

**PHA 5127**  
**Case Study 1**  
**Answer by Jeff Stark**

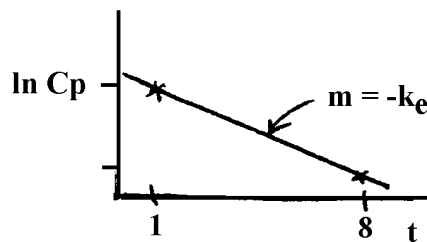
- I. Mr J.S., a 41 yr old, 60 kg, double amputee patient with G-ve pneumonia, was being treated with gentamicin and ampicillin. Gentamicin had been given as an iv bolus (0.5 mg/kg). Serum samples were obtained at 1 and 8 hours post injection, and the lab reported concentrations of 3 and 0.5  $\mu\text{g/ml}$ , respectively. Assume one compartment, first-order elimination for gentamicin.
- a. Calculate  $k_e$  and half-life of gentamicin in this patient.

Given:

Conc. Data	$C_{\mu\text{g/ml}}$	$t(\text{hr})$
	3.0	1
	0.5	8

Assume 1st order elimination, 1-compartment body model

(a) Calculate  $k_e$  and  $t_{1/2}$



$$-m = k_e = -\frac{\ln(3) - \ln(0.5)}{(1-8)\text{hr}} = 0.260\text{hr}^{-1}$$

$$t_{1/2} = \frac{\ln 2}{k_e} = 2.66\text{hr}^{-1}$$

b. Calculate  $V_d$ . Knowing that  $V_d$  in normal subjects = 0.25 L/kg, explain any observed deviations for this patient.

Recall: 
$$Cp_0 = \frac{D}{V_d}$$

This equation may be rearranged to give

$$V_d = \frac{D}{Cp_0}$$

In order to use this, however, we must know  $Cp_0$  (which was not given).

We can get  $Cp_0$  in two ways: (i) graphically or (ii) calculation. Since we do know  $k_e$ , we can use the familiar equation for an iv bolus dose which has 1<sup>st</sup> order elimination (and 1 compartment body model),

$$Cp(t) = Cp_0 \cdot e^{-k_e t}$$

Solving this for  $Cp_0$ ,

$$Cp_0 = Cp(t) \cdot e^{k_e t}$$

We can use either data point for this calculation. At  $t=1hr$ ,  $Cp(t) = 3.0 \mu g/ml$ . So,

$$\begin{aligned} Cp_0 &= (3.0 \text{mg} / \text{ml}) \cdot e^{(0.260 \text{hr}^{-1})(1 \text{hr})} \\ &= 3.9 \mu g/ml \end{aligned}$$

The iv bolus dose is  $D = (0.5 \text{ mg/kg})(60 \text{kg}) = 30 \text{ mg}$ .

Now to find  $V_d$ ,

$$V_d = \frac{30 \text{mg}}{3.9 \text{mg} / \text{ml}} \times \frac{1000 \text{mg}}{1 \text{mg}} \times \frac{1 \text{L}}{1000 \text{ml}} = 7.7 \text{L}$$

The normal  $V_d$  is 0.25 L/kg. For this patient this would be 15L.

The  $V_d$  for this patient is roughly one-half the value expected for a normal subject. This lower  $V_d$  is most likely attributed to the fact that this patient is an amputee.

c. Calculate total clearance of gentamicin.

$$Cl = k_e \cdot V_d$$

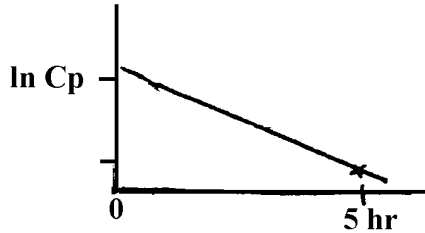
$$= (0.260hr^{-1})(7.7L) = 2.0L/hr$$

II. A 10 yr old, 25 kg patient suffering from Status Asthmaticus was given an iv bolus of aminophylline (500 mg). When serum concentrations were measured at 0 and 5 hours after injection, drug levels were found to be 35 and 14.4  $\mu\text{g/ml}$ , respectively. Assume a therapeutic range of (10-20)  $\mu\text{g/ml}$  for theophylline, 1 mg aminophylline is equivalent to 0.8 mg theophylline, and elimination occurs by a first-order process.

