1. S.T., a 32-year-old, 64 kg female with a serum creatinine of 0.9 mg/dL is to be given tobramycin. Calculate a maintenance dose which will produce a “peak” concentration of 7 mg/L one hour after the half-hour infusion has been started, and a trough concentration of 1 mg/L. Assume that the tobramycin will be administered as a one-half hour infusion. If S.T. was to be given tobramycin 5 mg/kg QD, what would be the calculated steady-state peak concentration one hour after starting the half-hour infusion? Also predict subsequent steady-state plasma concentration 12 hours after starting the infusion and at the trough.

\[
CL_{CR} = \frac{(140 - 32) \cdot 64}{85 \cdot 0.9} = 90 mL/ min = 5.42 L/ h
\]

\[V_d = 0.25 \cdot 64 = 16 L\]

\[k = 0.339 h^{-1}\]

\[C_{max} = \frac{7}{e^{-0.339 \cdot 0.5}} = 8.3 \mu g/ mL\]

\[\tau = \frac{\ln 8.3}{0.339} + 0.5 = 6.7 h \to 8h\]

\[D = 8.3 \cdot 0.339 \cdot 16 \cdot 0.5 \cdot \frac{(1-e^{-0.339 \cdot 8})}{(1-e^{-0.339 \cdot 0.5})} = 22.5 \cdot \frac{0.9336}{0.1559} = 135 mg\]

5mg/kg QD

\[C_{max} = \frac{320}{5.42 \cdot 0.5} \cdot \frac{(1-e^{-0.339 \cdot 5})}{(1-e^{-0.339 \cdot 24})} = 118.1 \cdot \frac{0.1559}{0.9997} = 18.4\]

measured peak:

\[C_{max}^* = 18.4 \cdot e^{-0.339 \cdot 0.5} = 15.5 \mu g/ mL\]

\[C_{12h} = 18.4 \cdot e^{-0.339 \cdot 11.5} = 0.37 \mu g/mL\]

\[C_{24h} = 18.4 \cdot e^{-0.339 \cdot 23.5} = 0.006 \mu g/mL (undetectable)\]
2. B.C. is a 30 year old 70kg woman with a serum creatinine of 0.9 mg/dl. An initial gentamicin dose of 100mg was infused of 30 minutes in the emergency room and you were consulted to provide a pharmacokinetic assessment. Calculate the plasma concentration of gentamicin one hour after the infusion was started (or 30 minutes post infusion).

Calculate CrCL (= CL\text{TOTAL})

\[
CL_{cr} = \frac{(140 - 30) \cdot 70}{85 \cdot 0.9} = 100mL/min = 6L/h
\]

And calculate \(V_d\) and \(k\)

\[
V_d = 0.25 \cdot 70 = 17.5L
\]

\[
k = \frac{CL}{V_d} = 0.34h^{-1}
\]

Find the true \(C_{\text{peak}}\)

\[
C_{\text{max}} = \frac{100}{6 \cdot 0.5} \cdot (1 - e^{-34.0.5})
\]

\[
= 33.3 \cdot (1 - 0.844)
\]

\[
= 5.2 \text{ g/mL}
\]

After 30 minutes:

\[
C = 5.2 \cdot e^{-0.34 \cdot 0.5} = 4.4 \text{ g/mL}
\]
3. The hepatic clearance of a drug in a patient is reduced by 50% due to chronic viral hepatitis. How is the total body clearance of the drug affected? What should be the new dose of the drug in the patient? Assume that the drug has only renal and hepatic elimination routes, and renal drug clearance ($F_{ren}=0.4$) and plasma drug protein binding are not altered.

