Question 33

The key to each answer below is that the Na/K ATPase uses energy (in the form of ATP) to pump sodium out of the basal side of the tubule epithelial cell (with chloride following due to charge) and potassium into the cell (which generally leaks back out of the cell across the basal membrane). One very important result of this activity is that intracellular sodium concentrations are <u>low</u>. In terms of kidney function, the action of the Na/K ATPase permits the following: (Students need above and **two** from the following list)

1. Water recovery: At the ascending limb of the Loop of Henle and at the collecting ducts, salt diffuses into the epithelial cell and is pumped into the interstitium. This does two things: it is responsible for generating a concentration gradient within the interstitial fluid (which ultimately allows water to be recovered at the collecting ducts) & it draws water out of the descending limb of the Loop. It is therefore the basis of water recovery.
2. Nutrient recovery: In the proximal tubule cell, the low intracellular sodium concentration provides the energy to drive glucose into the cell via a sodium/glucose coupled transporter at the apical membrane. (Glucose then diffuses down its concentration gradient into the interstitial fluid.)
3. Nutrient recovery: As #2, but can replace glucose with amino acids or nucleic acids or other organics or minerals or potassium & chloride. This permits the recovery of the molecules/ions important in maintaining normal physiological function.
4. Water recovery: Based on #'s 2 & 3, molecules/ions are transferred from the filtrate into the interstitial fluid. This makes the interstitial fluid osmotically concentrated and water follows. Most water reabsorption occurs in the proximal tubule due to these events for which Na/K ATPase provides, indirectly, the driving force.
5. pH regulation: The low intracellular sodium concentration (maintained by the Na/K ATPase) permits sodium coming into the cell across the apical membrane to be exchanged for H+ (and bicarbonate to be exchanged for chloride at the basal cell membrane). This facilitates maintaining normal body pH. At times of moderate acidosis, this activity is increase to excrete excess H+ through the urine and return body pH back to within the normal range.
6. pH regulation: As in #5, at times of acidosis, a sodium/ammonium ion (NH_4+) exchanger delivers H+ (in the form of NH_4+) into the urine. This ammonium results from the metabolism of the amino acid glutamine. The NH_3 generated from this metabolism combines with H+ within the cell to generate NH_4+. Thus getting rid of this ion represents getting rid of NH_3 and H+. This mechanism results in removing H+ from the body via the urine and facilitates return of body pH to within normal limits.
7. K+ regulation: The action of aldosterone at the distal tubule and collecting duct is to increase Na/K ATPase activity at the basal side of the epithelial cell and, in part, to increase K channels at the apical membrane. The net effect of the ATPase is to increase the rate at which K+ is secreted and removed from the body. This is very important in maintaining K+ within normal limits (necessary, in part, for normal nerve and muscle function).

Extra Credit: Eating salty French (Freedom?) fries results in the osmotic concentration of the blood rising (due to the salt). A rise in blood osmotic concentrations stimulates the release of vasopressin. This prompts 1) a rise in water recovery from the filtrate [increased water transfer from the collecting duct lumen to the interstitial fluid] and 2) a rise in thirst – hence a slurp of beer. (Chances are that the amount of vasopressin released is insufficient to promote significant vasoconstriction.) By increasing water recovery as well as fluid gain, the blood osmotic concentration is returned to acceptable levels but blood fluid volume, and therefore blood pressure, has now risen. A rise in blood pressure (along with alcohol itself) blocks further vasopressin release. A rise in blood pressure will also increase GFR and the volume of filtrate generated. Without vasopressin release, the collecting duct wall becomes impermeable to water, water is not recovered and hence, the extra fluid is eliminated as urine. (This will help to return blood pressure back to normal levels.) Therefore, vasopressin release under these conditions involves two steps: initially a stimulation of release followed by an inhibition of release.