CLEARANCE AND REABSORPTION OF WATER*

I. Glomerular Filtration Rate and Renal Plasma Flow

A. It would be extremely useful for both practical and theoretical reasons to be able to estimate the amount of plasma that is filtered by the glomeruli. However, the actual volume of plasma that passes through the glomerular filter cannot be measured easily. So instead, we use a stand-in called the **GLOMERULAR FILTRATION RATE or *GFR***.

1. We will use the concept of clearance (see last packet) to estimate the *GFR*. As such, it is important to keep in mind that:

a. **we are <u>not</u> really measuring the actual amount of plasma that is filtered** because:

b. the clearance equation assumes that venous levels of some substance are at zero -- that is, it is entirely removed in the clearance process. The equation then calculates the minimum volume of plasma that would need to be processed to account fully for all of the substance that is found in the urine. Since we know that filtration does not remove all of a substance -- it cannot (see last class) -- then the *GFR* is a **virtual volume**. The *GFR* is not the actual volume of plasma that is filtered.

? Could the entire amount of any freely-filterable substance present in the plasma ever completely transferred from the plasma to the filtrate? (Assume that there is still plasma present in the efferent glomerular arteriole -- i.e., assume that not all of the plasma passes across the glomerular membrane.)

c. In fact, the *GFR* is **the <u>MINIMUM</u> AMOUNT OF PLASMA THAT WOULD NEED TO FLOW THROUGH THE GLOMERULUS TO ACCOUNT FOR ENTIRE AMOUNT OF A CERTAIN SUBSTANCE THAT WE FIND IN THE URINE**.

NOTE: Most clearances, like the *GFR* are VIRTUAL, NOT REAL VOLUMES. The only exception to this is the renal plasma flow (RPF) (see below).

2. <u>To estimate *GFR*,</u> we need to find a substance that is:

a. **FREELY FILTERED** (unlike some large molecules that are only partially filtered).

b. **NEITHER SECRETED NOR REABSORBED** -- that is, the only avenue for its appearance or removal from the urine is via filtration. Obviously, if there are other pathways, we are measuring the sum of several processes.

c. It must be **some substance that is NOT METABOLIZED or PRODUCED by the body**. Obviously, if either of these processes occurs between the time we give it to the subject and the time that it is removed, we will miss-estimate the clearance of the substance.

d. It must not be toxic.

3. The substance that is used to estimate clearance is **INULIN**, a large polysaccharide of fructose that is not normally found in animals. It occurs naturally in some plants, such as tubers of the Jerusalem artichoke and it is considered a diet food since it isn't metabolized. Look on the

filtration curve given on page 6 of the previous class notes (#25). Note that inulin is freely filtered.

4. Thus, we use the **CLEARANCE OF INULIN as our standard of the *GFR***.

5. We will sometimes refer to a *GFR* based on inulin as $\boldsymbol{GFR_{in}}$.

? If the volume of filtrate that is produced equals the volume of plasma that leaves the glomerulus, what proportion of the amount of the material that entered the glomerulus via the plasma has moved to the filtrate if the substance is freely filterable (such as inulin)?
What happens if less plasma leaves than filtrate? More?
What are the obvious problems with the clearance concept as it relates to *GFR*?

HINT -- for these problems and for the one given earlier, think about how a filter works in lab -- use saline as an example of something that is freely filterable. Assume that we fill the filter, let is work for a while and then remove the fluid that has not yet passed through the filter. That material (that did not filter) is the equivalent of the plasma in the efferent glomerular arteriole. By analogy, inulin is like the salt in the saline solution. Why?

3. The concept of **RENAL PLASMA FLOW**

a. The **renal plasma flow (*RPF*) is a measure of the total amount of plasma that flows through the glomeruli and the prox. and distal convoluted tubules**. (Note that most plasma flows through both, but some only flows through one or the other).

b. If we use a substance that, unlike inulin, is **COMPLETELY CLEARED**, we can measure renal plasma flow.

1. the clearance for such a substance is not a virtual volume of plasma but instead is actually the volume of plasma that is cleared (since the venous levels of this substance really are at zero).

2. A substance that meets these criteria and the others dealing with metabolism and toxicity (see the requirements for measuring GFR) is **PARA-AMINOHIPPURINC ACID or PAH**.

i. Any PAH that is not filtered is almost all secreted if the initial plasma concentrations are low.

ii. So, we can assume that it is completely cleared. Thus:

1. *RPF* = Clearance of PAH

? Would it be possible to estimate *RPF* accurately when the [PAH] is very high? Explain.

4. **Filtration Fraction**: We have established (I hope) that not all of a material is ever filtered by the kidney. We can define the amount that is actually filtered by the **Filtration Fraction (*FF*)** that is given mathematically as:

2. $FF = \dfrac{GFR}{RPF}$

? Typical *FF* values for inulin are 0.15 to 0.2. Explain the ramifications of this measurement.

? For any substance that is freely filtered and not reabsorbed or secreted, what will be the value of its clearance as compared to inulin?
What will be *FF* for such a substance as compared to that of inulin?

B. The use of the GFR_{in} to determine if a substance is filtered only, or filtered and secreted, or filtered and reabsorbed:

1. For any substance that is **freely filtered but that is not handled in any other way (such as inulin)**, its **Clearance should equal the GFR_{in}** (that is the clearance for the freely-filtered only substance inulin).

