

JULY 2007  
QUESTION 2

Outline the sites and mechanisms of actions of diuretics. Give one example of each class and two side effects

**Diuretics** work in the kidney  
decrease sodium reabsorption along the nepron,  
increasing urinary sodium and water loss  
potency of action is determined by the site of action

### Proximal tubule

Carbonic anhydrase inhibitors -acetazolamide  
May be used in pts with hypercapnic COPD, otherwise use rare  
Inhibit  $\text{CO}_2 + \text{H}_2\text{O}$  rxn, producing less  $\text{H}^+$   
 $\text{Na}^+$  is transported via  $\text{Na}^+.\text{H}^+$  antiporter,  $\text{H}_2\text{O}$  follows  $\text{Na}$  to urine  
SE: metabolic acidosis, parathesias, fatigue

Osmotic agents -mannitol  
Minor overall effect, not commonly used in oedematous states  
alter osmotic forces, starlings forces favour movement into tubule  
disrupts the counter-current mechanism (CCM) also  
SE: pulmonary oedema, can cause acute reduction in ICP

### Thick ascending loop

Loop diuretics -frusemide  
Most common agent, maximal affect up to 25% filtered load  
block  $\text{Na}.\text{K}.\text{2Cl}$  symporter, decreasing  $\text{Na}$  reabsorption and disrupting CCM  
SE: hypokalaemia, hyponatraemia, hyperchloraemic acidosis

Osmotic agents considered to act here also via the CCM

### Distal convoluted tubule

Thiazide diuretics -hydrochlorothiazide  
Maximal affect up to 5% filtered load  
block the  $\text{Na}.\text{Cl}$  symporter in the apical membrane. decrease  $\text{Na}$  reabsorption (but dont affect the CCM)  
SE: hyperglycaemia due to decreased glycogenolysis and increased insulin secretion, gluconeolysis.  
hypokalaemia

### Late distal tubule

Potassium sparing diuretics -Spironolactone  
Maximal effect up to 2% filtered load (usually in combo with other agent)  
anatanogise the action of aldosterone, inhibiting  $\text{Na}.\text{K}.\text{ATPase}$  activity, reducing reabsorption of  $\text{Na}$  and decreasing secretion of  $\text{K}$   
SE: Hyperkalaemia, gynacomastia (men) and menstrual abnormalities due to sim receptors on the adrenal cortex

