Excretory Physiology

Urine production and eliminations are one of the most important mechanisms of body homeostasis
   → composition of blood is determined more by kidney function than by diet

all body systems are directly or indirectly affected by kidney function

kidney function is closely tied to circulatory system

typically referred to as “excretory system”

excretory wastes = metabolic wastes
   → chemicals & toxins produced by cells during metabolism

but we have several organs that serve an **excretory function** other than kidneys:
   1. **kidneys**
   2. **skin**
      sweat glands rid body of water, minerals, some nitrogenous wastes (ammonia)
   3. **lungs**
      rid body of CO2 from energy metabolism of cells
   4. **intestine**
      in addition to getting rid of undigested food residue
      feces also contains some metabolic wastes as well;
      bile pigments, salts, calcium, some toxins

Functions of Urinary System:
   1. removal of metabolic wastes
   2. elimination of toxins
   3. elimination of excess nutrients
   4. elimination of excess hormones
   5. regulation of fluid volume
   6. regulation of electrolytes
   7. regulation of acid base balance
   8. regulation of blood volume and pressure
   9. erythropoiesis
   10. calcium absorption

**Nephron**

nephron = functional units of kidneys

    each kidney is composed of over 1 million nephrons
two basic parts:

**nephric tubule**
- microscopic, highly convoluted tubule
- associated **blood supply**

**Nephric Tubule**

the nephric tubule is organized into several discrete structures

**Bowman’s Capsule**
- cup shaped mouth of nephron
- usually in cortex

**Proximal Convoluted Tubule**
- attached to Bowman’s Capsule
- highly coiled (convoluted)
- inner surface contains microvilli

**Loop of Henle**
- large loop consisting of:
  - descending limb &
  - ascending limb
- extends down into medulla

**Distal Convoluted Tubule**
- appears similar to PCT

**Collecting Tubule**
- many DCT’s drain into one collecting tubule
- bundles of collecting tubules = **pyramids**

**Blood Supply**

kidneys are highly vascularized

every minute, 1200 ml/min of blood flows through kidneys

\[ \rightarrow = \frac{1}{5} \text{th of cardiac output} \]

- 45 gallons/day
- all blood ~60x’s/day

**Glomerulus**
- dense capillary bed
- formed by afferent arteriole
- inside Bowman’s capsule

**Bowman’s Capsule + Glomerulus = Renal Corpuscle**
Efferent Arteriole
blood leaves glomerulus via efferent arteriole
[\rightarrow \text{artery} \rightarrow \text{capillary bed} \rightarrow \text{artery}]

Peritubular Capillaries
efferent arteriole divides into another capillary bed
surrounds the rest of the nephric tubule
(PCT-LH-DCT-CT)

Urinary Physiology

urine formation in nephrons occurs by:
1. filtration
2. reabsorption
3. secretion

1. Filtration

occurs in renal corpuscle:
Glomerulus \rightarrow \text{Bowmans Capsule}

water, salts, small molecules and wastes are filtered out of blood capillaries of glomerulus:

fenestrated capillaries
\rightarrow \text{act like sieve}

have higher filtration pressure than other capillaries of body

afferent arteriole is larger than efferent arteriole
\rightarrow \text{increases pressure in glomerulus}
presssure \sim 45\text{mmHg}
(vs 35 \text{mmHg} in most capillaries)

not all water leaks out, some is retained since proteins and solutes that remain in blood attract water by osmosis
(water follows salt)

if blood pressure is reduced
\rightarrow \text{urine formation slows down}

kidneys can maintain a fairly constant filtration rate by:
1. **renal autoregulation**
kidney adjusts its own resistance to blood flow despite changes in systemic blood pressure by constricting and dilating local arterioles
   = autoregulation

