23  The Urinary System
Taft College Human Physiology
• The primary organ of the urinary system is the kidney. It plays a key role in homeostasis by controlling blood composition, blood volume, and blood pressure in the process of making urine.

• Each minute 1300 mls of blood enters the kidney via the renal arteries and 1298-9 mls leave by the renal veins, so only 1-2 mls/minute leave as urine.

• We will look at what urine contains and why it is formed.
The Functions of the Kidney

1. **Regulates water balance** and eliminates excess water.

2. **Regulates salt concentration** of the body
   - These 2 functions help regulate blood volume, blood pressure, and blood composition.

3. **Eliminates nitrogenous wastes** that are toxic if retained. = wastes from the breakdown of proteins.
   - Most of these wastes are metabolized by the liver and made ready for excretion.
   - Other materials are also detoxified in the liver and excreted in the urine.

4. **Regulates H⁺ of blood.** Kidney actively excretes H⁺ as needed to maintain blood pH.

5. **Secretes erythropoietin** (EPO) that stimulates rbc production.
Water Balance

• Approximately 60% of your body weight is water.
• The kidney regulates total body water content and concentration of the water.

Water is taken in to body in 3 ways:
1. Food: water in food = 0.7 L/day
2. Drink: = 1.6 L/day
3. Metabolic production = 0.2 L/day (H₂O produced by chemical reactions in the body)

Water is discharged from the body in 3 ways:
1. Sweating = 0.6 L/day
2. Lungs = 0.3 L/day
3. Urine = 1.5 L/day

• Note – in both cases water lost and water uptake = about 2.5 L/day. This will vary by ambient temperature (Taft in August vs. January) and activity level.

• Job of kidney is to make sure water content of body stays in balance.
Waste Elimination

- There are many waste products that are formed as a byproduct of metabolism in the body.

- Several organs in the body are responsible for getting rid of these wastes.

- Examples:
  - Lungs: CO$_2$, H$_2$O, heat
  - Skin: salts, urea, water, heat
  - Kidney: another organ that rids the body of wastes.
    - Excess H$_2$O, urea, H$^+$, salts, heat
Gross Anatomy of Urinary System

- **Macroscopic Inspection of Urinary System**
- Blood supply = *renal arteries* deliver blood **high in nitrogenous waste (urea)** to each *kidney*.
- Blood exits kidneys by *renal veins*, **lower in nitrogenous waste (urea)** after wastes are filtered by kidney.
- The **ureters** collect urine from each kidney and deliver it to the *bladder*.
- The urine exits the bladder through a single **urethra** that leads to the external environment.
- 20-25% of resting cardiac output goes through kidney via renal arteries.
- Kidneys serve to filter this blood of wastes.
Urination (micturition, voiding)

- Urination (micturition, voiding) = stretch receptors in the bladder fire when bladder reaches certain volume (200-400 ml) to cause a micturition reflex in the spinal cord. There are 2 sphincters to control the exit of urine from the bladder.
- The urge to urinate occurs as the internal sphincter (smooth muscle) controlled by the autonomic nervous system relaxes and the bladder muscles contract.
- The external sphincter (skeletal muscle) muscle is under voluntary control and will allow one to urinate at will.
Microscopic Inspection of the Kidney

- The functional unit (where the work gets done) of the kidney is the nephron.
- There are approximately 1 million nephrons in each kidney.

