1. B.W. is a 50-year-old, 5’2”, 55kg female with a serum creatinine of 2.2 mg/dL. She is given gentamicin for soft tissue infections. Calculate the gentamicin concentration 1 hour after initiating the one-half hour infusion of a 200 mg dose, using the short-term infusion model.(2pt)

IBW = 45.5 + 2.3 \cdot 2 = 50.1 \text{ kg}

TBW < 120\% \text{ IBW}

\[
CL_{cr} = \frac{(140 - \text{age}) \cdot TBW}{\text{Cper} \cdot 85} = \frac{(140 - 50) \cdot 55}{2.2 \cdot 85} = 26.47 mL/\text{min} = 1.59 L/hr
\]

\[
V_d = 25\% \cdot \text{TBW} = 0.25 \cdot 55 = 13.75 L
\]

\[
k_e = \frac{CL}{V_d} = \frac{1.59 \text{ L/hr}}{13.75 \text{ L}} = 0.12 \text{ hr}^{-1}
\]

Short-term infusion (single dose):

\[
C = \frac{D}{CL \cdot T} \left(1 - e^{-k_e T}\right) \cdot e^{-k_e t} = \frac{200}{1.59 \cdot 0.5} \left(1 - e^{-0.12 \cdot 0.5}\right) \cdot e^{-0.12 \cdot 0.5} = 13.8 mg/L
\] (2pt)

2. S.H. with a CL of 6.1 L/hr, Vd of 17.5 L was given tobramycin 7mg/kg QD in a 30-minute-infusion. Predict the steady-state peak concentration at the end of infusion and subsequent steady-state plasma concentration 12 hours after starting the infusion. Assume S.H. weighs 60 kg. (2pt)

\[
k_e = \frac{CL}{V_d} = \frac{6.1 \text{ L/hr}}{17.5 \text{ L}} = 0.349 \text{ hr}^{-1}
\]

\[
C_{ss \ max} = \frac{D \cdot (1 - e^{-k_e T})}{CL \cdot T \cdot (1 - e^{-k_e T})} = \frac{7 \cdot 60 \cdot (1 - e^{-0.349 \cdot 0.5})}{6.1 \cdot 0.5 \cdot (1 - e^{-0.349 \cdot 24})} = 22.03 mg/L
\] (1pt)
\[ C_{ss} = C_{ss \, max} \cdot e^{-ke^{-t}} = 22.03 \cdot e^{-0.349 \cdot 11.5} = 0.398 \text{ mg/L} \] (1pt)

3. K. K., a 30-year-old, 65 kg, non-obese female patient with a gram-negative pneumonia, was being treated with gentamicin 100mg infused over 30 minutes every 8 hours at midnight, 8:00a.m., and 4:00 p.m. Blood samples were obtained just before the 8:00 a.m. and at 9:00 a.m to evaluate therapy and prevent toxicity. The gentamicin concentrations reported were 0.4 mg/L and 4.5 mg/L respectively. Assuming these concentrations represent steady-state levels, make a dosing adjustment to achieve a peak concentration of 8 mg/L. (2pt)

Calculating \( k \) by transposing \( C_{ss \, max} \) into the same interval as \( C_{ss \, min} \), so 7 hour interval between these two concentrations.

\[ k = \frac{\ln \frac{4.5}{0.4}}{7} = 0.346 \text{hr}^{-1} \] (1pt)

True peak concentration: \( C_{\text{max}} = \frac{4.5}{e^{-0.346 \cdot 0.5}} = 5.35 \text{mg/L} \)

True trough concentration: 0.4mg/L

\[ Vd = \frac{100}{0.346 \cdot 0.5} \cdot \frac{(1 - e^{-0.346 \cdot 0.5})}{(5.35 - 0.4 \cdot e^{-0.346 \cdot 0.5})} = 18.33L \]

\[ D = 8 \cdot 0.346 \cdot 18.33 \cdot 0.5 \cdot \frac{(1 - e^{-0.346 \cdot 8})}{(1 - e^{-0.346 \cdot 0.5})} = 25.37 \cdot \frac{0.937}{0.159} = 149.5 \text{mg} \] (1pt)
4. H.W., a 65-year-old, 5’4”, 60kg woman with a serum creatinine of 1mg/dL, has been started on 1g of vancomycin over 1 hour infusion q12h for the treatment of staphylococcal. Calculate initial peak and trough vancomycin concentration and steady-state peak and trough vancomycin concentration. (2pt)

\[ V_d = 0.178 \cdot \text{age} + 0.22 \cdot \text{TBW} + 15 \]
\[ = 0.178 \cdot 65 + 0.22 \cdot 60 + 15 \]
\[ = 39.77 \text{ L} \]

