Reabsorption and Secretion 1 and 2
Linda Costanzo, Ph.D.

OBJECTIVES:

After studying this lecture, the student should understand:

1. Definitions of reabsorption and secretion.
2. How to calculate filtered load, excretion rate, and reabsorption or secretion rate.
3. The glucose titration curve.
5. The pattern of urea transport along the nephron, and the relationship between urine flow rate and urea excretion.
6. The principle of non-ionic diffusion and its application to the excretion of weak acids and bases.

The nephron is lined by a single layer of epithelial cells that serve the functions of reabsorption and secretion. Reabsorption and secretion occur after filtration, modify the glomerular filtrate, and ultimately determine how much of each substance will be excreted in the urine. **Reabsorption** is the transport of a substance from the glomerular filtrate (or tubular fluid) into the peritubular capillary blood; in this way, a substance that was filtered is returned to the blood. **Secretion** is the transport of a substance from peritubular capillary blood into the tubular fluid.

Many substances are reabsorbed including: water, Na⁺, Cl⁻, HCO₃⁻, glucose, amino acids, Ca²⁺, phosphate, and urea. A few substances are secreted including: organic acids (e.g., PAH, salicylates), organic bases (e.g., morphine), H⁺, and K⁺.

Most transport processes involved in reabsorption and secretion are carrier-mediated and include: primary active transport, secondary active transport (cotransport and countertransport), and facilitated diffusion. A few substances are transported by simple diffusion (non-carrier-mediated). Water movement occurs by osmosis.
I. MEASUREMENT OF REABSORPTION AND SECRETION RATES

Figure 1. Processes of filtration, reabsorption, and secretion in a nephron. The sum of the three processes is excretion.

Filtered load \[= \text{GFR} \times [P]x \]

Excretion rate \[= V \times [U]x \]

Reabsorption or secretion rate \[= \text{Filtered load} - \text{excretion rate} \]

If the filtered load > excretion rate, there has been net reabsorption. If the filtered load < excretion rate, there has been net secretion. Units of filtered load, excretion rate, reabsorption or secretion rate are amount/time (e.g., mg/min, mmoles/min, mmoles/hour, mmoles/day)

**Note: for freely filtered substances, filtered load is calculated with the equation shown above. However, for substances bound to plasma proteins (i.e., not freely filtered), the filtered load calculation must be modified by the % free (unbound). For example, if a substance is 60% bound to plasma proteins (40% free), filtered load = GFR x total plasma concentration x 40%.
II. GLUCOSE REABSORPTION (Titration Curve) – Carrier Mediated, Cotransport

The cellular mechanism of glucose reabsorption is a Na⁺-glucose cotransporter in the luminal membrane of early proximal tubule. Glucose is freely filtered and, therefore the filtered load increases as the plasma glucose concentration increases. At low plasma glucose, all of the filtered glucose is reabsorbed and excretion is zero. At higher plasma glucose concentrations, the transporters for reabsorption become saturated and reabsorption levels off at the \( T_m \) level. Once there is saturation of reabsorption, any additional glucose filtered is excreted in the urine. **Threshold** is the point on the excretion curve where glucose first appears in the urine. Notice that threshold occurs at a lower plasma glucose concentration than does the \( T_m \), a phenomenon called **splay**. Splay occurs because of the low affinity of the Na⁺-glucose cotransporter and because of nephron heterogeneity (different nephrons have a different \( T_m \)).

Glucosuria (increased glucose in the urine) can occur in diabetes mellitus when an increased level of plasma glucose results in an increased filtered load that exceeds the reabsorptive capacity of the nephron. In pregnancy, glucosuria can occur because increased GFR leads to increased filtered load of glucose. In renal
**glucosuria**, there is a decreased $T_m$ due to decreased number or affinity of the Na'-glucose cotransporter (i.e., renal defect).

### III. PAH SECRETION (Titration Curve) – Carrier Mediated, Cotransport

![PAH Titration Curve](image)

**Figure 3.** PAH titration curve. PAH (para-aminohippuric acid) filtration, secretion, and excretion are shown as a function of plasma PAH concentration. $T_m$, Tubular transport maximum.