2. **renin-angiotensin system**
mainly controls systemic blood pressure in emergencies but will also increase pressure in glomerular capillaries
renin is secreted by cells in walls of DCT (juxtaglomerular cells) in response to:
   - decreased BP: below 80 mmHg
eg. hemorrhage, dehydration
direct sympathetic stimulation
renin activates angiotensin (plasma protein)
angiotensin causes vasoconstriction of arterioles throughout the body
   → raises blood pressure

3. **local chemicals**
some chemicals secreted by kidney have local effect on blood vessels
   - eg. prostaglandins (tissue hormones)
     → some vasodilators
     → some vasoconstrictors
   - eg. NO → vasodilator
   - eg. kallikrein (renal enzyme) → vasodilator
   - eg. adenosine
   - eg. endothelin

   **Sympathetic stimuli can override the above:**
   - renal autoregulation can be overridden by emergency or stress
   - sympathetic fibers trigger strong constriction of afferent arterioles
   - shunts more blood to heart, brain, muscles

   **filtrate** is essentially the same composition as plasma without formed elements or proteins
solutes (filtrate) enter Bowman’s capsule

2. Tubular Reabsorption

urine is not the same composition as this filtrate
needed nutrients are conserved
wastes and toxins are eliminated
blood levels of fluids, salts, acidity etc are actively regulated

reabsorption is more selective
occurs all along nephric tubule
overall, ~99% of glomerular filtrate gets reabsorbed
only ~1% of original filtrate actually leaves the body as urine

<table>
<thead>
<tr>
<th></th>
<th>Plasma</th>
<th>Filtrate</th>
<th>Reabsorbed</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Amount</td>
<td>%</td>
</tr>
<tr>
<td>Proteins</td>
<td>8,000</td>
<td>15</td>
<td>15</td>
<td>100.0%</td>
</tr>
<tr>
<td>Glucose</td>
<td>180</td>
<td>180</td>
<td>180</td>
<td>100.0%</td>
</tr>
<tr>
<td>Salts</td>
<td>1,498</td>
<td>1,498</td>
<td>1,486</td>
<td>99.1%</td>
</tr>
<tr>
<td>Water</td>
<td>180,000</td>
<td>180,000</td>
<td>178,500</td>
<td>99.2%</td>
</tr>
<tr>
<td>Urea</td>
<td>53</td>
<td>53</td>
<td>28</td>
<td>52.8%</td>
</tr>
<tr>
<td>Uric Acid</td>
<td>8.5</td>
<td>8.5</td>
<td>7.7</td>
<td>90.0%</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.4</td>
<td>1.4</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.4</td>
</tr>
</tbody>
</table>

different substances are reabsorbed back into blood from different parts of tubule:

Proximal Convoluted Tubule
~80% of materials to be reabsorbed are reabsorbed in PCT
cells lining PCT have microvilli more mitochondria
all small proteins, glucose, amino acids are reabsorbed
most water, most salts are reabsorbed some wastes

Loop of Henle
additional Cl⁺ and Na⁺ ions are reabsorbed by active transport
countercurrent mechanism:
high salt conc is maintained in medulla around loop
ascending limb is impermeable to water
creates high conc of salts

**Distal Convoluted Tubule & Collecting Tubule**

high salt conc around nephric tubule causes water reabsorption in
DCT and CT
both salt and water reabsorption is partially controlled by
hormones:

- Na\(^+\) & K\(^+\) by aldosterone
- H\(_2\)O by ADH & aldosterone (indirectly)

**Aldosterone:**

- secretion controlled by K\(^+\) & Na\(^+\) ion concentrations in tissue fluids
- also affect reabsorption of water
tied to renin secretion
diuretics tend to
- increase Na\(^+\) reabsorption
- and increase K\(^+\) loss

**AntiDiuretic Hormone:**

- No ADH \(\rightarrow\) tubules are practically impermeable to water \(\rightarrow\) release hypotonic urine
- with ADH \(\rightarrow\) tubules are permeable to water
  - osmosis causes water reabsorption
  - \(\rightarrow\) release hypertonic urine

