

Q12 Describe the renal handling of bicarbonate and the changes in urine pH along the nephron. (80% of marks) How is this affected by hypoventilation? (20% of marks) (Sept 2010)

The kidney freely filters 4000-5000mmol of bicarbonate (HCO_3) per day $\text{GFR (180) x } [\text{HCO}_3] (24) = 4230\text{mmol/day}$

Under normal conditions this bicarbonate is completely reabsorbed such that none is present in the urine. This is vital for acid base balance.

85% of filtered HCO_3 is reabsorbed in the proximal tubule:

- In the proximal tubule cell, H^+ and HCO_3 are formed from CO_2 and H_2O catalyzed by carbonic anhydrase
- HCO_3 crosses the basolateral membrane to enter the blood via the Na/HCO_3 symporter. The H^+ enters the tubular lumen via the Na/H^+ antiporter or the H^+ ATPase pump
- In the lumen, the H^+ ions combine with the filtered HCO_3 ions to form CO_2 and H_2O , which diffuse back into the cell to reform into H^+ and HCO_3
- The net effect is the resorption of one molecule of HCO_3 and one of Na from the tubular lumen into the bloodstream for each molecule of H^+ secreted into the lumen. This mechanism does not lead to the net excretion of any H^+ because the H^+ is consumed in the reaction with the filtered HCO_3 .
- Fluid entering the PT has a pH the same as plasma, approx. 7.4. By the end of the PT it has fallen to ~ 6.8 due to resorption of HCO_3 .

The Loop of Henle reabsorbs 10-15% through similar processes to that in the PT.

The remaining 0-5% of bicarbonate is absorbed in the distal tubule. The DT has limited capacity to absorb HCO_3 , so if the filtered load is high some will be excreted in the urine. H^+ is secreted into the lumen via a H^+ ATPase in the intercalated cells. Once again it reacts with filtered HCO_3 . HCO_3 transfer across the basolateral membrane involves a HCO_3/Cl antiporter rather than a HCO_3/Na symporter. Luminal pH can be as low as 4.4 by the end of the DT.

EFFECT OF HYPOVENTILATION

- Hypoventilation will result in an increase in PaCO_2
- This causes an intracellular acidosis
- In the cell, CO_2 reacts with H_2O to form carbonic acid, which dissociates to H^+ and HCO_3 . The HCO_3 is reabsorbed into the bloodstream, and the H^+ excreted into the tubular lumen where it reacts with filtered bicarbonate as mentioned above
- Excess H^+ is excreted as titratable acid and NH_4^+ ; these processes create new HCO_3 for absorption to compensate for the acidosis (this effect will take several days)