PAH is a prototype of a secreted substance. As with glucose, filtered load is linearly related to plasma concentration. Secretion is a carrier-mediated process in the proximal tubule, transporting PAH from peritubular capillary blood into tubular fluid (urine). At low plasma concentrations of PAH, secretion increases steeply with increasing concentration because plenty of carriers are available. As the concentration increases, the carriers saturate and reach $T_m$. Excretion is the sum of filtration and secretion; thus, excretion increases steeply at low plasma concentrations and then less steeply once secretion is saturated.

Think about the following question. To measure RPF with PAH, would you choose a plasma PAH concentration below $T_m$ or above $T_m$?

### IV. EXAMPLE OF UREA – Simple and Facilitated Diffusion

Urea is freely filtered across the glomerular capillaries, and then reabsorbed and secreted by the nephron by **passive** mechanisms (facilitated diffusion and simple
diffusion). Reabsorption of urea is greater than secretion, so there is net reabsorption (about 40% of the filtered urea is excreted in the urine). The sites for urea reabsorption are the proximal tubule and inner medullary collecting ducts. The site for urea secretion is the thin descending limb of Henle’s loop.

All urea transport in the nephron is passive. Whether reabsorption or secretion, urea is always moving down its concentration gradient. For urea transport to occur, there must be a concentration gradient and that portion of the nephron must be permeable to urea.

A. **Proximal tubule.** 50% of the filtered urea is reabsorbed in the proximal tubule by simple diffusion, down its concentration gradient. Where does this concentration gradient come from? The urea concentration in glomerular filtrate is identical to the urea concentration in blood (i.e., in Bowman’s space, there is no concentration gradient). As water is reabsorbed in the proximal tubule (the subject of later lectures), urea lags slightly behind, causing the urea concentration in the lumen to become slightly higher than the urea concentration in blood – this slightly higher luminal urea concentration becomes the driving force for urea reabsorption. The corollary is that the more proximal water reabsorption, the more urea reabsorption.

B. **Thin descending limb of Henle.** Because 50% of the filtered urea is reabsorbed in the proximal tubule, 50% remains in the lumen to enter the loop of Henle. Now, unexpected things happen. You will learn in later lectures that very high concentrations of urea are established in the interstitial fluid of the inner medulla (part of the corticopapillary osmotic gradient). The thin descending limbs of Henle pass through this high-urea region and, because they are urea-permeable, urea is secreted, down its concentration gradient, from the interstitial fluid and blood of that region into the nephron. More urea is secreted into thin descending limbs than was reabsorbed in the proximal tubule, and approximately 110% of the filtered load is now present in the lumen and enters the ascending limb of Henle’s loop.

C. **Thick ascending limb of Henle, distal tubule, cortical and outer medullary collecting ducts.** These segments are impermeable to urea, so no urea transport occurs. However, in the presence of ADH, water is reabsorbed in the late distal tubule and the cortical and outer medullary collecting ducts. If water is reabsorbed in these segments, urea is “left behind,” and the luminal urea concentration becomes very high (you will apply this fact in the next step).

D. **Inner medullary collecting ducts.** 110% of the filtered urea arrives at the inner medullary collecting ducts. Here, there is a specific transporter for facilitated diffusion of urea, UT1, that is turned on by ADH. In the
presence of ADH, urea is reabsorbed by the UT1, down its concentration gradient. About 70% of the filtered urea is reabsorbed, leaving 40% to be excreted. Urea that is reabsorbed by inner medullary collecting ducts in the presence of ADH, is added to the corticopapillary osmotic gradient in a process called urea recycling (i.e., urea that would otherwise have been excreted, is “recycled” into the corticopapillary gradient). In the absence of ADH, urea is not reabsorbed by inner medullary collecting ducts.

E. **Relationship between urine flow rate and urea excretion.** The higher the urine flow, the higher the urea excretion (see figure below). Why? Since all urea transport is passive, it depends on concentration difference. Therefore, urea reabsorption is related to water reabsorption as follows. Higher water reabsorption (lower urine flow rate) leaves more urea behind and creates higher luminal urea concentration, which drives higher urea reabsorption (lower urea excretion). Conversely, lower water reabsorption (higher urine flow) means less urea reabsorption (higher urea excretion).