3. **Tubular Secretion**

- cells of DCT and CT can secrete some substances
  - esp K\(^+\) and H\(^+\)
  - also NH\(_4\) and
  - some drugs (eg. penecillin)

  - can be active or passive processes

  - usually urine is slightly acidic
    - normal diet produces more acid than alkaline waste products

**Renal Clearance Rate**

- the concentration of wastes in blood leaving kidneys (renal vein) is usually lower than their conc in blood entering kidneys (renal artery)
  - \(\rightarrow\) blood is cleared of wastes

- can estimate filtration rate of kidneys
need chemical that is filtered but not reabsorbed
eg. creatinine (but some is secreted too)
eg. inulin

measure how much of a known amount appears in urine then

\[ \text{Glomerular Filtration Rate} = \text{Renal Clearance Rate} \]

Average Renal Clearance Rate
for most substances is \(~20\%\)\n\[ \rightarrow \text{ie. \sim20\% of materials in renal blood are filtered and not reabsorbed/transit} \]

requires many passes thru kidneys to completely rid blood of something

**Reabsorption & Secretion of Specific Nutrients**

1. **Glucose**
easily filtered
requires energy to reabsorb
minimum amount of glucose in plasma to cause glucose to appear in urine
\[ = \text{renal plasma threshold} \]
\[ = 180-200 \text{ mg/100 ml} \]

glycosuria/hyperglycemia
\[ \rightarrow \text{plasma glucose >200 mg/100ml} \]

2. **Amino Acids**
all require carriers for active transport
presence in urine may be due to:
excess amounts in blood
missing or defective carriers

<table>
<thead>
<tr>
<th>Amino Acid</th>
<th>Disease</th>
<th>Cause of Disease</th>
<th>Effects of Defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>cystine</td>
<td>Cystinuria</td>
<td>defective cystine carriers</td>
<td>kidney stones</td>
</tr>
<tr>
<td>tryptophane</td>
<td>Hartnup disease</td>
<td>defective tryptophane carriers</td>
<td>cells deficient in NAD and NADP</td>
</tr>
<tr>
<td>methionine</td>
<td>Homocystinuria</td>
<td>enzyme defect causes buildup of this intermediate product</td>
<td>speech defects, mental retardation</td>
</tr>
<tr>
<td>phenylalanine</td>
<td>Phenylketonuria</td>
<td>enzyme defect causes buildup of this intermediate product</td>
<td>severe mental retardation</td>
</tr>
</tbody>
</table>
3. **Sodium**

90% of filtered sodium is reabsorbed in PCT
additional 10% may be absorbed in LH due to effects of Aldosterone:
- without aldosterone
  - → 8% of rest is reabsorbed
  - → 2% is lost in urine (~30g/d)
- with aldosterone
  - → all 10% is reabsorbed
  - → urine has 0 sodium in it

4. **Potassium**

90% of filtered potassium is reabsorbed in PCT

high blood [K⁺]:
- may occur in metabolic acidosis
- can cause cardiac arrhythmias

low blood [K⁺]:
- can cause arrhythmias, muscle cramps

additional 10% may be absorbed in LH due to effects of Aldosterone:
- without aldosterone
  - → all 10% is reabsorbed
- with aldosterone
  - → stimulates secretion of K⁺ into DCT
    - up to 50x’s more than was originally filtered

diuretics cause
- greater reabsorption of sodium and
- increased loss of potassium
  - → may require KCl supplements

5. **Hydrogen Ions (H⁺)**

linked to potassium secretion

6. **Bicarbonate Ions (HCO₃⁻)**

usually all is reabsorbed
Urine Analysis

the kidneys perform their homeostatic functions of controlling the composition of internal fluids of body

the by product of these activities is Urine

urine contains a high concentration of solutes

in a healthy person, its volume, pH and solute concentration vary with the needs of body

during certain pathologies, the characteristics of urine may change dramatically

an analysis of urine volume, physical and chemical properties can provide valuable information on the internal conditions of the body