2. As we saw at the end of the notes for the last class, secretion and reabsorption both involve processes in addition to re-absorption.

a. In one case (**SECRETION**), additional substance is added to the filtrate and thus the total filtrate concentration of this substance is increased.

1. There are very few substances that are only secreted -- that is, there are few substances that are not filtered and only removed by secretion. Therefore, unless we know differently, we will always assume that something that is secreted has also been filtered.

2. **If a substance is both <u>freely</u>-filtered and also secreted, its clearance will be greater than the *GFR* (inulin clearance -- based entirely on filtering).**

b. In the other case, a substance is freely filtered and then **<u>REABSORBED</u>** from the filtrate.

1. Obviously, in this case, the Clearance for this substance will be less than the *GFR*.

2. Certain materials that are not freely filtered (such as proteins) will also give clearances that are less than the *GFR* -- knowledge of the expected filterability of the substance is obviously important.

c. In summary, if we know that a molecule is potentially freely-filterable, then the following relationships hold:

3. Clearance of X = GFR_{in} FILTERED ONLY

4. Clearance of X > GFR_{in} FILTERED AND SECRETED

5. Clearance of X < GFR_{in} FILTERED AND REABSORBED

? What should be the clearance of glucose at plasma concentrations that are below the T_m of glucose? (Give an exact value and rationale using the clearance equation). What will be the clearance of glucose above the T_m relative to the value for inulin?

D. Calculation of Tubular Reabsorption and Tubular Secretion:

1. The concept of **Filtered Load**: The amount of any substance that is filtered by the glomerulus per minute is called the filtered load. Mathematically it is given as:

6. Filtered Load = $GFR * P_a$

where P_a is the arterial plasma glucose concentration and Filtered Load is given as amount (usually mg) /min.

2. If a substance is also either secreted or reabsorbed, the amount of the substance in the urine will be changed.

? Glucose is freely filtered. Assume that C_{inulin} is 125 ml/min. and that the plasma glucose concentration is 100 mg/dl. What is the Filtered load for glucose?
In this same person, the $[glucose]_{urine}$ is 0 mg/ml. Describes the ways the kidney handles glucose.

E. Using Clearance to estimate the magnitude of transport for some substance; calculation of the renal blood flow.

1. We can write an equation that describes all avenues of movement of substance into or out of the urine:

7. Excretion = Filtered Load - Reabsorption + Secretion

Given this equation and the example above, what is the **apparent** rate of reabsorption of glucose?

2. **Renal Blood Flow (*RBF*)**: Up until now, we have only talked about plasma flow

? WHY

We can calculate the renal blood flow (RBF) by a very simple equation if we know the *RPF* and hematocrit:

8. $$RBF = \frac{RPF}{1 - hct}$$

II. The Mechanism by Which the Kidney Concentrates Urine.

A. Urine may be concentrated by two means:
1. Addition of solutes in the tubules
2. Removal of water from the prox. convol. tubules and collecting ducts.

Both mechanisms are important. However, we will concentrate on the removal of water since not only does a concentrated urine result, but we can also see how one part of the body's fluid balance regulatory system works.

The nephrons that are primarily involved in fluid balance are the juxtamedullary nephrons. In looking at fluid balance regulation, it will be important to look at what happens in all sections of the nephron that are after the glomerulus. We will be especially interested in the loop of Henle, the proximal convoluted tubule and the collecting duct.

B. OPERATION OF THE LOOP OF HENLE

1. The loop of Henle is largely responsible for producing a concentration gradient that runs from the boundary of the cortex and medulla to the pelvis (or papillary) region. In an individual who is not drinking tremendous volumes of fluids, this gradient will go from about 300 mOSM at the medullary/cortex border to 1200 mOSM at the papillary region. The question we now need to deal with is how this gradient is produced. We will approach this problem in terms of how such a gradient is (i) established and (ii) maintained.

2. The loop of Henle uses a **COUNTER-CURRENT MULTIPLIER** device to build the medullary concentration gradient.

a. The key of this device is that small constant increments of substances (such as Na^+) are added to the descending loop of Henle. As a result, concentration increases with each step of the descent towards the papillary region.

b. After the hairpin turn, substances are removed in the ascending loop. These same substances will diffuse back into the descending loop.

