Answers for Case Study 1 – Fall 2001

I. The elimination half-life (k_e) can be calculated as slope using a plot of natural log of Concentration versus time:

$Ke = (\ln C_1 - \ln C_2) / (t_2 - t_1)$

$Ke = (\ln 0.5 - \ln 3)/(8\text{-}1)$

$Ke = 0.256\ h^{-1}$

Half-life ($t_{1/2}$) is can then be calculated by:

$T_{1/2} = 0.693/Ke$

$T_{1/2} = 0.693/0.256\ h^{-1}$

$T_{1/2} = = 2.7\ h$

Volume of distribution (Vd) can be calculated by:

$Vd = Dose/C_0$

Where C_0 is the concentration in plasma when time = 0 or immediately after the dose is given.

To find C_0 you need the equation for a 1-compartment, 1st order elimination following i.v. bolus

$C = C_0\ e^{-Ket}$

or rewritten

$\ln C = \ln C_0 - Ke^*T$

rearrange to solve for C_0

$\ln C_0 = \ln C + Ke^*T$ or $C_0 = C\ e^{Ke^*T}$

plugging in the values using t = 1 and C = 3 ug/ml

$C_0 = 3\ e^{0.256^*1}$

$C_0 = 3.9$ ug/ml or 3.9 mg/L

Since we now have C_0 and we know the dose

Dose = 0.5 mg/mg body weight where the patient is 60 kg

Dose = 0.5 mg/kg * 60 kg = 30 mg

And the Vd is:

$Vd = 30\ mg / 3.9\ mg/L$

And the volume of distribution is

$Vd = 7.7\ L$

II. This problem is similar to the first problem except, the drug that we administer, aminophylline, is not the active drug BUT we measure the active drug, theophylline, in the blood AND 1 mg aminophylline = 0.8 mg theophylline

First calculate the elimination rate constant (Ke) as we did in Problem 1:

$Ke = (\ln C_1 – \ln C_2) / (t_2 – t_1)$
$Ke = (\ln 35 – \ln 14.4)/(5-0)$
$Ke = 0.178\ h^{-1}$

Half-life ($t_{1/2}$) is can then be calculated by:
$T_{1/2} = 0.693/Ke$
$T_{1/2} = 0.693/0.178\ h^{-1}$
$T_{1/2} = 3.9\ h$

Volume of distribution (Vd) can be calculated by:

$Vd = Dose/C_0$

Where C_0 is the concentration in plasma when time = 0 or immediately after the dose is given. Now remember, the dose given was 500 mg of aminophylline BUT we need to know how much theophylline that is equivalent to, so we convert

500 mg aminophylline * 0.8 mg theophylline / 1 mg aminophylline = 400 mg

So we actually gave a 400 mg dose of theophylline. Therefore the volume of distribution is

$Vd = 400\ mg / 35\ mg/L$

And the volume of distribution is

$Vd = 11.4\ L$

We now want to know how long it will take the patient to reach sub-therapeutic blood levels of theophylline. Knowing therapeutic levels are 10-20 ug/ml, we would like to know how long it would take to go below 10 ug/ml. Using the equation for a 1-compartment, 1st order elimination following i.v. bolus

$C = C_0\ e^{-Ket}$

or rewritten

$\ln C = \ln C_0 - Ke*T$

rearrange to solve for time

$T = -(\ln C - \ln C_0) / Ke$ or $T = -(\ln C/C_0) / Ke$

Plugging in C = 10 ug/ml, C_0 = 35 ug/ml, and Ke = 0.178 h^{-1}

$T = -(\ln 10/35) / 0.178$

T = 7 h for the patient's blood levels to go below 10 ug/ml

We now need to calculate the area under the curve (AUC) from t = 0 to infinity ($AUC_{0\rightarrow\infty}$) and we do this by using trapezoids.

The area of a trapezoid is the (average height of the sides) * the base or for a given time interval

AUC (t =1-2) = $(C_1 + C_2)/2 * (t_2 - t_1)$

Given the data set

AUC (0-1 h) = (35+30)/2 * (1-0) = 32.5 ug*h/ml
AUC (1-2 h) = (30+25)/2 * (2-1) = 27.5 ug*h/ml
AUC (2-4 h) = (17+25)/2 * (4-2) = 42 ug*h/ml
AUC (4-9 h) = (17+2)/2 * (9-4) = 60 ug*h/ml
AUC (9-16 h) = (2+7)/2 * (16-9) = 31.5 ug*h/ml

If we sum the AUC from t = 0 to 16 h we get 193.5 ug*h/ml. We still need to calculate from 16 h to infinity and we do this by

$AUC_{(t-\infty)} = C_x / Ke$

Where C_x is the last measured concentration, so in the this case the concentration at time = 16 h

$AUC_{(t-\infty)}$ = 2 ug/ml / 0.178 h^{-1} = 11.2

Now for AUC from t=0 through infinity we add the two parts

AUC (0-16h) + AUC (16h-infinity) = AUC (0-infinity)
193.5 ug*h/ml + 11.2 ug*h/ml = 204.7 ug*h/ml

III. This question is similar to Part B of Question #2. We assume a 1-compartment model with 1st order elimination. We are given a half-life of 8 h which give as an elimination rate constant of 0.087 h^{-1} because

$T_{1/2} = 0.693 / Ke$ or $Ke = 0.693 / t_{1/2}$
$Ke = 0.693 / 8 \text{ h} = 0.087 \text{ h}^{-1}$

We want to find how long it will take for the blood concentration to fall below 20 ug/ml. We do this by using the equation

$C = C_0 \, e^{-Ket}$

or rewritten

$\ln C = \ln C_0 – Ke*T$

rearrange to solve for time

$T = - (\ln C – \ln C_0) / Ke$ or $T = - (\ln C/C_0) / Ke$

Plugging in C = 20 ug/ml, C_0 = 53 ug/ml, and Ke = 0.087 h^{-1}

$T = - (\ln 20/53) / 0.087$

T = 11.2 h for the patient’s blood levels to go below 20 ug/ml