   High levels of angiotensin II $\Rightarrow \downarrow$ RBF $\Rightarrow \downarrow$ GFR

If the ultrafiltrate produced during glomerular filtration in a single day were excreted from the body unmodified, what would be lost in urine?

<table>
<thead>
<tr>
<th>Substance</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>180 L (180 kg)</td>
</tr>
<tr>
<td>Na$^+$</td>
<td>25,200 mEq (580 g)</td>
</tr>
<tr>
<td>Cl$^-$</td>
<td>19,800 mEq (701 g)</td>
</tr>
<tr>
<td>HCO$_3^-$</td>
<td>4320 mEq (264 g)</td>
</tr>
<tr>
<td>Glucose</td>
<td>14.4 g</td>
</tr>
</tbody>
</table>

Each of the above losses represents more than 10-fold the amount present in the entire extracellular fluid of the body.
Tubular Reabsorption:

Water and many solutes (e.g., Na+) are reabsorbed from the filtrate into the peritubular capillaries via membrane transporters.

**Filtered Load:**
Amount of a substance filtered into Bowman’s space per unit time

\[ \text{Filtered load} = \text{GFR} \times [P]_X \]

**Excretion Rate:**
Amount of a substance excreted in urine per unit time

\[ \text{Excretion rate} = \dot{V} \times [U]_X \]

**Reabsorption rate:**
Filtered load - Excretion rate

Filtered load must be greater than excretion rate for net reabsorption to occur.

### Example

**Na+**

- **Filtered Load:**
  - 180 L/day × 140 mEq/L
  - 25,200 mEq/day

- **Excretion Rate:**
  - 1 L/day × 100 mEq/L
  - 100 mEq/day

- **Reabsorption Rate**
  - 25,200 - 100 = 25,100 mEq/day
  - (99.4% of filtrate load)

Costanzo (Physiology, 4th ed.) – Figure 6.12

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**Glucose** is a good example for examining the basic underlying mechanisms of tubular reabsorption of nutrients.

**Two-step Process:**

1) **Na+-glucose cotransport**
   - Occurs at luminal membrane
   - Na+-glucose cotransporter (SGLT)
   - Secondary active transport

2) **Facilitated glucose transport**
   - Occurs at peritubular membrane
   - GLUT 1 / GLUT 2 transporters
   - Facilitated diffusion

Costanzo (Physiology, 4th ed.) – Figure 6.14
A glucose titration curve depicts the relationship between plasma glucose concentration and glucose reabsorption.

**Things to Note:**
- As the plasma [glucose] increases, the filtered load increases linearly.
- All glucose can be reabsorbed up to plasma [glucose] of 200 mg/dL.

**Transport Maximum (T_m):**
Point at which all transport proteins are fully engaged (saturated)

Glucose $T_m = 350$ mg/dL
- Glucose starts to appear in the urine at plasma [glucose] above 200 mg/dL.

**Sodium (Na+):**
- Single most abundant cation in filtrate
- 80% of active transport energy devoted to Na+ reabsorption
- Net reabsorption of > 99% of filtered load
Tubular Reabsorption:

**Sodium (Na⁺) Reabsorption**

**Early PCT**
- Active transport of Na⁺ drives system
  - Na⁺ (100%)
  - Glucose (100%)
  - Na⁺ (100%)
  - Amino acid (~100%)
  - Phosphate, lactate, or citrate (~100%)
  - Na⁺
- Lumen-negative potential: Co-transport of Na⁺, glucose and Na⁺-amino acid bring (+) charge in while leaving (-) in lumen
- "Highest priority" reabsorptive work

**Late PCT**
- Lumen-positive potential: Movement of Cl⁻ down its [gradient] leaves (+) charges in filtrate
- Na⁺ follows Cl⁻ through tight junctions driven by lumen-positive potential
- ↑ [Cl⁻]
- Na⁺, Cl⁻
Tubular Reabsorption:

Solute and water reabsorption are coupled and are proportional to each other in the PCT – Isosmotic reabsorption

Isosmotic Reabsorption:
1) Na$^+$ enters cell; water follows passively
2) Na$^+$ actively pumped out of basolateral membrane; water follows passively
3) Isosmotic fluids collect in lateral intra-cellular space; high osmotic pressure in peritubular capillary drives reabsorption

