Functions of the Kidneys

- Make urine
- Regulate blood volume and blood pressure
- Regulate plasma concentrations of $\text{Na}^+$, $\text{K}^+$, $\text{Cl}^-$, $\text{HCO}_3^-$, and other ions
- Help to stabilize blood pH
- Conserve valuable nutrients
- Assist the liver in detoxification and deamination

Anatomical Features of Kidneys

Kidneys are retroperitoneal

Figure from: Martini, Anatomy & Physiology, Prentice Hall, 2001
The Nephron

Vasa recta are associated with juxtamedullary nephrons.

Nephrons are the structural and functional units of the kidney.

Sympathetic nerve fibers from the ANS innervate the kidney.

Blood Flow Through Kidney and Nephron

Renal Corpuscle (Glomerulus + Capsule)

Podocytes form the visceral layer of the glomerular capsule. Their pedicels (foot processes) form filtration slits (or slit pores) that function in forming filtrate.

Efferent arteriole is smaller than the afferent arteriole.

This creates a high pressure (~55-60 mm Hg) in the glomerular capillary bed.
The Nephron

1. Glomerular capsule
2. PCT – simple cuboidal with a brush border
3. Thin segment of the descending nephron loop - simple squamous epithelium
4. Thick ascending nephron loop - cuboidal/low columnar
5. DCT - simple cuboidal with no microvilli (specialized for secretion, not absorption)

The order of the parts of the nephron is important to know.

Juxtaglomerular Apparatus

Juxtaglomerular cells (JG) - modified smooth muscle cells in the wall of the affenter arteriole that contract (and secrete renin)

Cells of the macula densa (MD) are osmoreceptors responding to solute concentration of filtrate

MD + JG cells = juxtaglomerular apparatus

---

Glomerular Filtrate and Urine Composition

<table>
<thead>
<tr>
<th>Substance</th>
<th>Plasma Concentration (mM)</th>
<th>Glomerular Filtrate Concentration (mM)</th>
<th>Urine Concentration (mL/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (Na⁺)</td>
<td>142</td>
<td>140</td>
<td>138</td>
</tr>
<tr>
<td>Chloride (Cl⁻)</td>
<td>103</td>
<td>103</td>
<td>103</td>
</tr>
<tr>
<td>Potassium (K⁺)</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Calcium (Ca²⁺)</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Magnesium (Mg²⁺)</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Glucose (Glu)</td>
<td>120</td>
<td>150</td>
<td>120</td>
</tr>
<tr>
<td>Creatinine (Cr)</td>
<td>1.7</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Creatinine (Cr)</td>
<td>1.7</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Blood urea nitrogen (BUN)</td>
<td>20</td>
<td>14</td>
<td>14</td>
</tr>
</tbody>
</table>

Glomerular filtrate is about the same composition as plasma: H₂O, glucose, amino acids, urea, uric acid, creatine, creatinine, Na, Cl, K, HCO₃⁻, PO₄³⁻. But notice how different the composition of urine is. Additionally, note that protein is not normally present in urine.
Urine Formation

Fluid from plasma passes into the glomerular capsule and becomes filtrate at an average rate of 125 ml/minute. This is known as the Glomerular Filtration Rate (GFR)

- **Glomerular Filtration (GF)** *Adds to volume of urine produced
  - substances move from blood to glomerular capsule

- **Tubular Reabsorption (TR)** *Subtracts from volume of urine produced
  - substances move from renal tubules into blood of peritubular capillaries
  - glucose, water, urea, proteins, creatine
  - amino, lactic, citric, and uric acids
  - phosphate, sulfate, calcium, potassium, and sodium ions

- **Tubular Secretion (TS)** *Adds to volume of urine produced
  - substances move from blood of peritubular capillaries into renal tubules
  - drugs and ions, urea, uric acid, H⁺

\[ \therefore \text{Urine formation } = \text{GF + TS - TR} \]