(or 0.7L/kg \cdot 60 = 42 L)

\[ \text{IBW} = 45 + 2.3(\text{height in inches}-60) \text{ kg} \]
\[ = 45 + 2.3 \cdot 4 \]
\[ = 54.2 \text{ kg} \]

\[ \text{TBW} < 1.2 \ast \text{IBW using TBW} \]

\[ CL_{cr} = \frac{(140 - \text{age}) \cdot \text{TBW}}{\text{Cp cr} \cdot 18.3} \]
\[ = \frac{(140 - 65) \cdot 60}{18.3} \]
\[ = 52.94 \text{ mL/ min} \]
\[ = 3.18 \text{ L/hr} \]

\[ k_e = \frac{\text{CL}}{V_d} = \frac{3.18}{39.77} = 0.08 \text{ hr}^{-1} \]

Two acceptable models: i.v. bolus and short-term infusion

1) i.v. bolus model

Initial peak and trough

\[ C_{\text{max}} = \frac{D}{V_d} = \frac{1000}{39.77} = 25.14 \text{ mg/L} \ (0.5 \text{ pt}) \]

\[ C_{\text{min}} = C_{\text{max}} \cdot e^{-k_{\text{el}}} = 25.14 \cdot e^{-0.08 \cdot 12} = 9.63 \text{ mg/L} \ (0.5 \text{ pt}) \]

Steady state peak and trough
\[
C_{ss \ max} = \frac{D}{Vd \cdot (1 - e^{-ke \cdot T})} = \frac{1000}{39.77 \cdot (1 - e^{-0.08 \cdot 12})} = 40.75 \text{mg} / L \quad (0.5\text{pt})
\]
\[
C_{ss \ min} = C_{ss \ max} \cdot e^{-ke \cdot T} = 40.75 \cdot e^{-0.08 \cdot 12} = 15.6\text{mg/L} \quad (0.5\text{pt})
\]

2) short-term infusion

Initial peak and trough
\[
C_{\ max} = \frac{D}{CL \cdot T} \cdot (1 - e^{-ke \cdot T}) = \frac{1000 \cdot (1 - e^{-0.08 \cdot 11})}{3.18 \cdot 1} = 24.18 \text{mg} / L
\]
\[
C_{\ min} = C_{\ max} \cdot e^{-ke(\tau - T)} = 24.18 \cdot e^{-0.08 \cdot 11} = 10.03 \text{mg/L}
\]

Steady state peak and trough
\[
C_{ss \ max} = \frac{D \cdot (1 - e^{-ke \cdot T})}{CL \cdot T \cdot (1 - e^{-ke \cdot T})} = \frac{1000 \cdot (1 - e^{-0.08 \cdot 11})}{3.18 \cdot 1 \cdot (1 - e^{-0.08 \cdot 12})} = 39.19 \text{mg} / L
\]
\[
C_{ss \ min} = C_{ss \ max} \cdot e^{-ke(\tau - T)} = 39.19 \cdot e^{-0.08 \cdot 11} = 16.26 \text{mg/L}
\]

5. K.T. is a 65-year-old, 5’7”, 105kg man with a serum creatinine concentration of 2.2mg/dL. He is going to receive vancomycin for a nafcillin-resistant S.aureus (NSRA) infection. Design a dosing regimen (dose and dosage schedule) that will produce peak concentration of 30mg/L and trough concentration of 10mg/L. (2 pt)

\[
Vd = 0.178 \cdot \text{age} + 0.22 \cdot \text{TBW} + 15
= 0.178 \cdot 65 + 0.22 \cdot 105 + 15
= 49.67 \text{L}
\]

\[
\text{IBW} = 50 + 2.3(\text{height in inches-60}) \text{ kg}
= 50 + 2.3 \cdot 7
= 66.1\text{kg}
\]

\[
\text{TBW} > 1.2 \cdot \text{IBW using ABW}
\]
ABW = IBW + 0.4(TBW - IBW) = 66.1 + 0.4(105 - 66.1) = 81.66kg

\[
CL_{cr} = \frac{(140 - age) \cdot ABW}{C_{pcr} \cdot 72} = \frac{(140 - 65) \cdot 81.66}{2.2 \cdot 72} = 38.66 mL/min = 2.32 L/hr
\]

\[
k_e = \frac{CL}{V_d} = \frac{2.32 L/hr}{49.67 L} = 0.047 hr^{-1}
\]

\[
\tau = \frac{\ln\left(\frac{C_{max}}{C_{min}}\right)}{k} = \frac{\ln\left(\frac{30}{10}\right)}{0.047} = 23.4 hr \approx 24 hr \quad (1 pt)
\]

Dose = \(V_d \cdot C_{max} \cdot (1 - e^{-k_e \cdot \tau}) = 49.67 \cdot 30 \cdot (1 - e^{-0.047 \cdot 24}) = 1 g \quad (1 pt)\)

1g q24h