

## RENAL GENERAL FUNCTIONS

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### Summary

The human organism is constantly in exchange with its environment as an open system. The organism receives and disposes e.g. fluid and electrolytes from/to its environment. The organism is very sensitive to the deprivation of fluid and electrolyte as compared to its tolerance to calorie (food) deprivation. The role of kidneys is to tightly regulate the balanced optimum conditions required by the cells for their normal activities. This balanced, optimum internal environment condition is referred to as “homeostasis”. Kidneys excrete the waste products of metabolism, produce, secrete and metabolize hormones, and regulate the pH and electrolytes balance. The kidneys are also involved in the oxygen carrying capacity of the blood by producing erythropoietin hormone which contributes to the regulation of the erythrocyte number in the circulation. Several systems integrate the renal functions with the activity of the endocrine system. Nutritional status can affect the renal tasks in many ways.

### 1. Introduction

In mammals the kidneys are paired bean-shaped organs responsible for the maintenance of the fluid and electrolytes homeostasis of the organism. The major functions of the kidneys justify their massive blood supply (about 20% of the cardiac output). A portion

of the plasma, which goes through the kidneys, is filtered into the tubules (GFR). Filtration is the first step in urine formation.

The kidneys have many functions, and therefore they are vitally essential organs. Loss of kidney function is a life-threatening situation. Among the most important functions of the kidneys are the regulation of water and ions including the pH balance of blood and the extracellular fluid. The kidneys also regulate the blood volume and composition. They can synthesize glucose (gluconeogenesis) and thus help the liver in the maintenance of blood glucose levels. Without kidneys the excretion of nonvolatile wastes is nearly impossible, not to speak about the excretion of excessive water.

The kidneys contribute also to the availability of oxygen in all tissues by regulating the number of red blood cells as they contribute to their maturation in bone marrow by secreting erythropoietin. The kidneys secrete a hormone-like enzyme called renin which cleaves angiotensinogen to convert it to angiotensin I, itself to be converted to angiotensin II under the effect of converting enzyme. The renin-angiotensin mechanism has a role in the regulation of systemic blood pressure. Thus kidney disease may be a reason for hypertension. Bone metabolism is also dependent on the activities of the kidneys as far as it concerns the involvement of the kidneys in calcium/phosphate homeostasis and active vitamin/hormone D synthesis.

On the other hand, several general regulatory systems of the body contribute to the kidney functions. Blood volume and its pressure as well as its oxygen content are critical for the healthy function of the kidneys. Several hormones participate in the control of water and ion excretion and reabsorption in kidney tubules. Brain, heart and adrenal glands secrete regulatory peptides and other hormones which also play a part in controlling kidney functions.

In this chapter, some of the vital kidney functions are discussed in greater detail.

## 2. Renal General Functions

The main functions of the kidneys can be categorized as follows:

1. Maintenance and balance of the body fluids. The kidneys control the volume of the plasma, thence controlling extracellular fluid volume, which will eventually have an effect on intracellular volume. The maintenance is achieved via the interaction of several hormones such as ADH from the hypothalamus and neurohypophysis, ANF from the heart and aldosterone from the adrenal cortex (see *Endocrinology*).
2. Maintenance of osmolarity and the electrolyte composition. Through variations in the concentration of ions excreted in urine, the kidneys keep the levels of these elements at their physiological values. The principal ions are  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$ ,  $\text{Ca}^{2+}$ ,  $\text{Mg}^{2+}$ , and  $\text{PO}^{4-}$ .
3. Maintenance of acid-base balance of body fluids by excreting the non-volatile acids and ammonium ions as well as by tubular reabsorption of bicarbonate.
4. Excretion of nitrogenous metabolic waste products such as urea, urate and creatinine. The composition, concentration and the volume of the body fluids and components constantly tend to change as a result of food and fluid intake

and metabolism. The kidneys function to regulate these elements and keep them at the homeostatic levels and hence maintain an optimum internal environment for the proper functioning of other vital organs of the body such as the heart and the nervous system.