3. Let's see how it works:

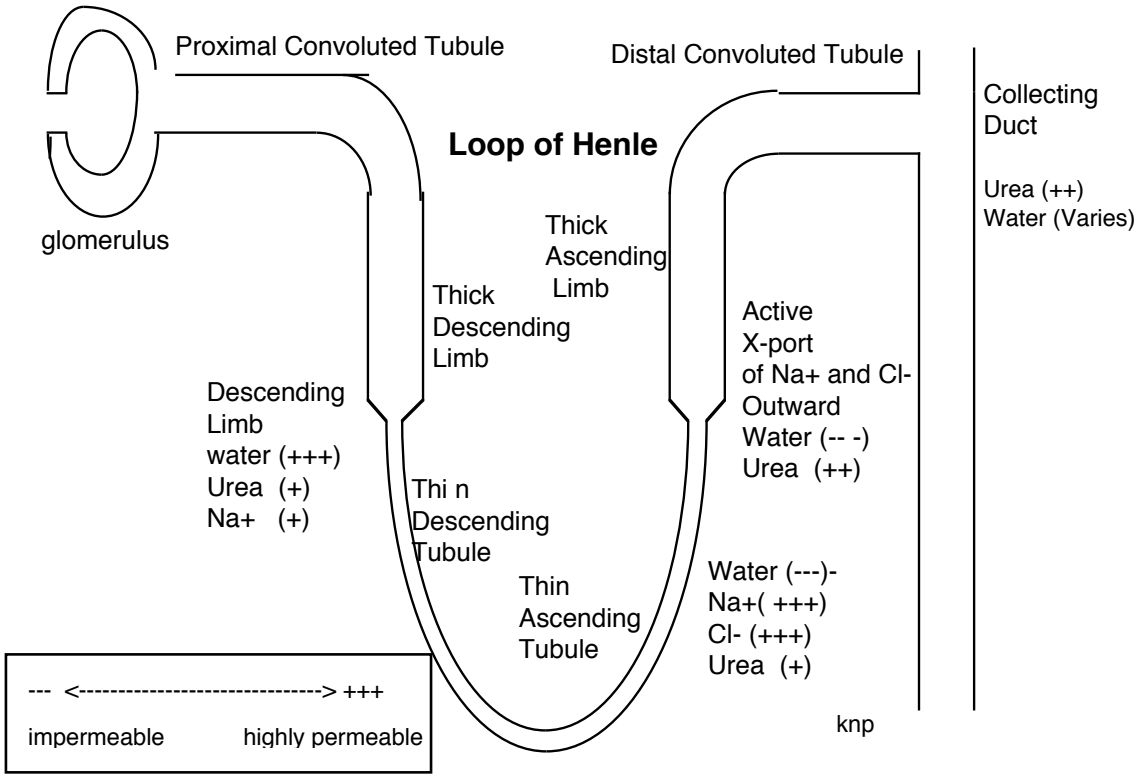
a. First, recall that:

1. The **descending limb** is highly permeable to water and less so to urea and Na^+.

2. The **Thin Ascending limb** is impermeable to water and is highly permeable to Na^+ and to Cl^- and is less so to urea.

4. The **Thick Ascending limb** is also impermeable to water, but it **actively transports NaCl** and is permeable to urea.

5. The **Collecting duct** has variable (hormonally regulated, see below) permeability to water and is permeable to urea.



b. Let's see how the medullary concentration gradient is established:

1. When fluid first enters the descending thin limb of the loop of Henle, it has a concentration that is iso-osmotic with the blood, its value is *ca* . 300 mOSM.

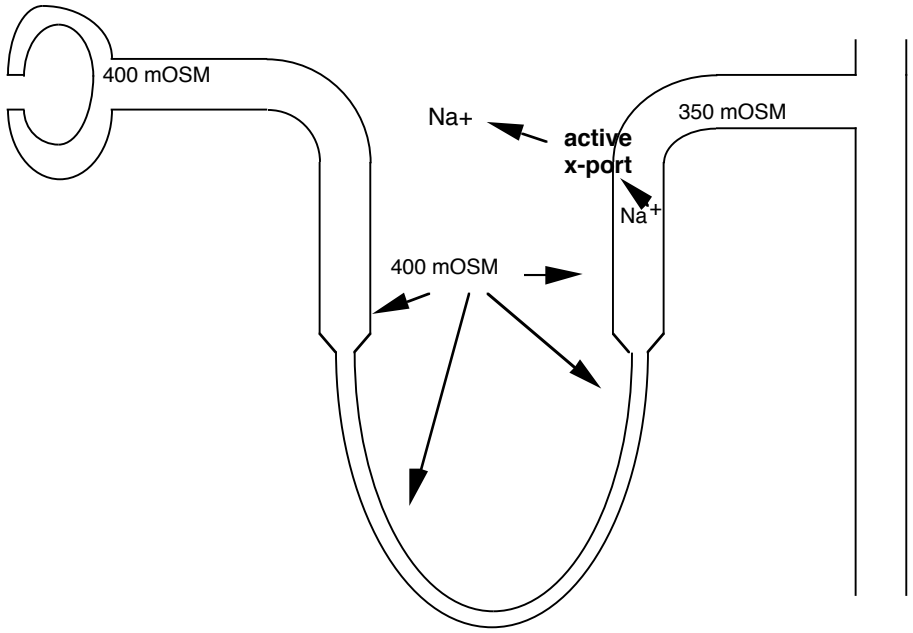
2. At the moment there is no medullary concentration gradient. Thus, no water leaves the descending limb nor does any urea or Na^+ enter.

3. Likewise, no net change in Na^+ or water occurs in the thin ascending limb.

4. However, **once the thick ascending limb is reached, Na^+ is actively transported out**

(a) **this Na^+ and accompanying Cl^- enters the medullary tissue.**

(b) Since the thick ascending limb is impermeable to water, the result is that the osmolarity within the tubule decreases (less Na^+ and Cl^- in the same volume). Thus, the picture looks like this:



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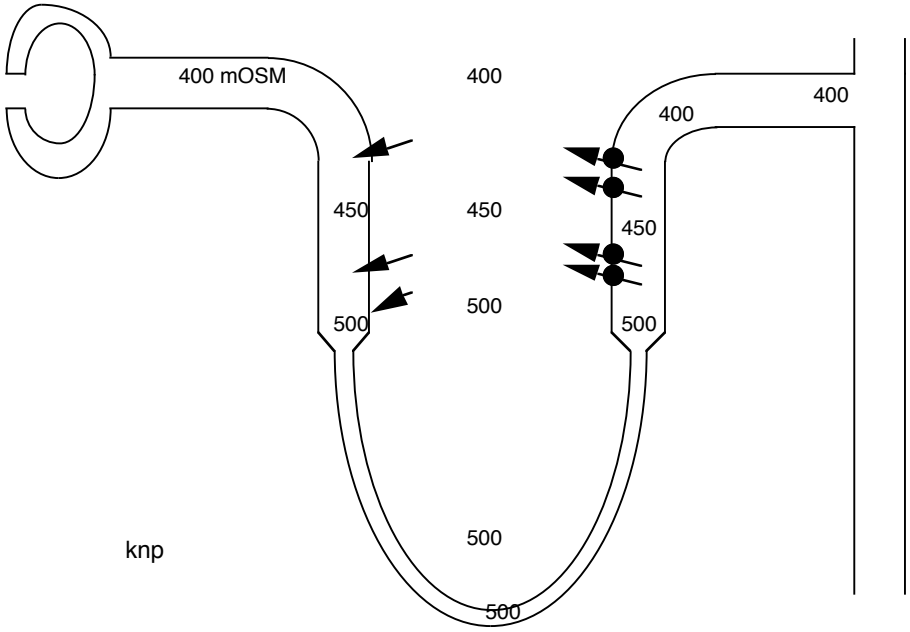
Na^+ is actively transported out of the thick ascending loop into the peritubular space, it can then diffuse back into the Desceding loop which is permeable to it. Notice that Cl^- follows the Na+ to maintain electroneutrality although in at least some cases it is the Cl^- that is transported and the Na^+ that follows passively. Also note that this entire schematic is to show how the gradient is produced -- normally the gradient is always present although it may change to some extent with changes in fluid balance.

5. Now, let's focus on the medullary tissues that surround the tubule. Due to active transport, the concentration of Na^+ and Cl^- are now higher than before the pumps were started up.

6. As a result, the medullary tissue now has [Na^+] and [Cl^-] greater than in the tubular fluid in the descending limb. And, for the same reason, the osmolarity of the medullary tissue is greater then the tubular fluid. The result is that Na^+ and Cl^- diffuse down their concentration gradients into the descending tubule. At the same time, some water

diffuses out. The result of both of these processes is that as the tubular fluid moves "down" the descending loop, its total osmotic concentration increases.

7. **<u>As the fluid moves up the thin ascending loop</u>**, not much happens when the gradient is initially being established. This is because, initially at least, the total osmotic concentration is heavily "layered" as a gradient that increases markedly. So after just a short time of operation, the system looks something like this:

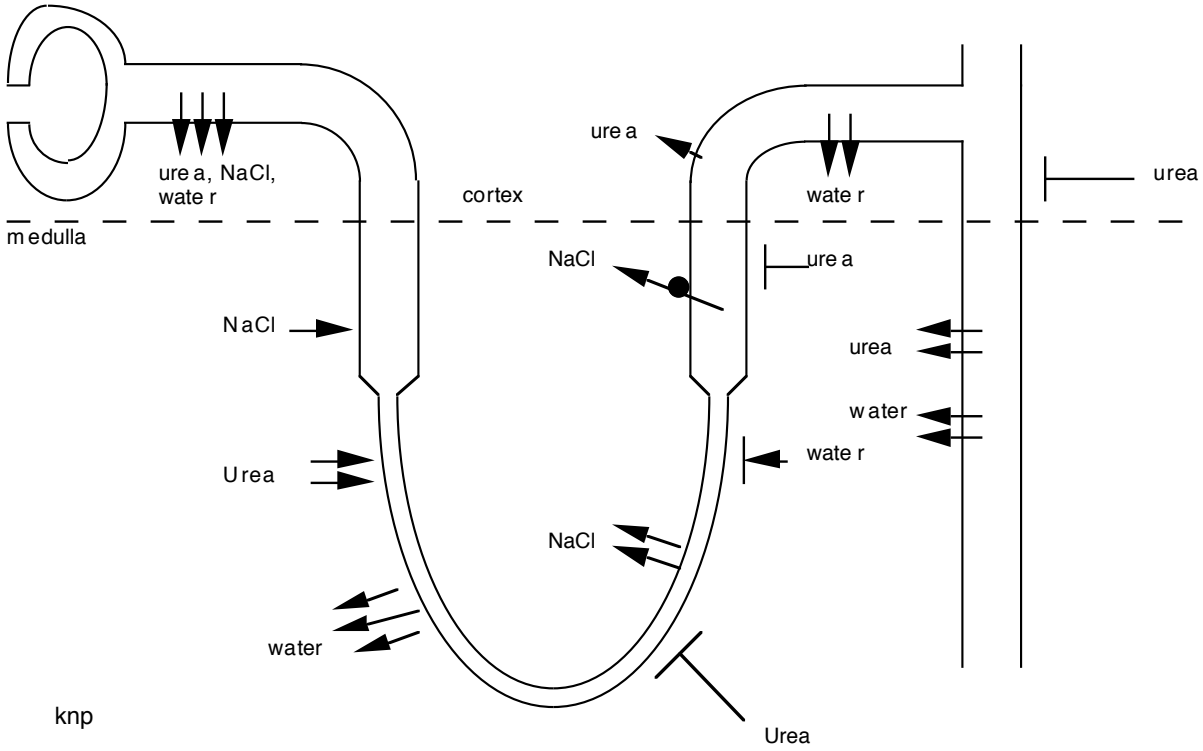


8. Once again, when the fluid reaches the thick ascending tubule, Na^+ is actively transported out and into the medullary tissues. This further raises the osmolarity of these tissues and maintains a concentration gradient for Na^+ entry into the descending loop.

