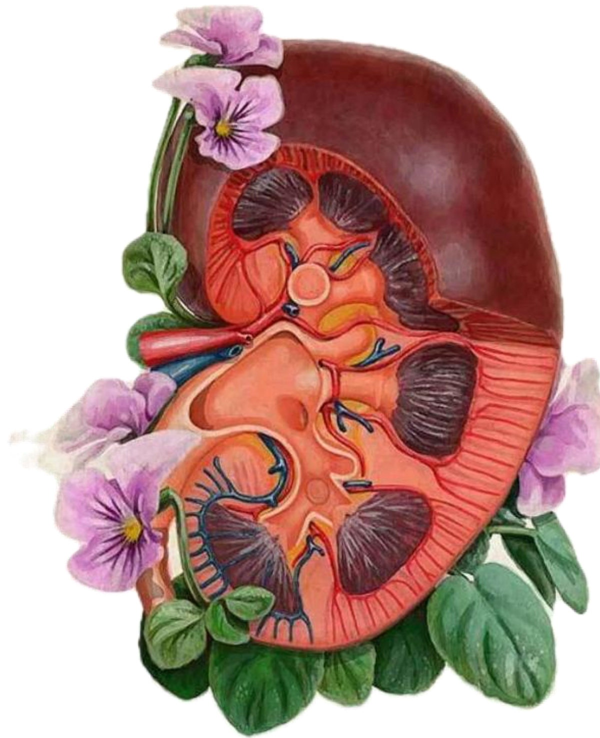
UGS Physiology Sheet #1 – V1



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In this lecture we will explore 1) kidney function, 2) its anatomy, 3) the basic process of urine formation. We will learn some basic principles essential for understanding the rest of the urinary system.

Functions of the Kidney

Kidneys are essential for life and perform many functions; failure of any of which can negatively affect our health or even be fatal.

1. Removal of waste substances from the blood, like creatinine and urea.
2. Acid-base balance.
3. Electrolyte Homeostasis
4. Hormones and enzyme release: like erythropoietin and Renin.
5. Activates Vit D.
6. Regulate body fluids and arterial blood pressure.
7. Gluconeogenesis.

1. Waste removal

The body's metabolism consistently produces harmful waste substances among the most prominent of which are nitrogen / ammonia containing compounds such as urea, creatinine, and uric acid. A build up in these substances, termed ***Azotemia***, can be toxic to the human body, especially to the CNS.

Urea is a product of protein metabolism. Protein breakdown produces amino acids that are deaminated producing ammonia, which is toxic and is therefore converted to urea; a less toxic substance that can be easily excreted by the kidney. The accumulation of wastes to the point of reaching toxic levels may result in ***Uremia***.

Creatinine is a result of muscle metabolism, and its production is proportional to muscle mass. This is important because this means that normally men will have higher creatinine levels than women, and body builders will have higher levels than normal individuals. Creatinine levels are very important clinically as they are used as a measure for kidney function (and thus health).

Kidney function is inversely proportional to serum creatinine levels, this means that if the creatinine levels are double the normal levels, half of the kidney, or half of the kidney's basic functional units (nephrons), are damaged or not working properly.

Kidney function is assessed through Kidney Function Tests (KFTs), the main one of which is called the **Glomerular Filtration Rate (GFR)**. GFR is inversely proportional to serum ***creatinine*** concentration.

$$\mathrm{GFR} \propto \frac{1}{[\mathrm{Creatinine}]}$$

Although urea levels are also indicative of kidney function, they are not used as a diagnostic tool because they are too easily influenced by external factors like diet.

The Molecular Weight (MW) of urea and creatinine are 60 g/mol and 114 g/mol respectively; This is important because sometimes you will be given lab values in either g/mL or mol/L units, so you must be able to convert between them. Revise conversions on your own.