5. Secretion of hormones including renin, erythropoietin and vitamin/hormone D<sub>3</sub>.
  - Renin is secreted by the granular cells of the juxtaglomerular apparatus. This hormone catalyzes the conversion of angiotensinogen to Angiotensin I (ANG I), which is further cleaved to ANG II under the effects on angiotensin converting enzyme produced by the endothelial cells. ANG II is a powerful vasoconstrictor and also regulates tubular reabsorption of Na, glomerular hemodynamics and tubuloglomerular feedback.
  - Erythropoietin is a protein produced by the renal cortical interstitial cells in response to hypoxemia. It stimulates the maturation of the red blood cell progenies in the bone marrow, thus increasing the number of erythrocytes and consequently increasing the O<sub>2</sub> transport capacity.
  - 1,25-Dihydroxycholecalciferol is the most active form of the vitamin D<sub>3</sub> secreted by the renal proximal tubule cells. This hormone plays an important role in the regulation of calcium and phosphate homeostasis.
6. Gluconeogenesis  
During prolonged fasting, the kidneys synthesize glucose from amino acids and other precursors and release it into the blood. Thus, like the liver, kidneys are gluconeogenic organs.

### 3. Body Fluid Compartments

About 60% of the human body in males is composed of water which is distributed intra- and extracellularly. The extracellular fluid is contained in the blood vessels as plasma and in between the body cells as the interstitial fluid. The actual percentage of body water depends on age, sex and the amount of adipose tissue as the total body weight. For instance, a man with 70 kg body weight is assumed to have 20% adipose tissue (14 kg) and 80% lean body mass (56 kg). It is known that the water content of lean body mass is fairly stable to about 73% which means 40.88 kg of it is water. If we consider that the water content of the adipose tissue is negligible, then in this example the total body water content is about 41 liters out of 70 kg body weight, i.e. 58% of the weight.

In the fetus, the proportion of the total body water in relation to the body weight may be as high as 94%, while in newborns it is 75% and in one-year-old children 60%. At puberty the proportion of water may temporarily increase, but at adulthood it reaches the steady state of 60% in men and 50% in women.

Ions are dissolved in the body water, and they play important roles in the cellular functions. Table 1 shows the average concentrations of anions and cations in ICF and ECF.

Ion	Plasma (mEq/L)	ICF (mEq/L)
<b>Cations</b>		
K <sup>+</sup>	4	140
Na <sup>+</sup>	143	12

Ca <sup>++</sup>	2	0.001
Mg <sup>++</sup>	1	38
Total	150	190
<b>Anions</b>		
Cl <sup>-</sup>	104	4
HCO <sub>3</sub> <sup>-</sup>	24	12
Phosphates	2	40
Protein	14	50
Other	6	88
Total	150	190

Table 1. Ionic composition of plasma and intracellular fluid (ICF).

The numbers depict the absolute amount of the ions and proteins. Therefore it may seem that there are more ions in the ICF than in plasma. In reality, the number of ions in both compartments must be the same because no osmotic concentration difference can exist on the two sides of the membranes. The difference is due to the presence of bound ions inside the cell, mainly Magnesium.

#### 4. Juxtaglomerular Apparatus (JGA) Releases Renin

In all nephrons, the portion of the tubule which marks the boundary between the ascending loop of Henle and the distal convoluted tubule courses between the afferent and efferent arterioles at the hilus of the glomerulus of its own nephron. This section of the tubule contains the macula densa cells and the entire area is known as the JGA. (Figure 1)

Therefore, the JGA is composed of three cell types:

1. Granular cells, which appear to be differentiated smooth muscle cells in the walls of the arterioles, particularly in the afferent arterioles (see Figure 2). These cells exhibit renin-containing secretory vesicles. The renin secretion is regulated by salt concentration sensed by the macula densa cells, and the arteriolar hydrostatic pressure. These cells are also extensively innervated by the sympathetic fibers whose excitation leads to the release of renin.
2. Extra-glomerular mesangial cells, which are located between the glomerulus and the macula densa cells. These cells communicate with the granular cells via gap junctions. (Figure 3)
3. The macula densa cells on the tubular wall. These cells participate in the regulation of renin secretion and the control of the glomerular filtration rate via tubuloglomerular feedback (TGF). The macula densa cells function as osmoreceptors which continuously sense and monitor the tubular fluid osmolarity (Na and Cl concentrations). When the concentration of the ions in the tubular fluid is increased, the macula densa cells send chemical signals through the extraglomerular mesangium of the JGA to the distal part of the afferent arteriole of the same nephron. This consequently leads to vasoconstriction, hence decreasing the glomerular blood flow and GFR.

