Deacon's Challenge

No 166 - Answer

A patient is found to have a serum digoxin concentration of 3.8 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 ug/L?

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First calculate the elimination rate constant (k_d) from the half life ($t_{1/2}$):

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

$$40 = \frac{0.693}{k_d}$$

$$k_d = \frac{0.693}{40} = 0.0173\ h^{-1}$$

Using the natural logarithmic form of the integrated first order rate equation:

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

where Cp_0 = initial concentration = 3.8 µg/L

Cp_t = final concentration = 2.0 µg/L

t = time for concentration to fall from 3.8 µg/L to 2.0 µg/L = ?

Substitute these values and solve for t:

$$\ln 2.0 = \ln 3.8 - 0.0173t$$

$$0.693 = 1.335 - 0.0173t$$

$$0.0173t = 1.335 - 0.693 = 0.642$$

$$t = \frac{0.642}{0.0173} = 37\ h \quad \text{(to 2 sig figs)}$$

Alternative forms of the integrated rate equation can be used:

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

$$2.0 = 3.8 \times e^{-0.0173t}$$

$$\frac{2.0}{3.8} = e^{-0.0173t}$$

$$0.526 = e^{-0.0173t}$$

$$\ln 0.526 = -0.0173t$$

$$-0.642 = -0.0173t$$

$$t = \frac{-0.642}{-0.0173} = \mathbf{37h}$$

2. $$\log_{10} CR = -0.30N$$

where CR = concentration ratio = Cp_t/Cp_0 and N = number of half-lives

$$\log_{10}(2.0/3.8) = -0.30N$$

$$\log_{10} 0.526 = -0.30N$$

$$-0.279 = -0.30N$$

$$N = \frac{-0.279}{-0.30} = 0.93$$

t = 0.93 half-lives = 0.93 x 40 = **37h**

Question 167

Current NICE guidelines for the use of newer agents in the treatment of Type 2 Diabetes recommend that GLP-1 agonists (e.g. exenatide) should only be continued after 6 months if the HbA1c concentration has fallen by at least 9 mmol/mol compared to baseline. If the biological within-subject variance is 5 $mmol^2/mol^2$, what analytical precision must the assay achieve in order to be able to detect a true fall of 9 mmol/mol with greater than 95% certainty?

Two tailed z-distribution:

P(%)	10	5	2	1	0.2	0.1
z	1.65	1.96	2.33	2.58	3.09	3.29

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