Deacon's Challenge No. 49 Answer

A 45-year old man is brought to casualty following a fit. He had been working alone late in a garage, when he was found by the security guard who called an ambulance. On admission, he has a large bruise on the left temple and is semi-comatose, he smells of alcohol. The admitting team request urea and electrolytes, glucose and an alcohol and blood gas estimation and arrange an urgent CT scan. The results are as follows:

Sodium	141 mmol/L	Potassium	4.5 mmol/L
Urea	3.5 mmol/l	Creatinine	105 µmol/L
Ethanol	270 mg/dL	Glucose	3.2 mmol/L
Hydrogen ion	39 nmol/L	PO2	11.6 kPa
PCO_2	3.8 kPa		

The CT scan does not show any bony injury or evidence of intracranial bleed. The neurological registrar is called and asks for an osmolal gap to help provide a quick estimation of whether there is a possibility that other toxic substances present in the garage, such as antifreeze, have been taken in any quantity.

The measured osmolality is 330 mOsm/Kg.

As duty biochemist you are asked to:

a) Calculate the osmolal gap
b) Show whether the alcohol concentration explains the observed osmolal gap, explaining any assumptions you make in the process.

MRCPath, May 2000

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a) Numerous equations have been proposed for the calculation of plasma osmo*lality* from the mol*ar* concentrations of the principal osmotically active species normally present in plasma – principally sodium and potassium (and their associated anions), glucose and urea. One such equation is:

$$\text{Osmolality}_{\text{Calculated}}\ (\text{mOsm/Kg}) = 2\,[\text{Na}^+] + [\text{urea}] + [\text{glucose}] \ldots\ldots\ldots\ldots(\text{i})$$

The concentration of sodium is multiplied by 2 to allow for the associated anions (mainly chloride and bicarbonate). Using this equation gives the following result:

$$\text{Osmolality}_{\text{Calculated}} = (2 \times 141) + 3.5 + 3.2 = \mathbf{289}\ \text{mOsm/Kg (3 sig figs)}$$

Alternative equations have been used which have been claimed to have superior accuracy. These include the following:

$$\text{Osmolality}_{\text{Calculated}}\ (\text{mOsm/Kg}) = 1.86\,[\text{Na}^+] + [\text{urea}] + [\text{glucose}] + 9 \ldots\ldots(\text{ii})$$

which gives: $(1.86 \times 141) + 3.5 + 3.2 + 9 = \mathbf{278}$ mOsm/Kg (3 sig figs)

$$\text{Osmolality}_{\text{Calculated}}\ (\text{mOsm/Kg}) = 1.86[\text{Na}^+ + \text{K}^+] + [\text{urea}] + [\text{glucose}] + 10 \ldots(\text{iii})$$

which gives: $1.86\,(141 + 4.5) + 3.5 + 3.2 + 10 = \mathbf{287}$ mOsm/Kg (3 sig figs)

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

$$\text{Osmolal gap (mOsm/Kg)} = \text{Osmolality}_{\text{Measured}} - \text{Osmolality}_{\text{Calculated}}$$

Using the above three calculated osmolalities the corresponding osmolal gaps can be calculated:

Equation (i):	Osmolal gap = 330 - 289	= **41** mOsm/Kg
Equation (ii):	Osmolal gap = 330 - 278	= **52** mOsm/Kg
Equation (iii):	Osmolal gap = 330 - 287	= **43** mOsm/Kg

b) Calculate the expected contribution of ethanol to the measured osmolality (i.e. the expected osmolal gap) by converting its concentration from mg/dL to mmol/L:

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

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

$$\text{Ethanol (mmol/L)} = \frac{270 \times 10}{46} = 59 \text{ mmol/L (2 sig figs)}$$

In every instance the calculated osmolal gap is less (not more) than the ethanol concentration which indicates that there is *no significant amount* of any other osmotically active species present.
Assumptions made in calculating osmolality include:

- That all the important osmotically active species are accounted for.
- That all ionic species are completely dissociated
- That the anions associated with Na^+ and K^+ are free to contribute to osmolality and are not part of a macromolecule (e.g. protein)
- That the activity of each species is the same as concentration i.e. the ions exhibit ideal behaviour.
- That the mol*al* concentration of each ion (mol/Kg *water*) is the same as molar concentration (mol/L *plasma*). This is not true since plasma is about 95% water.

It is not surprising that a range of formulae have been proposed and that they all give differing results. It is important to remember that an osmolal gap is calculated from 4 (or 5) individual measurements each with its own inherent impression so that the combined imprecision of the final result may be considerable. The reference range using equation (i) has been quoted as –10 to +10 mOsm/Kg. Furthermore, volatile solvents such as ethanol do not behave entirely as expected with some osmometers. ■

Question 50

You attempt to derive a reference range for TSH for an ethnic minority population.
The first 10 samples give the following results:

Result	n
Between 0.5 and 1.49 mU/L	5
Between 1.5 and 2.49 mU/L	3
Between 2.5 and 3.49 mU/L	0
Between 3.5 and 4.49 mU/L	1
Between 4.5 and 5.49 mU/L	1

On the basis of these results, what range of TSH values would encompass 95% of the ethnic minority population?

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