Renal Physiology

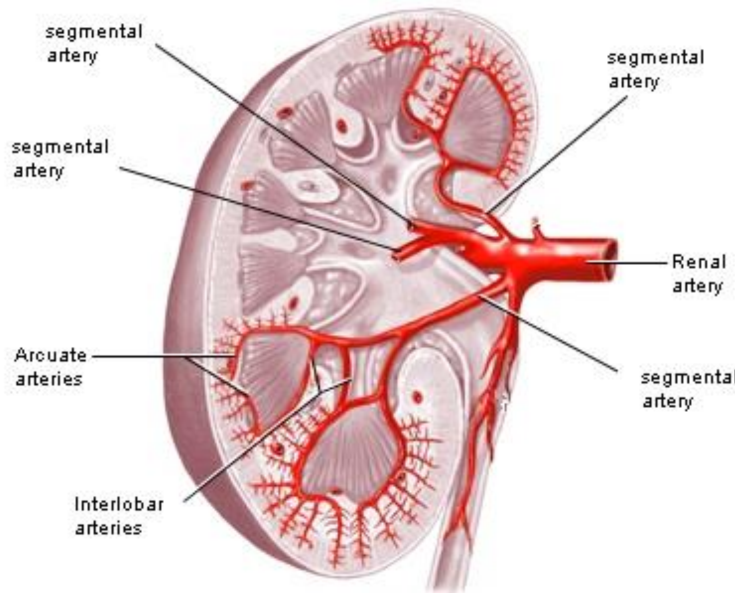
Kidneys are essential for life, without normal functioning kidneys we cannot survive.

What are the different functions of the kidney that without death may occur?

Regulate body fluids	As the kidneys are the key in the production of urine, they react to changes in the body's water level throughout the day. As water intake decreases, the kidneys adjust accordingly and leave water in the body instead of helping excrete it. In case of failure increase body fluids, hypervolemia, pulmonary edema and death
Regulate blood pressure	The kidneys need constant pressure to filter the blood. When it drops too low, the kidneys increase the pressure, malignant hyper tension is the main cause of renal failure
Electrolyte balance	Sodium, potassium, magnesium, phosphorus, and calcium levels are all controlled by the kidney, hyperkalemia may occur due to renal failure which causes arrhythmia. Calcium imbalance affects the bones.
Synthesis of erythropoietin	When the kidneys don't get enough oxygen, they send out a distress call in the form of erythropoietin, it stimulates the bone marrow to produce more oxygen-carrying red blood cells. In case of renal deficiency, anemia occurs.
Get rid of fixed acids	Acidosis may cause death
Synthesis of hormones	Erythropoetic factor and renin, 1,25 dihydroxycholecalciferol (Vitamin D)
Excretion and metabolization of hormones	Most peptide hormones (e.g. insulin, angiotensin II, etc)
Vitamin D3 is activated in the kidney	Has to do with calcium.
Target for hormones	E.g. ADH, aldosterone etc.
Remodification of blood	Once it leaves the kidneys it will contain more bicarbonate
Regulate acid-base levels	Through Bicarbonate and H^+
Excrete waste products	The kidneys filter out toxins, excess salts, and urea.
Foreign chemicals are excreted by the kidneys	Pesticides, food additives, toxins, drugs.
Make G from non CHO sources	make sugar from proteins at time of starvation (gluconeogenesis)

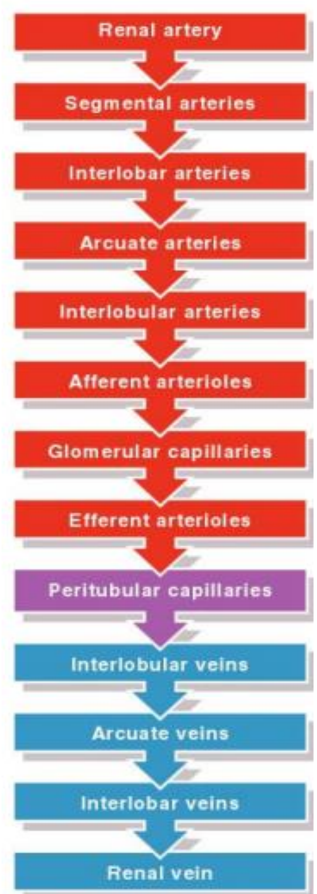
Renal Blood Flow

The blood supply that goes to the kidney is huge compared to its size, for example the skeletal muscles which are 40% of our body weight they receive less blood supply (1 litter at rest) than the two kidneys which all together may weight 200 grams (receive more than 1 litter), also the blood that goes to the kidneys is not only to nourish it with oxygen but so the kidneys can change the composition of this blood (remodification), but on the other hand, the blood goes mainly to the muscles according to their needs.