2. **Acid-base balance**

The human body can function only when blood pH is maintained within a narrow physiological range (7.35 – 7.45). This balance must be tightly regulated by buffering systems to ensure normal enzyme structure and function, and therefore normal metabolic activity. Even small deviations from this range can be life-threatening.

Our normal metabolism however continuously produces acidic products, putting our bodies under constant acidic attack and risk of developing metabolic acidosis. The body's primary way for defending against acidosis is through utilizing bicarbonate, which reacts with acid (H^+) to produce water and CO_2. CO_2 can be exhaled by the lung:

$$H^+ + HCO_3^- \rightleftharpoons H_2CO_3 \rightleftharpoons H_2O + CO_2$$

Our reserve of bicarbonate is limited, making it among body's most important resources. It must be conserved in the blood, as the body can't afford loss in the urine. Furthermore, the body needs to keep constantly producing bicarbonate to match its rate of constant consumption, which is also done by the kidney.

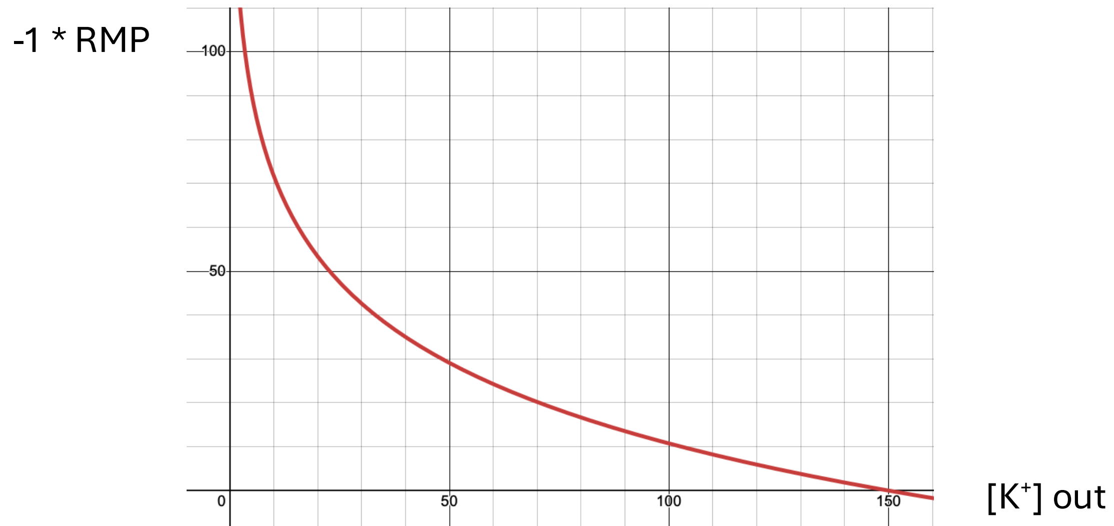
3. **Electrolyte homeostasis**

100 mEq/day of K^+ and 150 mEq/day of Na^+ are eliminated daily through the kidney; their main method of elimination. To maintain ionic balance elimination is equal to our daily ingestion.

Renal failure can cause hyperkalemia which affects resting membrane potential (RMP) making it less negative. An increase in $[K^+]$ in the blood from 4 mEq/L (normal) to 8 mEq/L changes RMP from roughly -90 to -70. This affects the excitability of the

heart and can cause lethal arrhythmia. Clinically if a patient presents with certain arrhythmia that are due to hyperkalemia (after performing an ECG), Hemodialysis should be performed right away to save this patient. Hypernatremia is less lethal.

Nernst Equation: $RMP = -61 \times log \frac{[K^+]\ in}{[K^+]\ out}$



4. Body fluid and arterial blood pressure regulation

Urine output is 1 mL/min ≈ 1.5 L/Day. Impaired urine formation and excretion will cause hypervolemia, resulting in malignant hypertension.