67% of solute absorbed in PCT
67% of water absorbed in PCT

---

Tubular Reabsorption:

**Sodium (Na$^+$) Reabsorption**

Na$^+$ moves freely into / out of the thin portions of the loop of Henle but there is no net reabsorption

Reabsorption mechanism is load-dependent; the more Na$^+$ delivered to the region, the more the region reabsorbs

The most potent diuretics, loop diuretics, work at this site (block cotransporters)

- Furosemide
- Bumetanide

Can block up to 25% of Na$^+$ reabsorption

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Costanzo (Physiology, 4th ed.) – Figure 6.22

Costanzo (Physiology, 4th ed.) – Figure 6.24
Tubular Reabsorption:

**Sodium (Na⁺) Reabsorption**

Like the loop of Henle, the DCT and collecting duct exhibit load-dependent Na⁺ reabsorption

---

**Early Distal Tubule**

- **Na⁺-Cl⁻ cotransporter**
- **Thiazide diuretics**
- **NaCl reabsorption inhibited by thiazide diuretics (block cotransporters)**

Water is NOT reabsorbed with solutes in this region (cortical diluting segment)

---

**Late distal tubule / Collecting duct**

- **Epithelial Na⁺ channels (ENaC)**
- **K⁺-sparing diuretics (Amiloride)**
- **Aldosterone regulates activity in cell:**
  1) ↑ ENaC proteins
  2) ↑ Na⁺-K⁺ ATPase
  3) ↑ enzymes (citric acid cycle)

NaCl reabsorption inhibited by K⁺-sparing diuretics (block ENaCs)

Water reabsorption is variable (hormone dependent)
### Tubular Secretion:

A few substances (e.g., organic acids / bases) are secreted from peritubular capillary blood into tubular fluid by way of membrane transporters.

**Filtered Load:**
Amount of a substance filtered into Bowman's space per unit time

\[
[\text{Filtered load}] = \text{GFR} \times [P]_x
\]

**Excretion Rate:**
Amount of a substance excreted in urine per unit time

\[
[\text{Excretion rate}] = V \times [U]_x
\]

**Secretion rate:**
Excretion rate - Filtration load
Excretion rate must be greater than filtration load for net secretion to occur.

**Example:**
- **PAH**
  - **Filtered Load**
    \[
    180 \text{ L/d} \times 0.1 \text{ g/L} = 18 \text{ g/d}
    \]
  - **Excretion Rate**
    \[
    1 \text{ L/d} \times 54 \text{ g/L} = 54 \text{ g/d}
    \]
  - **Secretion Rate**
    \[
    54 - 18 = 36 \text{ g/d}
    \]

### Tubular Reabsorption:

**A PAH titration curve** depicts the relationship between plasma PAH concentration and PAH secretion.

- **PAH**
  - **Unbound plasma [PAH]**
  - **Transporters for PAH located in peritubular capillaries of PCT**
  - **10% bound to blood proteins**

**Para-aminohippuric acid (PAH)**

**Things to Note:**
- As the plasma [PAH] increases, the filtered load increases linearly.
- As with reabsorption, a transport maximum exists for PAH.
- At [low] PAH, steep excretion rate; at [high], rate declines as \( T_m \) reached.
- Also transport antibiotics (e.g., penicillin).

*Costanzo (Physiology, 4th ed.) – Figure 6.12*

*Costanzo (Physiology, 4th ed.) – Figure 6.17*
Tubular Reabsorption / Secretion:

Along with nutrients, the reabsorption / secretion of ions is an important component of nephron physiology.

