Deacon's Challenge

No 193 - Answer

A patient in A&E with suspected adrenal crisis was given an iv dose of hydrocortisone at 18.00. The medical team on take wish to carry out a short synacthen test to confirm the diagnosis but there will be a significant contribution from the administered drug until its concentration has fallen to 10% of the peak value. Assuming that hydrocortisone elimination follows a single compartment (first order) model with a half-life of 2 h, what is the earliest time at which the test can be carried out?

The integrated form of the first-order rate equation is:

$$\boxed{Cp_t \quad = \quad Cp_0 \times e^{-kd.t}}$$

Where Cp_0 is the initial plasma concentration and Cp_t is the plasma concentration at time *t*. *kd* is the elimination rate constant.

There are several ways this equation can be utilised:

Method 1
Taking natural logarithms produces a useful linear form of the equation:

$$\boxed{\ln Cp_t \quad = \quad \ln Cp_0 - k_d.t}$$

k_d can be calculated from the half-life ($t_{1/2}$): $$k_d = \frac{0.693}{t_{1/2}}$$

Substitute $t_{1/2} = 2$h: $$k_d = \frac{0.693}{2} = 0.3465 \text{ h}^{-1}$$

Since we wish to find the time taken for the plasma concentration to fall to 10% (1/10), substitute $Cp_t = 0.1$, $Cp_0 = 1$ and $k_d = 0.3465$ and solve for *t*:

$$\ln 0.1 = \ln 1 - 0.3465t$$

$$-2.303 = 0 - 0.3465t$$

$$0.3465t = 2.303$$

$$t = \frac{2.303}{0.3465} = \mathbf{6.6\ h} \quad \text{(to 2 sig figs)}$$

Therefore it will take approximately 7 h for the cortisol concentration to fall by 90% so that the earliest the synacthen test can be performed is **1am the next day.**

Method 2
Re-arrange the integrated first-order rate equation:

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

($\ln Cp_0 - \ln Cp_t$) can be written $\ln (Cp_0/Cp_t)$ therefore: $k_d.t = \ln (Cp_0/Cp_t)$

Substitute $k_d = 0.693/t_{1/2}$: $\frac{0.693t}{t_{1/2}} = \ln (Cp_0/Cp_t)$

If N = number of half-lives (i.e. $t/t_{1/2}$) and CR is the concentration ratio (i.e. Cp_0/Cp_t) then the equation becomes:

$$\boxed{0.693N = \ln CR}$$

Substitute $CR = 1/0.1 = 10$ then solve for N:

$$0.693N = \ln 10 = 2.303$$

Therefore $N = \frac{2.303}{0.693} = 3.323$

and 3.323 half-lives = 3.323 x 2 = **6.6 h** (to 2 sig figs)

Question 194

A GP asks your help interpreting plasma creatinine results obtained on a 56 year old hypertensive patient. At diagnosis his plasma creatinine was 85 µmol/L. Six months later his plasma creatinine had risen to 110 µmol/L. Although the eGFR on both specimens was reported as >60 mL/min.1.73m^2 he is concerned that the patient may be developing renal disease. Is this increase significant? Your laboratory quotes a reference range (95% confidence limits for a Gaussian distribution) of 60-120 µmol/L with an analytical CV of 6.3% at all concentrations above 80 µmol/L. Assume an index of individuality of 0.46.

Table of z-distribution:

P (two sided)	0.10	0.05	0.02	0.01	0.002	0.001
z	1.65	1.96	2.33	2.58	3.09	3.29