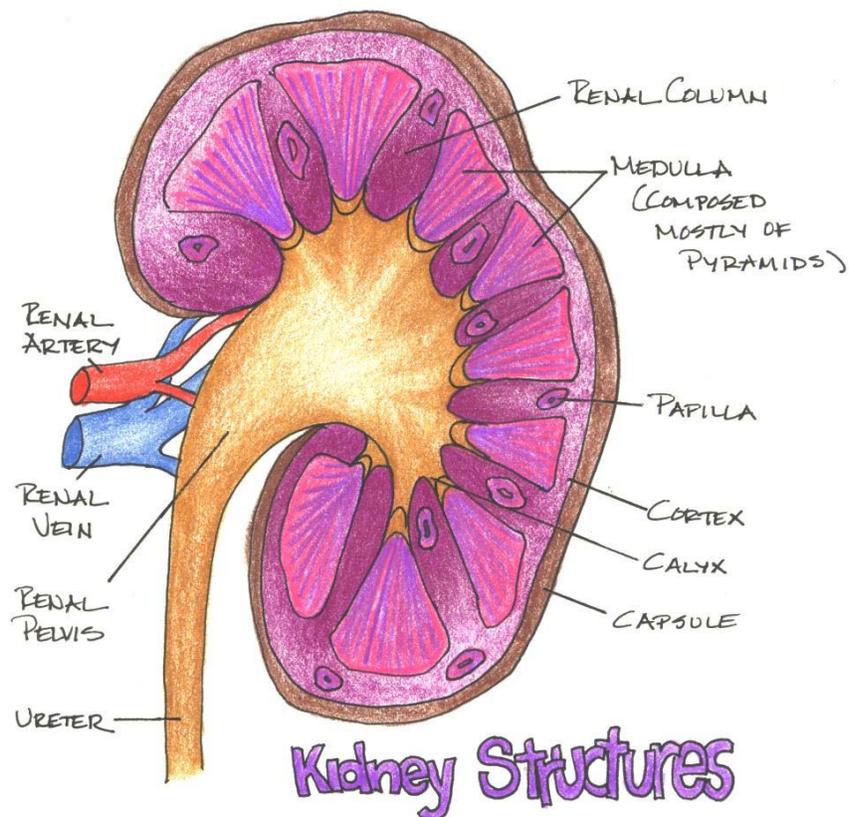


## Kidneys, Nephrons, and Urine Production

Part of the urinary system, our kidneys are vital organs that serve to remove waste from the bloodstream through ultrafiltration and the formation of urine, and to aide the body in maintaining proper hydration through a process called osmoregulation. Situated to the back of the abdominal wall, the kidneys are snugged up underneath the diaphragm, behind the liver on one side and the stomach on the other, partially shielded in the back by the 'floating' ribs.

Figure 1 illustrates the basic structure of a human kidney:

