

# Urine Concentration and Dilution

For the cells in the body to function properly they must be working in the optimal environment. This includes a correct and optimal fluid osmolarity, which is the concentration of electrolytes and other solutes in the plasma. This is sometimes referred to as the water balance, since, to a large extent, extracellular fluid sodium concentration and osmolarity are regulated by the amount of extracellular water.

The kidneys are the body's primary tool to maintain its water balance. They can/will preserve or excrete water based on the osmolarity in the body. By concentrating the ultrafiltrate in the tubular system (and thereby concentrating the urine) the body will excrete less water and by diluting the ultrafiltrate the body will excrete more water. This enables the body to maintain a very exact osmolarity at all time.

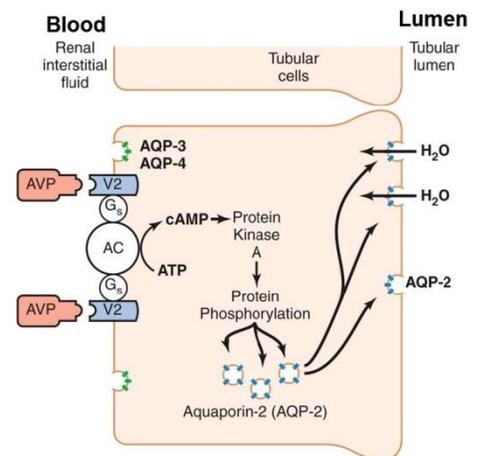
Normal body osmolarity is approximately 300 mOsm/L. The kidney has an ability to vary this tubular osmolarity (urine osmolarity) between 50-1200 mOsm/L. The body utilizes two different mechanisms to maintain an optimal osmolarity in the blood: ADH (anti-diuretic-hormone) and countercurrent multiplier mechanism.

## ADH

ADH will alter the permeability of the membrane in the distal tubule and collecting duct by inserting aquaporin-2 channels.

ADH binds to specific V2 receptors, which increases the formation of cAMP and activates protein kinase A. This causes a protein phosphorylation, which leads to insertion of aquaporin-2 channels. An aquaporin-2 channel is an intracellular protein placed on the luminal (toward tubule) side of the cell membrane. This protein acts as a channel allowing water to move from tubule into the cell.

The above action of ADH enables water to be reabsorbed, hence the name anti-diuretic-hormone. This mechanism can add up to 600 mOsm/L to the interstitial fluid osmolarity; about half of what the body is able to produce. The other half comes from the countercurrent multiplier mechanism.



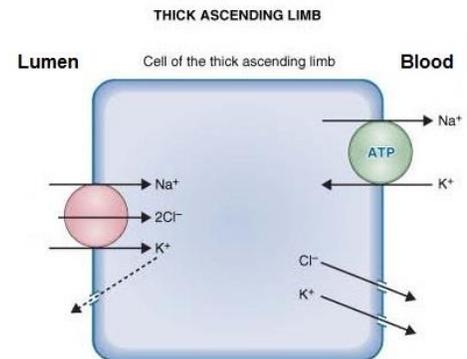
## Countercurrent Multiplication Mechanism

The countercurrent multiplication mechanism is actually a two-step process. Through repeating these two steps the kidney builds up the gradient seen in the loop of Henley.

## First Step or Single Effect

The first step in the process takes place in the thick ascending tubule, where the  $\text{Na}^+\text{-K}^+\text{-2Cl}^-$  transporter moves sodium from the tubule into the interstitial space. The process is by co-transport and the needed gradient is supplied by the  $\text{Na}^+\text{-K}^+\text{-ATPase}$  located in the basolateral membrane (remember, this is on the blood side of the cell, opposite the tubular [lumen] side of the cell).

In the thick ascending tubule, the loop's membrane is NOT permeable to water. In this part of the loop of Henle there are no aquaporin channels and the tight junctions between the epithelial cells that make up the membrane are no longer permeable for water (they are now really tight).

