1. A.M. is a 5’ 7”, 70 kg, 60 year old female who suffered a severe burn that has since been infected by S. aureus. Her Cpcreat is measured at 0.6 mg/dL. Design a dosing regimen of half-hour i.v. infusions of gentamicin that will give her a true peak concentration of 7 μg/ml and a true trough concentration of 0.5 μg/ml. For k_e use the creatinine clearance and the predicted volume of distribution and not the k_e for aminoglycoside equation from your equation sheet. (2pts)

First calculate τ, but in order to calculate τ you will need k_e, and for k_e you will need to know Clcr and Vd. To calculate Vd you need to know if this patient is obese or not.

IBW = 45.5 + 7*2.3 = 61.6 kg  70kg (TBW)<120%IBW
Use TBW for Clcr and Vd calculations
CLcr=(140-60)*70/(85*0.6)=109.80 mL/min=6.59 L/hr
Vd=0.25*70kg=17.5L
k_e =Cl/ V = (6.59L/hr)/17.5L=0.377 hr⁻¹
τ =ln(7/0.5)/0.377 +0.5= 7.5 hr~8 hour

Dose = 7μg/mL*0.377hr⁻¹*17.5L*0.5 hr*(1-e⁻(0.377hr⁻¹*8hr))/(1-e⁻(0.377hr⁻¹*0.5hr))=127.8 mg~130 mg

Dose 130 mg of gentamicin every 8 hours as a 0.5 hour i.v. infusion.

2. A.M. is given 130 mg gentamicin at 8:00 am. At 9:00 am a plasma sample is taken and yields a Cpmax' of 10.1 μg/mL. Another sample is taken one half hour before the next infusion to give a Cpmin' of 2.7 μg/mL. Calculate the actual k_e and Vd for A.M. and recommend a dosing change to give a true Cmax of 7 μg/ml. The dosing interval is 8 hours. (2pts)

First calculate the k_e
k_e = ln(10.1(μg/mL)/2.7(μg/mL))/6.5hrs = 0.201 hr⁻¹

Next in order to calculate the Vd you must calculate the true Cmax and Cmin

\[ C_{max} = 10.1(\mu g/mL)/e^{(-0.201hr⁻¹*0.5hr)} = 11.17 \mu g/mL \]

\[ C_{min} = 2.7(\mu g/mL)/e^{(-0.201hr⁻¹*0.5hr)} = 2.44 \mu g/mL \]

Now you can calculate a Vd

\[ Vd = 130mg*(1-e^{(-0.201hr⁻¹*0.5hr)})/(0.201hr⁻¹*0.5hr*(11.17(\mu g/mL)-2.44(\mu g/mL))e^{(-0.201hr⁻¹*0.5hr)}) = 13.80 L \]
Now you can calculate the new dose.
Dose = \[7(\mu g/mL) \times 0.201 \text{ hr}^{-1} \times 13.80L \times 0.5 \text{hr} \times (1-e^{-0.201 \text{hr}^{-1} \times 8 \text{hr}})/(1-e^{-0.201 \text{hr}^{-1} \times 0.5 \text{hr}})\]
= 81.20mg~80 mg

3. Calculate the new C_{min}. Is this acceptable for toxicity? What is the suggested target for the trough concentration? (2pts)

\[C_{min} = 7.0(\mu g/mL) \times e^{(-0.201 \text{hr}^{-1} \times 7.5 \text{hr})} = 1.55 \text{ mg}\]
Yes this is acceptable. We want to keep trough concentrations below 2 mg/L for gentamicin because trough concentrations greater than this are associated with renal toxicity. Usually renal function is restored once the drug is discontinued. Ototoxicity can also occur with trough concentrations exceeding 4 mg/L for more than 10 days. This drug accumulates in deep tissues.

4. J.B. is a 30 year-old male with a height of 5’10” and weighs 180 lbs. He is admitted for treatment of an acute pulmonary exacerbation. His serum creatinine is 0.9 mg/dL. His treatment is initiated with tobramycin 180 mg infused over 30 minutes every 8 hours. Calculate the predicted steady-state peak and trough concentrations. For k_e use Cl_{cr} and V_d again. (2pts)

\[\text{TWB} = 180 \text{lbs}/2.2(\text{lbs/kg}) = 81.82 \text{ kg} \quad \text{IBW} = 50+2.3 \times 10 = 73 \text{ kg} \quad 73 \text{kg} \times 0.2 + 73 \text{kg} = 87.6 \text{ kg}\]
\[\text{TBW} < 120\% \text{IBW use TBW}\]
\[\text{Vd} = 0.25 \times 81.82 \text{kg} = 20.46 \text{ L}\]
\[\text{CL}_{cr} = (140-30) \times 81.82 \text{kg}/(72 \times 0.9 \text{mg/dL}) = 138.89 \text{ mL/min} = 8.33 \text{ L/hr}\]
\[k_e = \text{CL/Vd} = 8.33 (\text{L/hr})/20.46 \text{L} = 0.407 \text{ hr}^{-1}\]
\[C_{max} = 180 \text{mg} \times (1-e^{(-0.407 \text{hr}^{-1} \times 0.5 \text{hr})})/(8.33 (\text{L/hr}) \times 0.5 \text{hr} \times (1-e^{(-0.407 \text{hr}^{-1} \times 8 \text{hr})})) = 8.28 \text{ mg/L}\]
\[C_{min} = 8.28 (\text{mg/L}) \times e^{(-0.407 \text{hr}^{-1} \times 7.5 \text{hr})} = 0.391 \text{ mg/L}\]

5. A patient is admitted with an acute drug overdose of tobramycin. A serum level is measured at 30 \(\mu g/mL\). Assuming an 9 hour half-life and no further drug absorption, how long dose it take for the serum level to drop to the upper limit of the therapeutic range (12 \(\mu g/mL\))? (2pts)

\[k_e = 0.693/9\text{hr} = 0.077\text{hr}^{-1}\]
\[12(\mu g/mL) = 30(\mu g/mL) \times e^{(-0.077 \text{hr}^{-1} \times t)} = \ln(12(\mu g/mL)/30(\mu g/mL))/0.077\text{hr}^{-1} = 11.9 \text{ hours}\]