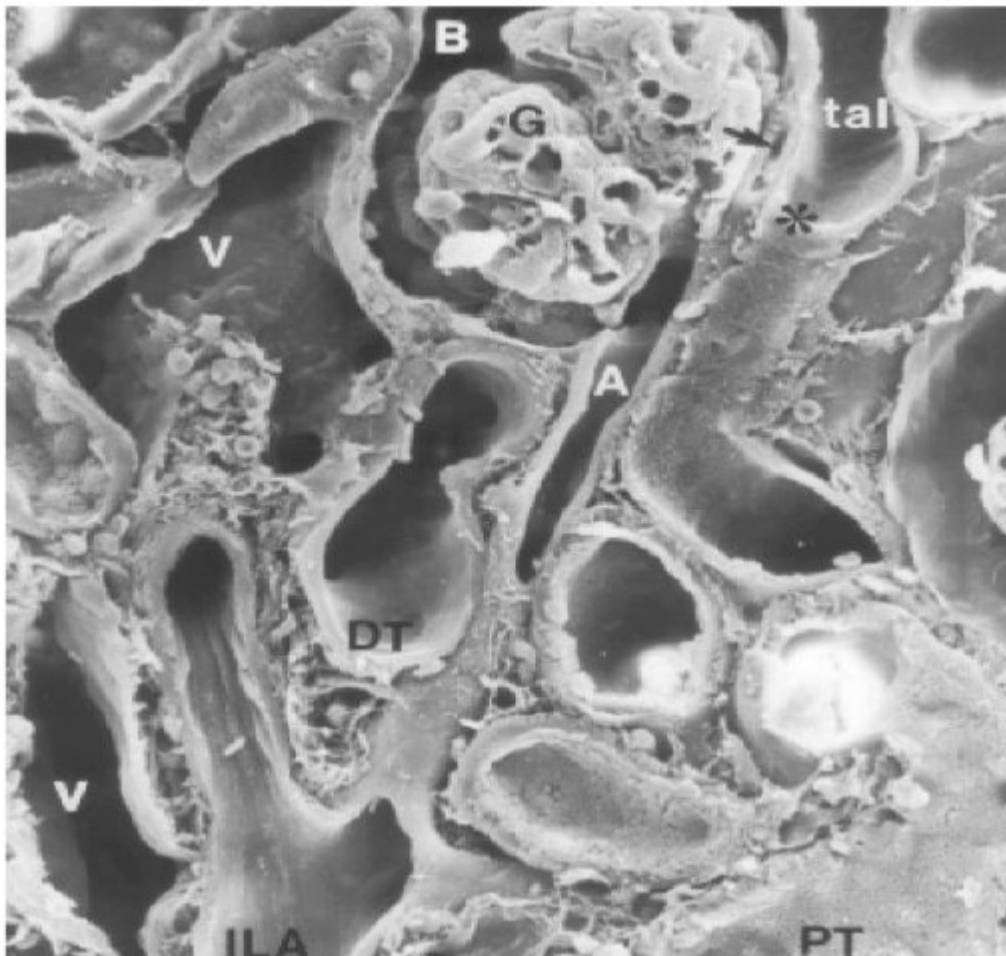


Figure 1. The glomerulus and its surroundings.

Along the interlobular artery (ILA) runs the vein (V). The artery divides into two afferent arterioles (A), from which one forms the glomerular capillaries (G). The black arrow points at the efferent arteriole. The star points at the macula densa cells which are part of the thick ascending limb of Henle (tal). PT: proximal tubules, TD: distal tubules, which is in close contact with its afferent arteriole (SEM photo from rat kidney, white line: 100  $\mu$ m).

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## Biographical Sketches

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