Notice what is happening. Water is flowing through the tubule (only a small amount exits in the descending loop). Its ultimate source is the glomerulus. By contrast, some of the Na^+ and Cl^- flow straight through but some is removed from the tubular fluid in the ascending thick tubule and put back into the descending loop. Thus, this Na^+ can be envisioned as cycling back and forth and never getting out of the medulla. The maximum amount of Na^+ that can be transported (the capacity of the system) is determined by the number of pump molecules. Initially they are not saturated but as more and more Na^+ is "trapped" by this recycling process and as the $[Na^+]$ becomes greater, they become saturated. This helps to determine the ultimate greatest concentration found in the medullary gradient (see diagram on p. 9). The greater the capacity of the ascending thick limb to pump out Na^+, the greater the amount that can be "trapped" in the limb and the greater the concentration gradient.

9. As this process is continuously repeated, the gradient gradually increases by the processes mentioned above: Na^+ enters the thin descending tubule as water leaves, thus the concentration increases as the papilla (renal pelvis) is approached -- by contrast, as the fluid ascends the thin section, some Na^+ diffuses out as the medullary concentration decreases; a large amount of Na^+ is pumped out in the thick ascending tubule, further

decreasing the osmolarity of the tubular fluid. After a while, a steady-state is reached that will appear like this:



The arrows indicate the direction of movement and the number of arrows the extent of movement. Lines that end with perpendicular lines (-I) indicate no permeability in that particular region for a certain substance. The principle active transport site is for Na+ in the thick ascending loop; note that everywhere NaCl is indicated together in fact the transport is via separate channels and/or transporters. The dotted line indicates the approximate position of the cortex medulla boundary.
This figure is re-drawn from Berne and Levy, *Physiology*, Mosby 1983, fig. 47-8.

We'll consider what happens with the urea, which also follows a cycle, a bit later in these notes.

10. The result of the action of all of the gradients produced by the thousands of juxtamedullary nephrons is that an osmotic gradient exists from the cortex to the papillary region of the medulla. It is caused primarily the distribution of Na^+ Cl^-, and urea that was mentioned above. Active transport of Na^+ and differential permeabilities of all ions and water are the factors responsible for this gradient.

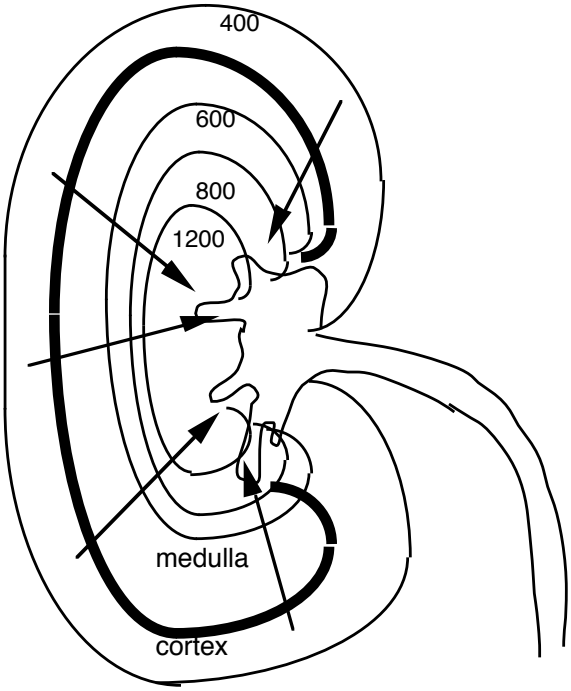
a. The size of this gradient (from the top to the bottom of the loop) is determined mainly by two factors:

1. The density of Na^+ transporters in the ascending tubule of the loop. The more, the greater the possible gradient.

2. The length of the ascending tubule: obviously, the longer, the more places for Na^+ transport to occur.

b. The system is maintained by the input of energy: active transport of Na^+ is required. Between the active transport of Na^+ in the ascending tubule and the other

active processes in the kidney, it is soon obvious why the kidney is one of the most metabolically active tissues in the body.



Lines within the medulla indicate a constantly increasing osmolarity of all tissues as one moves towards the renal pelvis.
The osmolarity inthe cortex is the same everywhere.
The arrows indicate the flow of the filtrate through the collecting ducts to the pelvis of the kidney. It is during this flow that the urine can be concentrated.

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Counter-current multipliers: many physiologists like to refer to the loop of Henle as a counter-current multiplier. Clearly, it is a counter-current system since the descending and ascending limbs pass near each other and the fluid flows in opposite directions. What about the multiplier part? Multiplication is repeated adding and that is exactly what this system does. By extracting Na^+ using active transport in the thick ascending segment, and then adding it to the descending limb and doing this repeatedly, the loop is performing a type of multiplication. Notice that unlike a counter-current exchanger (see respiration notes and see next section), the multiplier does not rely entirely on passive forces (beyond any active circulation) -- the counter-current multiplier requires active transport to build up a gradient.