Blood flow to the kidney is 22% of cardiac output, which means 1250 ml of blood/min, divided into 55% plasma and 45% cells.

Blood reaches the kidney through the renal artery (which is the fifth branch of the aorta at the level of the second lumber vertebra) the renal arteries divide into **segmental arteries** then **interlobar arteries**, **arcuate arteries**, **interlobular arteries** and finally become **afferent arterioles**. These afferent arterioles give rise to capillaries, called **lobular capillaries**, they join to form another **efferent arteriole**, this is like the portal circulation in the liver and pituitary gland, this is extremely important, then efferent arterioles again give rise to capillaries they surround the tubule, we call them **peritubular capillaries**, after this they join forming the **venules**, passing the same path as the arteries ending as renal vein.



Because the aorta is to the left of the midline, the right renal artery is longer. The inferior vena cava lies to the right midline making the left renal vein two times longer than the right renal vein. For this reason it is better to take the donor left kidney (short artery, long vein) & place it in the right pelvis of the recipient. Multiple arteries & veins can supply the kidney.

The A-V oxygen difference is small, however, O_2 consumption in the kidney is twice as that for brain. This O_2 consumption is directly related to Na^+ reabsorption. If filtration ration is high, Na+ reabsorption is high, O2 consumption is high.

How to measure Renal Blood Flow (RBF)?

Through this equation:

$$RBF = \frac{\text{Renal Plasma Flow}}{1\text{-Hct}}$$

So, if we assume that the RBF is 1250 ml and the Hematocrit is 45%, the Renal Plasma Flow is ≈ 685 ml.

How to measure Renal Plasma Flow (RPF)?

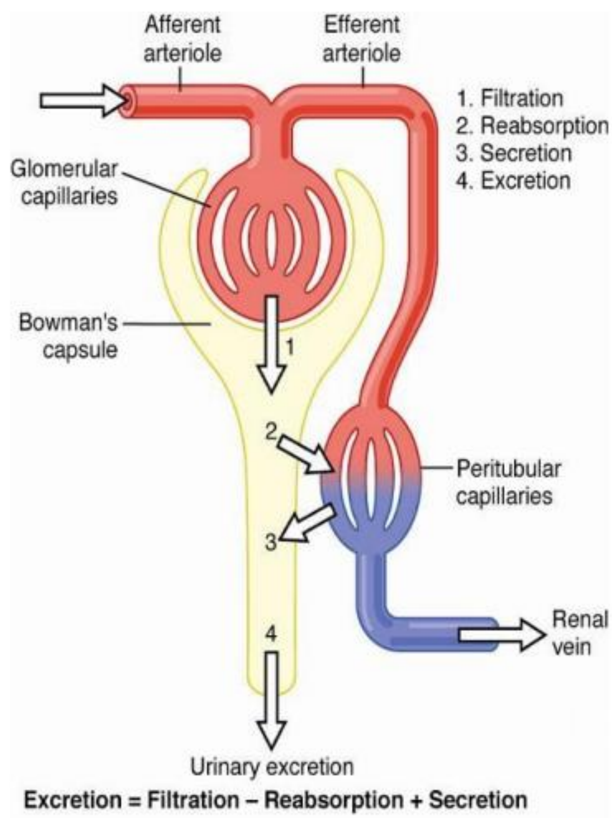
RPF: how much plasma enters both kidneys per minute. We use a substance X that is completely removed (cleaned) from the blood once it reaches the kidneys.

Each kidney has around one million nephrons, a nephron is a 4-5 cm long tubule, we can divide it anatomically into proximal, loop of Henle, distal, etc.

But physiologically we divide the nephron into two parts:

- Ultra filtration device the Glomerular apparatus
- Epithelium (The rest of the nephron), which is going to modify the ultra filtration.

