Proximal Convoluted Tubule

Summary for PCT:

At the end of the proximal tubule
- 65% of sodium and water is reabsorbed
- 50% of chloride and potassium
- close to 100% of filtered nutrients and bicarbonate is reabsorbed

Loop of Henle

- Contains a descending limb and ascending limb
- Structural organization of the epithelial cells that line up the walls of these limbs is different
  - descending limb is permeable to water and does not contain significant numbers of Na⁺/K⁺ pumps
  - ascending limb is impermeable to water but contains many Na⁺/K⁺ pumps
  - ascending limb also contains Na⁺-K⁺-2Cl⁻ co-transporters which use the Na⁺ concentration gradient to take up these electrolytes

The net result of this system is that sodium and chloride are removed from the tubules into the peritubular fluid of the medulla
Loop of Henle

This example with temperature shows what would happen if the vessel running through a system was linear. The fluid running through vessel would leave at a different temperature, and the system would cool down because the temperature would be “dragged” away.

By creating a loop system, heat is exchanged between the system and the vessel on its way down, and between the two parts of the loop on its way up. The fluid leaving the vessel is close to the original temperature and the temperature of the system is maintained.
Loop of Henle

Because of the arrangement of the loop of Henle, a similar counter current feedback loop system is set in motion.

- Sodium and Chloride are pumped out of the thick ascending loop into the surrounding fluid.
- This elevates the osmotic concentration in the around the whole loop system
- Since the descending loop is water permeable, water is pulled out of the descending loop, increasing the osmolarity in the descending loop
- As more concentrated fluid arrives at the ascending loop, it accelerates the pumping of solutes out of the ascending loop, making the interstitial fluid even more concentrated.

Loop of Henle

This cycle repeats with elevated concentrations delivered to the descending limb which in turn delivers these concentrations to the pumps in the ascending limb until a final equilibrium is reached

This system is called the countercurrent multiplication system.

- The result is the formation of an osmotic gradient in the medulla, from 300 mOsm at the cortex to 1200 mOsm in the deepest portion in the medulla.
- This is of extreme importance in the conservation of water.
The fact that the Vasa Recta neatly follows the Loop of Henle protects the formed gradient in the interstitial fluid of the medulla.

If the Vasa recta capillaries were of a linear nature, the osmolarity gradient would dissipate and never be able to form.

The loop form of the Vasa Recta maintains that salt gradient and reinforces it!
**Loop of Henle**

The final result in the Loop of Henle is:

- Re-absorption of another 15% of water
- Re-absorption of 40% of K$^+$, 25% of Na$^+$, 25% of Cl$^-$
- The Ultrafiltrate leaving the ascending limb is hypotonic to blood (100 vs 300 mOsm/L)
- An osmotic gradient is set up and maintained in the interstitial fluid of the medulla!

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**Distal Convoluted Tubule**

- Only 15-20% of the original filtrate arrives at the DCT
- DCT and Collecting ducts performs final adjustment of urine by means of Active secretion or absorption
Absorption:

- Re-absorption of Na\(^+\) and Cl\(^-\) occurs via a sodium-chloride symporter in the apical membranes of these tubules (of course, water follows by osmosis).
- The process is once again aided by Na/K pumps in the basolateral side of these cells.

- In the distal portions of the DCT, specific cells (chief cells) use specific Na\(^+\) channels in combination with Na/K pumps.
- Aldosterone has its effect on these cells, by promoting insertion of more such Na\(^+\) channels and Na/K pumps, thus increasing the capacity to re-absorb Na\(^+\).
Distal Convoluted Tubule

Secretion of K⁺
- In the previous method of reabsorption, K⁺ is secreted for every Na⁺ reabsorbed.
- Remember that Aldosterone from the adrenal glands is stimulated by excess K⁺, which thus promotes additional K⁺ secretion into the urine.
- Increased K⁺ levels in bloodstream also promotes the driving force for K⁺ into the lumen of the tubules.
Distal Convoluted Tubule

Secretion of $H^+$

- Occurs via at least 2 mechanisms in which **carbonic anhydrase** is involved
- In one mechanism, it results in HCl secretion in return for $Na^+$ and $HCO_3^-$ absorption.
- The combination of $H^+$ removal and addition of bicarbonate to the blood becomes important in control of blood pH.
- The other mechanism uses de-amination of proteins, elimination of the $NH_3$ group as $NH_4^+$, in return for a bicarbonate ion back into the blood stream.

Collecting Ducts

- Additional solute recovery of $Na^+$ occurs in exchange of $K^+$ via a similar aldosterone regulated mechanism.
- Bicarbonates are reabsorbed in exchange for chloride.
- Urea, being lipid soluble diffuses into the peritubular fluid of the medulla.
- In this section, when blood pH is low, proton pumps actively pump protons into the tubular lumen.
The major function of the collecting ducts is to regulate the re-absorption of the last amounts of water on its way to the bladder.

