TUBULAR TRANSPORT

Basic Relations. For a freely filtered solute, Filtered Load = Glomerular Filtration Rate x Plasma Concentration, or

FL = GFR x P

Note: If the solute is bound to proteins or restricted in filtration, then FL = WFL x F (Water Filtration Rate x Concentration of solute in the filtrate water).

Tubular Transport. Tubular transport rate (T) of a solute = Difference between Filtered Load and Excretion Rate (urine concentration times urine formation rate, U x V), or

T = FL - UV

If the filtered load is greater than the excretion rate (FL > UV or UV/FL < 1), then the solute is reabsorbed along the tubule. If excretion is greater than the filtered load (UV > FL or UV/FL > 1), then the substance is secreted by the tubule. Note that we can calculate only the net reabsorption or secretion, which may be the result of a combination of secretion and reabsorption in different segments of the nephron.

Relation to Clearance (C). If the clearance of a solute is greater than the clearance of inulin (=GFR), then the substance must be secreted. If the clearance of a solute is less than the clearance of **inulin**, the substance must be reabsorbed.

Fractional Excretion. The fraction of the FL that is excreted is called the fractional excretion, and can be calculated from C(solute)/C(inulin) or (U/P)solute / (U/P)inulin.

Reabsorption. Reabsorption may take place by transport through the tubule cells (transcellular) or through the space between the tubule cells (paracellular).

Paracellular transport is by passive diffusion or by solvent drag.

Transcellular transport may be mediated, passive, or a combination of the two Transcellular transport involves luminal and basolateral steps. Luminal steps may be by diffusion (through channels or through the membrane lipids), or mediated by cotransport (Na with glucose, amino acids or carboxylic acids), by exchange (H with Na), or by primary ATP driven pumps (H, K). Basolateral transport steps may be by primary active ATP driven pumps (Na- K, Ca, H), by facilitated carriers (glucose, amino acids other organic solutes), by coupled co-transporters (for HCO3 and Na, or for K and Cl), by exchangers (Na for Ca, HCO3 for Cl), or by passive diffusion through channels or through the membrane lipids.

Mediated reabsorption processes have a limiting maximal rate, i.e. they are saturable and show a tubular transport maximum (Tm or Vmax). They also exhibit a threshold, i.e. a plasma level after which the solute involved starts to appear in the urine. Some solutes, such a glucose, have a high threshold; they only appear in the urine at plasma levels much higher than normal. Other solutes, such as phosphate, have low threshold, i.e. they appear in urine at plasma levels only slightly above normal. Only the plasma levels of those solute with low threshold are regulated by the kidney. High capacity (Vmax), low affinity, transporters are usually located proximally. Low capacity, high affinity transporters are usually located more distally. This enhances the efficiency of reabsorption.

Splay. Because some nephrons have a lower reabsorbtive capacity than average, some substances begin to appear in urine before Tm is reached. This distribution of nephron reabsorbtive capacity is called Splay.

Secretion. Coupled anion/cation transporters mediate the transfer of certain organic solutes from renal interstitial fluid into the tubule cells. These solutes are actively accumulated in the cells, from which they exit into the tubule lumen along concentration or electrical gradients. Many drugs are secreted in this way by the tubule cells. Some substances (NH4, glucuronide and glycine conjugates) are produced by metabolism inside the tubule cells and then enter the tubule fluid; these are also said to be secreted.

At low plasma concentrations, many secreted solutes (for example, p-aminohipopurate or PAH) are extracted almost completely from the plasma as it goes through the kidneys. Secretory transport systems also exhibit saturability (Tm). Only when the plasma level is well below that required to reach Tm can such solutes be extracted efficiently from the blood perfusing the kidneys and their clearance approach the RPF. Since even at low concentrations, only about 90% of substances such as PAH are excreted in one pass through the renal circulation, their clearance is termed the effective RPF.