**Glomerular Filtration**

Glomerular filtrate is plasma that passes through
1) the fenestrae of the capillary endothelium,
2) the basement membrane around the endothelium, and
3) the filtration slits (slit pores) of the podocytes

This is called the 'filtration membrane'

Glomerular filtration is a mechanical process based primarily on molecule size

**Glomerular Filtration and Urine Formation**

Glomerular Filtration Rate (GFR) is directly proportional to the net filtration pressure

\[ \text{GFR } \approx 125 \text{ ml/min (180 L/day)} \]

Urine output is only 0.6 – 2.5 L per day (an average of about 1.8 L, or about 1% of glomerular filtrate)

- Blood pressure is the most important factor altering the glomerular hydrostatic pressure (and NFP).
- A MAP fall of 10% will severely impair glomerular filtration; a fall of 15-20% will stop it.

\[ \text{Net Filtration Pressure } = \text{force favoring filtration } – \text{forces opposing filtration} \]
\[ = (\text{HP } + \text{OP}) \]

NFP = HP + OP - (HP, + OP)
Summary of Factors Affecting GFR

<table>
<thead>
<tr>
<th>Factor</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasoconstriction</td>
<td></td>
</tr>
<tr>
<td>Afferent arteriole (Δ radius × GFR)</td>
<td>↓ GFR</td>
</tr>
<tr>
<td>Efferent arteriole (Δ radius × 1/GFR)</td>
<td>↑ GFR</td>
</tr>
<tr>
<td>Vasodilation</td>
<td></td>
</tr>
<tr>
<td>Afferent arteriole</td>
<td>↓ GFR</td>
</tr>
<tr>
<td>Efferent arteriole</td>
<td>↑ GFR</td>
</tr>
<tr>
<td>Increased capillary hydrostatic pressure</td>
<td>↓ GFR</td>
</tr>
<tr>
<td>Increased colloid osmotic pressure</td>
<td>↓ GFR</td>
</tr>
<tr>
<td>Increased capsular hydrostatic pressure</td>
<td>↓ GFR</td>
</tr>
</tbody>
</table>

Know this table – it’s important!

Three Major Ways of Regulating GFR

1) Autoregulation
- Maintains GFR despite changes in local blood pressure and blood flow (between 90 – 180 mm Hg mean systemic pressure)
- Myogenic (muscular) mechanism – contraction of afferent arteriolar vascular smooth muscle when stretched (increased BP); relaxation occurs when BP declines
- Tubuloglomerular mechanism – MD cells detect ↑ flow rate and/or ↑ osmolarity of filtrate in DCT → JG cells contract → afferent arteriole constricts → ↓ GFR

Three Major Ways of Regulating GFR

2) Neural (Autonomic) Regulation
- Mostly sympathetic postganglionic fibers = vasoconstriction of afferent arterioles ↓ GFR (conserves water, redirects blood to other organs)
- Stimulates juxtaglomerular apparatus to secrete renin
- May override autoregulatory mechanism at afferent arteriole

3) Hormonal Regulation
- Renin-angiotensin system – ↑ ECF volume and BP
- Atrial Natriuretic Peptide (ANP) - ↓ GFR, ↑ fluid loss (dilates afferent arteriole, constricts efferent arteriole)
Renin-Angiotensin System

**Renin** is released by the juxtaglomerular apparatus due to:
1. Decline of BP (Renin $\propto 1/\text{Pressure}$)
2. Juxtaglomerular stimulation by sympathetic NS
3. Decline in osmotic concentration of tubular fluid at macula densa (Renin $\propto 1/\text{[NaCl]}$)

