Deacon's Challenge
No 135 - Answer

A teenage male presents to A&E after a session of "binge drinking" with a plasma sodium concentration of 125 mmol/L and a body weight of 72 Kg. As no other cause can be found for his hyponatremia a diagnosis of "beer potomania" is made. Stating any assumptions you make, estimate the fluid excess in Litres.

The lowest urinary solute concentration achievable by the kidney is approximately 50 mmol/L. Therefore the maximum volume of urine (and free water clearance) is limited by solute availability. In beer potomania the ingestion of large volumes of fluid (with a low solute content), often aggravated by poor nutrition, results in insufficient solutes to excrete the excess volume of water. A dilutional hyponatraemia ensues with excess fluid shared between the ICF and ECF compartments.

Since sodium is mainly confined to the ECF and the concentrations of plasma and ECF sodium are equal:

Total ECF Na (mmol) = Plasma Na (mmol/L) x ECF vol (L)

Assuming there is no change in total body sodium after the binge drinking session and there is no sodium shift between compartments or significant changes in the concentrations of other osmotically active species:

Initial ECF Na (mmol) = Final ECF Na (mmol)

Therefore:

Initial plasma Na (mmol/L) x Initial ECF vol (L)
= Final plasma Na (mmol/L) x Final ECF vol (L)

The final plasma Na concentration is given as 125 mmol/L.

The initial plasma Na is unknown, but it would be reasonable to assume a "normal" value of 140 mmol/L.

The above expression still contains two unknowns – the initial and final ECF volumes. One solution would be to assume an initial ECF volume of 14 L (a typical value for an adult male). The calculation then becomes relatively straight forward:

$$14 \times 140 = \text{Final ECF vol (L)} \times 125$$

$$\text{Final ECF vol} = \frac{14 \times 140}{125} = 15.7\ \text{L}$$

$$\text{ECF excess vol} = \text{Final ECF vol} - \text{Initial ECF vol} = 15.7 - 14 = 1.7\ \text{L}$$

This ECF volume is then multiplied by 3 (since the ECF is normally approximately a third of total body water):

Fluid excess = 1.7 x 3 = **5.1 L**

It is possible to perform this calculation (and obtain a similar result) without assuming a value for the initial ECF volume:

Initial body wt (Kg) = Final body wt (Kg) - Water excess (Kg)

Substituting final body wt = 72 Kg

Initial body wt (Kg) = 72 - Water excess (Kg)

Assuming that initially the total body water was a normal 60% of body weight, and that a third of this was located in the ECF we can write:

$$\text{Initial ECF(L)} = (72 - \text{Water excess}) \times \frac{60}{100} \times \frac{1}{3}$$

$$= 14.4 - (0.2 \times \text{Water excess})$$

Assuming the excess water that accumulates is divided between the ECF and ICF in the normal ratio of 1:2, then the following expression can be written for the final ECF vol:

Final ECF (L) = Initial ECF (L) + (0.33 x Water excess)

= 14.4 - (0.2 x Water excess) + (0.33 x Water excess)

= 14.4 + (0.13 x Water excess)

Substituting these two ECF volumes and the plasma sodium concentrations into the original equation gives:

140 x {14.4 - (0.2 x Water excess)} = 125 x {14.4 + (0.13 x Water excess)}

which can be solved for water excess:

2016 - (28 x Water excess) = 1800 + (16.25 x Water excess)

(16.25 x Water excess) + (28 x Water excess) = 2016 - 1800

44.25 x Water excess = 216

$$\text{Water excess} = \frac{216}{44.25} = \mathbf{4.9\ L}$$

Question 136

A new drug for the treatment of rheumatoid arthritis is metabolised in vivo to its active metabolite (MW = 142) by a plasma enzyme. The metabolite is cleared by glomerular filtration. A patient (body weight = 75 Kg, GFR = 100 mL/min) failed to respond to treatment. Kinetic studies showed that the patient's enzyme obeyed simple Michaelis-Menten kinetics with respect to drug concentration (K_m = 80 µmol/L and V_{max} = 5 µmol/min/L plasma). Calculate the maximum achievable steady state plasma concentration (in mg/L) and comment on the significance of this result if the therapeutic range for the metabolite is 80-140 mg/L.