1. A 32-year-old 70 kg male received a kidney transplant, and is treated with cyclosporine 250 mg BID. His trough level is measured and comes back 80 ng/mL. Design a new dosing regimen based on this information with a Cmax of 400 ng/mL and a Cmin of 150 ng/mL. (Cyclosporine is rapidly absorbed).

\[ V_d = 4.5 \times 70 = 315(L) \]

\[ C_{\text{max}} = \frac{F \times D}{V_d} + C_{\text{min}} = \frac{0.3 \times 250 \times 1000}{315} + 80 = 318(ng/ml) \]

\[ K_e = \frac{\ln(318) - \ln(80)}{12} = 0.115(h^{-1}) \]

\[ T_{au} = \frac{\ln(400) - \ln(150)}{0.115} = 8.52(h) = 8(h) \]

\[ Dose = \frac{C_{\text{max}} \times [1 - e^{(-k_e \times T_{au})}] \times V_d}{F \times S} = \frac{400 \times [1 - e^{(-0.115 \times 8)}] \times 315 \times 1000}{0.3 \times 1} = 252 \times 10^6(ng) \]

Dose regimen is 250 mg tid.

2. A 57-year-old, 50 kg woman with congestive heart failure, was admitted to the hospital for possible digoxin toxicity. Her serum creatinine was 2.8 mg/dL, and her dosing regimen at home had been 0.25 mg digoxin (tablets) daily for a year. Her digoxin plasma concentration on admission was 3.8 μg/L. How long will it take for the digoxin concentration to fall from 3.8 to 2 μg/L if no further doses are given?

\[ Cl_{\text{cr(female)}} = \frac{(140 - 57) \times 50}{85 \times 2.8} = 17.44(ml/min) \]

\[ Cl = \frac{S \times F \times Dose}{\tau \times C_{ss}} = \frac{1 \times 0.7 \times 0.25 \times 1000}{1 day \times 3.8 \mu g/l} = 46.05(L/day) \]

\[ V_d = 3.8L/day \times IBW + 3.1 \times Cl_{\text{cr}} = 3.8 \times 50 + 3.1 \times 17.44 = 244(L) \]

\[ K_e = \frac{Cl}{V_d} = \frac{46.05}{244} = 0.189(/day) \]
\[ T = \frac{(\ln C_1 - \ln C_2)}{k_e} = \frac{(\ln 3.8 - \ln 2)}{0.189} = 3.4 \text{(day)} \]

3. An 82 kg male became nauseated after receiving i.v. aminophylline 90mg/h for several days. A plasma sample for theophylline was obtained and the infusion was discontinued. Ten hours later a second plasma sample was obtained. The reported plasma theophylline concentrations were 40μg/mL and 20μg/mL, respectively. Estimate the hourly dose of aminophylline required to maintain the plasma theophylline concentration at 15mg/L. (Use aminophylline \( S = 0.85 \), \( V_d = 0.5 \text{L/kg} \))

\[
Ke = \frac{(\ln C_1 - \ln C_2)}{(t_2 - t_1)} = \frac{(\ln 40 - \ln 20)}{10} = 0.639/10 = 0.0693 \text{(h}^{-1}\text{)}
\]

\[
V_d = 0.5 \text{L/kg} \times 82 \text{kg} = 41 \text{(L)}
\]

\[
Cl = Ke \times V_d = 0.0693 \times 41 = 2.84 \text{(L/h)}
\]

\[
MD = \frac{Cl \times Css}{F \times S} = \frac{2.84 \times 15}{1 \times 0.85} = 50.11 \text{(mg/h)}
\]

4. A 34 year old female patient (54 kg, SeCr 1.1 mg/dl) received a 30 mg methotrexate loading dose I.V. followed by a 30 mg/h infusion over 36 hours. Her levels at 24h and 48h were 12.2 μM and 0.76 μM, respectively. Calculate the anticipated methotrexate level at 60 hours.

\[
K_1 = \frac{\ln(C_1/C_2)}{t} = \frac{\ln(12.2/0.76)}{12} = 0.231 \text{(h}^{-1}\text{)}
\]

\[
t_{1/2_1} = 0.693/0.231 = 3 \text{ (h)}
\]

\[
t \text{ at } 0.5 \mu M
\]

\[
t = \frac{\ln(C_1/C_2')}{K_1} = \frac{\ln(12.2/0.5)}{0.231} = 13.8 \text{ (h)}
\]

\[
t_{1/2_1} = 3 \text{ h} \quad t_{1/2_2} = 10 \text{h}
\]

\[
K_2 = 0.693/10 = 0.0693 \text{ (h}^{-1}\text{)}
\]
T = 60 - 13.8 - 36 = 10.2 (h)

\[ C_{p_{60h}} = 0.5 e^{-0.0693 \times 10.2} = 0.25 \mu M \]