Potassium (K⁺):

- Balance essential for excitable tissue function
- Utilizes both reabsorption and secretion mechanisms for regulation

K⁺ reabsorption is handled by the α-intercalated cells:

- Relatively uncommon; most often associated with low K⁺ diet

K⁺ reabsorption is handled by the principal cells:

- Associated with individuals having normal / high K⁺ diet
- The magnitude of K⁺ secretion is determined by the size of the electrochemical gradient

Costanzo (Physiology, 4th ed.) – Figure 6.30

Costanzo (Physiology, 4th ed.) – Figure 6.31
Tubular Reabsorption / Secretion:

Along with nutrients, the reabsorption / secretion of ions is an important component of nephron physiology

**Phosphate** (HPO$_4^{2-}$):
- Important ion for bone and as a urinary buffer for H$^+$
- Only reabsorbed at PCT

**Parathyroid hormone** blocks reabsorption
- G-protein coupled system inhibits Na$^+$-phosphate cotransport leaving phosphate in tubule lumen

**Psuedohypoparathyroidism:**
Although circulating levels of PTH are high, PTH cannot produce its phosphaturic effects due to renal cells being resistant to PTH action

---

**Calcium** (Ca$^{2+}$):
- Important ion for bone and excitable tissue function
- Pattern of reabsorption similar to sodium
- Regulation of Ca$^{2+}$ occurs at DCT
Regulation of Urine Volume / Concentration:

The kidneys keep the solute load of body fluids constant, at about 300 mOsm

Corticopapillary osmotic gradient:
A gradient of osmolarity in the interstitial fluid of the kidney from the cortex to the papilla that allows the kidney to vary urine concentration / volume

What solutes contribute to the osmotic gradient?

What mechanisms deposit these solutes in the interstitial fluid?

1) Countercurrent multiplication
2) Urea recycling

Regulation of Urine Volume / Concentration:

1) Countercurrent Multiplication

A function of the loops of Henle, which deposit NaCl in the deeper regions of the medulla

Things to Recall:

1) The thick, ascending limb of the loop of Henle reabsorbs NaCl
2) The thick, ascending limb of the loop of Henle is impermeable to water
Regulation of Urine Volume / Concentration:

1) **Countercurrent Multiplication**

- **Step 1:** NaCl reabsorbed from ascending loop, descending limb equilibrates with interstitial fluid.
  - SINGLE EFFECT
  - New fluid (300 mOsm) enters descending limb from PCT, equal volume displaced from ascending limb.
  - High osmolarity fluid "pushed" down.

- **Step 2:**
  - TUBULAR FLOW

The size of the corticopapillary gradient depends on the length of the loop of Henle (Humans = 1200 mOsm).

---

**Note:**
- Constant 200 mOsm difference between two limbs of the loop of Henle
- Limit of NaCl pump power

---

Regulation of Urine Volume / Concentration:

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**Note:**
- Constant 200 mOsm difference between two limbs of the loop of Henle
  - Limit of NaCl pump power
Regulation of Urine Volume / Concentration:

The kidneys keep the solute load of body fluids constant, at about 300 mOsm

2) Urea Recycling

A function of the collecting ducts, which deposit urea in the deeper regions of the medulla

Urea enters the interstitial fluid via diffusion from the inner medullary collecting ducts and moves down gradient into ascending limb of loop of Henle via facilitated diffusion

Regulation of Urine Volume / Concentration:

The vasa recta are specialized capillary beds that serve the medulla and papilla of the kidney

Vasa recta participates in countercurrent exchange
- Countercurrent multiplier established gradient (active process)
- Countercurrent exchange maintains gradient (passive process)

- Only 5% of renal blood flow serves medulla (‘sluggish’ flow)
- Capillaries permeable to both water and solutes

Capillary osmolarity matches interstitial osmolarity

Picks up water additional lost from the loop of Henle

Costanzo (Physiology, 4th ed.) – Figure 6.39

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.16, 25.7
Formation of Concentrated Urine (~ 1200 mOsm)

1) The PCT pulls out solutes and water in equal proportions (~ 67%)

   **Remember:** Isosmotic reabsorption

2) The thick, ascending limb of the loop of Henle actively reabsorbs NaCl (Na⁺-K⁺-2Cl⁻ cotransporter); cells impermeable to water

   ADH increases activity of Na⁺-K⁺-2Cl⁻ cotransporters leading to enhanced single effect (e.g., steeper gradient)

3) In early DCT, NaCl reabsorbed (Na⁺-Cl⁻ cotransporter); cells impermeable to water

   Filtrate osmolarity reduced to ~ 80 mOsm

4) In late DCT, the principle cells are permeable to water in the presence of ADH

