Overview of Renal Function

Anatomy/Function of the Kidney

- Structure/Function
  - 1% of body mass
  - 25% of cardiac output
  - Passes total blood volume every 4-5 minutes
  - Filters 180 l per day and reabsorbs 178.5 l of it
  - Produces 1.5 l of acidic (pH~6) urine per day
  - 5% increase in filtration would generate 9 l urine per day!
  - Regulation of kidney ensures that this does not happen.
Nephron Structure

- Closed end of tubule forms a bowl for the glomerulus
- Glomerulus is extension of capillaries, creates ultrafiltrate of blood that passes to Bowman’s capsule
- Urine passes through collecting duct to renal pelvis
- Tubule
  - One-cell thick
  - Proximal tubule
  - Loop of Henle
  - Distal tubule
- 1 million nephrons/kidney

Osmoregulatory Organs: Prototypical Transport Systems and the Mammalian Kidney
Transport Systems: Prototype

External, Lumen (apical surface)

Internal, Interstitial space (basal surface)

Transport Systems: Specific Example

- ATPase removes Na⁺ and absorbs K⁺
- K⁺ diffuses and crosses into tubular lumen through special channels
- Net K transporter, driven by ATP-ase
**Na⁺ Transport**

![Diagram showing Na⁺ transport in the kidney](image)

- **Passive cotransport:** Na⁺ and glucose move together.
- **Active transport:** Na⁺ is transported against its concentration gradient using ATPase.
- Channels facilitate movement of ions.

**H⁺ transport driven by Na⁺ transport**

![Diagram showing H⁺ transport](image)

- **Passive Antiporter:** H⁺ and Na⁺ move together.
- **Proton Production:** H⁺ reacts with CO₂ and H₂O to form HCO₃⁻ and CO₂.
- **CA (carbonic anhydrase):** Catalyst for the proton reaction.
- **Basolateral membrane:** HCO₃⁻ moves to the basolateral side.

*Bioengineering 6000 CV Physiology*
Functional Overview

- **Contents:**
  - Water + urea, NaCL, KCL, phosphates, etc.
  - Color and odor product of diet, e.g., asparagus
- **Process:**
  - Filter everything out (and take back what is worth keeping)
  - Reabsorption of water and salts
  - Secretion of additional unwanted substances

Renal Circulation

- **Afferent arteriole**
- **Glomerulus**
  - 10% of blood crosses to tubule
  - 100 ml/minutes
- **Efferent arteriole**
- **Secondary capillaries**
  - Loops: vasa recta
- **Veins**
Nephron Functional Overview

- Most water and minerals taken out of the filtrate
- Each region of tubule has different function
- “Renal clearance”
  - Amount of plasma from which a substance is completely removed from the body [ml/min]
  - Function of filtration, reabsorption, and secretion

Example: Glucose Regulation

- Normal glucose clearance is zero (i.e., no net loss)
- Filtration is complete
- Reabsorption complete (to a limit of about 320 mg/min)
- Clearance increases for excess plasma glucose
- Diabetics have low reabsorption and can accumulate glucose in urine
Detailed Passage Through the Nephron

1. Glomerular (filtration)
2. Proximal (reabsorption)
3. Loop of Henle (concentration)
4. Distal (reabsorption/secretion)
5. Collecting Duct (reabsorption/secretion)

Glomerular Structure
Glomerular Filtration

- Filtrate excludes only red blood cells and large proteins
- Rate depends on:
  - Hydrostatic pressures
  - Colloid osmotic pressure
  - Hydraulic permeability
- Net pressure is +10 mm Hg
- Permeability very high
  - Capillaries fenestrated
  - Filtration slits in glomerulus

Regulation of Filtration

Goal: maintain constant filtration under variations in arterial pressure
- Myogenic autoregulation: rise in blood pressure causes first stretch, then contraction of afferent arteriole
- Osmotic autoregulation
  - Macula densa: Sensor cells for osmolarity and flow of distal tubule; release substances to control afferent arterial flow
  - Granular cells control smooth muscle by releasing renin
- Central regulation:
  - Sympathetic innervation of afferent arteriole
  - Responds to blood loss (constriction) and hypertension (dilation)
  - Also causes constriction of parts of glomerulus to further reduce filtration
  - Powerful mechanism, can override autoregulation
Renin-Angiotensin System

- Renin, enzyme released from the granular cells by
  - reduced renal blood pressure
  - reduced solute delivery to distal tubule
  - sympathetic stimulation
- Angiotensin I, released from the kidneys by
  - rise in Renin
- Angiotensin II, result of Angiotensin I cleavage by
  - ACE
- Angiotensin II causes
  - at low levels, constriction of efferent arterioles, raises glomerular filtration
  - at higher levels constriction of both efferent and afferent arterioles, reduces glomerular filtration
  - increase reabsorption of Na⁺ (and water) in distal tubule
  - release of aldosterone (adrenal cortex) and vasopressin (pituitary) which increases reabsorption of Na⁺ and water in distal tubule

