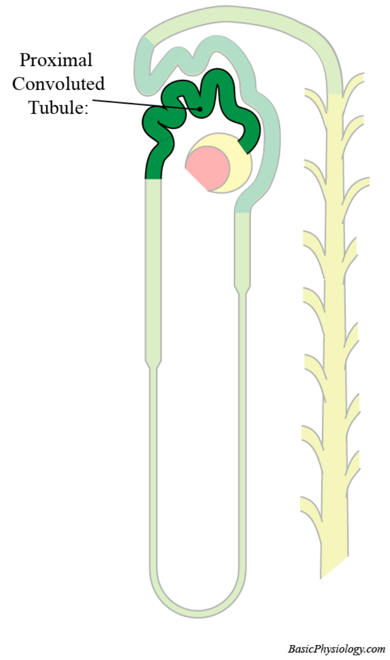
F.3.3. The Proximal Convoluted Tubule

A. Introduction:

1.
Now that a HUGE amount of pre-urine has been filtrated from the blood in Bowman's capsule (120 ml/min = 7.2 litre/hour = 173 l/day!), what is going to happen to all that fluid?

2.
This is the task of the rest of the nephron and is determined by the function of:
1) the proximal convoluted tubule
2) the loop of Henle
3) the distal convoluted tubule
4) and the collecting ducts.

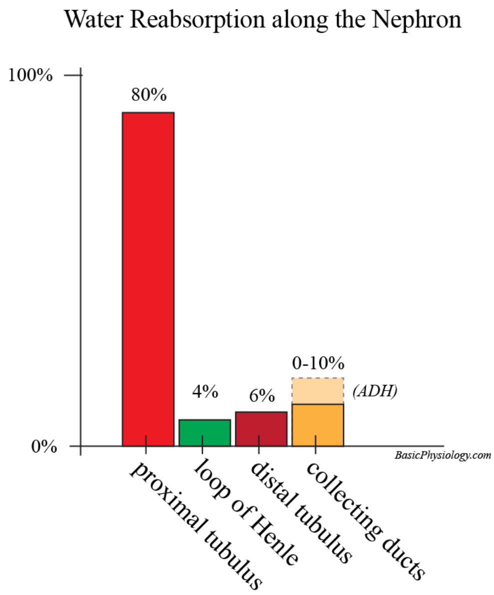
3.
In general, two things will happen:
a. **Re-absorption**: most of the water and solutes will flow back from the filtrate to the blood.
b. **Secretion**: there will also be some secretion of specific solutes, from the blood, into the pro-urine.



B. Re-absorption of water:

1.
The major task of the **proximal** convoluted tubule is to transport most of the water back to the blood.

2.
In fact, as you can see in this graph, 80% of all the water reabsorption takes place in the proximal convoluted tubule while the remainder 20% is re-absorbed by the other parts of the nephron.



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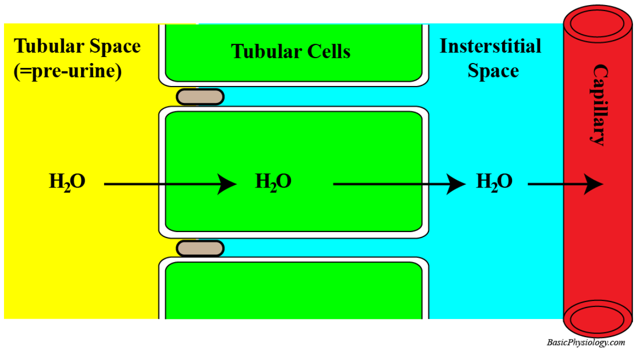
<td>3.
This huge water transport takes place from the tubular space, through the tubular cells, to the interstitial space and then, through the capillary walls, back into the blood stream.</td>
<td colspan="2">
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<td>4.
This water transport is dictated by the osmotic pressure differences in all these spaces.</td>
<td>5.
This is determined, at the same time, by an active reabsorption of many solutes in the pre-urine to the blood that ‘sucks’ the water with it.</td>
<td>6.
That is why we need to discuss in more details the transport mechanisms in the proximal tubule.</td>
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C. Re-absorption of solutes:

<table>
<tr>
<td>1.
This is a fairly complicated process that takes place, in different ways and degrees along the tubular system and the collecting ducts.</td>
<td>2.
There are two pathways for the re-absorption of water and solute:
a. through the cells bordering the tubule; the transcellular route
b. through the gaps between these border cells; the paracellular route.</td>
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<td>3.
The transcellular route means that the transport has to cross the luminal cell membrane to get into the cell and then has to travel through the cell and then has to cross the basolateral membrane at the other side of the cell to get out of it.</td>
<td>4.
The paracellular route looks simpler but can be hindered by the tight junctions that couple the cells to each other.</td>
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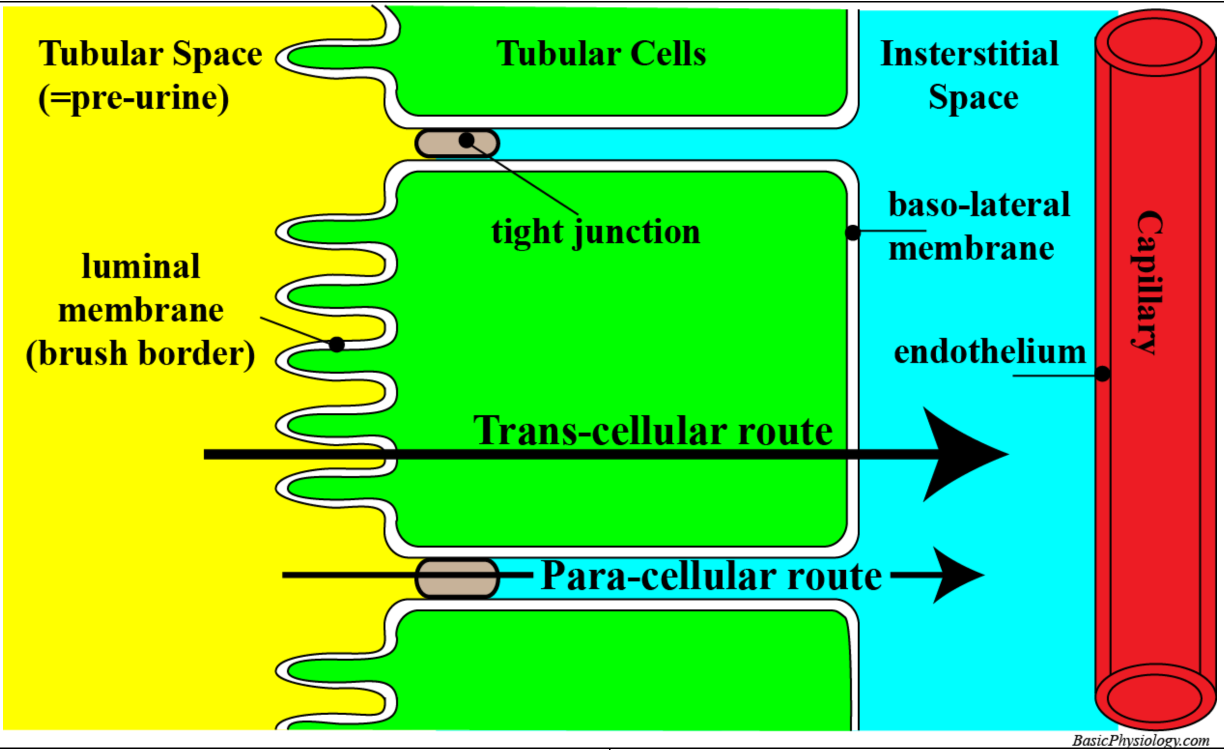


