1. M.W., an 11-year-old, 36 kg female, is receiving 300mg of valproic acid q12h for absence seizures. While the seizure frequency has declined with this therapy, she is still experiencing a few (1-2) absence seizures per day. M.W. has no obvious signs of side effects from the valproic acid therapy and has normal renal and hepatic function. What is the expected trough concentration for M.W. on her current regimen?

\[
CL = 0.013 \times 36 = 0.468 L/h
\]

\[
Vd = 0.14 \times 36 = 5.04 L
\]

\[
k_e = \frac{CL}{Vd} = \frac{0.468}{5.04} = 0.09 h^{-1}
\]

\[
C_{\text{min}} = \frac{F \cdot S \cdot D}{Vd} \cdot e^{-k_e \cdot \tau} = \frac{300}{5.04} \cdot e^{-0.09 \cdot 12} = 90.13 \cdot 0.34 = 30.64 mg/L \approx 31 mg/L
\]
2. B.K., a 59-year-old, 67 kg female, was admitted to the coronary care unit with a diagnosis of acute myocardial infarction. B.K. has a history of mild chronic renal failure, a serum creatinine of 1.7mg/dL. B.K. developed premature ventricular contractions (PVCs) which were unresponsive to lidocaine. Calculate a parenteral loading dose of procainamide designed to achieve a plasma concentration of around 7mg/L and an i.v. maintenance infusion rate that will maintain an average plasma concentration of 6mg/L.

\[ Vd = 2 \cdot 67 = 134L \]

\[ LD = \frac{C_p \cdot Vd}{F \cdot S} = \frac{7 \cdot 134}{1 \cdot 0.87} = 1078.2mg \approx 1100mg \]

\[ CL_{cr} = \frac{(140 - 59) \cdot 67}{85 \cdot 1.7} = 37.56mL/min \approx 2.25L/h \]

\[ CL_{renal} = 3 \cdot 2.25 = 6.75L/h \]
\[ CL_{acet} = 0.13 \cdot 67 = 8.71L/h \]
\[ CL_{other} = 0.1 \cdot 67 = 6.7L/h \]
\[ CL_{total} = 6.75 + 8.71 + 6.7 = 22.16L/h \]

\[ MD = \frac{C_{cr,ave} \cdot CL \cdot \tau}{F \cdot S} = \frac{6 \cdot 22.16 \cdot 1}{1 \cdot 0.87} = 152.83mg \approx 150mg \]
3. S.S. has been taken 250mg of quinidine sulfate orally q6hr but has been admitted to hospital and is now unable to take this medication. What intramuscular (i.m.) dose of quinidine gluconate would be equivalent to 250mg quinidine sulfate p.o. q6h? Show calculations.

for quinidine sulfate:

\[
Amount_{Drug \text{ absorbed}} = F \cdot S \cdot D = 0.7 \cdot 0.82 \cdot 250 = 143.5\text{mg}
\]

for quinidine gluconate:

\[
D_{\text{new dosage form}} = \frac{Amount_{\text{quinidine sulfate absorbed}}}{F_{\text{new dosage form}} \cdot S_{\text{new dosage form}}} = \frac{143.5}{1 \cdot 0.62} = 231.45\text{mg} \approx 250\text{mg}
\]
L.P., a 66-year-old, 72 kg male (SrCr 1.6mg/dL), has been taking 0.25mg of digoxin tablets orally for his CHF, and at 9.00am on the day of admission, a digoxin plasma concentration of 1.1µg/L was measured. He was continued on his outpatient maintenance dose. On the fifth day, just before his morning dose (four doses of digoxin have been administered each day at 9.00am), a second digoxin sample was obtained. Using the expected pharmacokinetic parameters, calculate L.P.’s digoxin concentration on the morning of the fifth day.

\[ \frac{CL_{CR}}{72} = \frac{140 - 66}{72 \cdot 1.6} = 46.25mL / \text{min} \]

\[ CL = 0.33 \cdot 72 + 0.9 \cdot 46.25 = 65.39mL / \text{min} \approx 3.9L / h \approx 93.6L / \text{day} \]

\[ Vd = 3.8 \cdot 72 + 3.1 \cdot 46.25 = 416.98L \approx 417L \]

\[ k_e = \frac{CL}{Vd} \cdot \frac{93.6}{417} = 0.22 days^{-1} \]

\[ C_{\text{min(sum)}} = C_{\text{measured}} \cdot e^{-k_e \cdot t_1} + \frac{F \cdot D}{Vd} \cdot \left[ e^{-k_e \cdot t_1} + e^{-k_e \cdot t_2} + e^{-k_e \cdot t_3} + e^{-k_e \cdot t_4} \right] \]

\[ = 1.1 \cdot e^{-0.22 \cdot 4 \text{days}} + \frac{0.7 \cdot 250}{417} \cdot \left[ e^{-0.22 \cdot 4 \text{days}} + e^{-0.22 \cdot 3 \text{days}} + e^{-0.22 \cdot 2 \text{days}} + e^{-0.22 \cdot 1 \text{day}} \right] \]

\[ = 0.456 + 0.42 \cdot [0.41 + 0.52 + 0.64 + 0.8] \]

\[ = 1.45 \mu g / L \]
5. Y.T., a 46-year-old, 55 kg female, is to be given carbamazepine as an anticonvulsant agent. Calculate a daily dose that will produce an average steady-state plasma concentration of approximately 8mg/L. How would you administer that dose?

\[
MD = \frac{C_{ss,ave} \cdot CL \cdot \tau}{F \cdot S} = \frac{8 \cdot 3.52 \cdot 24}{0.8 \cdot 1} = 844.8 \text{mg / day} \approx 800 \text{mg / day}
\]

Initial dose of 200-400mg with increase of 200mg every 7 to 14 days till the final dose of 800mg/day.