PHA 5127
Case Study 1 (answer key)
Fall 2002

**Question 1.**
A 10 yr old, 25 kg patient suffering from Status Asthmatics was given an iv bolus of aminophylline (800 mg). When theophylline plasma concentrations were measured at 0.5 and 5 hours after injection, drug levels were found to be 35 and 14.4 mg/L, respectively.
(Assume a therapeutic range of 10-20 mg/L for theophylline, 1 mg aminophylline is equivalent to 0.8 mg theophylline and elimination occurs by a first-order process.)

(1) Calculate ke and half-life of theophylline in this patient.

$$k_e = \frac{\ln(C_2 / C_1)}{(t_1 - t_2)} = \frac{\ln(14.4/35)}{(0.5-5)} = \mathbf{0.2\ h^{-1}}$$

$$t_{1/2} = \frac{\ln 2}{k_e} = \frac{0.693}{0.2} = \mathbf{3.5\ hrs}$$

(2) Calculate Vd of theophylline in this patient.

$$C_t = C_0 \cdot e^{-ke \cdot t}$$
$$C_0 = C_t \cdot e^{ke \cdot t} = 14.4 \cdot e^{0.2 \cdot 5} = 38.6 \text{ mg/L}$$
$$V_d = \frac{Dose}{C_0} = \frac{800}{38.6} = \mathbf{16.6\ L}$$

(3) How long will it take before the patient is subtherapeutic?

$$C_t = C_0 \cdot e^{-ke \cdot t}$$
$$10 = 38.6 \cdot e^{-0.2 \cdot t}$$
t = **6.8 hrs**

It will take 6.8 hrs after the dosing.

Or

$$C_t = C_5 \cdot e^{-ke \cdot (t-5)}$$
$$10 = 14.4 \cdot e^{-0.2 \cdot (t-5)}$$
t = **1.8 hrs**

It will take 1.8 hrs after 5-hour sampling time.

**Question 2.**
A 41 yr old, 60 kg male patient with gram-negative pneumonia, was being treated with gentamicin and ampicillin. Gentamicin had been given as an iv bolus (2 mg/kg). The concentration-time profile of gentamicin after first dose in this patient was shown as following:
(Assume first-order elimination for gentamicin.)

(1) Calculate the $AUC_{0\text{-}10}$ of cefaclor using trapezoidal rule.

First, need to find out the drug concentration at time zero ($C_0$),

$$k_e = \frac{\ln(C_2 / C_1)}{(t_1 - t_2)} = \frac{\ln(1.5 / 4.2)}{(2 - 6)} = 0.26\ \text{h}^{-1}$$

$$C_t = C_0 \cdot e^{-\text{ke}\cdot\text{t}}$$
$$C_0 = C_t \cdot e^{\text{ke}\cdot\text{t}} = 5.5 \cdot e^{0.26\cdot 1} = \mathbf{7.1\ mg/L}$$

Then, using trapezoidal rule: $AUC_{t1\text{-}t2} = \frac{(C_1 + C_2)}{2} \cdot (t_2 - t_1)$

| Time (h) | Conc(mg/L) | $AUC_{t1\text{-}t2}$ |
|---|---|---|
| 0 | **7.1** | |
| 1 | 5.5 | 6.3 |
| 2 | 4.2 | 4.9 |
| 3 | 3.3 | 3.8 |
| 4 | 2.5 | 2.9 |
| 6 | 1.5 | 4.0 |
| 8 | 0.9 | 2.4 |
| 10 | 0.5 | 1.4 |
| $AUC_{0\text{-}10}$ | | **25.7** |

The sum of individual AUCs is **25.7 mg*h/L.**

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

$$AUC_{10\text{-}\infty} = \frac{C_x}{k_e} = \frac{0.5}{0.26} = 2.0\ \text{mg*h/L.}$$

$AUC_{0\text{-}\infty} = AUC_{0\text{-}10} + AUC_{10\text{-}\infty} = 25.7 + 2.0 = \mathbf{27.7\ mg*h/L.}$