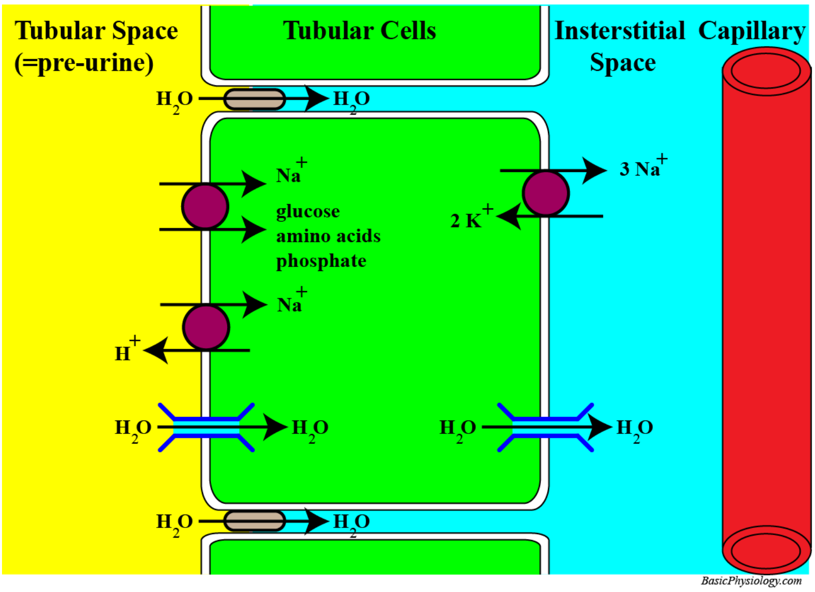
5. In some areas of the tubule, as in the proximal tubule, the tight junctions are very permeable to water. However, in other areas, such as in the thin part of the loop of Henle, the tight junctions are very 'tight' and pretty impermeable to water (*see later*).	6. Once water and solutes have successfully passed the tubular cell, or the tight junctions, they find themselves in the **interstitial** space on the other side of the tubular cell and now have to cross the capillary membrane to get 'back' into the **plasma**.

Link: F6. Loop of Henle

D. The Transcellular Route:

1. The most important route is the **transcellular** route (through the cell).	2. For this system we need a series of active **transporters** both at the luminal membrane and the baso-lateral membrane:
3. **The sodium-potassium pump:** This pump is well known in many places in the body (in nerves and muscles for example). In the kidney tubule, it is located at the basolateral membrane and interacts with the interstitial fluid. And, as everywhere else in the body, it pumps 3 sodium ions out of the cell in exchange for 2 potassium ions into the cell.	4. **The co-transporters:** There are also many co-transporters active in the tubular cells. A few examples are those transporting glucose, phosphate and amino acids. A sodium ion travels together with these substances into the cell.
5. **Counter-transporters:**	6. **Water channels:**

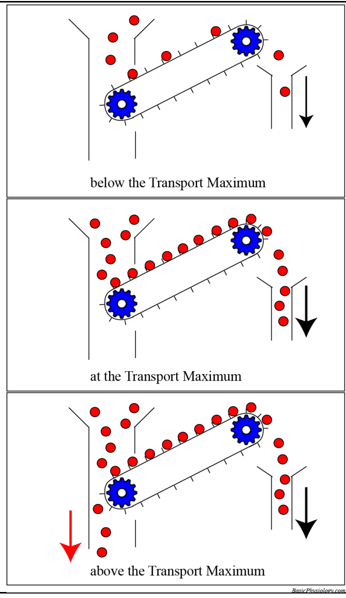
There are also transporters that exchange one solute for the other. In this case, sodium ions are exchanged for hydrogen ions.	In addition, as more solutes gets into the cell, the osmotic pressure will increase, which in turn will attract water to flow through the water channels from the tubular space into the cell.



7. And, as the solutes are pumped out of the cell, through the basolateral membrane into the interstitial space, water will follow them too.	8. In effect, as you can expect, water follows the pathway created by the solutes. This is how, in the proximal tubule, 70-80% of the water is reabsorbed.

E. Transport Maximum:

1. Since all these solutes are transported, through the cell and its cell membranes, by some type of (co-) transporter, there could be a situation in which the transporters are working at full capacity and are therefore saturated.	2. Then, if more solutes became available, the transporter would not be able to transport these extra solutes from the pre-urine towards the capillaries.
3. A classic example of such a situation is the transport of **glucose**.	
4. Normally all glucose gets filtrated in the glomeruli, flows into the proximal tubules where it gets transported back to the blood.	

