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### **Functional unit of kidney-P-3**

Function The kidneys are responsible for several vital functions, including electrolyte and volume regulation, excretion of waste products, acid-base balance, synthesis of hormones such as erythropoietin, and metabolism of low molecular weight proteins. The glomerulus The kidneys receive from 20 to 25% of the cardiac output; this is approximately 1,200 ml/min of renal blood flow or 600 ml/min of renal plasma flow (RPF). The filtration fraction (FF) represents the proportion of the RPF that passes into the renal tubules, and is normally 20%; this means that glomerular filtration rate (GFR) is 120 ml/min (180 L per day) in an average 60 kg person.

The GFR is the product of the Ultrafiltration Coefficient (Kf) and the net filtration pressure (the change in P),  $GFR = K_f (\Delta P)$  where  $\Delta P$  represents the sum of the Starling forces across all capillary beds, and Kf is determined by the surface area available for filtration and the hydraulic conductivity of the glomerular capillary wall. Variation in any of the mentioned components may alter the GFR. In short, filtration at a single glomerulus occurs because of four major components: (1) Kf; (2) hydraulic pressure gradient, favoring passage of water and molecules; (3) transcapillary oncotic pressure, favoring intravascular maintenance of free water and solutes; and (4) the glomerular flow rate.

The Proximal Convoluted Tubule From the 160 to 180 L of ultrafiltrate produced per day, only 1.5 to 2 L of urine is excreted. Reabsorption of 60 to 65% of free water and NaCl occurs in the PCT. Additionally, most of the potassium, phosphate, HCO<sub>3</sub>, and nearly all nutrients, such as glucose and amino acids, are reabsorbed in this segment. The solute and water reabsorption in the proximal tubule is isotonic, with a minimum change in luminal osmolarity.

This site of the nephron is also responsible for active solute secretion, hormone production, and renal gluconeogenesis. The Loop of Henle Reabsorption of 30 to 40% of sodium occurs in this segment with important changes in urine osmolarity.

The loop of Henle divides into three segments:

- (1) The thin descending limb (TDL),
- (2) The ascending thin limb (ATL)
- (3) Thick ascending limb (TAL).

The TDL is permeable to water and small solutes. In contrast, the ATL and TAL are impervious to water but permeable to solutes. The furosemide-sensitive  $\text{Na}^+\text{-K}^+\text{-2Cl}^-$  cotransporter (NKCC2) is located in the apical membrane of the TAL cells of juxtamedullary nephrons.

These solutes are reabsorbed from the tubular fluid into the interstitium, increasing its osmolarity. This hypertonicity contributes to the flow of free water from the TDL into the renal interstitium. This process is known as the countercurrent mechanism. Urine becomes hypertonic as it passes through the TDL and hypotonic in the TAL, the diluting segment of the nephron. The reabsorbed water returns to the circulation along the vasa recta. The Distal Nephron The DCT is responsible for the fine-tuning of urine. It contributes 5 to 10% in the reabsorption of filtered sodium and chloride, as well as with  $\text{K}^+$  secretion. Just as the loop of Henle, the DCT is water-impermeable, further diluting the urine. The following cluster of transporters accomplishes solute reabsorption:  $\text{Na}^+\text{-K}^+$  ATPase: it expresses at the basolateral membrane of the distal nephron. It contributes to  $\text{Na}^+$  reabsorption in two different ways: (1) it maintains the intracellular  $\text{Na}^+$  concentration low and  $\text{K}^+$  concentration high, and (2) it generates an electronegative gradient towards the inside of the cell.

The DCT is the nephron segment that expresses the highest activity of  $\text{Na}^+\text{-K}^+$  ATPase. Thiazide-sensitive  $\text{Na-Cl}$  cotransporter (NCC): it is a cotransporter that mediates the majority of  $\text{Na}^+$  and  $\text{Cl}$  reabsorption. The expression of NCC is limited to the DCT. Amiloride-sensitive  $\text{Na}^+$  transporter (ENaC) and Renal outer medullary potassium channel (ROMK): ENaC generates an electrogenic gradient that mediates the potassium secretion through ROMK. The more sodium reabsorbed through ENaC; the more potassium is excreted through ROMK.

Aldosterone, an adrenal hormone stimulated by hyperkalemia and hypovolemia, favors this process. Acid-base ionic channels:  $\text{H}^+$  and  $\text{HCO}_3^-$  are secreted through intercalated cells type A and B, respectively, located in the collecting duct.