- Blood supply associated with each nephron:
  - The renal artery (High in urea) branches to supply ~$10^6$ afferent arterioles that deliver arterial blood to the renal corpuscle (combination of the glomerulus and glomerular capsule) where non-selective filtration takes place.
  - The blood leaves the renal corpuscle via the efferent arteriole.
  - The efferent arterioles divide into a network of peritubular capillaries associated with the loop of the nephron (loop of Henle).
  - The peritubular capillaries unite to ultimately leave the kidney via the renal vein (Low in urea).
Another View of Blood Supply to and from Nephron

- The **functional unit** (where the work gets done) of the kidney is the **nephron**.
- There are approximately **1 million nephrons** in each kidney.
- Blood supply associated with each **nephron**
  - The **renal artery** (High in urea) branches to supply ~10⁶ **afferent arterioles** that deliver arterial blood to the **renal corpuscle** (combination of the glomerulus and glomerular capsule) where non-selective filtration takes place.
  - The blood leaves the renal corpuscle via the **efferent arteriole**.
  - The efferent arterioles divide into a network of **peritubular capillaries** associated with the loop of the nephron (loop of Henle).
  - The peritubular capillaries unite to ultimately leave the kidney via the **renal vein** (Low in urea).
Urine Production Within Nephron

- Plasma = filtrate enters the nephron through the glomerular capsule (Bowman’s capsule) within the renal cortex where it collects in a cup like space.
- Its flows to the proximal convoluted tubule to the loop of the nephron (Loop of Henle) that descends and ascends in the renal medulla.
- The filtrate continues to the distal convoluted tubule in the cortex and then enters the collecting duct that carries urine deep into the medulla of the kidney.
- Now that urine is in its final form it travels through the ureter to the bladder.
3 Basic Processes within the Nephron

1. **Non-selective filtration** – Occurs in the **renal corpuscle**. Substances small enough to pass through the glomerulus and glomerular capsule filter into the nephron. **All materials** (glucose, H₂O, urea (and other waste products), amino acids(protein), ions (Na⁺) move from the blood into the nephron.

2. **Selective reabsorption** – As filtrate passes through nephron and collecting tubule, useful materials (glucose 100%, H₂O 99%, urea 53% (and other waste products), amino acids (protein) 95%, ions (Na⁺) 99%, are returned back into capillaries. Note: the kidney is only 47% efficient in removing the nitrogenous waste = urea.

3. **Secretion** – As fluid passes through the nephron and collecting tubule it gains some material (H⁺ to control blood pH, K⁺, some reabsorbed urea) from the blood.

![Diagram of the nephron with labeled processes](image-url)
Summary – 3 Processes in Nephron

1. Nonselective Filtration
   - peritubular capillaries (blood)
   - Glucose
   - Water
   - Urea
   - Protein
   - Ions (Na+)
   - Filtrate

2. Selective Reabsorption
   - glucose 100%
   - water 99%
   - Na+ 99%
   - Urea 53%

3. Secretion
   - H+
   - Reabsorbed urea

Renal Corpuscle

Nephron and Collecting Duct
1. **Non-selective Filtration** (glomerular filtration)
   - Blood is filtered into capsule and through a membrane due to blood pressure. About 16-20% of plasma volume becomes filtrate. 180 L/day filtrate.
   - Everything is filtered except formed elements of blood and plasma proteins.
   - Filtrate = glucose, H₂O, urea (and other waste products), amino acids (proteins), ions (Na⁺).
2. Selective Reabsorption (tubular reabsorption)
- Selective reabsorption is the movement of materials from the nephron and collecting duct, back into the blood (peritubular capillaries).
- Returning most (99%) of the filtered water and solutes back into the blood stream is a critical nephron function.
- The active transport of Na\(^+\) sets up an osmotic, chemical and electrical gradients that promotes reabsorption of the other solutes and water by osmosis. The active transport of materials requires a lot of ATP (6% of body total for renal tubules).
2. **Selective Reabsorption** (tubular reabsorption)
   - The ascending portion of the loop of the nephron is impermeable to water so no water can be reabsorbed.
   - This increases the water concentration in the ascending limb.
   - 90% of solutes and water have been reabsorbed by the time the filtrate makes it to the distal convoluted tubule.
2. **Selective Reabsorption** (tubular reabsorption)