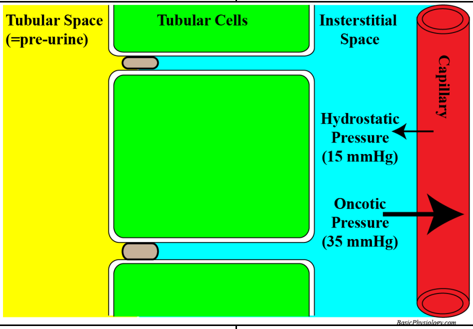
5. Normally **ALL** glucose goes back to the blood.	
6. But in diabetes for example, there is sometimes more glucose in the blood than normal.	
7. If this concentration is too high, then the transport maximum for glucose is reached.	8. Then, some glucose will NOT be reabsorbed and this will then appear in the urine! This is a very important tool to **diagnose** diabetes!

F. The Paracellular Route:

1. This transport pathway goes between the tubular cells and through the tight junctions.	2. In the proximal convoluted tubule, the tight junctions are very permeable to water and to small ions (calcium etc.). Driven by the osmotic differences induced by the transcellular route, a lot of water is 'sucked' from the tubular space to the interstitial space through the paracellular route.
3. Obviously, there is no active transport along this route! (*There are no membranes stupid!)*	

G. Peritubular capillaries:

1. Once the water and its solutes have reached the interstitial space, they now need to flow into the peritubular capillaries.	2. This works (again!) with the laws of the **Starling exchange system**. Remember? (*link*).
3. Also remember that the blood that flows in these peritubular capillaries has already gone through the glomeruli.	4. There, in the glomeruli, they have lost a lot of water and solutes, except for the proteins (which were not filtered).
5. So, in the plasma in the peritubular capillaries, there are a lot of proteins whereas	6. In addition, the blood pressure (also called the **hydrostatic pressure**) has decreased because

in the interstitial fluid there is little or none. This will create a strong **oncotic pressure.**	of flow resistance in the glomeruli and in the efferent arteriole.
	
7. These two forces, the oncotic pressure and the hydrostatic pressure, oppose each other.	8 But the ‘sucking’ oncotic pressure (35 mmHg) is much higher than the weak hydrostatic pressure (15 mmHg).
9. Therefore, there is a strong inward force to ‘suck’ the water, with its solutes, from the interstitial space back into the plasma and the blood.	10. You may remember, in the capillaries in normal tissues, that something similar also happened, which, at the end of the capillaries, created a **net negative pressure**.
11. In the peritubular capillaries in the kidneys, the net filtration pressure **is negative along its whole length!**	12. This therefore leads to a large re-absorption of water and solutes back into the blood.

H. Tubular Secretion:

1. Hey! The tubular cells also transport stuff the other way; from blood to the pre-urine! This is the opposite direction of reabsorption; i.e. **secretion**!	2. Again, this secretion requires active transporters but these transport in the opposite direction, from the interstitial fluid to the pre-urine in the tubular space.
3. The major components that are excreted are stuff that the body wants to get rid of, such as bile salts, uric acid and keto-acids.	4. These transporters are not very specific so they can also transport and secrete molecules that are not common (“exogenous”) in our body (exogenous = produced outside our body).

5. Examples of such 'exogenous chemicals' are drugs such as penicillin, but also dangerous chemicals such as toxins.	6. Please note that there is also a transport maximum for this type of secretion. If there is too much of something, it will not get transported; in this case to the urine i.e., it will remain in the body.

I. Regional differences in reabsorption and regulation:

1. The proximal convoluted tubule reabsorbs the largest amount of water and solutes from the pre-urine.	2. This consists of 70-80% H_2O, 60-70% sodium, all the glucose and amino acid molecules and much more.
3. The rest of the reabsorption is performed in different ways and to different degrees by the other parts of the tubular system.	4. After the proximal convoluted tubule, the distal convoluted tubule is the next important part.
5. This will be discussed in F.3.4. Distal Convoluted Tubule.	6. But first, the pre-urine flows into the Loop of Henle! (*next page*).

J. At the end of the proximal tubule, what has been reabsorbed?

1. Just to show how important the function of the proximal tubule is, I have listed all the components that are being reabsorbed in this proximal tubule.	
2. **Compounds**: • Amino acids • Glucose • Lactate • Proteins • Urea • Uric acid • Vitamins	3. **Ions**: • Na^+ • K^+ • Ca^{2+} • Mg^{2+} • Cl^- • HCO^{3-}
4. And finally (and most importantly): **H_2O (water!)** *lots of it*	