Proximal Tube Reabsorption

- 70% of salts reabsorbed
  - Active pumping (via K/Na pump on basolateral)
  - Water and Cl⁻ follow Na⁺ passively (and perhaps co-transport)
  - Glucose and amino acids follow in co-transport
  - Other substances concentrated in filtrate
- By loop of Henle
  - 75% of filtrate reabsorbed
  - Iso-osmotic with cells/plasma (300 mosm/L)
  - Phosphates, Ca²⁺, and other electrolytes reabsorbed as needed
Proximal Tube Secretion

- Organic anions (OA\(^{-}\))
  - K/Na pump creates Na\(^+\) gradient for exchanger
  - Non-specific mechanism for many OA's, both endogenous and exogenous
  - Drugs can alter transport through competitive binding
  - Co-administration of secreted ions with a drug can slow secretion (removal) of the drug because they can compete with the drug.

Loop of Henle

Concentration of Urine

- Descending limb
  - High passive H\(_2\)O transport
  - Interstitial osmolarity climbs (see below)
  - Thin cells
  - Almost no active salt transport, low salt permeability
- Thin ascending segments
  - Highly permeable to NaCl
  - Very low permeability to H\(_2\)O
  - No active salt transport
- Thick ascending limb
  - Active transport of NaCl
  - Low H\(_2\)O permeability
  - Reduces osmolarity
**Distal tubule**

**Adjustment of urine content**

- **Reabsorption:**
  - $\text{Na}^+$, $\text{Cl}^-$, $\text{HCO}_3^-$
  - Active transport of NaCl
  - Water follows salts (permeability controlled by ADH)

- **Secretion:**
  - $\text{H}^+$, $\text{NH}_3$, $\text{K}^+$
  - $\text{K}^+$
    - Occurs when elevated in the body
    - Na/K pumps into tubular cells, leaks into tubule through channels

- **Regulation/Feedback**
  - Distal tubule is close to glomerulus so regulation based on osmolarity in tubule
  - Concentrates urine
  - Salt transport under endocrine control
  - Aldosterone: enhanced Na$^+$ reabsorption and K$^+$ secretion

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**Collecting Duct**

**Final concentrating of urine**

- **Water permeable**
  - Permeability controlled by ADH through cAMP signaling that increases aquaporin formation
  - Interstitial space is hypertonic (mostly from NaCl and urea)

- **Secretion of $\text{K}^+$, $\text{H}^+$, $\text{NH}_3$**

- **Reabsorption of $\text{Na}^+$, $\text{Cl}^-$, $\text{HCO}_3^-$**
  - $\text{Na}^+$ by active transport
  - Regulated by aldosterone
  - Determines water movement and urine concentration

- **Reabsorption of urea**
  - End of duct very permeable to urea
  - Regulated by ADH by increase in urea transporters
Concentration of Urine

- Ability to concentrate urine depends on
  - Length of loop of Henle (kangaroo rat has very long one)
  - Gradient of osmolarity
  - Countercurrent mechanisms to maintain osmotic gradient (see below)
- Salt glands (e.g., marine birds)
  - Active salt transport via Na⁺/K⁺ pump and Na⁺/Cl⁻ cotransport
  - 2-3 times blood osmolarity

Aldosterone and ADH

- Aldosterone:
  - Releases from adrenal cortex
  - Increases Na⁺ reabsorption
- Antidiuretic Hormone (ADH)
  - Also called vasopressin
  - Released from pituitary in response to angiotensin II, osmotic and blood pressures
  - Increase water reabsorption
- Atrial Natriuretic peptide (ANP)
  - Released from atrium in response to pressure
  - Inhibits release of renin and ADH to increase urine production
Countercurrent Multiplier

**Active**
- Loop with active transporters between the arms loops
- Leads to cumulative concentration increase
- Requires:
  - Active Transport between arms
  - Constant flow into loop
- Concentration gradient along the entire arm is greater than between arms.

**Passive**
- Passive system reduces the gradient, e.g., reducing heat loss to the heat sink.

Countercurrents in the Kidney

1) Active transport of salt
   - Increased osmolarity
   - Lower water permeability
2) Osmotic passive transport of water
   - Low NaCl, urea permeability
3) Passive diffusion of urea
   - Only place with high urea permeability
4) Osmotic diffusion of water
   - Produces high osmolarity filtrate and bottom of loop
5) Diffusion of salt
   - Low water permeability
   - Produces low osmolarity filtrate at top of loop
   - Overall effect is concentration of urine
Counter Currents: Role of Vasa Recta

- Vasa recta parallel to loop
- Counter current mechanism plays key role in maintaining strong blood flow without disrupting osmolarity gradient

Urine Production Summary

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  - Water + urea, NaCl, KCl, phosphates, etc.
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