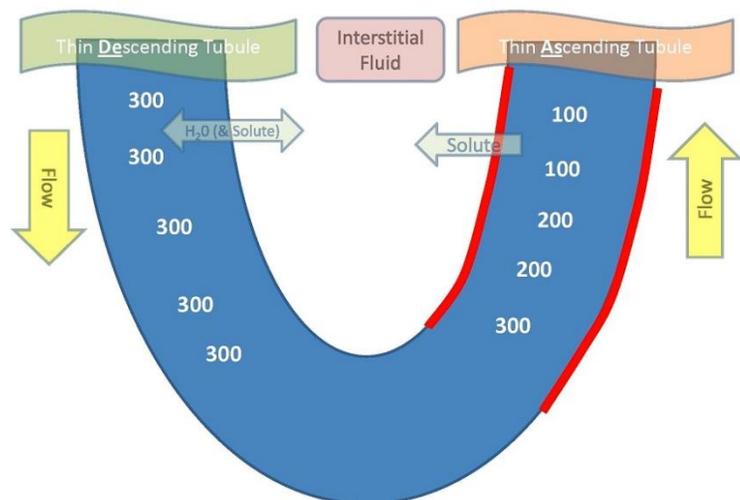


When  $\text{Na}^+$  is transported out of the tubule into the interstitial tissue without water following the osmolarity will increase in the interstitial tissue. Interestingly, ADH will increase the activity of the  $\text{Na}^+\text{-K}^+\text{-2Cl}^-$  transporter and therefore enhance the effect of this process. Remember, the amount of ADH goes up when the body osmolarity goes up in order to preserve water.

## Second Step or Continual Flow of Fluid Through the Tubule

Obviously, I'm describing a hypothetical situation with fluid being static in the tubule and let it be known that there is a continuous flow of fluid through the tubular system at all time. In order to explain what is happening it is necessary to view the process in this hypothetical step-wise manner.

With the flow being a continuous flow it is obvious that more ultrafiltrate with an osmolarity of 300 mOsm/L will enter the descending part of the loop of Henley thereby pushing the now hyperosmolar tubular fluid ahead of it.



In the interstitial fluid a gradient will start to build due to the differences in membrane permeability between the descending and ascending part of the tubule.

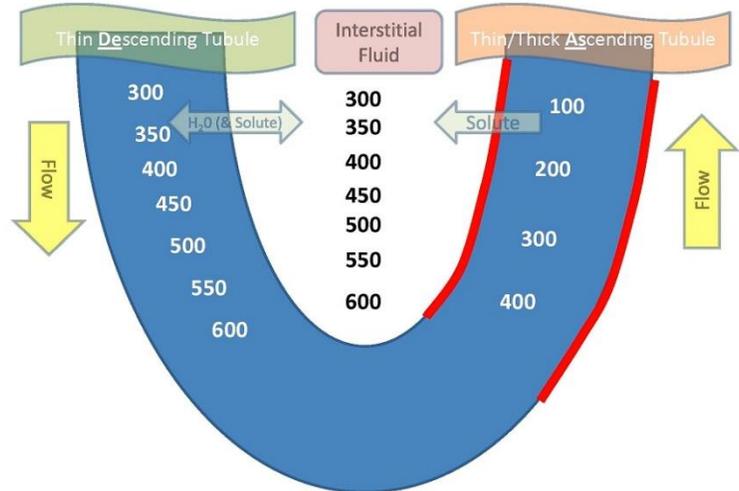
### Third Step or Multiplication

When you repeat step one and step two continuously it becomes clear that a gradient will form in the interstitial tissue compartment. As shown each repeat of the two steps increases, or multiplies, the gradient.

The size of the corticopapillary osmotic gradient depends on the length of the loop of Henley, which is why the medullary nephrons, although fewer, are the "heavy lifters" among the kidney nephrons.

This two-step process establishes the corticopapillary osmotic gradient.

Two special features of the renal medullary blood flow contribute to the preservation of this concentration gradient: low medullary blood flow and the vasa recta.