5. Activation of vitamin D

For our body to absorb Ca^{++}, Activated Vit D (D_3, Calcitriol, or 1,25-dihydroxycholecalciferol) is needed, which is activated by the kidney. Decrease in serum calcium may result in osteoporosis and fracture.

6. Enzyme and hormone secretion

The kidney produces enzymes and hormones like renin and erythropoietin respectively. Renin is crucial for the Renin – Angiotensinogen pathway that produces Angiotensin II (AT_2), a hormone that regulates arterial blood pressure (ABP). Erythropoietin secretion is increased in hypoxic conditions to stimulate RBC production, therefore renal failure causes anemia.

7. Gluconeogenesis

The kidney supports the liver during fasting or low-carbohydrate (keto) states by synthesizing glucose.

Internal Anatomy and Structure

Perfusion: the kidney is a reconditioning organ.

We have two kidneys with a total weight of about 250 g, with each kidney weighing approximately 115–170 g. They receive blood through the renal artery and return the remaining blood through the renal vein. The renal blood flow (RBF) is around 1250 mL /min, which is about 25% of the cardiac output (CO) assuming that the CO $\approx 5L/min$.

When you adjust the blood flow to the mass of the tissue (mL/g/min), you find that the kidney receives blood at around 4 mL / gram / minutes; the blood flow received is higher than almost any tissue (besides the carotid bodies). This is **not** because the kidney needs this much blood and oxygen to match its demand. Although its metabolic activity is high, it is not sufficient to justify such a large blood supply.

Organ	Blood flow (ml/g/min)	[A-V O_2] difference (Vol %)
Kidney	4.2	1.4
Heart	0.8	11
Carotid body	20	0.5
Muscle	0.03	6

This is well demonstrated when you look at the extraction ratio (ER) of different organs. The kidney has a relatively low oxygen extraction, as indicated by the small arteriovenous (A–V) O_2 difference. This means it receives more blood than it actually needs for oxygen consumption. The kidney receives high blood flow because the body requires it to modify blood composition (e.g., by adding or removing substances), rather than simply to meet metabolic needs.

In contrast, the heart receives only the amount of blood necessary to meet its metabolic demand. This is illustrated by the large A-V O_2 difference. This difference is also reflected in mechanisms of injury: during ischemia, the heart is highly susceptible to hypoxia, whereas kidney injury typically occurs through different mechanisms.

Internal structures

The kidney mainly consists of the cortex and the medulla, and each kidney has around 1 million nephrons, the kidney's functional unit. The Cortex is 1 cm thick and appears granular, where each granule represents a glomerulus, a capillary bed that delivers blood

to the nephron (1 glomerulus per nephron so around 1 million glomeruli). The Medulla appears striated and contains the tubular component of the nephrons.

Renal blood supply

We have the Renal Artery (delivering 1250 mL / min of blood) and the Renal vein (receiving 1249 mL / min of blood; 1 mL / min got filtered in the kidney).

The renal artery enters the kidney through the hilum and then branches progressively to form the: (Veins follow the reverse pathway)

Segmental, interlobar, arcuate (cortex–medulla junction), interlobular arteries.

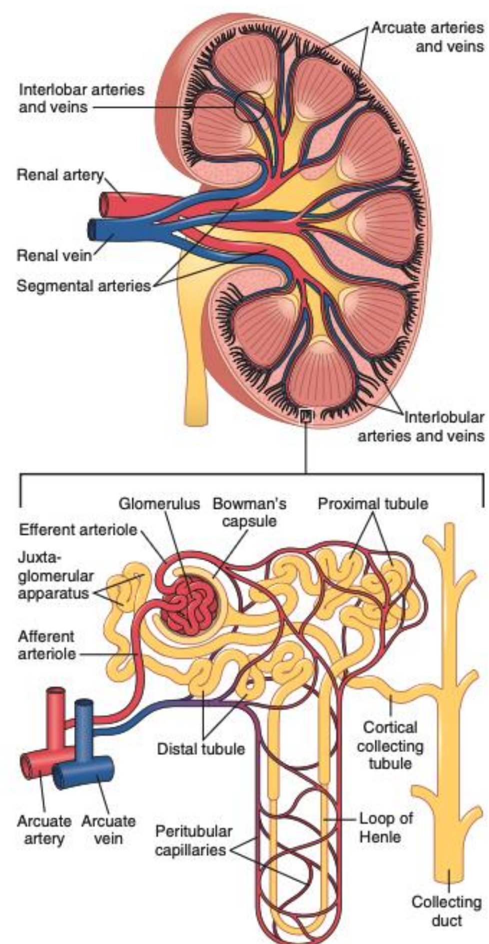
This branching is only relevant in blood distribution. This is for anatomy.

