PROXIMAL TUBULE FUNCTION

Magnitude of Proximal Tubule Reabsorption

Since \( P_{Na} = 145 \text{ mEq/L} \) and \( GFR = 180 \text{ L/day} \), then \( 26100 \text{ mEq Na/day} \) (equivalent to Na in 1.566 kilogram salt) are filtered. Only 300 mEq Na/day are excreted in the urine. Thus, about 99% is reabsorbed by the kidneys.

Most of the **Na reabsorption** takes place in the proximal tubule. The \( (TF/P)_{\text{inulin}} = 3 \) by the end of the proximal convoluted tubules(PCT). This indicates that only 1/3 of the filtered water remains by the end of the PCT and two thirds have been reabsorbed. The Na concentration in fluid sampled at the end of the PCT equals that in plasma, \( (TF/P)_{Na} = 1 \). So, 2/3 of the filtered Na must also have been reabsorbed along the PCT.

The osmolarity of the fluid along the PCT remains nearly equal to that in plasma \( (TF/P)_{osm} = 1 \). So 2/3 of all filtered solutes are reabsorbed along with 2/3 of the filtered water along the PCT. This is called isoosmotic reabsorption.

**Transport in the S1 Proximal Tubule Segment**

**Mechanisms:** Luminal Na entry into S1 PCT cells via **Na/H exchange** (25% of the amount reabsorbed), and via **cotransport with glucose** (5%) and **amino acids** (2%) and **carboxylic acids** (1%), for a total of 33% of S1 Na reabsorption. The rest of the Na (66%) is reabsorbed...
passively by solvent drag through the paracellular pathway. Of the Na that enters the S1 PCT cells, about 3/4 is transported from the PCT cells into the interstitial space by the Na-K ATPase at the basolateral side and the rest is extruded via basolateral 3HCO3-Na cotransport.

S1 is poorly permeable to Cl and urea, which rise in concentration along S1, compensating in part for the decrease in concentrations of HCO3, glucose, amino and carboxylic acids, phosphate and sulfate.

Water reabsorption along S1 is due to a small (4 mOsm/L) osmotic gradient (lumen hypotonic) due to preferential reabsorption of NaHCO3, Na with glucose, amino and carboxylic acids and an extremely high permeability to water, due to abundance of aquaporin water channels in PCT cell membranes.

When delivery of poorly reabsorbed solutes to the PCT increases (such as glucose in diabetes mellitus, HCO3 when carbonic anhydrase is inhibited, or excess filtered saline), osmotic water reabsorption and paracellular passive Na reabsorption by solvent drag decrease and an osmotic diuresis may develop in which up to 66% of filtered Na and water (66 ml/min) may be excreted as slightly hyperosmotic urine.

Transport in the S2-S3 Proximal Tubule Segments

Along the S2 and S3 segments, the major transport process is the reabsorption of NaCl through parallel Cl-/formate- and Na+/H+ exchanges at the luminal cell membrane.

Water reabsorption along S2 and S3 is driven by a small (4 mOsm/L) effective osmotic radiant generated by the lower osmotic effect of intraluminal Cl- (reflection coeff. = 0.8), compared to peritubular HCO3-, glucose, and amino acids (reflection coeff. = 1), in spite of similar intrac and peritubular total osmolarities. The water permeability in these segments is also very high.

Proximal Tubule Transport Regulation

Regulation of Na+ and water reabsorption along the proximal tubule is by glomerular-tubular (GT) balance: tubular reabsorption changes in proportion to the filtered load; percent or fractional reabsorption remains constant. GT balance is due to intratubular and peritubular factors.

Intratubular factors: At the high tubule flow rate associated with high GFR, the decrease in the luminal concentrations of HCO3, glucose, and amino acids along the PCT are less marked than at normal GFR. Thus, the more distal cells in S2 and S3 are exposed to higher concentrations of these solutes when GFR is higher. High concentrations promote the reabsorption of these solutes, coupled with Na which, in turn, increases the osmotic reabsorption of water.
Peritubular factors: When GFR increases due to a rise in efferent resistance there is an increase in peritubular capillary oncotic pressure (Ponc) and a decrease in peritubular capillary hydrostatic pressure (Phydro), both of which reduce interstitial fluid pressure and promote fluid and Na reabsorption proportionally to the increase in GFR. (Note: oncotic pressure is the osmotic pressure developed by plasma proteins.)

When mean arterial pressure (MAP), afferent resistance or oncotic pressure (Ponc) change, there are adjustments of GT balance that lead to changes in fractional reabsorption of Na and water along the PCT. Decrease in MAP, increase of afferent arteriole resistance, or increase of peritubular capillary Ponc (common in dehydration and volume depletion) lead to increases in proximal fractional reabsorption of Na and water by reducing peritubular Phydro and/or interstitial fluid pressure. The reverse occurs when MAP increases, afferent resistance decreases, or peritubular capillary Ponc decreases (common in overhydration or volume expansion).

Other factors: In addition to intratubular factors and peritubular Starling forces (physical factors), proximal tubule Na transport is also regulated by hormones, such as AII and catecholamines.