By the time fluid enters the collecting ducts, roughly 85% of the water has been re-absorbed back into the bloodstream.

Due to Na\(^+\) re-uptake and additional water re-uptake, osmolarity at the entrance of the collecting ducts is now back iso-osmotic with blood (\(\sim\) 300 mOsm/L).

The distal part of the DCT and the collecting ducts are rather impermeable to water.

If nothing changes at this point, the amount of fluid and remaining electrolytes/chemicals ending up as urine would equal to

\[(15\% \text{ of } 125 \text{ ml/min}) \times 60 \times 24 = 27 \text{ L/day}\]

The osmolarity would remain the same as when it enters the DCT collecting ducts: 100 mOsm/L (hypoosmotic to blood - diluted)

The main function of the collecting tubules is thus to dramatically adjust this in order to prevent extreme water loss.
Collecting Ducts

• This regulation is under the influence of ADH.
• ADH results in the insertion of specific water channels in the membranes of the collecting duct cells that face the lumen (apical side).
• The higher the amount of circulating ADH, the more water channels inserted, the more permeable the collecting ducts become to water.
• Also remember that due to the action of the loop of Henle, an osmotic gradient in the medulla has been created: 300 mOsm at the cortex area to 1200 mOsm at the deepest portions of the medulla.

Collecting Ducts

Cross-section of kidney tubule

Collecting duct cell

Medullary interstitial fluid

Vasopressin

Vasopressin receptor

Aquaporin-2 water pores

Second messenger signal

cAMP

Storage vesicles

600 mOsm

700 mOsm

300 mOsm

Pilosa
Collecting Ducts

- When filtrate thus passes through collecting ducts made water permeable via ADH action, it will result in an osmotic movement of water out of the collecting ducts.
- With normal ADH levels, the osmolarity of the fluid in the collecting ducts will equilibrate with the osmolarity of the medulla.
  - The formed urine will end up having an osmolarity of 1200 mOsm/L; thus 4 x more concentrated than blood plasma.
  - Urine volume ~ 1200 ml/day (~ 0.83 ml/min). This is thus 0.66 % of the GFR.
Effects of ADH (vasopressin) and Osmolarity change along the nephron
**Summary of Actions**

**Diuretics:**

Are drugs that slow renal absorption of water and thereby cause diuresis, an elevated water flow and urine production.

Many diuretics work by decreasing Na$^+$ reabsorption

- **Loop diuretics:**
  - Work by decreasing action of Na-K-Cl pumping in the ascending loop
  - Result is more salts leaving the nephron into the bladder with more water
  - Side effect is that K$^+$ is lost as well creating possible **hypokalemia**
  - Ex: Furosemide

- **Thiazide diuretics:** drugs that work on DCT and block the Na-Cl symporter (thiazide diuretics such as Diuril)

- **Potassium sparing diuretics:** try to prevent hypokalemia
  - Inhibit action of aldosterone in collecting duct (Ex: spinolactone)
  - Block apical Na-leakage channel in the lumen (Ex: amiloride)

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**Rest of Urinary System**

Rest of urinary system transports, stores and eliminates
- Ureters
- Bladder
- Urethra
Ureters

• Pair of muscular tubes, containing bands of longitudinal and circular smooth muscle
• Extend from renal pelvis to the bladder
  – Peristaltic contractions force urine toward the urinary bladder
Bladder

- Hollow, muscular organ
  - Reservoir for the storage of urine
  - Contraction of detrusor muscle voids bladder
- Internal features include
  - Trigone
  - Neck
  - Internal urethral sphincter
  - Ruggae

Detrusor muscle is part of the muscularis layer. It contains an inner and outer layer of longitudinal smooth muscle, with a circular layer sandwiched in between.
Urethra

- Extends from the urinary bladder to the exterior of the body
- Passes through urogenital diaphragm (external urinary sphincter)
- Differs in length and function in males and females

Micturation Reflex

Urination is coordinated by the micturition reflex

- It is initiated by stretch receptors in wall of bladder
- Urination requires coupling micturition reflex with relaxation of external urethral sphincter
Micturation Reflex

1. Stretch receptors activated
   Signal travels to pons micturation center

2. PS signal travels down spine

3. PS signal Inhibits Symp. Fibers that relax the bladder

4. In sacral area, PS fibers activate the detrusor muscle (contraction)

5. PS fibers also inhibit the sympathetic fibers that control the internal urethral sphincter (causes relaxation)
   • Also inhibits somatic fibers that contract the external sphincter.