Given:	C( $\mu\text{g/ml}$ )	t(hr)
	35.0	0
	14.4	5

Note: 1 mg aminophylline = 8 mg theophylline

a. Calculate  $t_{1/2}$ ,  $k_e$ ,  $V_d$  and  $CL$  for theophylline in this patient.



$$k_e = -m$$

$$= -\frac{\ln(35.0) - \ln(14.4)}{(0 - 5)hr}$$

$$= 0.178 \text{ hr}^{-1}$$

$$t_{1/2} = \frac{\ln 2}{k_e} = \frac{0.693}{0.178hr^{-1}} = 3.9hr$$

To calculate  $V_d$ , we can use the  $Cp_0$  expression solved for  $V_d$ :

$$Cp_0 = \frac{D}{V_d}$$

or

$$V_d = \frac{D}{Cp_0}$$

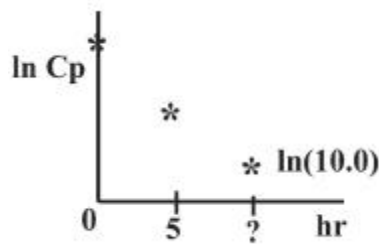
$$V_d = \frac{500\text{mg(aminoph)}}{35.0\text{mg/ml(theoph)}} \times \frac{0.8\text{mg theoph}}{1.0\text{mg aminoph}} \times \frac{10^3\text{mg}}{1\text{mg}} \times \frac{1\text{L}}{10^3\text{ml}}$$

$$= 11.4\text{ L}$$

$$Cl = k_e \cdot V_d$$

$$= (0.178\text{hr}^{-1})(11.4\text{L}) = 2.0\text{L/hr}$$

b. How long will it take before the patient is subtherapeutic ?



Since we know  $Cp_0$  and  $k_e$ , we can calculate the concentration at any time point.

Likewise, we can calculate the time point at which a given concentration is reached.

$$Cp(t) = Cp_0 \cdot e^{-k_e t}$$

We need to solve this for the time  $t$  at which  $Cp(t) = 10.0\ \mu\text{g/ml}$ .

$$e^{-k_e t} = \frac{Cp(t)}{Cp_0}$$

Taking the natural log of both sides gives:

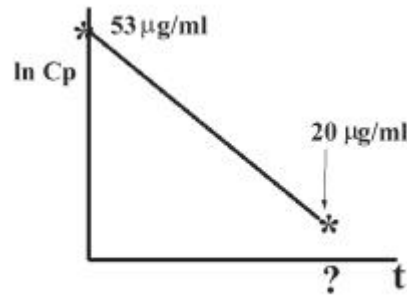
$$-k_e t = \ln(Cp(t)/Cp_0)$$

$$t = -\frac{1}{k_e} \cdot \ln(Cp(t)/Cp_0)$$

$$= -\frac{1}{(0.178\text{hr}^{-1})} \cdot \ln(10.0/35.0)$$

$$= 7.0\text{ hr}$$

III. A patient is admitted to the ER upon ingesting an overdose of theophylline. A serum drug level was measured at 53  $\mu\text{g/ml}$ . Assuming an 8 hour  $t_{1/2}$  and no further drug absorption, determine how long it would take for the serum level to drop to the upper limit of the therapeutic range (20  $\mu\text{g/ml}$ ).



to solve this problem, we can use the same equation used in question 2(b). Here, we let  $C_{p0} = 53 \mu\text{g/ml}$ .

$$k_e = \frac{\ln 2}{t_{1/2}} = \frac{0.693}{8\text{hr}} = 0.087\text{hr}^{-1}$$

$$= -\frac{1}{(0.087\text{hr}^{-1})} \cdot \ln(20/53) = 11.2\text{hr}$$