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.

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

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

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

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

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

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

5mg/kg QD

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

measured peak:

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

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

\[C_{24h} = 18.4 \cdot e^{-0.339 \cdot 23.5} = 0.006 \mu g/mL \text{ (undetectable)}\]
2. L.F., a 28-year-old, 75 kg male, is receiving 100 mg of tobramycin infused IV over a 30 minute period q8h. His serum creatinine has increased from 1 mg/dL to 1.8 mg/dL over the past 24 hours. Since his renal function appears to be decreasing, three plasma samples were obtained to monitor serum gentamicin concentrations as follows: just before a dose; one hour after that same dose; and eight hours after that dose (two troughs and one peak level). The serum tobramycin concentrations at these times were 4 mg/L, 8 mg/L, and 5 mg/L, respectively. Calculate the volume of distribution, elimination rate constant, and clearance of tobramycin for L.F. Also, using the pharmacokinetic parameters calculated for L.F. above, develop a dosing regimen that will produce reasonable peak (10 mg/L) and trough (1 mg/L) concentrations of tobramycin.

\[
k = \frac{\ln \left( \frac{8}{5} \right)}{7} = 0.067 h^{-1}
\]
\[
C_{\text{max}} = \frac{8}{e^{-0.067 \cdot 0.5}} = 8.3 \text{ mg/L}
\]
\[
t_{1/2} = \frac{0.693}{0.067} = 10.3 h
\]
\[
V_d = \frac{100}{0.067 \cdot 0.5} \cdot \frac{\left(1 - e^{-0.067 \cdot 0.5}\right)}{\left(8.3 - 4 \cdot e^{-0.067 \cdot 0.5}\right)} = 2985 \cdot \frac{0.033}{4.43} = 22.2 L
\]
\[
\text{↑pre-dose level}
\]
\[
Cl = k \cdot V_d = 0.067 \cdot 22.2 = 1.49 L/h
\]
\[
= 25 \text{ mL/min}
\]

**True Peak = 10 mg/L**

\[
\tau = \frac{1}{0.067} + 0.5 = 34.8 \rightarrow 36 h
\]

\[
D = 10 \cdot 0.067 \cdot 22.2 \cdot 0.5 \cdot \frac{\left(1 - e^{-0.067 \cdot 36}\right)}{\left(1 - e^{-0.067 \cdot 0.5}\right)} = 7.44 \cdot 0.91 = 205 mg \Rightarrow 200 mg \text{ q36h}
\]

**Measured Peak = 10 mg/L**

\[
\tau = \frac{1}{0.067} + 1.5 = 35.8 \rightarrow 36 h
\]

\[
C_{\text{max}} = \frac{10}{e^{-0.067 \cdot 0.5}} = 10.3 \text{ mg/L}
\]

No difference
3. A patient was given 80 mg gentamicin over 30 minutes (i.v.) from 9:30 to 10:00 am. The following two serum levels were measured: 6.5 µg/ml at 10:30 am and 1.2 µg/ml at 5:00 pm. Calculate:

a. the elimination rate constant $k$

$$k = \frac{\ln \frac{6.5}{1.2}}{6.5} = 0.26 h^{-1}$$

b. the elimination half-life

$$t_{1/2} = \frac{0.693}{0.26} = 2.7 h$$

c. the peak concentration at 10:00 am

$$C_{\text{max}} = \frac{65}{e^{-0.26-0.5}} = 7.4 \mu g/mL$$

d. the trough concentration at 5:30 pm

$$C_{\text{min}} = 1.2 \cdot e^{-0.26-0.5} = 1.1 \mu g/mL$$

e. the volume of distribution

$$V_d = \frac{80}{0.26 \cdot 0.5} \cdot \frac{(1-e^{-0.26-0.5})}{(7.4-1.1 \cdot e^{-0.26-0.5})} = 615.4 \cdot \frac{0.122}{6.434} = 11.7 L$$

f. the clearance

$$CL = 0.26 \cdot 11.7 = 3.0 L/h \text{ or } 51 mL/min$$
4. A patient is admitted with an acute theophylline overdose. A serum level is measured at 45 µg/ml. Assuming an 8 hour half-life and no further drug absorption, how long does it take for the serum level to drop to the upper limit of the therapeutic range (20 µg/ml)?

\[
k = \frac{0.693}{8} = 0.087 \text{ hr}^{-1}
\]

\[
20 = 45 \cdot e^{-0.087 \cdot t}
\]

\[
\frac{20}{45} = e^{-0.087 \cdot t}
\]

\[
\ln(0.44) = -0.087 \cdot t
\]

\[
-0.811 = -0.087 \cdot t
\]

\[
t = 9.3 \text{ hr}
\]