11. **Blood Supply of the Medulla**: As was mentioned earlier, the living tissue in the medullary region is nourished by rather low flow using blood vessels that are called the ***vasa recta*** .

a. You might expect that any blood flow into the medulla would remove the gradient built up in the loops of Henle.

b. That would be the case if it were not for the fact that each vasa recta vessel acts as a **counter-current exchange**r (not multiplier). As the blood in each vessel moves down the medulla towards the renal pelvis, it becomes more concentrated since it is permeable to all ions and water. However, as it rises towards the cortex, the concentration decreases and salts flow back out and the water remains in. Thus, the vasa recta flow only makes a minor disturbance on the size of the gradient.

C. **Use of the Medullary Concentration Gradient to Remove Water**

1. We stated earlier that the purpose of the concentration gradient produced by the medullary counter-current multiplier was to concentrate urine. However, what we have seen so far instead suggests more of futile cycle. The only thing that has happened appears to be that we have created a Na^+, Cl^-, and urea merry-go-round that serves no obvious purpose. Overall, although the loop does remove some water and solutes (the tubular volume is somewhat reduced in the loop), this removal is not the major water conservation mechanism of the kidney.

2. **Fluid arriving at the Distal Convoluted Tubule**: Some additional water will be removed in the cortex/medullary border since the fluid that arrives there from the ascending thick segment is HYPO-OSMOTIC to the cortical tissue. Recall that this is because Na^+ and Cl^- were removed in the thick segment. Moreover, this part of the tubule is not water permeable.

3. **The distal convoluted tubules (DCT)**: more about this area in a moment but suffice it to say for now that:

a. further transport of Na^+ out may occur here. This movement is typically balanced by movement of K^+ into the tubular fluid (a Na^+/K^+ pump is involved; this operation is under the control of the hormone **aldosterone**. More about it shortly.

b. The DCTs are also water permeable. To the extent that fluid arriving there might be somewhat hypo-osmotic, water is lost.

c. As a consequence, the concentration of urea in the tubular fluid increases to a level greater than the surrounding tissues. Some of this urea diffuses out (down its concentration gradients) and it may re-enter the tubule eventually at on the descending loop (thereby also helping to build the gradient). enters

4. **The Collecting Ducts** (CD, collecting tubules):

a. Next, the tubular fluid flows from where the collecting ducts start (at the cortical-medullary boundary) "down" to the pelvis of the kidney. In the process, it passes through the entire concentration gradient created by the loops of Henle (see top of the previous page).

b. Let's assume that the **collecting ducts are very water permeable**. (*We will see in a moment that t**heir permeability varies***):

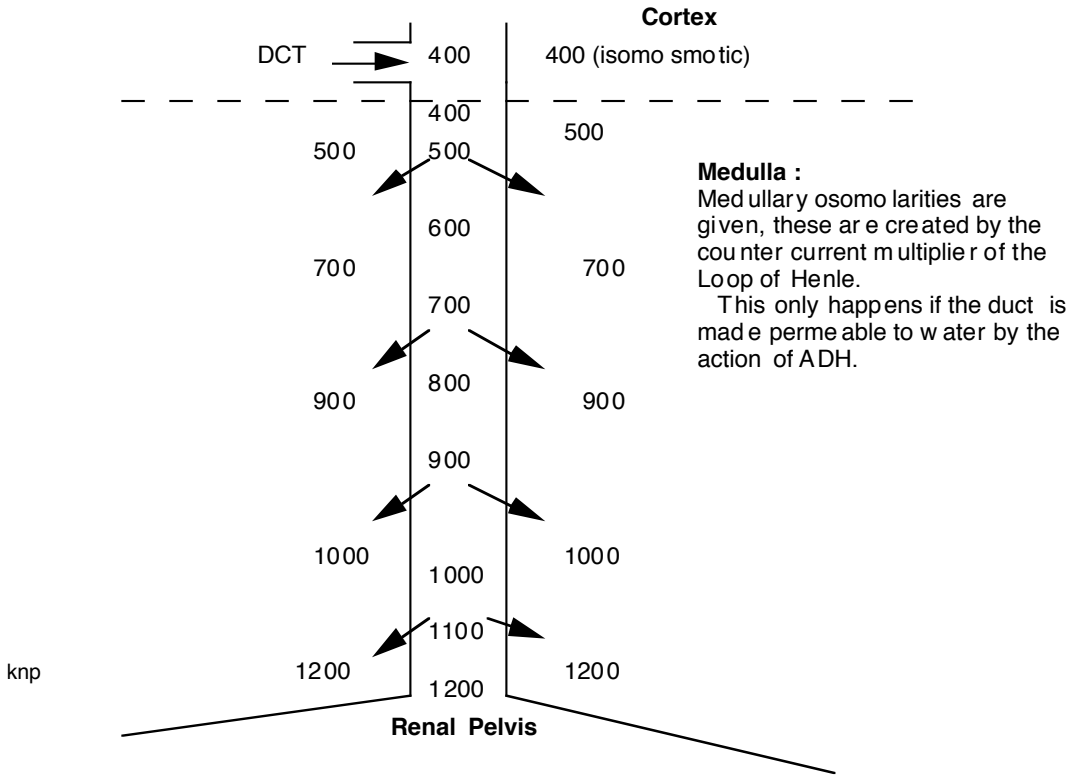
1. Recall that at the top of the CD, the conc. of the tubular fluid and the surrounding tissues are the same -- i.e., they are essentially iso-osmotic.