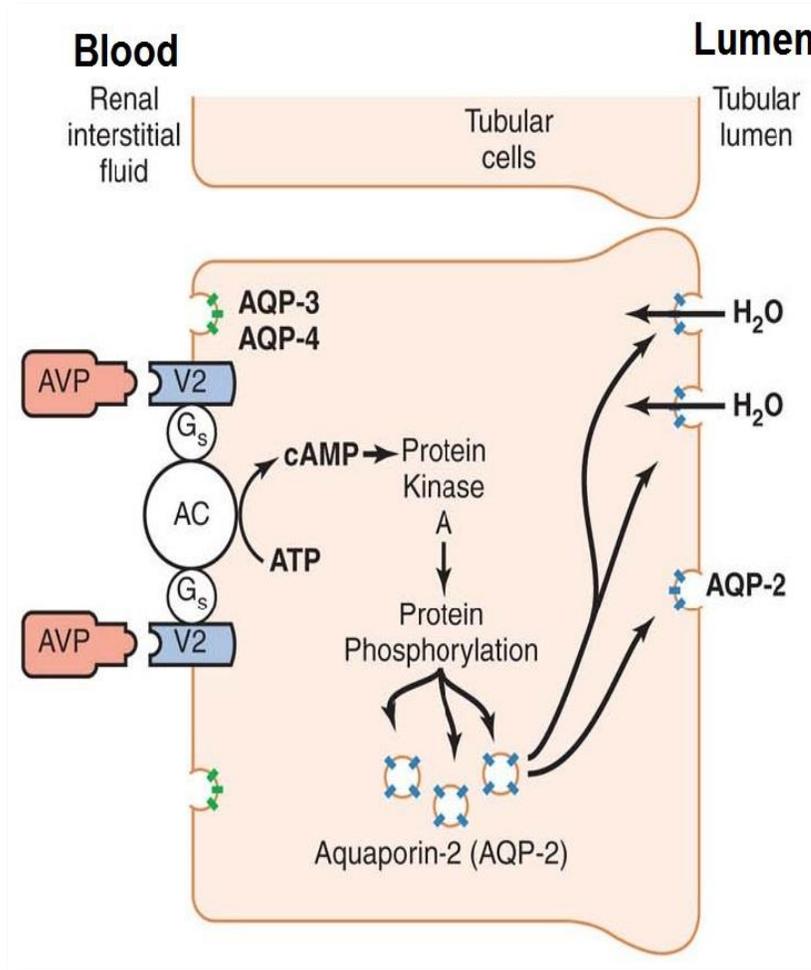
### Vasa Recta

Vasa recta branches off the efferent arteriole and surround the loop of Henley in its entirety. It provides blood flow to the medulla and papilla. Vasa recta is a capillary blood system and as such the exchange taking place across the membranes is purely passive.

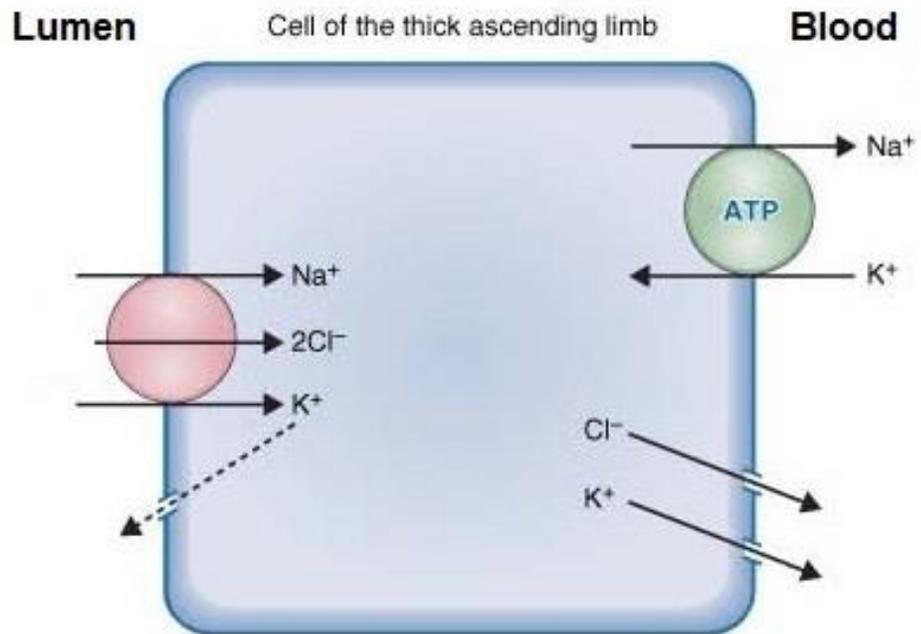
The other purpose of the vasa recta is to help maintain the corticopapillary osmotic gradient established by the countercurrent multiplication.