   Formation of Concentrated Urine (~ 1200 mOsm)
   
   • 1 ml fluid / min produced (~ 1.5 L urine / day)
Regulation of Urine Volume / Concentration: Dilute or concentration urine can be formed depending on the presence / absence of antidiuretic hormone (ADH)

Formation of Concentrated Urine (~ 1200 mOsmil)
- 1 ml fluid / min produced (~ 1.5 L urine / day)

5) In collecting duct, the principle cells are also permeable to water in the presence of ADH

- ADH increases urea recycling in the inner medullary collecting duct via the insertion of urea UT1 transporters
  - Urea flows down concentration gradient; enhances corticopapillary osmotic gradient

Formation of Dilute Urine (~ 75 mOsmil)
- 15 – 19 ml fluid / min produced (~ 22.5 L urine / day)

1) The PCT pulls out solutes and water in equal proportions (isosmotic reabsorption)

2) The thick, ascending limb of the loop of Henle actively reabsorbs NaCl (Na⁺-K⁺-2Cl⁻ cotransporter); cells impermeable to water

Corticopapillary osmotic gradient diminished in absence of ADH (↓ transporter activity)

3) In early DCT, NaCl reabsorbed (Na⁺-Cl⁻ cotransporter); cells impermeable to water

4) Late DCT collecting ducts impermeable to water; limited NaCl reabsorbed

Limited urea recycled
Regulation of Urine Volume / Concentration:

**Diuretics** are chemicals that elevate rates of urination

**Pharmacological Drugs:**
- Treat hypertension / edema

1) **Loop diuretics**
   - Block Na⁺ reabsorption in thick, ascending loop of Henle
   - Most potent diuretic
   - Furosemide

2) **Thiazide diuretics**
   - Block Na⁺ reabsorption in early distal convoluted tubule
   - Isoren

3) **K⁺ sparing diuretics**
   - Block Na⁺ reabsorption in late DCT / collecting ducts
   - Amiloride

Pathophysiology:

Conditions which affect ADH release / action can lead to abnormal urine flow rates

**Inappropriate Formation of Dilute Urine**
**Central Diabetes Insipidus:**
- Circulating levels of ADH abnormally low
  - Cause: Trauma / tumor
  - Treatment: Drugs which act as ADH analogues (e.g., dDAVP)

**Nephrogenic Diabetes Insipidus:**
- Circulating levels of ADH normal; principal cells of kidney unresponsive to hormone
  - Cause: Defect in 2nd messenger system (e.g., genetic)
  - Treatment: Thiazide diuretics; triggers ↑ water reabsorption in PCT

**Inappropriate Formation of Concentrated Urine**

**Syndrome of Inappropriate ADH (SIADH):**
- Circulating levels of ADH abnormally high
  - Cause: Trauma / tumor
  - Treatment: Drugs which block ADH activity (e.g., demeclocycline)
Urine:

Physical Characteristics of Urine:

1) Color & Transparency
   - Dilute = clear / pale yellow
   - Concentrated = deep yellow

2) Odor
   - Fresh = slight odor
   - Old = ammonia-like odor

3) pH
   - Acidic (pH ~ 6)

Micturition:

Incontinence:

- The inability to voluntarily control micturition

Parasympathetic activity
Sympathetic activity
Somatic motor nerve activity
Parasympathetic activity
Sympathetic activity
Somatic motor nerve activity

Detrusor muscle contracts; internal urethral sphincter opens
External urethral sphincter opens

(~ 10 mL remains following voiding)

Reflexive urination

(e.g., toddler)

Allow or inhibit micturition as appropriate

Inhbits micturition by acting on all three spinal efferents

Promotes micturition by acting on all three spinal efferents

Afferent impulses from stretch receptors
Simple spinal reflex

Urinary bladder filling stretches bladder wall

Brain

Higher brain centers

Pontine micturition center

Pontine storage center

Spinal cord

Parasympathetic activity
Sympathetic activity
Somatic motor nerve activity
Parasympathetic activity
Sympathetic activity
Somatic motor nerve activity

Inhibits

Micturition

Incontinence

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.22