2. As the tubular fluid starts to descend towards the kidney's pelvis, it is surrounded by tissue that is HYPEROSMOTIC with respect to it.

3. As a result, water leaves the CD (in response to the osmotic gradient). The circulation carries this water away. The fluid remaining in the tubule is now higher in overall osmotic concentration.

4. However, as it falls towards the pelvis of the kidney, it encounters tissues that are even more concentrated. Thus, a gradient that favors the movement of water from the tubule to the surrounding tissues and blood stream is maintained and water continues to flow out.

5. The net result of all of this is that the urine volume is greatly reduced, water is conserved for the body and the concentration of solutes in the urine is increased.



During the same process, urea becomes more concentrated as water leaves. The result is that urea begins to diffuse out of the CD fluid into the medullary tissues and eventually into the descending loop of Henle (recall that they are permeable to urea). Thus, the urea circulates between the CD/DCT and the descending loop. Furthermore, notice that as urea leaves, this makes the CD fluid more dilute than it would be otherwise and thus allows more water to be reabsorbed. Finally, note that this "urea cycling" will have its largest effect (most urea cycled) if the CD tubules are permeable to water. If they are not (see next section) urea cycling is not nearly as important of a process.

III. ENDOCRINE CONTROL OF FLUID AND ION BALANCE

A. Variables in the regulation of fluid and ion balance:

1. The extra-cellular fluid's composition has a profound effect on the conditions within all cells, besides on conditions of certain extra-cellular systems such as blood pressure. The **solute in the ECF at greatest concentration is NaCl**.

2. Regulated variables:

a. **Osmolarity.** This is one of those global variables, like *p*H, that affects every cell and the function of many proteins.

b. Osmolarity is closely tied to other variables, including **blood pressure, blood volume**, and **NaCl delivery to certain parts of the glomerulus**. Regulation of one of these variables will tend to affect the others.

3. **Receptors** used to sense the conditions of the ECF.

a. **STRETCH RECEPTORS**. As volume, pressure, or osmolarity changes, the degree of stretch of these receptors change and a signal is generated by associated neurons. These receptors fall into two different groups that are distinguished according to whether or not low or high pressures/volumes excite them.

1. **Low Pressure Baroreceptors --** these become more active as pressures drop below critical values. A good example is associated with the pulmonary vasculature (associated with converting enzyme in the renin-angiotensin system (see below)).

2. **High Pressure Baroreceptors:** these respond more and more as pressures become high. Examples are in the aortic arch, carotid sinus, and afferent arterioles of the glomerulus, and in the atria of the heart (atrial naturitic factor).

b. In addition, there are also specialized cells located in the hypothalamus known as **OSMORECEPTORS** that will respond to as little as a 1% change in plasma osmolarity.

c. All of these sensors are ultimately linked to a number of different neuronal or hormonal systems that control the ECF.

B. Water Conservation and Anti-Diuretic Hormone

1. In response to high osmolarity, low ECF volume, and/or low blood pressure, **ANTI-DIURETIC HORMONE (ADH) or VASOPRESSIN** is released. This is a small peptide, nine amino acids long, that is produced in specialized cells in the hypothalamus near the baroreceptors and then moves to and is released from the posterior pituitary.

a. A **DIURETIC** is something that causes increased loss of water (i.e., copious dilute urine).

b. Anti-diuretic Hormone is therefore a hormone that stops diuresis. When a lot of vasopressin is released, a small volume of relatively highly concentrated urine is formed.

c. The mechanism of **ADH** is simple: it **increases the permeability of the collecting tubule walls to water**.

1. Thus, water can easily leave the tubules and urine is concentrated.

2. By contrast, if little ADH is being secreted, the tubules are relatively impermeable to water and the urine is dilute. It should be mentioned that ADH also causes an increase in the rate of active re-absorption of Na^+ and urea permeability of the thick ascending limb, thereby further increasing the medullary concentration gradient.

d. Thus, in situations where water needs to be retained (such as high osmolarity, low pressure or low volume), ADH is released and more water is reabsorbed from the collecting ducts. The medullary concentration gradient makes this possible. If permeability is high, as the urine moves down the collecting duct through the medulla, it equilibrates to the increasing concentration by losing water.

B. Regulation of Total Blood Volume via Ion Balance:

1. The ADH system is obviously very important in maintaining proper amounts of water in the body. It works by regulation of the re-absorption of water. It is also a very fast-acting system.

2. Equally important are 3 longer-term regulators of total ionic balance. All are especially concerned with Na^+.

a. ALDOSTERONE: this is a type **MINERALO-CORTICOID**, that is, a steroid hormone from the adrenal cortex that influences ionic balance.