  Modification means taking from the ultra filtrate nephron to capillaries (re absorption) adding to ultra filtrate (secretion)



1. **Glomerular Filtration** passage of part of the plasma from the glomurle capillaries to bowman's capsule, somewhat variable, not selective (except for proteins), averages 20% of renal plasma flow
2. **Tubular Reabsorption** is the flow of Glomerular filtrate from the nephron into the peritubular capillaries, or from the urine into the blood, highly variable and selective to most electrolytes (e.g. Na+ , K+ , Cl-) and nutritional substances (e.g. glucose) are almost completely reabsorbed; most waste products (e.g. urea) are poorly reabsorbed.
3. **Filtrate Secretion** is the transfer of materials from peritubular capillaries to renal tubular lumen. highly variable; important for rapidly excreting some waste products (e.g. H^+ and K^+), foreign substances (including drugs), and toxins.
4. **Excretion of urine**

   Excretion = filtration– reabsorption + secretion

   Filtration is passive, secretion and reabsorption happens through active diffusion, primary active, or secondary active.

Anatomical parts of the Kidney

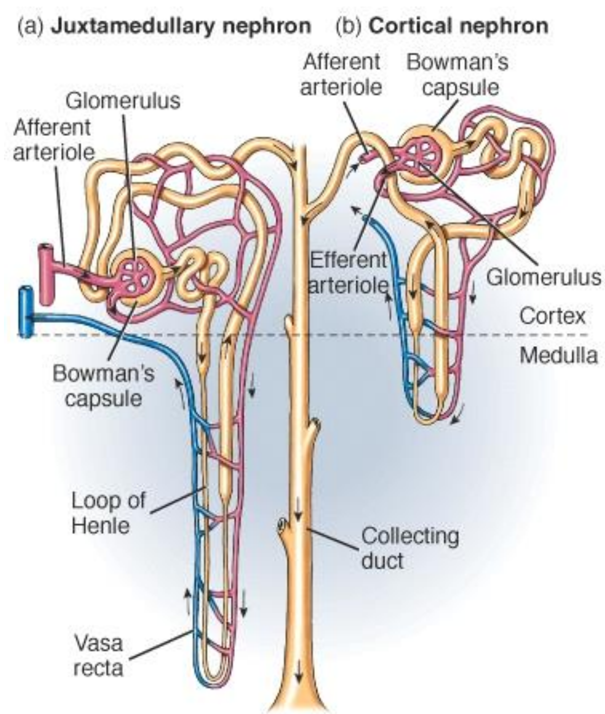
- Cortex The renal cortex is the part of the kidney where **ultra filtration** occurs, looks granular because we have glomurle capillaries, 1 million of them.

- Medulla contains the structures of the nephrons responsible for maintaining the salt and water balance of the blood. It contains tubules for **secretion** and **reabsorption.**
  - Outer medulla
  - Inner medulla

➢ Cortical atrophy : glomerulonephrits
➢ Medullary atrophy : tubular nephritis

Types of nephrons

- Cortical nephrons
  - Located in the outer cortex.
  - Short Loop of Henle
- Juxtamedullary nephrons
  - 15-20% of nephrons
  - Located at the borders between the cortex and the medulla
  - Long loop of Henle
  - Important in urine concentration



Glomerular filtration

First step of urine formation

Glomurle Filtration Rate GFR *is volume of plasma filtered from the glomurle capillaries to the bowman's space in the 2 million nephrons in both kidneys per unit time*.

Glomurle filtration rate (GFR) is used to classify kidney disease it can tell how much functioning nephrons are left, if 2 million nephrons working GFR should be 125 ml/min in a 25yrs old male weighing 70kg, 10-15% less in females.

- **Stage 1**

Decrease Renal Reserve

50-100% decrease in GFR

The other 50% of the nephrons they can compensate and maintain absolutely normal homeostasis for example if a one kidney is donated the patient is left with half the nephrons, but maintenance of normal homeostasis can be achieved, no food restriction

- **Stage 2**

Renal Insufficiency

20-49% Decrease in GFR

Has symptoms, the earliest sings is isosthenuria or polyuria with isotonic urine. Azotemia, anemia, and hypertension appear too. but can survive with salt and protein restrictions we do not need to give him medication

- **Stage 3**

Renal Failure

All signs and symptoms of uremia (urine in the blood) are present.

