Deacon's Challenge No. 78 Answer

A patient is found to have a serum digoxin concentration of 3.5 µg/L. Digoxin was stopped. Assuming a half life of digoxin in the serum of 40 hours, how long would it take for the serum digoxin concentration to fall to 2.0 µg/L?

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The elimination of digoxin follows first order kinetics and the integrated form of the rate equation is:

$$\ln Cp_t = \ln Cp_0 - k_d.t$$

where ln represents the natural logarithm (i.e. to the base *e*) and

Cp_0 = initial concentration = 3.5 µg/L
Cp_t = target concentration at time t = 2.0 µg/L
t = time taken to reach target concentration
i.e. for digoxin concentration to fall from 3.5 µg/L to 2.0 µg/L
k_d = elimination rate constant.

The value for k_d is not given, only the half-life ($t_{1/2}$). $t_{1/2}$ is the time taken for the plasma concentration to fall by a half. The relationship between k_d and $t_{1/2}$ can be derived as follows:

By definition when one half-life has passed the concentration is one half of the initial value i.e. $Cp_t = Cp_0/2$. Substitution into the integrated form of the first-order rate equation above gives:

$$\ln Cp_0/2 = \ln Cp_0 - k_d.t_{1/2}$$

Moving the $-k_d$.t1/2 term to the left hand side (which then becomes positive) and the ln Cp0/2 term to the right-hand side (which becomes negative) gives:

$$k_d.t_{1/2} = \ln Cp_0 - \ln Cp_0/2$$

Subtracting one logarithm from another is the same as calculating the log of one number divided by the other so that $\ln Cp_0 - \ln Cp_0/2$ can also be written $\ln 2.Cp_0/Cp_0$. The Cp_0 terms cancel leaving ln 2. Substitution of ln 2 for $\ln Cp_0 - \ln Cp_0/2$ gives:

$$k_d.t_{1/2} = \ln 2$$

ln 2 is 0.693 and rearrangement gives the following useful expression relating k_d to $t_{1/2}$:

$$k_d = \frac{0.693}{t_{1/2}}$$

k_d can therefore be obtained by substituting $t_{1/2}$ = 40 h:

$$k_d = \frac{0.693}{40} = 0.017\ h^{-1}$$

Values for k_d, Cp_0 and Cp_t can now be substituted into the integrated form of the first-order rate equation and solved for t:

$$\ln 2.0 = \ln 3.5 - 0.017\ t$$

using the calculator to obtain the natural logarithms (i.e. to the base *e*, NOT 10) of 2.0 and 3.5 gives:

$$0.693 = 1.252 - 0.017\ t$$

which can be rearranged and solved for t:

$$0.017\ t = 1.252 - 0.693 = 0.559$$

$$t = \frac{0.559}{0.017} = \mathbf{33\ h}\ \text{(2 sig figs)}$$

N.B. An alternative useful relationship between t, $t_{1/2}$ and the ratio of Cp_0/Cp_t can be derived enabling calculation of t in a single step:

$$t = 1.44.\ t_{1/2}.\ln (Cp_0/Cp_t)$$

Exam tip: The same integrated form of the first order rate equation can be used to calculate clearance of a tumour marker, radioactive decay and exponential growth (in which –kd becomes positive and $t_{1/2}$ is known as the doubling time). ■

Question 79

A 75-year old woman has a convulsion after a partial hip replacement. She is found to have a serum sodium concentration of 108 mmol/L. Her estimated weight was 55 Kg. Calculate the volume of 2.7% saline required to increase her sodium concentration to 125 mmol.L (Atomic weights of sodium 23, chlorine 35.5).

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