**Actions of Angiotensin II**
- Stabilizes systemic blood pressure and extracellular fluid volume

**Summary of Reabsorption and Secretion**

<table>
<thead>
<tr>
<th>Process</th>
<th>PCT</th>
<th>Distal</th>
<th>Collecting Duct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reabsorption</td>
<td>Glucose, amino acids, urea, uric acid, NaCl, HCO$_3$⁻</td>
<td>H$_2$O, Na$^+$, Cl$^-$, K$^+$, NO H$2$O</td>
<td>H$_2$O, urea</td>
</tr>
<tr>
<td>Secretion</td>
<td>Creatinine, H$^+$, Some drugs</td>
<td>Urea</td>
<td>-</td>
</tr>
</tbody>
</table>

Tubular Reabsorption in PCT

- 65% of filtrate volume is reabsorbed in the PCT

Tubular reabsorption - reclaiming of substances in filtrate by body (tubule $\rightarrow$ blood)

- Peritubular cap: 1) Low hydrostatic pressure 2) High COP 3) High permeability
- All uric acid, about 50% of urea, and no creatinine is reabsorbed
- Renal threshold is the plasma level (concentration) above which a particular solute will appear in urine, e.g., 180 mg/dL
Reabsorption in the PCT

<table>
<thead>
<tr>
<th>Substance</th>
<th>Mechanism of Reabsorption</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺ (Cl⁻)</td>
<td>Primary Active Transport</td>
<td>Na⁺ reabsorption is the driving force for most other reabsorption</td>
</tr>
<tr>
<td>H₂O</td>
<td>Osmosis</td>
<td>Closely associated with movement of Na⁺ (Obligatory water reabsorption)</td>
</tr>
<tr>
<td>Glucose</td>
<td>Secondary Active transport</td>
<td>Limited # of molecules can be handled ( T_m = 375 \text{ mg/min} ) attract H₂O</td>
</tr>
<tr>
<td>Amino Acids</td>
<td>Secondary Active transport</td>
<td>Three different active transport modalities; difficult to overwhelm</td>
</tr>
<tr>
<td>Other electrolytes</td>
<td>Secondary Active transport</td>
<td></td>
</tr>
</tbody>
</table>

Secretion in the PCT and DCT

In the DCT potassium ions or hydrogen ions may be secreted in exchange for reabsorbed sodium ions. Reabsorption of Na⁺ in the DCT is increased by the hormone, aldosterone.

Other compounds are actively secreted as well, e.g., histamine, ammonia, creatinine, penicillin, phenobarbital.

Summary of Events in the Nephron

1. Filtrate produced
2. Reabsorption of 65% of filtrate
3. Obligatory water reabsorption
4. Reabsorption of Na⁺ and Cl⁻ by active transport (NO H₂O reabsorption)
5. Facultative reabsorption of water (ADH is needed)
6. Absorption of solutes and water by vasa recta to maintain osmotic gradient
The mechanism shown is called the "countercurrent multiplier". Countercurrent multiplier allows the kidneys to vary the concentration of urine. Vasa recta maintains the osmotic gradient of the renal medulla so the countercurrent multiplier can work.

Approximate normal osmolarity of body fluids

Reduced osmolarity of tubular fluid due to action of countercurrent multiplier

The mechanism shown is called the "countercurrent multiplier". Countercurrent multiplier allows the kidneys to vary the concentration of urine. Vasa recta maintains the osmotic gradient of the renal medulla so the countercurrent multiplier can work.

Urea, Uric Acid, and Diuretics

Urea
- Product of amino acid catabolism
- Plasma concentration reflects the amount or protein in diet
- Enters renal tubules through glomerular filtration
- 50% reabsorbed
- Rest is excreted

Uric Acid
- Product of nucleic acid metabolism
- Enters renal tubules through glomerular filtration
- 100% of filtered uric acid is reabsorbed
- 10% secreted and excreted

A diuretic promotes the loss of water in the urine. Anything that adds more solute to tubular fluid will attract H₂O and can function as a diuretic to increase the volume of urine, e.g., glucose (osmotic diuretic).

