1. R.P., a 55-year-old, 70 kg male (SrCr 1.6mg/dL), has been taking 0.25 mg 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 third day, just before his morning dose (two 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 third day. (2 points)

CrCL = ((140-55)*70)/(72*1.6) = 51.6 ml/min
CL = 0.33 *70+ 0.9* 51.6 = 69.5 ml/min = 100.1 L/day
Vd = 3.8 * 70 + 3.1* 51.6 = 426 L
k_e = Cl/Vd = 100.1/426 = 0.235 day^{-1}

\[ C_{min(sum)} = C_{measured} \cdot e^{-k_e \cdot t_1} + \frac{F \cdot D}{V_d} \cdot \left[ e^{-k_e \cdot t_1} + e^{-k_e \cdot t_2} \right] = 1.1 \cdot e^{-0.235 \cdot 2 \cdot \text{days}} + \frac{0.7 \cdot 250}{426} \cdot \left[ e^{-0.235 \cdot 2 \cdot \text{days}} + e^{-0.235 \cdot 1 \cdot \text{day}} \right] \]

= 0.687+0.41*(0.625+0.791)
= 1.27 ug/L
2. M.J. is a 40 year old 65 kg male with intermittent asthmatic who presents to the emergency room with severe dyspnea, coughing, and wheezing. He is treated there with aerosol albuterol (S=0.8), but only partially clears. He is then given 400 mg of IV aminophylline over 30 minutes. Thirty minutes after the loading dose was administered (60 minutes from time zero) the theophylline concentration was 15 µg/ml. He has normal liver, kidney, and cardiac function and is afebrile. He is not receiving any other drugs. After the loading dose, M.J. was started on an IV aminophylline constant infusion of 55 mg/hr, Solu-Medrol IV and albuterol nebulization. Eight hours after the first serum level, a second level was 9 µg/ml.

A. Calculate the actual volume of distribution. (1 point)

\[
V_d = \frac{Dose \cdot F \cdot S}{C_p} = \frac{400 \text{mg} \cdot 1 \cdot 0.8}{15 \text{mg} / L} = 21.3L
\]

B. Calculate total body clearance. (1 point)

\[
CL = \frac{2 \cdot R_o}{(C_1 + C_2)} + 2 \cdot V_d \cdot (C_1 - C_2) \cdot \frac{2 \cdot 0.8 \cdot 55 \text{mg} / h}{(9 + 15 \text{mg} / L)} + \frac{2 \cdot 21.3L \cdot (15 - 9 \text{mg} / L)}{(15 + 9 \text{mg} / L) \cdot 8h} = 3.67 + 1.33 = 5L / h
\]

C. Calculate the additional IV aminophylline loading dose necessary to increase his level from 9 µg/ml back to 15 µg/ml. (1 point)

\[
LD = \frac{\Delta C_p \cdot V_d}{S \cdot F} = \frac{6 \text{mg} / L \cdot 21.3L}{0.8 \cdot 1} = 160mg
\]

D. Calculate the IV aminophylline infusion rate necessary to maintain his level at 15 µg/ml after the second loading dose. (1 point)

\[
MD = \frac{C_p,ss \cdot CL}{S \cdot F} = \frac{15 \text{mg} / L \cdot 5L / h}{0.8 \cdot 1} = 94mg / h
\]
3. R.J. is a 65-year-old male weighing 60 kg with a serum creatinine of 1.0 mg/dL with CHF. Calculate a maintenance dose that will achieve an average plasma digoxin concentration of 1.5 µg/L. If the patient had a serum creatinine of 5 mg/dL, what would be the estimated loading dose? (1 point each)

\[
Cl_{\text{creat}}(\text{male}) = \frac{(140 - \text{age})(\text{weight})}{72 \cdot \text{Scr}} = \frac{(140 - 65) \cdot 60}{72 \cdot 1} = 62.5 \text{mL/min}
\]

\[
CL = 0.33 \text{mL/kg/min} \cdot \text{weight/kg} + 0.9 \cdot CL_{\text{Cr}}(\text{mL/min}) = 0.33 \cdot 60 + 0.9 \cdot 62.5 = 76.1 \text{mL/min} \approx 109.6 \text{L/day}
\]

\[
MD = \frac{C_p, ss \cdot CL \cdot \tau}{S \cdot F} = \frac{1.5 \text{µg/L} \cdot 109.6 \text{L/day} \cdot 1 \text{day}}{0.7 \cdot 1} = 234.8 \text{µg}
\]