Let $RL =$ residual liver function $= [Cl_{h}]_{hepatitis}/[Cl_{h}]_{normal}$

$1 - Fren =$ fraction of drug metabolized

$[Cl_{h}]_{hepatitis} = RL \times [Cl_{h}]_{normal}$

Substituting for $[Cl_{h}]_{normal}$ with $Cl_{normal}$ $(1 - Fren)$,

$[Cl_{h}]_{hepatitis} = RL \times Cl_{normal} (1 - Fren)$

Assuming no renal clearance deterioration due to hepatitis,

$Cl_{hepatitis} = [Cl_{h}]_{hepatitis} + [Cl_{R}]_{normal} = RL \times Cl_{normal} (1 - Fren) + Cl_{normal} Fren = Cl_{normal} / RL (1 - Fren) + Fren$

Dose$_{hepatitis}$/Dose$_{normal}$=$[Cl_{hepatitis}]/[Cl_{normal}]=RL(1-Fren)+Fren$

Substituting with $RL = 0.5$ and $Fren = 0.4$:

Dose$_{hepatitis}$/Dose$_{normal}$=$[Cl_{hepatitis}]/[Cl_{normal}]=0.3+0.4=0.7$ (or 70%)

The adjusted dose of the drug in the hepatic patient would be 70% of the normal subject due to a 50% decrease in hepatic function in the above case ($Fren = 0.4$).
4. A 3 month old infant, born at full-term gestational age, is admitted to Shands Hospital for possible pneumonia. The infant weighs 3.5 kg. Ampicillin 175 mg iv q6h and Gentamicin 5 mg iv q8h (30 min infusion) is started. On day 3 of therapy, gentamicin serum concentrations are drawn as listed below:
Gentamicin dosing schedule 06-14-22 h.
Gentamicin peak serum conc. 6.6 µg/ml drawn at 0700 on 4/23.
Gentamicin trough serum conc. 1.1 µg/ml drawn at 1330 on 4/23.

a. Determine the estimated $k_e$ and $t_{1/2}$ of gentamicin in this patient.

\[
k = \frac{\ln \left( \frac{6.6}{1.1} \right)}{6.5} = 0.276 h^{-1}
\]

\[
t_{1/2} = \frac{0.693}{k} = 2.5 h
\]

b. Calculate the dose and dosage schedule necessary to achieve a peak serum gentamicin concentration of at least 10 µg/ml.

\[
C_{\text{max}} = \frac{6.6}{e^{-0.276 \cdot 0.5}} = 7.6 \mu g / mL
\]

\[
C_{\text{min}} = 1.1 \cdot e^{-0.276 \cdot 0.5} = 0.96 \mu g / mL
\]

\[
Vd = \frac{5}{0.276 \cdot 0.5} \cdot \left( \frac{1 - e^{-0.276 \cdot 0.5}}{7.6 - 0.96 \cdot e^{-0.276 \cdot 0.5}} \right) = 36.36 \cdot \frac{0.129}{6.76} = 0.69 L
\]

\[
\tau = \frac{\ln \left( \frac{10}{1} \right)}{0.276} + 0.5 = 8.8 h (8h)
\]

\[
D = 10 \cdot 0.276 \cdot 0.69 \cdot 0.5 \cdot \left( \frac{1 - e^{-0.276 \cdot 8}}{1 - e^{-0.276 \cdot 0.5}} \right) = 0.952 \cdot \frac{0.89}{0.129} = 6.6 mg \Rightarrow 7 mg q8h
\]
5. K. T., a 62-year old, 60-kg woman with a serum creatinine of 1 mg/dL, has been started on 500 mg of vancomycin every 8 hours for the treatment of staphylococcal infection. What are the expected peak and trough vancomycin concentrations for her at steady state?

\[ V_d = 0.17(62)+0.22(60)+15=10.54+13.2+15=38.74 \text{ L} \]

\[ CL \cong Cl_c = 0.85 \cdot \frac{(140 - 62)(60)}{72 \cdot 1} = 55.25 \text{ mL/min} = 3.32 \text{ L/h} \]

\[ Ke = \frac{CL}{V_d} = \frac{3.32}{38.74} = 0.0857 \text{ h}^{-1} \]

\[ C_{ss \ max} = \frac{S \cdot F \cdot Dose}{V_d} \cdot \frac{(1)(1)(500)}{(38.74)} \cdot \frac{1}{1 - e^{-0.0857 \cdot 8}} = 26.0 \text{ mg/L} \]

\[ C_{ss \ min} = C_{ss \ max} \cdot e^{-k \cdot \tau} = 26.0 \cdot e^{-0.0857 \cdot 8} = 13.1 \text{ mg/L} \]