Urine
- Urine composition varies depending upon:
  - Diet
  - Level of activity
- Major constituents of urine:
  - H₂O (95%)
  - Creatinine (remember, NONE of this is reabsorbed)
  - Urea (most abundant solute), uric acid
  - Trace amounts of amino acids
  - Electrolytes
  - Urochrome (yellow color), urobilin, trace of bilirubin
- Normal urine output is 0.6-2.5 L/day (25-100 ml/hr)
- Output below about 25 ml/hour = kidney failure (oliguria -> anuria)
Terms to know…

- Anuria – absence of urine
- Diuresis – increased production of urine
- Dysuria – difficult or painful urination
- Emuresis – uncontrolled (involuntary) urination
- Glycosuria (glucosuria) – glucose in the urine
- Hematuria – blood in the urine
- Oliguria – scanty output of urine
- Polyuria – excessive urine output

Elimination of Urine

Flow of Urine

- nephrons
- collecting ducts
- renal papillae
- minor and major calyces
- renal pelvis
- ureters
- urinary bladder
- urethra
- outside world

Know this…

Ureters and Urinary Bladder

Ureters
- retroperitoneal tubes about 25 cm long
- carry urine from kidneys to bladder by peristaltic contractions

Urinary bladder (cyst(o)) - temporary storage reservoir for urine
- Smooth muscular layer runs in all directions (detrusor muscle) under parasympathetic control.
- Contraction compresses the bladder and causes urine to flow into urethra
- Internal sphincter is thickening of detrusor muscle at neck of bladder – closed when detrusor is relaxed; open when detrusor contracts
Note the long male urethra (about 18-20 cm). There are three sections to the male urethra:
- Prostatic urethra
- Membranous urethra
- Penile urethra

Note the short urethra in females (about 4 cm).

Micturition (Urination) Reflex

Fluid and Body Compartments

About 40 L of fluid (avg. adult male; less in females due to greater proportion of body fat)

Major forces affecting movement of fluid between compartments:
1) Hydrostatic pressure
2) Osmotic pressure

‘Compartments’ commonly behave as distinct entities in terms of ion distribution, but ICF and ECF osmotic concentrations (about 290 mOsm/L) are identical. This is because H2O is free to flow between compartments and any disturbance in osmolarity is quickly corrected by H2O movement.
Body Fluid Ionic Composition

ECF major ions:
- sodium, chloride, and bicarbonate

ICF major ions:
- potassium, magnesium, and phosphate (plus negatively charged proteins)

You should know these chemical symbols and charges of ions.

Fluid (Water) Balance

- urine production is the most important regulator of water balance (water in = water out)

Major Regulators of H₂O Intake and Output

- Regulation of water intake
  - increase in osmotic pressure of ECF → osmoreceptors in hypothalamic thirst center → stimulates thirst and drinking

- Regulation of water output
  - Obligatory water losses (must happen)
    - insensible water losses (lungs, skin)
    - water loss in feces
    - water loss in urine (min about 500 ml/day)
  - increase in osmotic pressure of ECF → ADH is released
    - concentrated urine is excreted
    - more water is retained
    - LARGE changes in blood vol/pressure → Renin and ADH release
Dehydration and Overhydration

Dehydration
- osmotic pressure increases in extracellular fluids
- water moves out of cells
- osmoreceptors in hypothalamus stimulated
- hypothalamus signals posterior pituitary to release ADH
- urine output decreases

Severe thirst, wrinkling of skin, fall in plasma volume and decreased blood pressure, circulatory shock, death

Overhydration
- osmotic pressure decreases in extracellular fluids
- water moves into cells
- osmoreceptors inhibited in hypothalamus
- hypothalamus signals posterior pituitary to decrease ADH output
- urine output increases

‘Drunken’ behavior (water intoxication), confusion, hallucinations, convulsions, coma, death

Osmolarity and Milliequivalents (mEq)