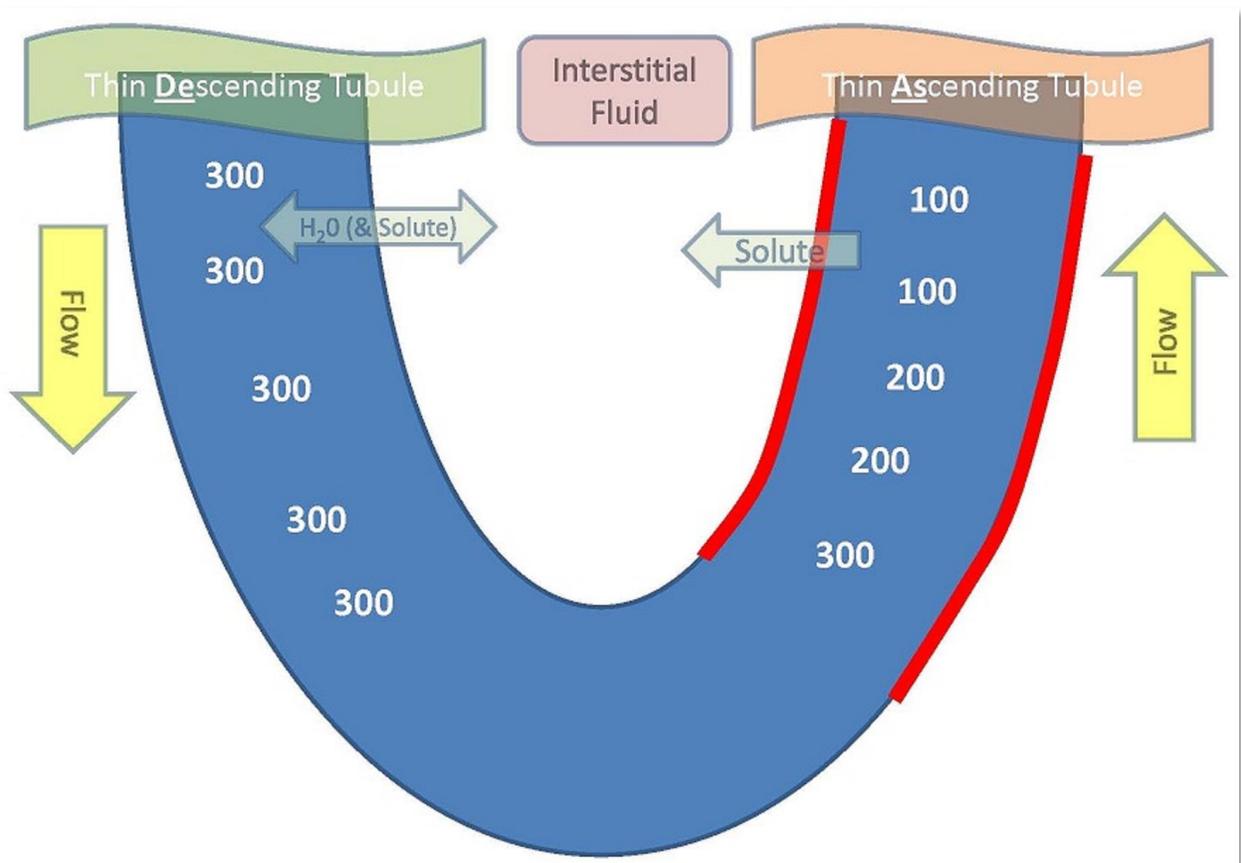
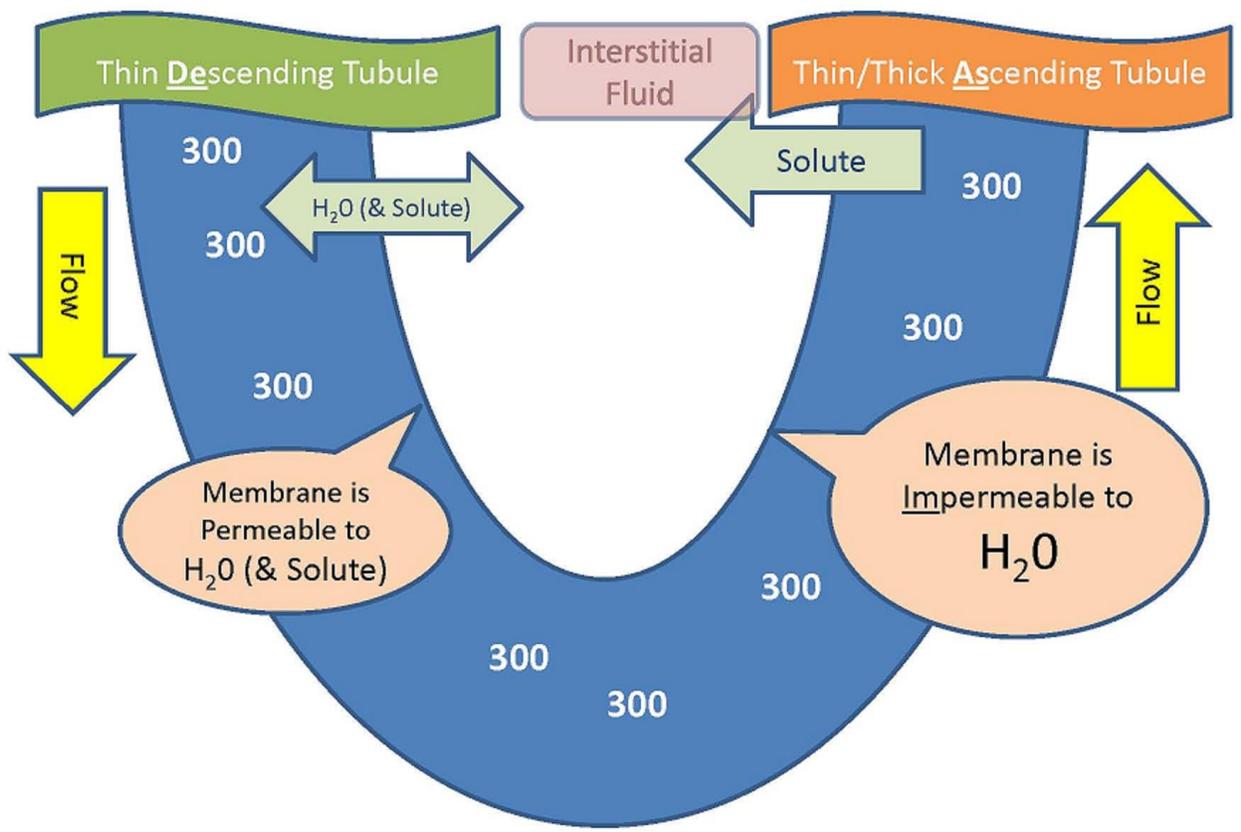
Vasa recta is highly permeable to solutes in the blood. As blood slowly descends into the medulla toward the papillae, it becomes progressively more concentrated, partly by solute entry from the interstitium and partly by loss of water into the interstitium. By the time the blood reaches the tips of the vasa recta, it has a concentration equal to the surrounding interstitial fluid, which would be about 1200 mOsm/L. As the blood ascends toward the cortex (afferent arteriole) it becomes progressively less concentrated as solutes diffuse back out into the medullary interstitium and as water moves into the vasa recta. This exchange of solutes and water is called the countercurrent exchange (not to be confused with the countercurrent multiplication).