Physical Characteristics

1. Volume
   normal = 1000 – 1800ml/day (2-3.5 pints)
   influenced by:
   blood pressure
   blood volume
   temperature
   diuretics
   mental state
   general health

2. Specific Gravity
   weight compared to water
   water = 1.000
   measures solute concentration
   average range: 1.008 - 1.030

3. Color
   normal = yellow-amber (from hemoglobin breakdown)
   influenced by:
   ratio of solutes
   → >solute conc.
   = darker yellow to brownish
   → <solute conc.
   = less color to colorless
   diet (eg. beets)
   blood in urine
4. **Transparency**
   turbid indicates mucus, bacteria or cells

5. **Odor**
   normal = musty
   diabetics → sweet odor

6. **pH**
   normal urine is slightly acidic: 5.0 - 7.8
   influenced by:
   diet
   eg. high protein → acidic
   vegetables → alkaline
   metabolic disorders:
   eg. lungs, kidneys, digestive system, etc

7. **Cells and Castings**
   normally find epithelial cells and some bacterial cells and varous cells casts
   Bacteria
   < 100-1000/ml = contamination by normal flora
   >100,000/ml = indicates active colonization of urinary system
   RBC’s & WBC’s
   presence is almost always pathological
   inflammation of urinary organs
   pus from infections

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**Chemical Characteristics**

1. **Water**
   normally is 95% of total urine volume
   remaining 5% consists of solutes

2. **Normal Solutes**
   mostly wastes or excess amounts of nutrients, hormones, etc
   organic – mainly ‘nitrogenous’ compounds:
   **urea** (95% of N wastes)
   from deamination of amino acids
   **creatinine**
   from breakdown of energy transferring molecule especially in muscle cells
   **uric acid**
   from breakdown of nucleic acids
inorganic –
chlorides and salts
ammonia – N containing cmpd, not much produced, very toxic
phosphates
sulfates

3. Abnormal Solutes
normal constituents of plasma
usually do not appear in urine:
   too large to be filtered out
   all is reabsorbed

a. albumin (protein)
normally too large to filter out
presence indicates increased permeability of glomerular membrane due to:
   injury
   high blood pressure
   irritation
   toxins

b. glucose
normally, all is filtered and all reabsorbed
body reabsorbs as much as is needed
when it appears in urine indicates high blood sugar concentrations
   \( \rightarrow \) symptom of diabetes mellitis

c. ketones
produced when excessive quantities of fats are being catabolized
high quantities may be caused by:
   diabetes
   starvation
   dieting
   \( \rightarrow \) too little carbohydrates in diet

Other Functions of Kidneys

in addition to their primary role in removing metabolic wastes and excess nutrients and hormones from the body, kidneys also:

5. Control rate of erythropoiesis

kidneys produce hormone = erythropoietin that regulates erythropoiesis:
   hypoxic \( \rightarrow \) secretes more erythropoietin
   excessive \( O_2 \) inhibits hormone production
testosterone enhances kidney production of erythropoietin
estrogen and progesterone have no effect

6. Affects the absorption of Calcium from intestine
activates Vitamin D circulating in blood

7. Help to regulate blood pressure & volume
renin-angiotensin mechanism

   lower BP:
   → kidneys release enzyme = renin
   → renin triggers production of angiotensin II
   → angiotensin causes:
     vasoconstriction → raises BP
     release of ADH → conserves water to raise BP

helps maintain high filtration pressure in Renal corpuscles

blood pressure is directly affected by the volume of fluids retained or removed from body:

greater volume → increases BP
   eg. excessive salts promote water retention
lower volume → decreases BP
   eg. dehydration
   eg. internal bleeding

Kidneys can directly affect blood volume by altering salt and water reabsorption under influence of Aldosterone and ADH

   eg. Aldosterone promotes salt retention and therefore water retention by kidneys
   eg. ADH promotes water retention by kidneys

8. Regulate pH of body fluids

able to actively secrete excess hydrogen ions