1. Aldosterone is released in response to low [Na^+] or low total fluid volume.

2. It acts on the cells of the **distal convoluted tubules** to cause greater uptake of Na^+ from the tubular fluid. The re-absorbed Na^+ goes back into the blood. In the process, **K^+ is traded for Na^+** and the K^+ is eliminated while Na^+ is conserved.

i. Like all steroids, aldosterone acts by binding to a cytoplasmic receptor found in its target cells and then this complex acts as a transcription factor that increases the expression of certain proteins (for example, Na^+ /K= pumps).

ii. The result is increased mitochondrial development and more proteins for the transport of Na^+ out of the tubules.

iii. The additional Na^+ in the blood will indirectly cause more water to be retained. This produces an increased tissue and blood fluid volume and raises the blood pressure.

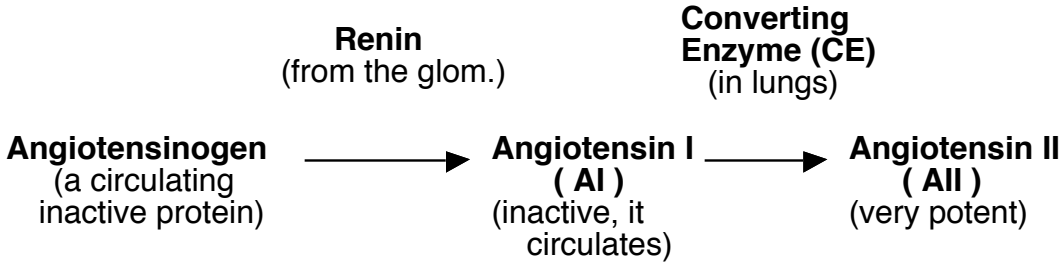
? Why does an increased blood volume raise BP?
? Why is mitochondrial development increased?

b. **RENIN-ANGIOTENSIN SYSTEM**: This system is rather complex.

1. **RENIN** is an enzyme that is released by the specialized glomerular cells in response to low glomerular blood flow, low plasma Na^+, low BP, or low blood volume (these are all obviously related).

2. Renin works on a circulating protein called **ANGIOTENSINOGEN**, which it converts to **ANGIOTENSIN I (also called AI)**.

3. In the lungs, AI is converted by a substance called **CONVERTING ENZYME** to **ANGIOTENSIN II (also called AII).** AII is the active enzyme in the system.



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Note that angiotensinogen, although having the -ogen ending typical of zymogen forms of enzymes, is not an enzyme. It is simply an inactive form of AI -- waiting in the blood to be activated when needed. In this sense, it is like some clotting factors in the blood.

d. **Actions of Angiotensin II:**

1. Constriction of the pre-glomerular capillary
2. Increased release of ADH
3. Increased release of aldosterone
4. Inhibition of atrial natriuretic hormone (see below).

All of these factors will result in an expansion of the blood volume

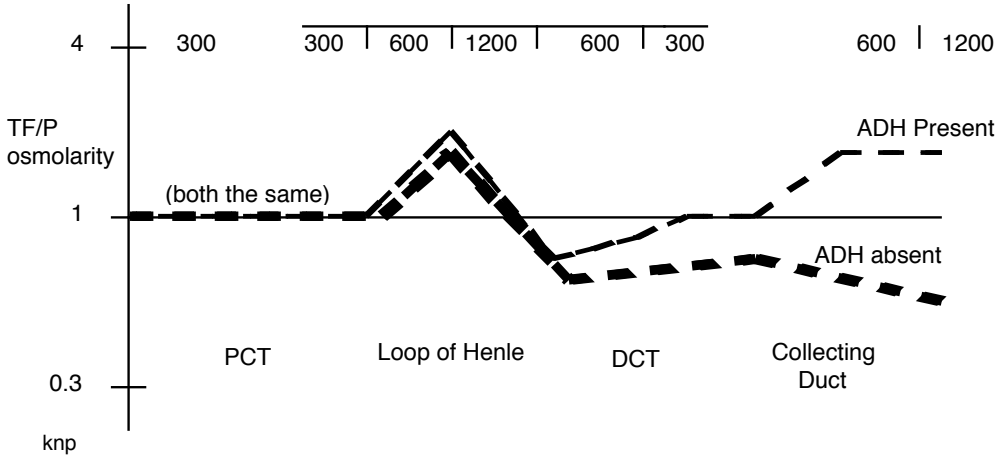
c. . **ATRIAL NATRIURETIC PEPTIDE**: this peptide is produced by certain modified myocardial cells in the atria in response to high levels of stretch (high blood pressure).

1. it tends to cause the **INCREASED LOSS OF Na^+**.
2. Thus, it works to **reduce blood volume and blood pressure**.

Final note*: This discussion of the kidney and its regulating hormones has been simplified considerably over what actually happens*.

Review:

1. *Be able to explain the graph below. As part of that explanation, know where tubular volume is reduced, where different substances are added or removed and be able to explain why the ADH present and absent graphs are different***.**



The osmolarity of tubular fluid (TF) compared to plasma (P) in different parts of the nephron as a function of the presence or absence of ADH (vasopressin).

Note that through the PCT the two concentrations (TF and P) are the same, TF increases in the descending portion of the loop and then decreases in the ascending loop (see notes). Notice that ADH affects concentrations in the DCT and CD although the cells of the CD are the most influenced targets of its action (see notes). Notice that the effect of ADH is to cause the urine to become concentrated over what it would be in the absence of ADH.

(Redrawn from Berne and Levy, *Physiology*, Mosby 1983, fig 45-7

2. *Why is a nephron filter used instead of a series of active transport systems to remove only what isn't needed?*