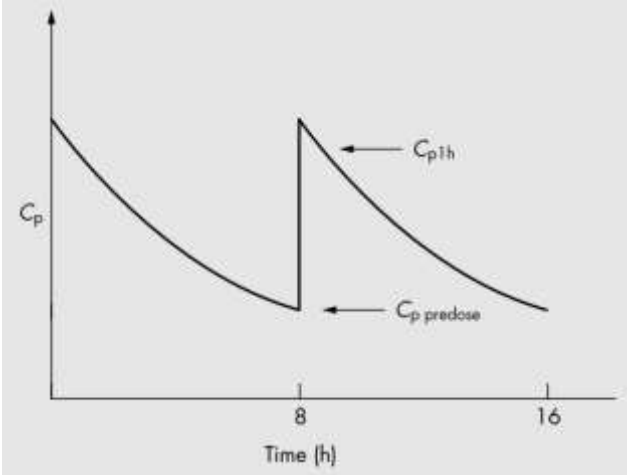
PHA 5127 Dose Optimization I Case Study 6, 2013

1. A patient was given a 100 mg IV bolus dose every 8 hr. At steady-state, two plasma samples were taken and respective concentrations were measured. The first sample was taken right before administration of the i.v. bolus dose (predose) and the second sample was taken 1 hour post dose (C_{p1h}). Measured concentrations for C_{p1h} and $C_{p\ predose}$ were 9.6 mg/L and 2.9 mg/L, respectively. Please calculate the drug's: elimination rate constant (k_e), half-life ($t_{1/2}$), volume of distribution (V_d), clearance (CL), and average steady-state concentration (C_{ss}).



2. You wish to begin a patient on a constant rate infusion of Drug X. The drug concentration is 10 mg/L before the start of the constant rate infusion. The volume distribution of the patient is 10 L and elimination rate constant is 0.4/hr.

   A. Please compute the infusion rate (k_0) necessary to achieve a steady state drug concentration (C_{ss}) of 20 mg/L.

   B. In order to reach the steady-state directly, what should be the loading dose? Remember the drug concentration was 10 mg/L before infusion.

3. True or False

   A. For a multiple IV bolus regimen, if the dosing interval is the same, the shorter the half-life the more pronounced the differences between peak and trough concentrations. (T F)
   B. For a multiple IV bolus regimen, the longer dosing interval, the longer it will take to achieve steady state. (T F)

C. For a multiple IV bolus regimen, the accumulation degree is larger in patients with higher clearance. (T F)
D. It takes more time to reach steady state for a drug with a higher degree of accumulation. (Assuming loading dose is not given, and dosing interval is the same.) (T F)