If serum creatinine increases to 5 mg/dL:

\[
Cl_{\text{creat}}(\text{male}) = \frac{(140 - \text{age})(\text{weight})}{72 \cdot \text{Scr}} = \frac{(140 - 65) \cdot 60}{72 \cdot 5} = 12.5 \text{mL/min}
\]

\[
Vd = 3.8 \cdot \text{weight/kg} + 3.1 \cdot CL_{\text{Cr}} = 3.8 \cdot 60 + 3.1 \cdot 12.5 = 267 \text{L}
\]

\[
LD = \frac{Vd \cdot C_p_0}{S \cdot F} = \frac{267 \text{L} \cdot 1.5 \text{µg/L}}{0.7 \cdot 1} = 572.1 \text{µg} \approx 600 \text{µg}
\]

Please note:

If the student uses an S of 1, the answers will be:

Maintenance Dose = 165 µg

And the loading dose = 400.5 µg

Please accept either answer.
4. T.D. weighs 40 kg and has been receiving 300 mg of aminophylline every 6 hours for several days. A plasma theophylline sample drawn immediately before a scheduled dose was 5.0 mg/L. Estimate the peak plasma concentration after each dose and the expected half-life based upon the observed trough concentration of 5.0 mg/L. (1 point each)

\[ V_d = 0.5 \text{ L/kg} \times 40 \text{ kg} = 20 \text{ L} \]

\[ C_{\text{max}} = C_{\text{min}} + \frac{(S)(F)(Dose)}{V_d} = 5 \text{ mg/L} + \frac{(0.8)(1.0)(300 \text{ mg})}{20 \text{ L}} = 17 \text{ mg/L} \]

\[ k_e = \ln \left( \frac{17}{5} \right)/6 \text{ hr} = 0.204 \text{ hr}^{-1} \]

\[ t_{1/2} = 0.693/k_e = 3.4 \text{ hours} \]
5. S.C., is a 62 year old, 50 kg woman with CHF, has been admitted to the hospital for possible digoxin toxicity. Her serum creatinine level was 3 mg/dL and her dosing regimen at home had been 0.25 mg of digoxin daily for many months. The digoxin plasma concentration on admission was 4 μg/L. How long will it take for the digoxin concentration to fall from 4 μg/L to 2 μg/L? (1 point) Calculate a daily dose that will maintain her digoxin concentration at 2 μg/L. (1 point)

\[ Cl_{CR} \text{ for females} = (0.85) \frac{(140 - \text{age})(\text{weight})}{72 \times SCr} = (0.85) \frac{(140 - 62)(50)}{72 \times 3} = 15.3 \text{ml/min} \]

Total \( Cl_{digoxin} \) (ml/min) for patients with CHF = (0.33 mg/kg/min)(weight) + (0.9) \( \times \) (\( Cl_{cr} \))
= (0.33)(50) + (0.9)(15.3) = 30.3 ml/min = 43.6 L/day

or you can use a more patient-specific approach:

\[ Cl = \frac{(S)(F)(Dose/\tau)}{Css(ave)} = \frac{(1)(0.7)(250 \mu g \text{ / day})}{Css(ave)} = 43.75 \text{ L/day} \]

\[ V_{digoxin} (L) = (3.8L/kg)(\text{weight}) + (3.1)(Cl_{cr}) = (3.8)(50) + (3.1)(15.3) = 237 \text{ L} \]

\[ k = \frac{Cl}{V} = \frac{43.75 \text{ L/day}}{237 \text{ L}} = 0.184 \text{ day}^{-1} \]

\[ \text{half life} = \frac{\ln(C_1)}{ke} = \frac{\ln(4)}{0.184 \text{ day}^{-1}} = 3.8 \text{ days} \]

\[ \text{Maint. Dose} = \frac{(Cl)(Cssave)(\tau)}{S \times F} = \frac{(43.75)(2)(1)}{1 \times 0.7} = 125 \mu g \text{ daily} \]