- If it were not for reabsorption, plasma volume would be gone in 20 minutes.
- Plasma volume of average person = 3L. Total volume of plasma runs through kidney about 60 times/day.
- However, 99% is of fluid is reabsorbed.
3. **Secretion** (tubular secretion)
   - This is movement of materials from the blood (peritubular capillaries) into the nephron and collecting tubules.
   - Some important materials that are secreted are:
     - **H⁺** - to control blood pH.
     - **K⁺** - to remove excess K⁺ ions. High levels can effect heart contraction.
     - Eliminate urea that has been reabsorbed.
     - Some drugs that are not in filtrate.
<table>
<thead>
<tr>
<th>Substance</th>
<th>Plasma (total)</th>
<th>Filtered (enters glomerular capsule/day)</th>
<th>Reabsorbed (returned to the blood/day)</th>
<th>Urine (excreted/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>3 L</td>
<td>180 L</td>
<td>178.5 L = 99%</td>
<td>1.5 L = 1%</td>
</tr>
<tr>
<td>Proteins</td>
<td>20 g</td>
<td>2 g</td>
<td>1.9 g = 95%</td>
<td>0.1 g = 5%</td>
</tr>
<tr>
<td>Sodium ions</td>
<td>9.7 g</td>
<td>580 g</td>
<td>575 g = 99%</td>
<td>4.6 g = 1%</td>
</tr>
<tr>
<td>Bicarbonate ion</td>
<td>4.6 g</td>
<td>275 g</td>
<td>275 g = 100%</td>
<td>0 g = 0%</td>
</tr>
<tr>
<td>Glucose</td>
<td>3 g</td>
<td>180 g</td>
<td>180 g = 100%</td>
<td>0 g = 0%</td>
</tr>
<tr>
<td>Urea</td>
<td>4.8 g</td>
<td>53 g</td>
<td>28 g = 53%</td>
<td>25 g = 47%</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.03 g</td>
<td>1.6 g</td>
<td>0 = 0%</td>
<td>1.6 g = 100%</td>
</tr>
</tbody>
</table>
As noted earlier, the kidney plays a main role and water balance. Birds and mammals (including man) have the ability to excrete **hypertonic urine** = urine that is more concentrated than their body fluids (up to 4X that of blood).

Let's see how the production of hypertonic urine is accomplished in a nephron.

Units = in milliosmoles/L = 1/1000 of an osmole.

Osmolarity = molecular weight of substance / # particles each molecule releases in solution.

In other words, the total number of dissolved particles per liter or the solute concentration. Don't worry about units.
Urine Formation

• The loop of nephron is primarily responsible for this ability to concentrate urine.

• An osmotic gradient is established in the medulla around the loop of nephron as follows:
  
  • **Na⁺ (and K⁺ Cl⁻) moves out of ascending limb by active transport but is impermeable to water.** This makes filtrate with more water and less solutes (100 mOsm).
  
  • **The opposite condition exists in the descending limb.**
  
  • **Water moves out of the descending limb by osmosis but is impermeable to salt.** This makes the tubular fluid more concentrated as it descends (1200 mOsm at bottom).
Urine Formation

• Note the movement of water and salt from the loop of Henle.
• This sets up the gradient in the medulla of the kidney to allow the concentration of urine if needed.
• The final events to concentrate urine can occur in the collecting duct. See next slide.
Urine Formation

• $H_2O$ moves out of distal convoluted tubule and collecting duct by osmosis. This makes medulla interstitial space near the cortex more dilute (400 mOsm). As the filtrate moves down the collecting duct and more water moves out, the filtrate = urine becomes more concentrated.

• The permeability in collecting duct is controlled by antidiuretic hormone (ADH) from the pituitary gland.

• An increase in ADH causes increased permeability, which leads to increased reabsorption of water, and therefore reduced urine production.

• Aldosterone influences salt reabsorption.