- Recall that osmolarity expresses total solute concentration of a solution
  - Osmolarity (effect on H₂O) of body solutions is determined by the total number of dissolved particles (regardless of where they came from)
  - The term ‘osmole’ reflects the number of particles yielded by a particular solute (milliosmole, mOsm, = osmole/1000)
    • 1 mole of glucose (180g/mol) > 1 osmole of particles
    • 1 mole of NaCl (58g/mol) > 2 osmoles of particles
- An equivalent is the positive or negative charge equal to the amount of charge in one mole of H⁺
  - A milliequivalent (mEq) is one-thousandth of an Eq
  - Used to express the concentration of CHARGED particles in a solution

Electrolyte Balance

Electrolyte balance is important because:
1. It regulates fluid (water) balance
2. Concentrations of individual electrolytes can affect cellular functions

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Normal plasma concentration (mEq/L)</th>
<th>Major mechanism(s) regulating retention and loss</th>
</tr>
</thead>
</table>
| Na⁺         | 140                                 | 1. Renin-angiotensin pathway  
2. Aldosterone (Aldosterone II, Na⁺, K⁺)  
3. Natriuretic peptides |
| Cl⁻         | 105                                 | Follows Na⁺  
1. Secretion at DCT (aldosterone sensitive) |
| K⁺          | 4.0                                 | 1. Renin-angiotensin pathway  
2. Parathyroid hormone  
3. Vitamin D (dietary uptake from intestines) |
| Ca²⁺        | 3.0                                 | 1. Calcitonin (children mainly)  
2. Parathyroid hormone  
3. Vitamin D (dietary uptake from intestines) |
Summary Table of Fluid and Electrolyte Balance

<table>
<thead>
<tr>
<th>Condition</th>
<th>Initial Change</th>
<th>Initial Effect</th>
<th>Correction</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in H2O intake (change in H2O levels)</td>
<td>↓ H2O intake</td>
<td>↓ H2O in the ECF</td>
<td>↑ H2O in the ECF</td>
<td>↓ H2O in the ECF</td>
</tr>
<tr>
<td>Change in Na+/H2O reabsorption (change in Na+ levels)</td>
<td>↓ Na+/H2O reabsorption</td>
<td>↓ Na+ concentration, ↓ ECF osmolarity</td>
<td>↑ Na+ concentration, ↑ ECF osmolarity</td>
<td>↓ Na+ concentration, ↓ ECF osmolarity</td>
</tr>
<tr>
<td>Change in volume (change in Na+ levels)</td>
<td>↓ volume, ↓ Na+</td>
<td>↓ H2O output, ↓ ECF volume, ↓ ECF osmolarity</td>
<td>↑ H2O output, ↑ ECF volume, ↑ ECF osmolarity</td>
<td>↓ H2O output, ↓ ECF volume, ↓ ECF osmolarity</td>
</tr>
</tbody>
</table>

You should understand this table

Acid/Base Buffers

A buffer resists changes in pH

<table>
<thead>
<tr>
<th>Buffer</th>
<th>Type</th>
<th>Speed</th>
<th>Eliminate H+ from body?</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical</td>
<td>Physical (first line of defense)</td>
<td>Seconds</td>
<td>No</td>
<td>Bicarbonate, phosphate, proteins (ICF, plasma proteins, Hb)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>Physiological</td>
<td>Minutes</td>
<td>Yes (indirectly as CO2)</td>
<td>H2O + CO2 → H+ + HCO3-</td>
</tr>
<tr>
<td>Renal</td>
<td>Physiological</td>
<td>Hours - Days</td>
<td>Yes</td>
<td>H+ excretion, HCO3- excretion/volatilization*</td>
</tr>
</tbody>
</table>

* Normal plasma [HCO3-] = 25 mEq/L

Acidosis and Alkalosis

If the pH of arterial blood drops to 6.8 or rises to 8.0 for more than a few hours, survival is jeopardized

1. Whether the cause is respiratory (CO2) or metabolic (other acids, bases)
2. Whether the blood pH is acid or alkaline

Respiratory system compensates for metabolic acidosis/alkalosis
Renal system compensates for respiratory acidosis/alkalosis