5 – 19% Decrease in GFR

- **Stage 4**

End Stage Renal Failure

<5%

At this stage, dialysis or transplantation are necessary for survival. Is an administrative term rather than medical term. It means that person should be covered by government insurance, because replacement therapy is mandatory.

There are different classifications to levels of GFR, the numbers are not specific but according to the policies of each country and insurance companies, but the bottom line is that all depend on the value of GFR.

Filtration is a bulk flow, anything with the molecular weight lees than the 70 can be filtered, urea and creatinine for example are freely filtered.

- **Urea** *comes from the breakdown of proteins*.
- **Uric acid** comes from the breakdown of nucleic acid.
- **Creatinine** *comes from break down of muscle phosphocreatine*.
- **Bilirubin** *comes from hemoglobin metabolism*.

These waste products must be removed and they are removed only in the kidney, renal failure means the elevation of these three substances? If you want to measure renal damage you measure urea creatinine levels in the plasma, if they are double it means you have 50% of your nephrons functioning only, they also gives us an idea about GFR.

filtration barrier (the capillaries, bowmen's epithelium, basement membrane) is negatively charged, it means that sometimes a substance that is positively charged with a molecular weight of 70 might penetrate it, and other times a substance with weight a little less than 70 but cannot penetrate due to its negative charge, proteins are negatively charged so usually they do not cross, if the barrier's negative charge is lost then proteins are expected to cross, for example albumin might be found in the urine, in a case called albuminurea.

We have four forces (starling) affecting filtration

1. Hydrostatic pressure in the glomurle capillary
   This force is equal to 60 mmhg (systemic 30 mmhg)
2. Colloid osmotic pressure in the capillary
   Due to albumin 32 mmhg
3. Hydrostatic pressure in bowmen's capsule
   18mmhg
4. Colloid osmotic pressure in bowman's capsule = zero due to absence of proteins

Filtration is flow, any flow is governed by Ohm's law, (ohms law states that flow is directly proportional to driving force, inversely proportional to resistance (resistance is an expression to show difficulty of how the process is going to occur, permeability is inversely proportional to resistance))

$$\text{GFR (flow)} = \frac{\text{Driving Force}}{\text{Resistence}}$$

$$\text{Permeability} = \frac{1}{\text{Resistence}}$$

GFR = Driving Force x Permeability

Protein concentration here is going to increase by 20%. This means that the osmotic pressure will increase by 20%, well. At one end it will be 28; while at the other end it will approach 36. In the middle area, it is about 32. This number is not found in the tabulated values. Flow is unit per time GFR, so GFR can be modified by modifying the driving forces which are the starling forces mentioned above.

The filtration pressure is equal to 10 mmHg (60-(32+18)). The 60 and the 50 are the sums of the inward and outward aforementioned Starling forces.

To calculate the filtration coefficient, we use the third equation (GFR equation). Since we know that the GFR is 125mL/min, and we know that the driving force is 10 mmHg. The filtration coefficient is the result of dividing the GFR by the driving force, which results in 12.5.

If the 10 mmHG are gone, we would have no GFR.

Where does this force come from (I apologize for the next part, but the Dr. did not do a good job explaining it).

Permeability

We will trace the pathway from the aorta to the afferent arteriole. At the aorta, the pressure is 2/3 diastole + 1/3 systole = which is almost 100 mmHg.

We pass the arterial system, and at the beginning of the afferent arteriole, the pressure is 85. At the end it is 60 mmHg. At the efferent end it becomes 59 mmHg.

The efferent at the beginning 59 mmHg, at the end it becomes 18 mmHg.

At the peritubular capillaries from 18 mmHg it becomes 8 mmHg, which will then be divided among the veins until it reaches the renal end where it becomes 4.

What do these numbers mean?

The systemic circulation starts at the left ventricle and ends at the right ventricle. From heart (A) to arteries (B) to arterioles (C) to capillaries (D) then to veins (E). Pressure at the A is 100, at B is 85, at C is 35, at D 15. At E it is zero. The flow from A to B is the cardiac output and from B to C is the cardiac output.

The change of pressure at (B) is 15, at (C) it is 50, at (D) it is 20, and at E it is 15. As we move further, the resistance decreases. The total peripheral resistance is equal to the sum of all resistances from A to B to C to D to E. 50% of the resistance resides in the arterioles due to the drop of pressure.