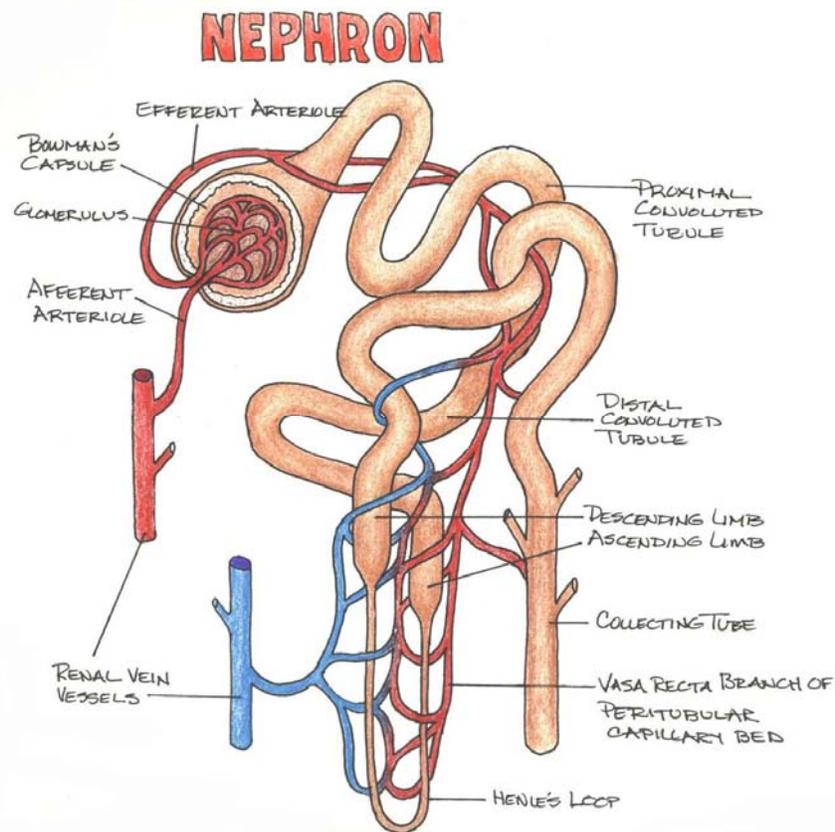


**Figure 1: Basic Kidney Structure**

Structures called nephrons residing in the cortex and medulla produce urine from filtrate removed from the bloodstream, passing it to the bladder via a series of collecting tubules that

continuously merge, ultimately reaching the renal pelvis and finally the ureter. The question is, “Exactly how is urine produced?” It can hardly pass into the bladder until it actually exists. In order to understand that process, we have to take a deeper look into the structure of the kidney – specifically looking to the nephron and the renal vessels, since this is where waste products leave the blood and enter kidney tissue.

There are about one million nephrons in a kidney, each feeding into a nest of collecting ducts. A nephron is a rather intricate structure and it serves two basic purposes: to filter and remove waste products and maintain the body’s water supply. At one end of the nephron, residing in the cortex, is an approximately 0.2mm diameter structure known as the Malpighian Corpuscle,<sup>1</sup> and about 3.0cm away at the other end, a collecting duct. A complicated array of blood vessels intertwine this structure. Figure 2 shows the basic organization of a nephron:

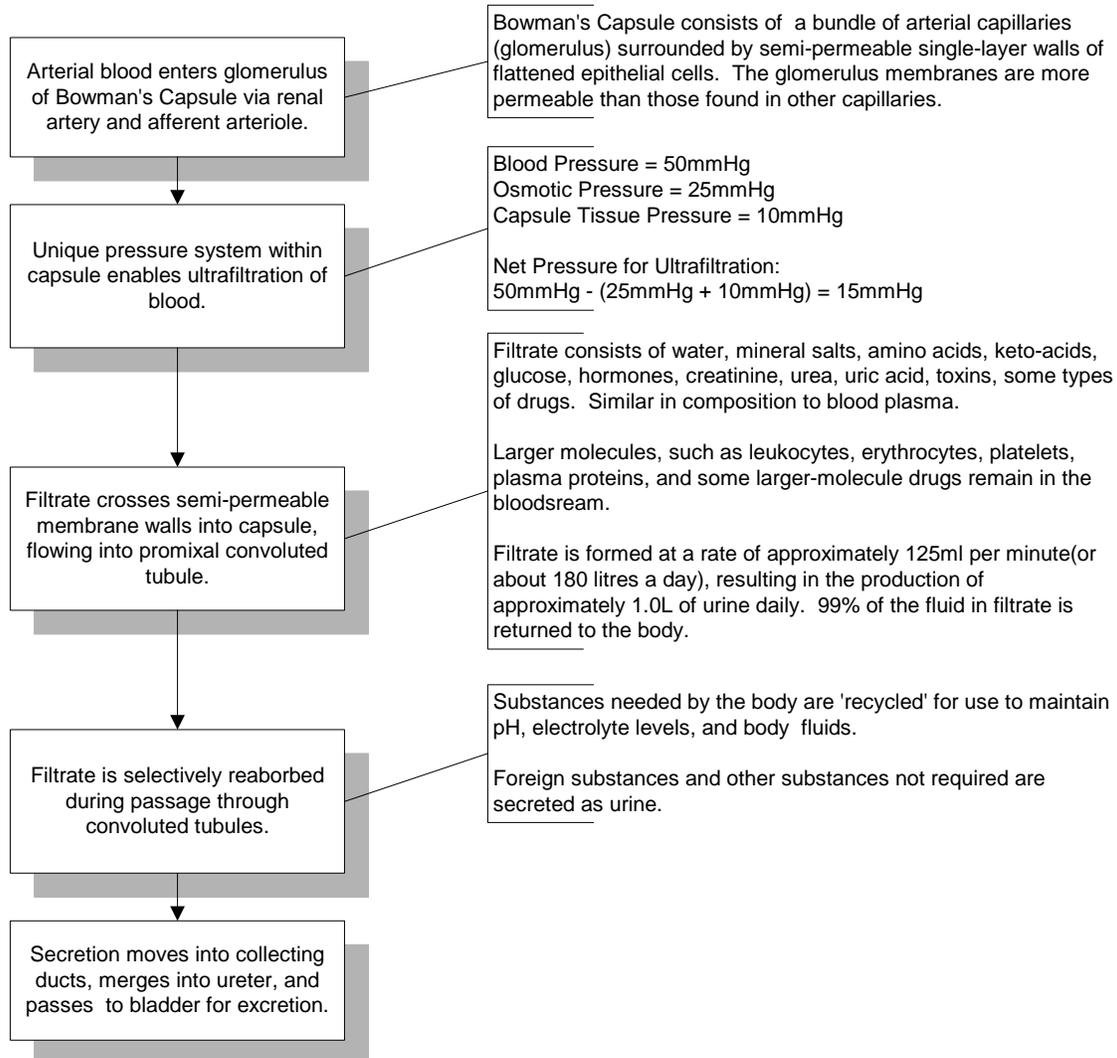


**Figure 2: Kidney Nephron**

<sup>1</sup> <http://www.thefreedictionary.com/>, Malpighian Corpuscle: 1. A mass of arterial capillaries enveloped in a capsule and attached to a tubule in the kidney. Also called *Malpighian body*, *renal corpuscle*; after Marcello Malpighi. This is considered the ‘closed’ or ‘blind’ end of a nephron.

Osmoregulation and the production of urine literally keeps the entire organism properly 'afloat.' Without correct kidney function, the human body would collapse quite quickly into a highly toxic and unstable state.<sup>2</sup>

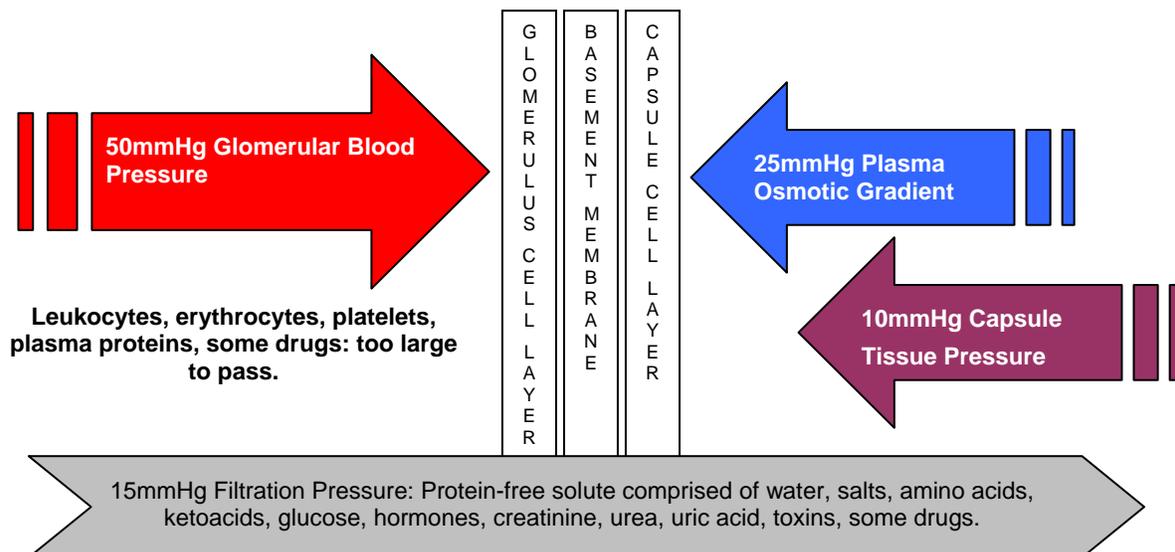
A simple flow diagram outlining the process can help provide a basic overview and understanding of the process before diving into the details:



**Figure 3: Urine Production Overview**

<sup>2</sup> Kidney dialysis treatment is a process that can be provided for patients suffering from certain kinds of kidney failure, but it is not a viable, long-term solution to waste removal or osmotic regulation.

