TOPIC 21: THE URINARY SYSTEM: REABSORPTION, SECRETION, AND URINE CONCENTRATION

I. Tubular Reabsorption
   A. Introduction
      1. Highly selective process
         a) Need to get essential materials out of tubules and back in blood
         b) Most wastes, other than urea, are too big to be reabsorbed and so are excreted in the urine
      2. Examples of reabsorption rates (Table 18.1)
         a) 99% of filtered water (47 gallons/day)
         b) 100% of filtered sugar (2.5 pounds/day)
         c) 99.5% of filtered salt (0.36 pounds/day)
   B. Process of Reabsorption: Transepithelial Transport
      1. Reabsorption requires molecules to cross two membranes: apical membrane and basolateral membrane (Fig 18.13)
      2. Two types of reabsorption (Fig 18.14)
         a) active: at least one of the steps requires energy (Fig 18.14a)
         b) passive: none of the steps requires energy (Fig 18.14b, c)
   C. Reabsorption of Na⁺ in the Proximal Tubule (Fig 19.14a)
      1. Na⁺ uses facilitated diffusion to cross apical membrane, going down concentration gradient from tubular lumen into proximal tubule epithelial cell. Can do so either by cotransport with glucose or an amino acid, or by counter transport with H⁺
      2. Na⁺ actively crosses basolateral membrane using the Na⁺-K⁺-ATPase pump which moves Na⁺ against concentration gradient from tubular cell into into interstitial fluid; then it passively diffuses into blood plasma.
   D. Reabsorption of Na⁺ in the Distal Tubule (Fig 19.14b)
      1. Na⁺ uses facilitated diffusion to cross apical membrane, going down concentration gradient from tubular lumen into proximal tubule epithelial cell. Can do so two ways:
         a) cotransport with Cl⁻ ions.
         b) through Na⁺ channels. If done this way, electrical balance must be maintained by passive movement of Cl⁻ into cell or K⁺ out of cell.
      2. Low plasma Na⁺ causes release of hormone aldosterone which causes increased reabsorption of Na⁺ by causing existing channels to open and stimulating synthesis of new channels and new Na⁺-K⁺-ATPase pumps (fig 19.15)
   E. Reabsorption of substances via Na⁺ Dependent Secondary Active Transport (Figs 19.14a & 18.15)
      1. Glucose and amino acids and other nutritionally important compounds are moved against their concentration gradients by secondary active transport
      2. These substances are co-transported across apical membrane along with the Na⁺ and then diffuse across basolateral membrane.
      3. Note that it is actually the Na⁺-K⁺-ATPase pump in the basolateral membrane that drives this process by keeping the concentration of Na⁺
low in the tubular cell so that a concentration gradient exists from tubular lumen into tubular cell
4. So they get a free ride with the Na⁺; **if no Na⁺, the pump shuts down and nothing is transported by secondary mechanisms.**
5. Glucose reabsorption (Fig 18.15)
   a) The maximum transport rate for glucose is ~ 375 mg/min
   b) Under normal conditions, ~ 125 mg/ml is reabsorbed
   c) If you have more than 375 mg/min that is available for reabsorption, the excess ends up in the urine
      (1) People with diabetes mellitus have high levels of plasma glucose, and end up excreting a lot of glucose in the urine because it all can not be reabsorbed

F. Reabsorption of substances via **Na⁺ Dependent Passive Processes**
1. Chloride ions (Cl⁻) (Fig 19.14a)
   a) passively follow the electrical gradient of Na⁺
2. Water molecules (in PROXIMAL TUBULES ONLY; see below for water reabsorption in distal tubules)
   a) osmotically follow Na⁺ across the membrane from proximal tubules to interstitial fluid (Fig 18.14b)
3. Urea reabsorption (in PROXIMAL TUBULES ONLY; see below for urea reabsorption in distal tubules)
   a) follows concentration gradient established by water leaving the tubules (Fig 19.5)
      (1) water leaves tubules, which increase tubular concentration of urea relative to the interstitial concentration, so it flows down its concentration gradient into the interstitial fluid
      (2) although half of the urea is reabsorbed, the other half is excreted, which in humans works just fine.
      (3) note: urea buildup due to renal failure is only mildly toxic compared to buildup of H⁺ and K⁺

G. Reabsorption of Phosphate (also true for Ca⁺⁺ and some other electrolytes)
1. The normal reabsorption rate of phosphate equals normal plasma concentrations of phosphate
2. If you ingest excess phosphate above normal plasma concentrations, the excess is not reabsorbed and so is excreted in the urine = **very tight regulation compared to glucose**
3. Parathyroid hormone can alter the reabsorption rates of electrolytes to conserve them if need be.

II. Tubular Secretion
A. General
1. Supplemental mechanism to filtration to get rid of substances
2. Essentially is the reverse of tubular reabsorption

B. Secretion of H⁺
1. When ECF is too acidic (i.e., too much H⁺), H⁺ is secreted passively (i.e., moves by diffusion from peritubular capillaries to tubular system.)