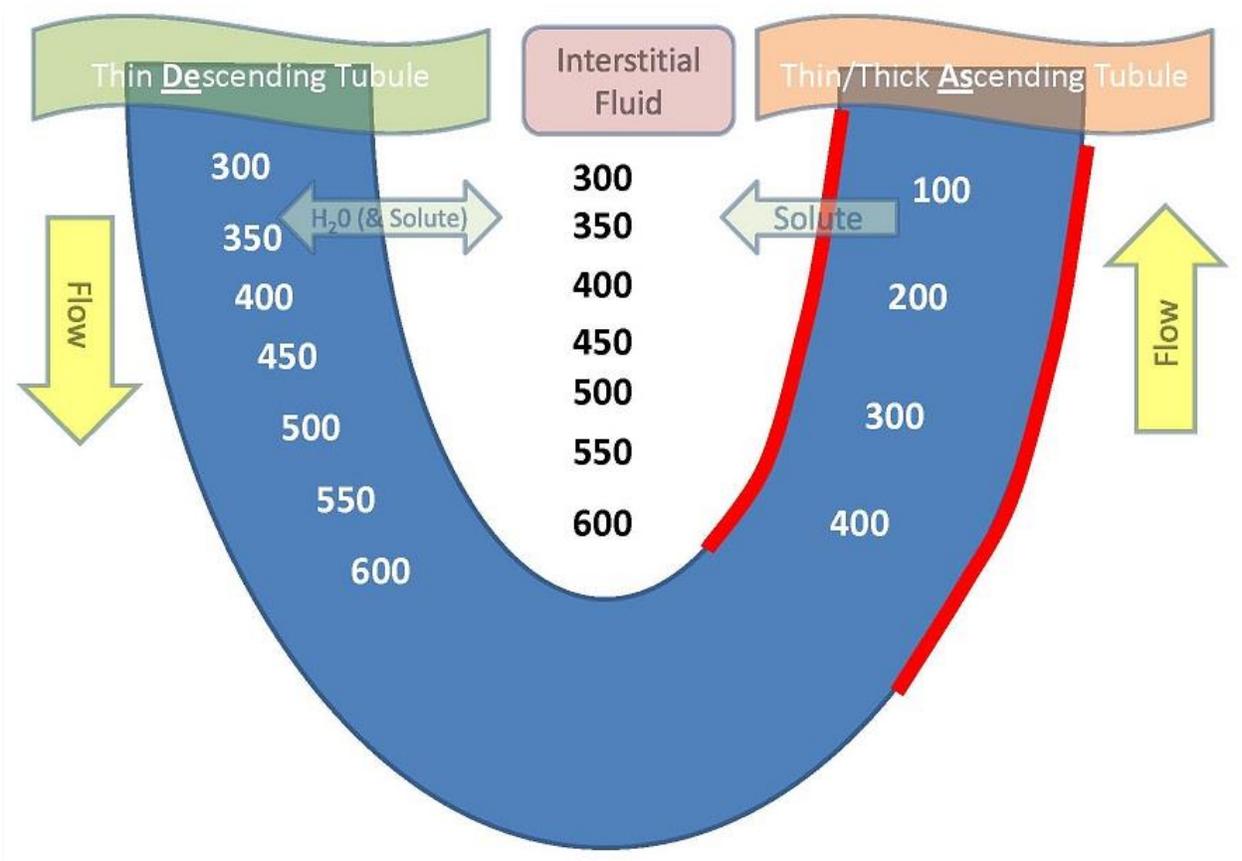
Blood leaving the vasa recta is actually slightly more concentrated (325 mOsm/L) than the blood entering vasa recta. Some of the solute from the corticopapillary osmotic gradient was picked up and will be carried back to the systemic circulation. The gradient will not dissipate, which would seem to occur with a higher concentration leaving vasa recta, because the mechanisms of countercurrent multiplication and urea recycling (ADH) continuously replace any solute lost.



### THICK ASCENDING LIMB







## References

### Textbooks

Costanzo LS. (2009) Physiology 4<sup>th</sup> Ed. Philadelphia: Saunders

Guyton & Hall (2011) Textbook of Medical Physiology 12<sup>th</sup> Ed. Philadelphia: Saunders

### Pictures

Costanzo LS. (2009) Physiology 4<sup>th</sup> Ed. Philadelphia: Saunders

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