Q16 Describe the biochemical abnormalities, and the mechanisms by which they arise, that may be observed in a patient who is taking frusemide (March 2012)

Frusemide is a 'loop diuretic' which acts by inhibiting the Na/K/2Cl symporter in the thick ascending limb of the loop of Henle.

Blockade of the symporter stops resorption of Na, K and Cl. This is turn stops movement of K back into the lumen via K channels (K 'recycling'). Normally this would create a positive potential in the lumen, which drives Na, Mg, K and Ca paracellularly into the interstitium.

Hence frusemide has a broad range of effects on biochemistry:

- HYPONATREMIA → due to blockade of sodium reabsorption via the triple symporter and loss of paracellular resorption. 25% of the filtered sodium load is reabsorbed in the TAL so a significant amount can be lost through the urine with frusemide.

- HYPOKALAEMIA → Due to blockade of the triple symporter and loss of the paracellular resorption of K, hence excretion in urine

- HYPOCHLORAEMIA → due to blockade of the triple symporter

- HYPOMAGNESAEMIA → due to loss of paracellular resorption of Mg which would normally driven by the positive potential caused by K movement into the lumen

- HYPOCALCAEMIA → due to loss of paracellular diffusion of Ca. Usually any luminal Ca will then be reabsorbed in the early distal tubule, but hypocalcaemia may occur.

- HYPERURICAEMIA → reduction in renal uric acid secretion due to increased uric acid resorption in proximal tubule secondary to volume depletion, and also competition from frusemide for secretion via the organic acid transporter in the proximal tubule

- HYPERGLYCAEMIA → frusemide decreases the rate of glycolysis in human RBCs and may reduce the sensitivity of insulin-induced skeletal muscle uptake

- METABOLIC ALKALOSIS → loss of chloride in the urine causes a hypochloraemic metabolic alkalosis