C. Secretion of K⁺ (Fig 19.20)
1. K⁺ must be closely regulated: if K⁺ too low in ECF = hyperpolarization of nerve and muscle cell membranes (= reduced excitability); high K⁺ in ECF increases membrane excitability, especially in the heart, which can lead to cardiac arrhythmias
2. K⁺ actively moved in opposite directions by reabsorption in the proximal tubule and secretion in the distal tubule.
3. The active transport of Na⁺ during Na⁺ reabsorption results in the secretion of K⁺, because Na⁺-K-ATPase pump moves Na⁺ and K⁺ in opposite directions
4. K⁺ secretion, not K⁺ filtration or reabsorption, is the process regulated by the kidneys to maintain proper amounts of K⁺.
   a) If plasma K⁺ is too high
      (1) The increased plasma K⁺ directly increases aldosterone production, which increases K⁺ secretion and hence excretion in the urine
   b) If plasma K⁺ is too low
      (1) aldosterone production reduced, so secretion of K⁺ is decreased = less K⁺ in the urine.
5. Problems with K⁺ secretion
   a) Because low plasma Na⁺ also stimulates aldosterone production to increase Na⁺ reabsorption, conservation of Na⁺ can inadvertently eliminate K⁺ via the aldosterone mechanism
   b) K⁺ secretion is also inversely related to H⁺ secretion, so if H⁺ secretion is increased under high acid conditions, that can result in an inadvertent increase in K⁺
D. Waste Ions
1. Separate secretory carriers for waste ions
2. Involved in removal of:
   a) unwanted endogenous substance, such as prostaglandins
   b) foreign inorganic chemicals, such as pesticides and drugs
      (1) note that the liver ionizes many foreign substances so they can be eliminated by this process in the kidneys
3. Secretion of waste ions not regulated; basically as many of these substances as possible are secreted and eliminated in urine.
III. Urine Concentration (Figs 19.6 and 19.7)
A. Overview
1. Need to be able to produce urine of varying concentrations.
   a) If you have consumed a lot of water, you need to be able to produce dilute urine so that you don’t lose too many ions.
   b) If you have been sweating a lot, you need to conserve water and so produce concentrated urine.
2. The way this is accomplished is by
   a) Using the loop of Henle to maintain a concentration gradient within the interstitial fluid of the renal medulla;
   b) Passing the collecting tubule through this concentration gradient.
   c) The collecting tubule is selective permeably to water.
d) If you need to conserve water, the collecting tubule is made permeable to water so water leaves the collecting tubule and is removed from the urine.

e) If you need to eliminate water, the collecting tubule is made impermeable to water, and all the water in the collecting tubule ends up in the urine.

f) You must look at Figure 19.7 to see how this works!

B. Countercurrent Multiplication

1. The descending loop of Henle is permeable to water, and does not transport Na⁺

2. The ascending loop of Henle is not permeable to water, but has active Na⁺ transport systems that can pump out Na⁺ against an osmotic pressure of 200 mosm/liter.

3. Na⁺ is pumped out of the ascending loop, which increases the osmolarity of the interstitial fluid, which causes water to passively leave the descending loop.

4. The water leaving the descending loop causes the fluid in the loop to increase in osmotic pressure; the water is absorbed by the vascular component surrounding the loop of Henle.

5. Net result: the fluid leaving the loop has an osmotic pressure of 100, and a concentration gradient from 300 to 1400 mosm/liter exists in the interstitial fluid of the renal medulla.

6. Urea is pumped out of the collecting duct and contributes to this concentration gradient

7. The vasa recta (the part of the vascular system around the Loop of Henle) also helps maintain this gradient by contributing ions and absorbing water.

C. Controlling Urine Concentration (Fig 19.10)

1. The collecting tubule runs through the concentration gradient as it heads toward renal pelvis

2. The distal and collecting tubules are impermeable to water, so the urine is hypotonic with an osmotic pressure of 100 mosm/liter. HOWEVER, in the presence of vasopressin (used to be called Anti-Diuretic Hormone) the distal and collecting tubules become permeable to water; the more vasopressin present, the more permeable these tubules become to water.

3. Vasopressin is produced by the hypothalamus, and stored in the posterior pituitary; the hypothalamus controls the release of vasopressin from the posterior pituitary.

4. Vasopressin activates a cAMP system in cells of late distal tubule and collecting ducts that causes more water channels to be inserted into basolateral membrane. (Fig 19.11)

a) If ECF is too concentrated (i.e. too many solutes and not enough solvent (water), vasopressin is released, and water diffuses out of distal and collecting tubules (and is picked up by the peritubular capillaries) which makes the urine less dilute and more concentrated.
b) If ECF is too dilute (i.e., not enough solutes and too much solvent (water), vasopressin is not released, water is not reabsorbed in the distal and collecting tubules, and the urine is dilute.
c) Range of urine concentration is 100 to 1400 mosm/liter
d) Note that urine production can not be completely halted, even when dying of thirst. Your body will use any available water to produce a very concentrated urine to get rid of wastes. When you die of thirst, you literally piss your life away.