Lecture 25, 15 November 2005
Osmoregulation (Chapters 25-28)

Vertebrate Physiology
ECOL 437 (aka MCB 437, VetSci 437)
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1. Osmoregulation
2. Kidney Function

Text:
Chapters 25-28

-Exam Thursday
Kidney Processes- overview

1. **FILTRATION**
   blood --> filtrate

2. **REABSORPTION**
   filtrate --> blood

3. **SECRETION**
   blood --> filtrate

All 3 involved in final Urine Composition

Hill et al. 2004, Fig. 27.6
Filtration Regulation:

1. **Myogenic** props. of afferent arteriole resist stretch

2. Secretions from cells of **juxtaglomerular apparatus** (where distal tubule passes near bowman’s capsule)
   - **Macula densa** cells (distal tubule)
     - monitor osmolarity and flow in distal tubule
     - paracrine hormonal activity on afferent arteriole
   - **Granular or juxtaglomerular** cells (afferent arteriole)
     - release **renin** which alters blood pressure...
Filtration Regulation:

Renin (from granular cells) released in response to
- low renal BP,
- low solute [ ] in distal tubule,
- or sympathetic activation

Renin leads to activation of Angiotensin II which
causes systemic vasoconstriction to inc. BP
stimulates aldosterone from adrenal cortex
vasopressin (ADH) from post. pit.
(these promote salt, water reabsorption)

3. Sympathetic innervation (reduce GFR)
- afferent vasoconstriction
- decreased space between podocytes

Renal Clearance:

Volume of plasma cleared of a substance by the kidney.

(Filtration, Reabsorption, Secretion)

Inulin (=GFR) b/c neither reabsorbed nor secreted

If clearance > GFR = secretion
If clearance < GFR = reabsorption
1. **FILTRATION**  
   blood --> filtrate

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   filtrate --> blood

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Reabsorption:

of 180 L/day filtered, ~178.5 L reabsorbed in humans

Lots of **active transport of salts** and other substances

Tight junctions not so tight in proximal tubule, so water can move from filtrate to plasma

Because of reabsorption (and secretion),  
Renal clearance does NOT often equal GFR

(Eckert 14-19)
Reabsorption limit – Glucose example

Tm at 300 mg/min/100ml plasma

Reabsorption:

Proximal Tubule

70% filtered Na\(^+\) actively reabsorbed
(by Na\(^+\)/K\(^+\)ATPase pump in basolateral membrane)
Cl\(^-\) and water follow

75% of filtrate is reabsorbed
including glucose and amino acids (Na\(^+\) dependent)
also, phosphates, Ca\(^+\), electrolytes as needed

Parathyroid hormone controls phosphate and Ca\(^+\) reabsorp.
triggers calcitriol production (Vit. D) for Ca\(^+\)

At end of proximal tubule filtrate is isoosmotic with plasma
(~300mOsm)
however, remaining substances are 4x concentrated
Sodium Reabsorption:

![Diagram of Mammalian Kidney showing sodium reabsorption](Eckert_14-12)

[See Hill et al. 27.16]

Mammalian Kidney

Sodium and Glucose Reabsorption:

(a)

![Diagram of Mammalian Kidney showing sodium and glucose reabsorption](Eckert_14-13)

(See Hill et al. 2004, 27.16)
Reabsorption:

**Loop of Henle**

- **Descending limb**
  - no active NaCl transport
  - low urea and NaCl permeability
  - permeable to water

- **Ascending thin limb**
  - no active NaCl transport
  - but permeable to NaCl
  - low urea permeability
  - low water permeability

- **Ascending thick limb**
  - NaCl transported out of tubule
  - low water permeability

One driver of concentrating mechanism of nephron:

- **Angiotensinogen** → **Renin** → **Ang. I** → **ACE in lung** → **Ang. II** → aldosterone from adrenal cortex

Another driver of concentrating mechanism of nephron:

- **Collecting Duct**
  - permeable to water
  - hormone control (ADH/vasopressin)
  - water (via aquaporins) follows osmotic gradient
  - permeable to Urea in inner medulla
-ADH role in water reabsorption/urine concentration

- Renin -> Ang. II
- Ang. II -> ADH
- Baroreceptor input (atrial and arterial)
- EtoH inhibits ADH release
Atrial Natriuretic Peptide (ANP)
-released by atrium cells in response to stretch (elevated BP)

-opposite effect of renin-angiotensin system
-decreases sodium reabsorption
-therefore increased urine production
-ANP inhibits release of ADH, renin, aldosterone