Then the afferent arterioles, **glomerular capillaries**, efferent arterioles, **peritubular capillaries.** What the doctor cares about.

They exist for each nephron. These are the 4 important branches that affect kidney function and physiology

The renal circulation is unique in having two capillary beds, the glomerular and peritubular capillaries; this also exists in the pituitary and liver. This creates two opportunities or sites for exchange for each nephron.

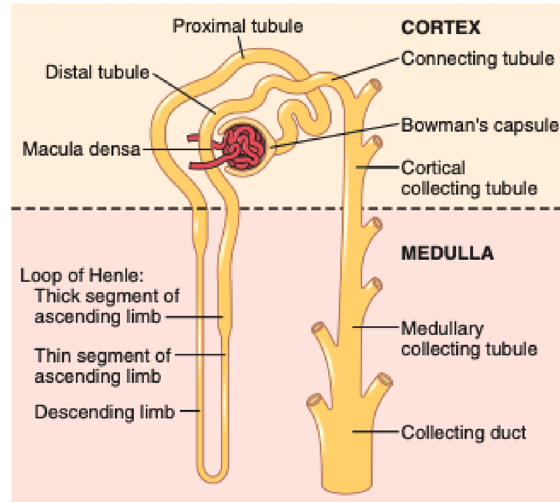
Glomerular capillaries are where large amounts of fluid and solutes (except the plasma proteins) are *filtered* to begin urine formation, and **peritubular** capillaries are sites of *reabsorption and secretion* to the nephron.



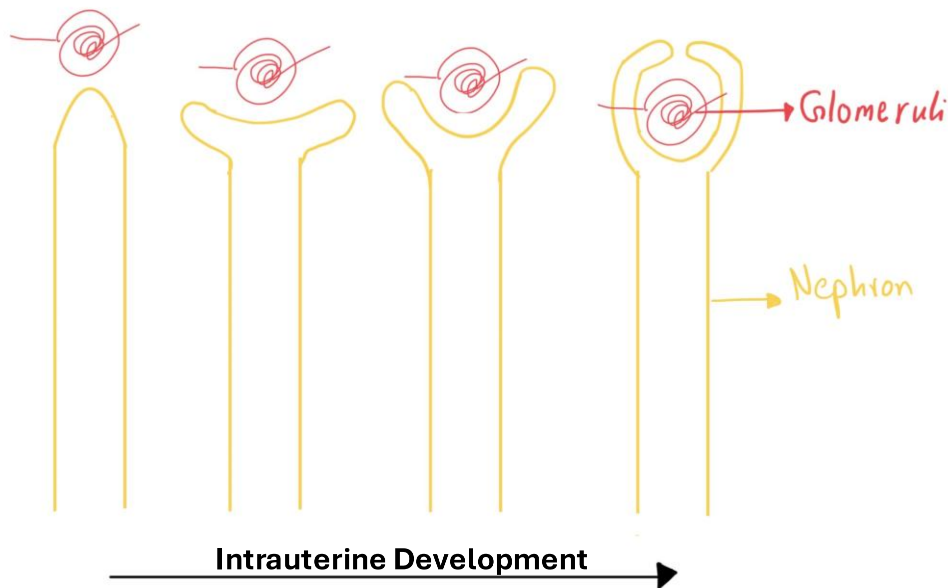
Nephrons are the functional unit

Each nephron is a long, convoluted tubule around 5–6 cm in length. It consists of several segments:

1. Afferent arteriole
2. Glomerular capillaries
3. Bowman's capsule
   beginning of the PCT
4. Proximal convoluted tubule (PCT)
5. Loop of Henle
6. Distal convoluted tubule (DCT)
7. Collecting duct (final segment; it has multiple parts with different functions)
   a. Cortical
   b. Outer medullary
   c. Inner medullary



Note: The glomerulus becomes enclosed in the Bowman's capsule during development.



We can divide nephrons into (10 nephron tubular segments or) to 2 main **functional** parts:

1) Ultra filtration device (Glomerulus and Bowman's Capsule)
   a. filters plasma without affecting proteins
   b. Dysfunction leads to Glomerulonephritis pathology
2) Epithelium that modifies the ultra-filtrate (rest of the tubule)
   a. Modifies through reabsorption and / or secretion
   b. Dysfunction leads to Tubulo nephritis pathology

Regional differences in nephron structure

We have 2 main types of nephrons: **Cortical and Juxtamedullary Nephrons**.

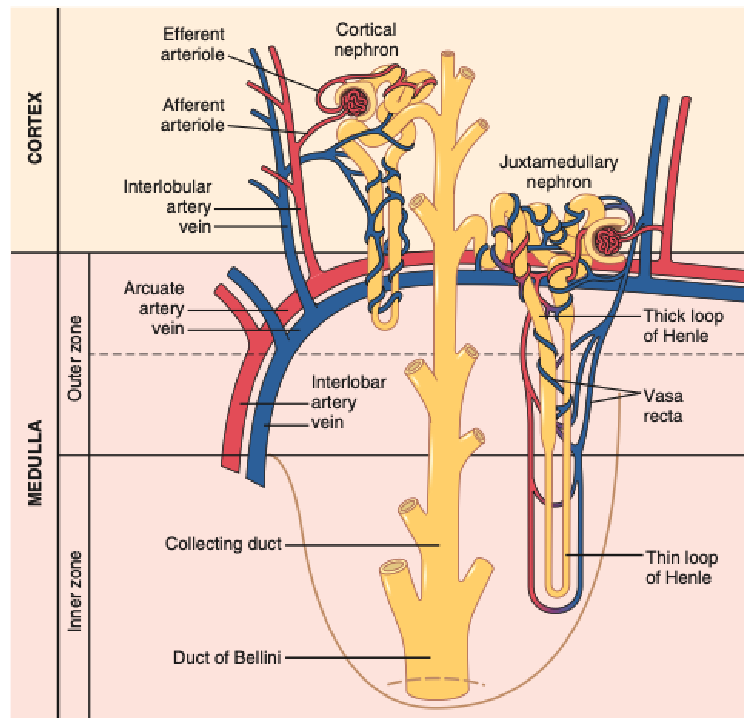
Although each nephron has all the components described earlier, there are some differences, depending on how deep the nephron lies within the kidney mass.

Cortical Nephrons (85%):

- Have their glomeruli located in the outer cortex
- short loops of Henle that penetrate only a short distance into the medulla

Juxtamedullary nephrons (15%):

- Have long loops of Henle that dip deeply into the medulla
- Their peritubular capillaries are called *vasa recta* and penetrate deeply into the medulla with the loop of Henle
- They are important for the concentration of urine, allowing its osmolarity to reach as high as 4 times the osmolarity of plasma (1200 vs 300 mOsm)



Urine Formation: 3 steps

The kidneys receive about 1250 mL/min of blood, which represents approximately 25% of the cardiac output (CO), so the renal blood flow (RBF) = 1250 mL/min. However, not all of this blood is relevant for filtration. Blood cells are too large to be filtered, as the filtration barrier prevents substances with a molecular weight > ***70,000 MW*** from passing through. Therefore, we focus on plasma, which makes up about 55% of blood volume (1 - Hematocrit). This gives us the Renal Plasma Flow (RPF) ≈ 650 mL/min.

$$RPF = RBF \times (1 - Hematocrit)$$

Glomerular filtration

Filtration in the kidney occurs by bulk flow, meaning movement of fluid and solutes together **due to pressure. It is not diffusion**, which applies to individual molecules, each moving down its own concentration gradient.