• Urea diffuses from the collecting duct near the turn of the loop of Henle (deep in the medulla) adding to the high concentration of solutes in the interstitial space(1200 mOsm)
How Urine Concentration is Controlled

There are **2 hormones** that regulate non-selective filtration and selective reabsorption in the kidney: **Aldosterone** and **Antidiuretic Hormone (ADH)**

1. **Aldosterone**
   - Aldosterone is a hormone produced by the adrenal gland (cortex).
   - **Aldosterone increases Na\(^+\) reabsorption by the kidney.**
   - **Aldosterone** activates active transport proteins to move Na\(^+\) from the filtrate to the peritubular capillaries.
   - Na\(^+\) moving out of the nephron increases the amount of water being reabsorbed and **reduces urine production**.
   - So, if **low aldosterone**, more Na\(^+\) and water are in the urine as they are not transported out. (**More urine is produced**).
How Urine Concentration is Controlled

What triggers aldosterone to be produced?

2 things:

1. Drop in Na\(^+\) ion concentration in blood.
2. Drop in blood pressure as measured by juxtaglomerular apparatus located on afferent arterial.
   • High blood pressure is necessary for filtration.

**Diuretics –** diuretics act by:

1. Inhibiting Na\(^+\) transport (reabsorption) in kidney.
2. Decreasing water reabsorption by the collecting duct

*People taking diuretics have to urinate more often and excrete more Na\(^+\).*
How Urine Concentration is Controlled

2. **ADH (antidiuretic hormone)**
   - ADH is released by *pituitary gland* (produced by cells in hypothalamus). It works by controlling permeability of collecting duct to water. It increases the permeability of the collecting ducts to water.
   - The increased permeability leads to increased reabsorption of water and reduced urine production.

No ADH Present - Collecting Duct is NOT permeable to water and large volume of urine is produced.

ADH Present - Collecting Duct is permeable to water and a small volume of urine is produced.
How Urine Concentration is Controlled

What triggers release of ADH by pituitary?

1. Increased concentration of solutes and blood as monitored by the hypothalamus.
   - Example: dehydration

2. Decreased blood pressure. As a monitored by stretch receptors in aorta and carotid arteries.
   - Example: Hemorrhage.
   - Both act to cause ADH release.
   - ADH increases water reabsorption.
   - ADH decreases solute concentration in blood.
   - ADH reduces urine production.

![Diagram](image.png)
Hypothalamus directs release of ADH

Brain: “thirst”

High [ADH] increases kidney permeability to H₂O

Increase in solutes

Homeostasis: total solute concentration ~ 280 mM

Brain: “quench”

Decrease in solutes

[ADH] drop decreases kidney permeability to H₂O

ADH release slows
Effects of Drugs

**Diuretics**

- Substances that slow renal reabsorption of water and cause diuresis (elevated urine flow rate) and therefore reduces blood volume.
  - Prescribed to treat hypertension by lowering blood volume.

*Prescription diuretics. These act by inhibiting reabsorption of filtered Na. Examples:*

- **Lasix** (furosemide) act on ascending limb to inhibit Na 2K Cl symporters. So more salt stays in tubule and water with it.
- **Thiazide** (e.g. chlothiazide Diuril) acts in DCT by inhibiting Na Cl symporters.
- Excess K may be lost in DCT with above two examples.
  - So, may need a K supplement.
- **Spironolactone** (Aldactone) acts to inhibit aldosterone by blocking Na leakage channels. These are K sparing diuretics.
Effects of Drugs

**Diuretics – increase urine production.**

- **Alcohol** prevents release of ADH from pituitary, therefore there is greater urine production.
- **Caffeine** (coffee, sodas) inhibits Na\(^+\) reabsorption, so Na\(^+\) and water are higher in urine.

**Antidiuretics – decrease urine production.**

- **Nicotine, morphine, barbiturates** – all stimulate ADH production.
Why is urine yellow?

- Due to pigment created when old red cells are recycled. Hemoglobin breaks down and part of the heme portion becomes bilirubin which is excreted as a similar pigment in the urine.