Now let's dig in and get started. We'll start at the 'blind' end, where we find Bowman's Capsule.<sup>3</sup> Blood is delivered into the capsule via the afferent arteriole after branching out from the renal artery. Here the hydrostatic pressure builds to approximately 50mmHg because the diameter of this arteriole is slightly larger than the downstream, or efferent, arteriole.<sup>4</sup> Between these two vessels lies the glomerulus, a bundle of capillaries of single-cell-wall thickness with quite permeable (fenestrated) membranes. The glomerulus is surrounded by Bowman's capsule and in between lies a basement membrane associated with the capillary; both of these membranes are embedded with glyco-proteins carrying a strong negative charge. The osmotic pressure (recall this is the opposing fluid pressure from the other side of the membrane) is about 25mmHg. This would leave a net pressure of close to 25mmHg, but we have to take into account the tissue pressure of the capsule itself, which is around 10mmHg.<sup>5</sup> This leaves a net pressure of approximately 15mmHg against the membranes from the glomerulus into the capsule.



**Figure 4: Ultrafiltration**

<sup>3</sup> <http://www.thefreedictionary.com/>, Bowman's Capsule: 1. A double-walled, cup-shaped structure around the glomerulus of each nephron of the vertebrate kidney. It serves as a filter to remove organic wastes, excess inorganic salts, and water; after Sir William Bowman, British surgeon, (1816-1892).

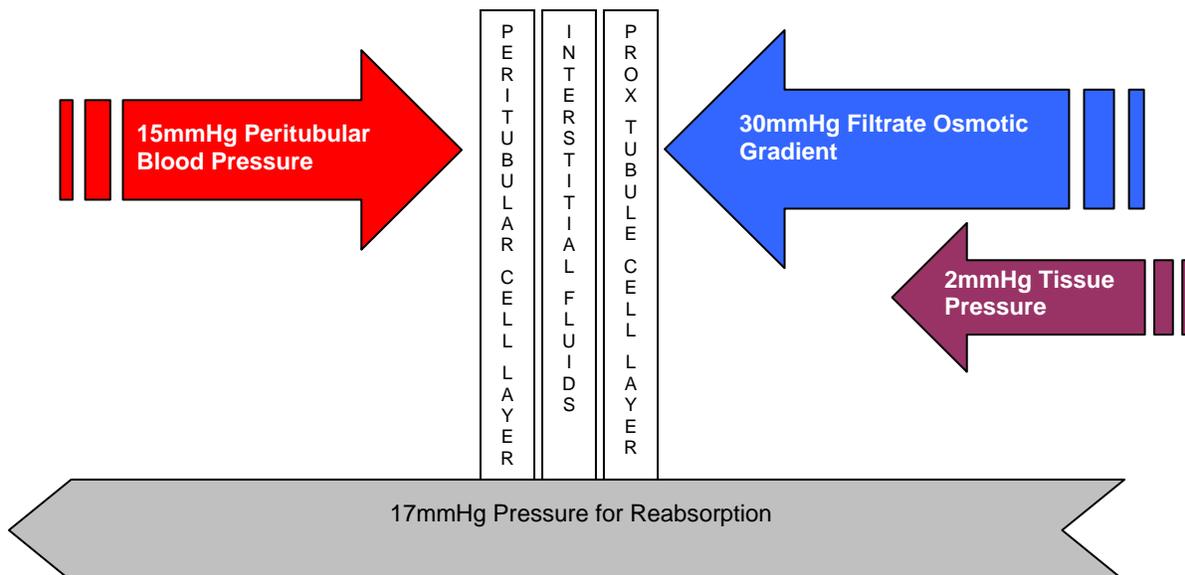
<sup>4</sup> There are two capillary beds connected in series within the blood-supply system of the nephron. The glomerulus, a capillary bed specific to the capsule, and the peritubular, which are fed from the efferent arteriole.

<sup>5</sup> Figures in Kapit and Ross&Wilson differ slightly. The figures from Kapit, p60, are being quoted here.

Given the high permeability of the membrane structures (fenestrated capillary endothelium and slits in the capsule podocytes (uniquely shaped epithelial cells), this large difference in pressure means that any blood constituents small enough will pass through the membranes, leaving those too large to pass (or those that are also negatively charged and thus repelled by the negatively charged glyco-proteins) generally remaining in the bloodstream (and *that* is ultrafiltration at its finest).

In a healthy human, the glomerular filtration rate (GFR) of the two kidneys together is about 125ml/min which yields approximately 1ml/min of urine. This poses a simple math problem: what happens to the other ninety-nine percent of the filtrate, if only about one percent is passed as urine?

