Deacon's Challenge
No 97 - Answer

A 14-year old boy was admitted in an intoxicated state having been suspected to have consumed an unknown quantity of methylated spirit (a mixture of ethanol and methanol). He weighed 55 Kg. The following laboratory results were obtained on a blood sample taken within 15 minutes of admission:

Urea	*2.9 mmol/L*
Sodium	*136 mmol/L*
Potassium	*4.2 mmol/L*
Glucose	*3.2 mmol/L*
Osmolality	*325 mOsm/Kg*
Ethanol	*185 mg/dL*

a) Estimate his serum methanol concentration in mg/dL and the volume of methanol he consumed (volume of distribution 0.6L/Kg, density 0.791 g/mL) stating any assumptions you make or limitations of this approach.

b) Why is the toxicity associated with this methanol dose likely to be less than if he had consumed an equivalent volume of pure methanol?

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a) First calculate the expected osmolality from the concentrations of species normally making the major contribution (Na, K, urea and glucose). Several equations have been proposed but the following is widely accepted as giving the best estimate:

$$\underset{\text{mOsm/Kg}}{\text{Osmolality}} = 1.86\,\underset{\text{mmol/L}}{[Na^+]} + \underset{\text{mmol/L}}{[\text{Glucose}]} + \underset{\text{mmol/L}}{[\text{Urea}]} + 9$$

Substituting values for Na^+, glucose and urea concentrations:

$$\text{Calculated osmolality} = (1.86 \times 136) + 3.2 + 2.9 + 9$$
$$= 268 \text{ mOsm/Kg (to 3 sig figs)}$$

The difference between this calculated value and the measured osmolality is the osmolal gap:

$$\underset{\text{mOsm/Kg}}{\text{Osmolal gap}} = \underset{\text{mOsm/Kg}}{\text{Measured osmolality}} - \underset{\text{mOsm/Kg}}{\text{Calculated osmolality}}$$

and represents the unmeasured osmotically active species (in this case mainly ethanol and methanol).

$$\text{Osmolal gap} = 325 - 268 = 57 \text{ mOsm/Kg}$$

Assuming ethanol and methanol are the major unmeasured species contributing to the osmolal gap:

$$[\text{Ethanol}] + [\text{Methanol}] = 57 \text{ mmol/L}$$

Therefore: $[\text{Methanol}] = 57 - [\text{Ethanol}]$

First convert the ethanol result to mmol/L:

$$\text{MW ethanol } (C_2H_5OH) = (2 \times 12) + (6 \times 1) + 16 = 46$$

$$\text{Ethanol (mmol/L)} = \frac{\text{Ethanol (mg/dL)} \times 10}{\text{MW}} = \frac{185 \times 10}{46} = 40 \text{ mmol/L}$$

Therefore; $\text{Methanol (mmol/L)} = 57 - 40 = 17 \text{ mmol/L}$

Converting this result to mg/dL:

$$\text{MW methanol } (CH_3OH) = 12 + (4 \times 1) + 16 = 32$$

$$\text{Methanol (mg/dL)} = \frac{\text{Methanol (mmol/L)} \times \text{MW}}{10}$$

$$= \frac{17 \times 32}{10} = \mathbf{54\ mg/dL} \text{ (to 2 sig figs)}$$

$$\text{Volume of distribution } (V_d) = \frac{\text{Amount of methanol in body}}{\text{Plasma concentration}}$$

First correct the V_d for body weight (55 Kg):

$$V_d \text{ (L)} = V_d \text{ (L/Kg)} \times \text{Body wt (Kg)}$$
$$= 0.6 \times 55 = 33 \text{ L}$$

Substituting this value and the plasma methanol (in mg/L) in the expression for (V_d) gives

$$33 \text{ (L)} = \frac{\text{Amount of methanol in body (mg)}}{54 \times 10}$$

$$\text{Amount of methanol in body} = 33 \times 54 \times 10 = 17{,}820 \text{ mg}$$

To convert to volume (mL) of methanol use the relationship for density:

$$\text{Density} = \frac{\text{Weight}}{\text{Volume}}, \quad \text{so that:} \quad \text{Volume} = \frac{\text{Weight}}{\text{Density}}$$

Since we need the volume in mL, the density is in g/mL and the amount of methanol in the body is in mg, the density must be multiplied by 1,000 to convert it to mg/mL.

$$\text{Volume (mL)} = \frac{17{,}820}{0.791 \times 1{,}000} = \mathbf{22.5\ mL} \text{ (to 3 sig figs)}$$

Assuming that all of the methanol ingested is absorbed and none of it is metabolised or excreted then the volume of methanol ingested is also **22.5 mL.**

b) Methanol itself is relatively non-toxic but is metabolised by the action of alcohol and aldehyde dehydrogenases to formaldehyde and formic acid. Formic acid is considered to be the main cause of metabolic acidosis. Ethanol is also metabolised by alcohol dehydrogenase, but the enzyme has a much higher affinity for this substrate. Therefore in the presence of ethanol the metabolism of methanol is slowed and the formation of toxic metabolites reduced.

Question 98

A buffer solution (pH 4.74) contains acetic acid (0.05 mol/L) and sodium acetate (0.05 mol/L) i.e. it is a 0.1M acetate buffer. Calculate the pH after addition of 2 mL of 0.025M hydrochloric acid to 10 mL of the buffer.