If your urine matches these colors you are hydrated.

If your urine matches these colors you are de-hydrated and you should drink more!

If your urine matches these colors you are seriously de-hydrated or could have blood in your urine. You should contact a doctor!
Creatinine Clearance

• Creatinine (energy store) is produced in skeletal muscle from creatine phosphate at a steady rate.
• Creatinine is cleared by the kidney as fast as it is made. So, if blood level raises (>1.5 mg/dl) it is usually an indicator of poor renal function.
• Better is a measure of renal creatinine clearance as expressed by how effectively the kidneys remove it from the plasma in a 24 hour period.

= Kidney Function
Creatinine Clearance

Renal creatinine clearance is equal to:

\[
\text{Urine creatinine level in 24 hr sample} \times \text{urine volume in ml/min over 24 hrs} \div \text{Plasma creatinine level}
\]

- Normal = 140ml/min
- The reason creatinine is used to determine glomerular filtration rate (kidney function) is because it is only filtered, not reabsorbed or secreted by nephron. Therefore 100% of the amount filtered is excreted in the urine.
Disorders of Kidney

**Nephritis**
- Bacterial infection of kidney. Usually see protein (proteinuria), white cells, bacteria, nitrate in urine.
- Nephritis is treated with antibiotics. If not successful, hemodialysis (machine performs function of kidney) or kidney transplant is necessary.

**Diabetes insipidus**
- Loss of ability to secrete ADH, increased urine flow (5-20 L/day).

**Renal failure**
- Decrease or cessation of glomerular filtration. 2 types: acute & chronic
  - **Acute** – Abrupt stop. Less than 250 ml of urine/day. Causes: decreased CO, blood volume, damage to renal tubules (toxins, drugs), kidney stones.
  - **Chronic** – progressive irreversible decline in glomerular filtration rate (GFR). Causes: glomerulonephritis, pyelonephritis, trauma to kidney.
  - 75% of nephrons can be lost before noticeable (renal insufficiency).
RENAL CORPUSCLE
Glomerular filtration rate: 105–125 mL/min
Filtered substances: water and all solutes present in blood (except proteins) including ions, glucose, amino acids, creatinine

DISTAL CONVOLUTED TUBULE
Reabsorption (into blood) of:
- Water 10–15% (osmosis)
- Na⁺ 5%
- Cl⁻ 5%
- Ca²⁺ variable

PROXIMAL CONVOLUTED TUBULE
Reabsorption (into blood) of filtered:
- Water 65% (osmosis)
- Glucose 100%
- Amino acids 100%
- Na⁺ 65%
- K⁺ 65%
- Cl⁻ 50%
- HCO₃⁻ 80–90%
- Ca²⁺, Mg²⁺ variable
- Urea 50%

Secretion (into urine) of:
- H⁺ variable
- Ammonia variable
- Urea variable
- Creatinine small amount

LOOP OF HENLE
Reabsorption (into blood) of:
- Water 15% (osmosis in descending limb)
- Na⁺ 20–30% (ascending limb)
- K⁺ 20–30% (ascending limb)
- Cl⁻ 35% (ascending limb)
- HCO₃⁻ 10–20%
- Ca²⁺, Mg²⁺ variable

Secretion (into urine) of:
- Urea variable

LAST PART OF DISTAL TUBULE AND COLLECTING DUCT
Reabsorption (into blood) of:
- Water 5–9% (insertion of water channels stimulated by ADH)
- Na⁺ 1–4%
- HCO₃⁻ variable amount
- Urea variable

Secretion (into urine) of:
- K⁺ variable amount to adjust for dietary intake (leakage channels)
- H⁺ variable amounts to maintain acid-base homeostasis (H⁺ pumps)

Tubular fluid leaving the collecting duct is dilute when ADH level is low and concentrated when ADH level is high.