Deacon's Challenge No. 35 Answer

A 60 mg dose of a drug is given to a male experimental subject who weighs 80 kg. Assuming that the drug is completely absorbed and distributed evenly throughout the total body water, estimate the potential peak plasma level. If the drug were distributed only within the extracellular compartment, what would the plasma level be?

MRCPath, November 2003

When a bolus of a drug is given, provided it is totally absorbed and not excreted or metabolized then the volume of distribution (V_D) is obtained by dividing the amount of drug given by its plasma concentration. i.e.

$$V_D = \frac{\text{Dose given}}{\text{Plasma concentration}}$$

If the volume of distribution and the dose given are both known, then this equation can be rearranged to calculate the plasma concentration:

$$\text{Plasma concentration} = \frac{\text{Dose given}}{V_D}$$

In this question we are told the dose given (60mg) and asked to calculate the plasma concentration assuming different volumes of distribution:

If the drug is distributed throughout body water, then V_D is the volume of total body water (TBW).
The body's total water content is approximately 60% by weight.

Therefore for an 80 kg man, total body water $= 80 \times \frac{60}{100} = 48$ litres (assuming that 1kg = 1L)

so that plasma concentration $= \frac{60}{48} = 1.25$ mg/L

If the drug is distributed throughout the extracellular fluid (ECF) only, the VD is the volume of the ECF. Approximately a third of the total body water is contained in the ECF. Therefore for an 80 kg man:

$$\text{ECF Vol (L)} = \text{TBW Vol (L)} = \frac{48}{3} = 16 \text{ L}$$

so that plasma concentration $= \frac{60}{16} = 3.75$ mg/L ■

Question No. 36

The incidence of the Gilbert genotype is common in the US and Europe. If the incidence of the variant bilirubin-UGT (UGT1A1) promoter associated with Gilbert's in a population is 9%, what proportion of the population carry at least one copy of the variant promoter? (Assume Hardy-Weinberg equilibrium applies).

MRCPath, November 2003