![Figure 4](image_url)

V. **NON-IONIC DIFFUSION – Weak Acids and Bases**

Many substances secreted by the proximal tubule are weak acids (e.g., PAH, salicylic acid) or weak bases (e.g., quinine, morphine). Weak acids and bases exist in two forms, charged and uncharged, and the relative amount of each form depends on pH. **Weak acids** have an acid form, HA, and a conjugate base form, A\(^-\). At low pH, HA predominates; HA is uncharged. At high pH, A\(^-\) predominates; A\(^-\) is charged. For **weak bases**, the base form is B and the conjugate acid is BH\(^+\). At low pH, BH\(^+\) (charged) predominates; at high pH, B (uncharged) predominates.

With respect to renal excretion of weak acids and bases, the relevant points are: (1) relative amounts of charged and uncharged species in the urine vary with
urine pH, and (2) only the uncharged species (“non-ionic”) can diffuse across the cells.

A. **Weak acids.** To illustrate the role of non-ionic diffusion in excretion of weak acids, consider the example of salicylic acid. (For simplicity, we will call both forms, HA and A⁻, salicylate.) Like PAH, salicylate is filtered and then secreted by the organic acid secretory mechanism in proximal tubule. Consequently, the urine concentration of salicylate becomes higher than the blood concentration, and there is a concentration gradient across the cells. In urine, there is both the HA and A⁻ forms, but only HA (uncharged) can "back-diffuse" across the cells, from lumen to blood, down this concentration gradient. At **acid urine pH**, HA predominates, there is more “back-diffusion,” and the clearance of salicylate decreases (see figure below). At **alkaline urine pH**, A⁻ predominates, there is less “back-diffusion,” and the clearance of salicylate increases.

The principle is used for treating **aspirin overdose**. By intentionally alkalinizing the urine, more A⁻ is created in the urine, and total salicylate excretion is increased.

B. **Weak bases.** The effect of non-ionic diffusion on excretion of weak bases is the opposite. The weak base is filtered and secreted, causing a higher urine concentration than blood concentration. In the urine, there is both BH⁺ and B forms, but only B (uncharged) can back-diffuse across the cells, from lumen to blood, down this concentration gradient. At **alkaline urine pH**, B predominates, there is more back-diffusion from urine to blood, and the clearance of the weak base is decreased. At **acid urine pH**, BH⁺ predominates, there is less back-diffusion, and the clearance of weak base is increased.

![Figure 5](image)

VI. **PRACTICE QUESTIONS**

1. The plasma concentration of inulin is 2 mg/ml, the plasma concentration of X is 2 mg/ml, the urine concentration of inulin is 260 mg/ml, the urine
concentration of X is 120 mg/ml, and the urine flow rate is 1 ml/min. Is there net reabsorption or net secretion of X and what is the rate? (Assume that X is not protein-bound.)

2. Glomerular filtration rate is 110 ml/min. The plasma concentration of Y is 100 mg/ml and Y is 70% bound to plasma protein. Urinary excretion of Y is 4 g/min. Is there net reabsorption or secretion of Y and what is the rate?

3. In untreated type I diabetes mellitus, glucose is excreted in the urine. Based on the titration curve for glucose, how would you explain the glucosuria?

4. To measure renal plasma flow with the clearance of PAH, should the plasma concentration of PAH concentration be below the $T_m$ or above the $T_m$ for PAH secretion?

5. A person takes an overdose of morphine (a weak base). To increase the urinary excretion of morphine, would you acidify or alkalinize the urine?

ANSWERS

1. Net reabsorption of X; 140 mg/min
2. Hint non protein-bound or ultrafilterable concentration of Y in plasma is 30 mg/ml. Net secretion; 700 mg/min
3. Plasma glucose concentration is higher than the renal threshold for glucose excretion
4. Below $T_m$ (To measure RPF with clearance of PAH, renal vein PAH is assumed to be zero. For this to be true, or nearly true, all PAH in the RPF must be cleared by a combination of filtration and secretion, and secretion must not be saturated.)
5. Acidify the urine (Shift equilibrium toward increased BH$^+$ in urine, decreased B, less back-diffusion from urine to blood, increased excretion)