

**(Key to Case Study1)**

**Case study 1.**  
**(PHA5127)**

**Fall 2003**

**Question 1.**

A 80 year old, 70-Kg patient with pneumonia, was being treated by an iv. bolus of gentamicin ( 0.5 mg / kg ). Serum samples were taken at 0.5 and 6 hours post injection, and the lab reported drug concentrations of 3.41 $\mu$ g/ml, and 0.83  $\mu$ g/ml, respectively. Assume gentamicin follows one compartment, first-order elimination.

1.) Calculate the half-life of gentamicin in this patient.

$$Ke = \frac{\ln(C_2 / C_1)}{t_1 - t_2} = -\frac{\ln(0.83/3.41)}{0.5 - 6} = 0.26(\text{hr}^{-1})$$

$$t_{1/2} = \frac{0.693}{0.26} = 2.66(\text{hr.})$$

2.) Calculate the volume of distribution of gentamicin in this patient.

$$\text{Dose} = 0.5 \times 70 = 35 \text{ (mg)}$$

$$\text{Recall: } C_t = C_0 \cdot e^{-Kt} \text{ then } C_0 = C_t \cdot e^{Kt} = 3.41 \cdot e^{0.26 \cdot 0.5} = 3.88(\mu\text{g} / \text{ml})$$

$$\text{Then: } Vd = \frac{\text{Dose}}{C_0} = \frac{35}{3.88} = 9.0(\text{l})$$

3.) Can you predict what is the drug concentration two half-lives after iv. bolus injection.

$$t = 2 \cdot 2.66 = 5.32(\text{hr.})$$

$$C_t = C_0 \cdot e^{-Kt} = 3.88 \cdot e^{-0.26 \cdot 5.32} = 0.97(\mu\text{g} / \text{ml})$$

**Or :**

Recall the definition of half-life. In one half-life,  $C_{t_{1/2}} = 0.5 * C_t$ . Then two half-lives,

$$C_{2t_{1/2}} = 0.5 \cdot C_{t_{1/2}} = 0.5 \cdot 0.5 \cdot C_t = 0.25 \cdot 3.88 = 0.97(\mu\text{g} / \text{ml})$$

## Question 2.

A 25-year-old, 60-kg female patient was given an iv. bolus of a aminophylline, ( 200 mg ). Theophylline concentration-time profiles after the first dose was given as following (table). Given the fact that 1mg of aminophylline is equivalent to 0.8mg theophylline and elimination occurs by first-order kinetics, please answer the following questions.

Table1. Theophylline concentration-time profiles after iv. bolus of aminophylline.

t(hr)	Con (ug/ml)	AUC(t1-t2)
0	<b>9.64</b>	
1	7.89	<b>8.76</b>
3	5.29	<b>13.18</b>
5	3.55	<b>8.84</b>
7	2.38	<b>5.92</b>
12	0.87	<b>8.13</b>
AUC 0-12		<b>44.83</b>

1.) Calculate the  $AUC_{0-12}$  of theophylline by using trapezoidal rule.

$$K_e = \frac{\ln(C_2 / C_1)}{(t_1 - t_2)} = \frac{\ln(0.87 / 7.89)}{(1 - 12)} = 0.2(\text{hr}^{-1})$$

$$\text{Again: } C_t = C_0 \cdot e^{-K_e \cdot t} \text{ Then, } C_0 = C_t \cdot e^{K_e \cdot t} = 0.87 \cdot e^{0.2 \cdot 12} = 9.64(\mu\text{g} / \text{ml})$$

$$\text{Then, using trapezoidal rule: } AUC_{1-2} = \frac{(C_1 + C_2)}{2} \cdot (t_2 - t_1)$$

The final answer is: 44.83 mg\*h/L.

2.) Calculate the  $AUC_{0-\infty}$ .

$$AUC_{12-\infty} = \frac{C_t}{K_e} = \frac{0.87}{0.2} = 4.35(\text{mg} \cdot \text{hr} / \text{L})$$

$$\text{Then, } AUC_{0-\infty} = AUC_{0-12} + AUC_{12-\infty} = 44.83 + 4.35 = 49.18(\text{mg} \cdot \text{hr} / \text{L})$$