Design a dosing regimen of amikacin to achieve a steady-state true peak concentration of 25 mg/L and concentration of 2 mg/L at 12 h after the start of dosing, assuming a twice-daily regimen via IV infusion of 0.5 hour for a specific patient: male, 35 years of age, 6’5” in height, 312 lbs. (2 pts)

Weight of 312 lbs is equivalent to 142 kg.

\[ IBW_{male} = 50 + 2.3(77 - 60) = 89.1 \text{ kg} \]

\[ TBW = \frac{312}{2.2} = 142 \]

Volume of distribution of amikacin can be estimated from the body weight:

\[ V_d = 0.26[IBW + 0.38(TBW - IBW)] = 0.26[89.1 + 0.38 \times (142 - 89.1)] = 28.4 \text{ L} \]

\[ k_e = \frac{-\ln(25) - \ln(2)}{0 - 11.5} = 0.22 \text{ h}^{-1} \]

\[ V_d = \frac{Dose}{k_e T} \cdot \frac{(1 - e^{-k_e T})}{C_{p_{max}} - (C_{p_{min}})e^{-k_e T}} \rightarrow \frac{Dose}{0.22 \times 0.5} \cdot \frac{1 - \exp(-0.22 \times 0.5)}{25 - 2 \exp(-0.22 \times 0.5)} = 28.4 \text{ L} \]

\[ Dose \sim 700 \text{ mg} \]

Dosing regimen is 700 mg IV infusion for 0.5 h, twice-daily.
An hour after the end of a 30-min intravenous infusion of 400 mg Drug X, the plasma level was 34 mg/L. Nine hours after the end of infusion, the plasma level was 3 mg/L. Predict the plasma level 12 hours after the start of dosing. Assuming that the drug was dosed at steady state, with an interdosing interval of 12 hours and a one-compartment body model, estimate the volume of distribution. (2 pts)

\[ k_e = -\frac{\ln(34) - \ln(3)}{1 - 9} = 0.303 \text{ h}^{-1} \]

First we estimate the drug concentration immediately after infusion and designate this as \( C_{p_{\text{max}}} \).

\[ 34 = C_{p_{\text{max}}} \exp(-0.303 \times 1) \]

\[ C_{p_{\text{max}}} = \frac{34}{\exp(-0.303 \times 1)} = 46 \text{ mg/L} \]

12 hours after the start of dosing is 11.5 hours after the end of infusion

\[ C(t = 11.5 \text{ h}) = 46 \times \exp(-0.303 \times 11.5) = 1.41 \text{ mg/L} \]

To compute the volume of distribution, we use the following equation:

\[ V_d = \frac{Dose}{k_e T} \times \frac{(1 - e^{-k_e T})}{C_{p_{\text{max}}} - (C_{p_{\text{min}}})e^{-k_e T}} = \frac{400}{0.303 \times 0.5} \times \frac{1 - \exp(-0.303 \times 0.5)}{46 - 1.41 \exp(-0.303 \times 0.5)} = 8.29 \text{ L} \]
Design a dosing regimen (dose and dosing interval) for gentamicin to achieve steady state peak and trough concentrations of 20 mg/L and 6 mg/L, respectively, assuming a short-term infusion of 2 hour infusion duration. The approximately gentamicin volume of distribution is 0.3 L/kg. The patient characteristics are: male, 45 years of age, 5'9", 225 lbs, serum creatinine is 1.8 mg/dL. Use Cockcroft-Gault equation to estimate the clearance of gentamicin. Round the dose to the nearest 50 mg. (3 pts)

\[
IBW_{male} = 50 + 2.3(69 - 60) = 70.7 \text{ kg}
\]

\[
TBW = \frac{225}{2.2} = 102.3 \text{ kg} \gg 120\% \text{ IBW} = 84.8 \text{ kg}
\]

We need to compute the adjusted body weight

\[
ABW = IBW + 0.4(TBW - IBW) = 70.7 + 0.4(102.3 - 70.7) = 83.3 \text{ kg}
\]

Use the adjusted body weight to compute the creatinine clearance

\[
CL_{cr} = \frac{(140 - 45)83.3}{72 \times 1.8} = 61 \text{ mL/min}
\]

Converting the units for creatinine clearance,

\[
CL_{gentamicin} = 61 \frac{\text{mL}}{\text{min}} \times \frac{60 \text{ min/h}}{1000 \frac{\text{mL}}{L}} = 3.66 \text{ L/h}
\]

\[
V_d = 0.3 \frac{L}{kg} \times 102.3 \text{ kg} = 30.7 \text{ L}
\]

\[
k_e = \frac{CL}{V_d} = \frac{3.66}{30.7} = 0.12 \text{ h}^{-1}
\]

\[
\tau = \frac{\ln\left(\frac{C_{\text{max}}}{C_{\text{min}}}ight)}{k_e} + T = \frac{\ln\left(\frac{20}{6}\right)}{0.12} + 2 \approx 12 \text{ h}
\]

\[
Dose = C_{\text{max(desired)}}k_eV_dT \frac{1 - \exp(-k_e\tau)}{1 - \exp(-k_eT)} = 20 \times 0.12 \times 30.7 \times 2 \times \frac{1 - \exp(-0.12 \times 12)}{1 - \exp(-0.12 \times 2)} = 527 \text{ mg} \sim 550 \text{ mg}
\]

The dosing regimen is 550 mg q12h
Using the information from the previous question, use the Dettli’s aminoglycoside $k_e$ equation to estimate the dosing regimen. $k_e = 0.00293 \times CL_{cr} + 0.014$, where $CL_{cr}$ is in mL/min (1.5 pts)

$$k_e = 0.00293 \times 61 + 0.014 = 0.193 \, h^{-1}$$

$$\tau = \frac{\ln \left( \frac{C_{\text{max}}}{C_{\text{min}}} \right)}{k_e} + T = \frac{\ln \left( \frac{20}{6} \right)}{0.193} + 2 \approx 8h$$

$$V_d = 0.3 \frac{L}{kg} \times 102.3 \, kg = 30.7 \, L$$

$$Dose = C_{\text{max}}(\text{desired}) \times k_e \times V_d \times T \frac{1 - \exp(-k_e \tau)}{1 - \exp(-k_e T)} = 20 \times 0.193 \times 30.7 \times 2 \times \frac{1 - \exp(-0.193 \times 12)}{1 - \exp(-0.193 \times 2)} = 667 \, mg \sim 650 \, mg$$

The dosing regimen is 650 mg q8h.
TRUE or FALSE (1.5 pts)

(1) Creatinine is an exogenous marker for GFR. (F)
(2) Creatinine itself has high plasma protein binding. (F)
(3) Creatinine is metabolized by the liver. (F)
(4) Creatinine is constantly formed by the muscle. (T)
(5) Creatinine excretion is affected by renal disease. (T)
(6) Serum creatinine measurement is a routine, fast and reliable estimate of creatinine clearance. (T)