This is where the unique structure of nephrons and dual-capillary beds come into play. About eighty-five percent of the nephrons in each kidney reside in the cortex, with short loops of Henle dipping into the outer region of the medulla. The other fifteen percent or so have much longer tubules and loops, reaching quite deeply into the medulla, and these play a role in water conservation. Reabsorption of water and a certain amount of blood constituents takes place in a process that is (loosely defined) an approximate reverse of ultrafiltration: Reabsorption.



**Figure 5: Reabsorption**

In order to fully understand and appreciate the complexity of this process, we have to break it apart into steps, first looking at the movement of fluids from the proximal nephron tubule to the interstitial fluid between the tubule and peritubular capillaries, then looking at how the fluid is moved into the capillaries from the interstitial fluid.

The proximal tubule cell walls are less permeable than those of the capsule. This means that some small solutes will not transport through the membrane and will therefore have a significant impact on solute concentration; this contributes to the condition of the high osmotic pressure gradient (30mmHg). Approximately 65% of the water and practically all of the nutrient content of the filtrate will be reabsorbed from the proximal tubule across interstitial fluid and into the capillaries, due to the unique asymmetrical structure of the tubular cells and the many  $\text{Na}^+$  -  $\text{K}^+$  pumps situated in the baso-lateral membrane. The unique cell structure prevents  $\text{Na}^+$  from moving back into the lumen of the tubule (there are no pumps on that side of the cell) once it has moved down its concentration gradient into the cell. It can only be pumped out into interstitial fluid. Since  $\text{Na}^+$  is positively charged, it will attract and take along negative ions,  $\text{Cl}^-$  being the most abundant and easily transported.

When a  $\text{Na}^+$  and a  $\text{Cl}^-$  molecule are transported from the lumen into interstitial fluid (which happens in large quantities), the osmotic gradient is affected (the active particles have left the lumen and have been added to the fluid). This creates favorable conditions for reabsorption of water, causing 370 water molecules to follow in bulk, in order to maintain osmotic stability. Thus, the reabsorption of  $\text{Na}^+$  and  $\text{Cl}^-$  is the driving force behind water movement from tubule lumen to interstitial fluid.

The unique microvilli structure (brush border) of the tubule cells on the lumen side also provides for the secondary active transport of glucose, amino acids, lactate, and phosphate (these molecules co-transport with  $\text{Na}^+$ , and the various mechanisms will not work unless a molecule of  $\text{Na}^+$  and one of the other substances is present). This structure creates a one-way system that ensures balanced reabsorption of these substances. Additionally, the proximal tubules play a role in maintaining pH balance, regulating calcium, magnesium, and phosphorus concentrations, as well as providing a means for secreting organic acids and bases from the bloodstream to the lumen for waste removal.

At this point, we've seen the reabsorption of a great deal of water and nutrients back into the bloodstream, and filtrate content is more concentrated with products being removed from the body. Reabsorption of much of the remaining water and salt continues in the distal tubule,

and it gets even more complex at this point due to an intricate regulating process involving sympathetic nerve impulses that constrict either the afferent or efferent arterioles, depending upon negative tubuloglomerular feedback regulating each individual nephron; this incredible feedback system isolates the absorption function from changes in systemic blood pressure, and controls the delivery of filtrate to the distal tubules by regulating the GFR. All things being equal and in balance, the volume of urine leaving the body equates to about one percent of the amount of filtrate, or somewhere between 1.0 and 1.5L daily.

In between the proximal and distal convoluted tubules lies the Loop of Henle. This loop is enmeshed in capillaries as previously discussed. The loops, particularly that 15 percent extending deeply into the medulla, play a role in conserving water in the body. This is regulated by the presence or absence of anti-diuretic hormone (ADH). During times of plenty, the reabsorption of water is prevented in the ascending limb of the tubule because the absence of ADH renders the membrane impermeable. This results in higher volume and more dilute urine. During times of water deprivation, ADH production is stimulated in the hypothalamus and it is released from its storage location in the posterior pituitary, due to the rise in osmotic pressure of blood plasma sensed by osmoreceptors. With the presence of ADH, the latter portions of the distal tubule and the collecting ducts become water-permeable, allowing reabsorption of water to continue into the interstitial fluid of the medulla. This results in a lower volume, higher concentrate urine.

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