ADH acts in stippled region of collecting duct

Urine can be 100-1200 mOsm in humans (plasma about 300)
Secretion:
From plasma into tubule of nephron

K+, H+, NH3, organic acids, organic bases
Organic anions (OA⁻):
Liver conjugates toxins and waste to glucuronic acid
Secreted into tubule lumen and excreted
Na/K-ATPase

Hill et al. 2004, Fig. 27.14
(Eckert 14-30)
Secretion:

-K+ secretion if, and only if, Na+ reabsorption (Na/K-ATPase)

-Can lead to unfavorably low levels of K+ if aldosterone acting to reabsorb Na+

or

-High K+ levels can affect heart function so excess stored in tissue as result of insulin action
Countercurrent Exchangers

Countercurrent Multipliers

See p.736 in your text
Urine concentrating ability

1200 mOsm in humans
9000 mOsm in kangaroo rats
9600 mOsm in *Perognathus* (mouse)

- Length of loops of henle
- Corticomedullary concentration gradient

(Knut Schmidt Nielsen 1997)


**Countercurrent Multiplier**

(Hill et al. 2004, Fig 27.12)
(Hill et al. 2004, Fig 27.12)

**Countercurrent Multiplier**

Urine concentrating ability

- Vasa Recta

- Loops of Henle only in Mammals and Birds -> Hyperosmotic Urine

(Eckert 14-18)
Osmoregulatory Mechanisms

- Similar mechanisms in nasal salt glands of birds and reptiles, mammalian kidney, rectal glands of sharks, gills of marine fishes, etc.
- Regulated by similar hormones as well.

(protons, $\text{Na}^+$/K+, symporters)

Non-mammalian kidneys:

- Only birds also have loops of henle

- Freshwater fish with more and larger glomeruli to make lots of dilute urine

- Some marine fish without glomeruli or bowman’s capsule – urine formed by secretion, ammonia secreted by gills

- Osmoregulation also via extrarenal organs...
Salt Glands

Shark *rectal glands* to dispose of excess NaCl
- Blood hyperosmotic to seawater, but less salt
- More urea and TMAO (trimethylamine oxide)
- NaCl actively secreted
Shark Rectal Salt Glands

**Salt-secreting cells:**
- Na/K-ATPase pump in basolateral membrane
- generates gradient for Na+ by which Na⁺/2Cl⁻/K⁺ cotransporter drives up [Cl⁻] in cell
- Cl⁻ across apical membrane
- Na⁺ follows paracellularly down electrochemical gradient (and H₂O)
- apical membrane **impermeable** to urea and TMAO
- therefore iso-osmotic secretion with lots of NaCl

... slightly different in birds and lizards →

Salt Glands

**Nasal/orbital salt glands** of birds and reptiles - especially species in **desert** or **marine** environments.

**Hypertonic NaCl secretions** (2-3x plasma osmolarity)

 Allows some birds to **drink salt water** and end up with osmotically free water
**Fish Gills**

Chloride cells involved in osmoregulation

- (recall Pelis et al. paper on smolting)
- lots of mitochondria to power ATPases
- mechanism similar in nasal glands (birds and reptiles), and shark rectal gland

Hill et al. 2004, Fig 26.7
Freshwater fish:
The mechanism basically reversed to allow uptake of salt from water against concentration gradient

Sea ↔ Freshwater

Switch between getting rid of excess salt in seawater and taking up salt in freshwater

Growth hormone and cortisol for → sea
   (more active chloride cells with more Na/K-ATPase activity)

Prolactin for → freshwater

(recall Pelis et al. paper on smolting)
pH regulation

**Acid Secretion**

CO$_2$ via lungs, H$^+$ via kidneys
(skin and gills can also play role)

**Proximal tubule and loop of henle:**
Na$^+$/H$^+$ antiporter (driven by Na/K-ATPase)

**Distal tubule and collecting duct:**
A-type cells with proton pump and anion exchanger
Ultrafiltrate buffered by bicarbonate, phosphates, and ammonia allowing for more acid secretion

e.g., $\text{NH}_3 + \text{H}^+ \rightarrow \text{NH}_4^+$

**pH regulation**

**Base Secretion** (opposite A-type cells)

**Diagram**

- Tubular lumen
- Blood
- NH$_3$
- Glutamine (Gln)
- Deamination
- α-Ketoglutarate
- H^+
- ATPase
- Na^+
- Apical membrane
- Basolateral membrane

If low on ammonia, deaminate amino acids
**pH and osmoregulation:**

(b)

Antiporter to get rid of protons (acid) and gain Na⁺

Mammalian Kidney

(Eckert 14-13)