- *Bulk flow* is the movement of the entire fluid (and everything dissolved in it) driven by a pressure gradient.
- *Diffusion* is the movement of dissolved substances within a fluid driven by a concentration gradient.

The efferent arteriole is narrower than the afferent arteriole. This difference increases resistance and makes the glomeruli have high hydrostatic pressure, around 60 mmHg, which is much higher than systemic (30 mmHg) or lung (7-10 mmHg) capillary hydrostatic blood pressure values. This means that for the entire glomerular capillary bed there will be net filtration and fluid will move from the blood vessel to the Bowman's capsule. The filtration fraction (FF) is 20%, meaning about 20% of the RPF is filtered. Glomerular Filtration Rate (GFR) ≈ 125 mL/min. The remaining fluid ≈ 525 mL/min continues into the efferent arteriole.

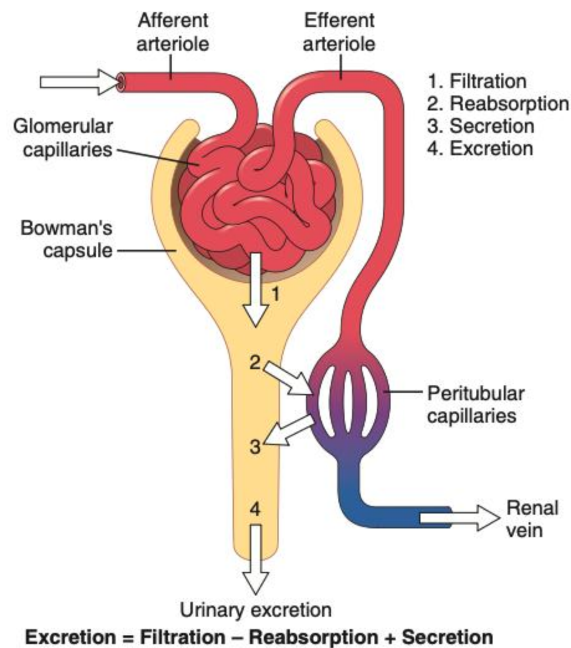
Freely filtered fluids are fluids that have the same concentration in the plasma as they do in Bowman's capsule and tubular fluid. This is typically true for electrolytes, small molecules, and most substances except proteins.

Peritubular capillary selective modification (reabsorption and secretion)

After filtration, the filtrate enters the tubular system, where selective processes occur in the peritubular capillaries. Since we know that we produce 1 mL/min of urine, then 124 mL/min get reabsorbed (>99%).

Although this is true for the whole fluid volume, there is selective control over specific substances and their concentrations, and they can be selectively reabsorbed or even secreted. Penicillin for example is actively secreted into the nephron. *Inulin* however is neither absorbed nor secreted (we will discuss inulin more later). Potassium (K^+) is a good example of complex renal handling: It is filtered, reabsorbed and secreted again.

So, for any substance: Excretion = F + S – R. These are the basic 3 steps for urine formation.



The last part of this lecture made more sense to be on the next sheet to reduce repetition and improve flow.

Changes v0 → v1:

1. Styling and punctuation.
2. Page 4: extra brief explanation about Gluconeogenesis.
3. **Page 9**: fixed (RBF to RPF) equation (from division to multiplication).
4. Page 9: extra explanation about bulk flow vs diffusion.
5. Page 10: added note about missing content.