1. A patient was given 90 mg gentamicin over 30 min (i.v.) from 8.30 to 9.00 a.m. The following two serum levels were measured: 5µg/mL at 9.30 a.m. and 1.5µg/mL at 4.00 p.m. Calculate:
   a. elimination rate constant,
   b. elimination half-life
   c. peak concentration at 9.00 a.m.
   d. trough concentration at 5.30 p.m.

a. 
\[ k = \frac{\ln \frac{5}{1.5}}{6.5} = 0.185h^{-1} \]

b. 
\[ t_{1/2} = \frac{0.693}{0.185} = 3.75h \]

c. 
\[ C_{\text{max}} = \frac{5}{e^{0.185 	imes 0.5}} = 5.48\mu g / mL \]

d. 
\[ C_{\text{min}} = 1.5 \cdot e^{-0.185 \times 5} = 1.14\mu g / mL \]
2. M.W. is a 51-year-old, 65 kg male with glomerular nephritis. His creatinine clearance is reasonably good, but he has a serum albumine concentration of 2.4 g/dL. M.W. is receiving 350 mg/day of phenytoin and has a steady-state phenytoin concentration of 8mg/L. What would his phenytoin concentration be if his serum albumin were normal? (assume a normal albumin concentration is 4.4 g/dL and a fraction unbound of 0.1)

\[
C_{P_{normal}} = \frac{C_{P'}}{(1-\alpha) \cdot \frac{P'}{P_{NL}}} + \alpha
\]

\[
C_{P_{normal}} = \frac{8 \text{mg/L}}{(1-0.1) \cdot \frac{2.4 \text{g/dL}}{4.4 \text{g/dL}}} + 0.1 = \frac{8 \text{mg/L}}{0.9 \cdot 0.55 + 0.1} = 13.45 \text{mg/L}
\]
3. Show for both high and low extraction drugs, how doubling the protein binding will affect the resulting unbound and total serum levels. What recommendations would you make for dose adjustments? Assume constant rate infusion and steady state.

**High**

\[ CL = Q \]

\[ \bar{C} = \frac{R_0}{Q} \]

\[ \bar{C}u = fu \cdot \bar{C}u = \frac{fu \cdot R_0}{Q} \]

- \( fb \uparrow, fu \downarrow \) \( \bar{C}u \downarrow \)
- \( \rightarrow \) increases the dose

**Low**

\[ CL = fu \cdot CL_{int} \]

\[ \bar{C} = \frac{R_0}{fu \cdot CL_{int}} \]

\[ \bar{C}u = \frac{R_0}{CL_{int}} \]

- \( fb \uparrow, fu \downarrow, \bar{C}u \leftrightarrow \)
- \( \rightarrow \) no change in dose
4. K.L., a 75 kg male smoker with chronic obstructive pulmonary disease, is to be started on an oral regimen of aminophylline (85% of which is theophylline). The pharmacokinetic parameters for this patient are \( V_d \) (0.5 L/kg), CL (80 mL/h/kg) and F (1.0).

Design an oral dosage regimen of aminophylline (100- and 200 mg tablets are marketed) for this patient to attain and maintain a plasma concentration within the therapeutic range (10-20 µg/ml). The absorption of theophylline is complete and rapid.

\[
CL = 6 \text{ L/h}, \quad V_d = 37.5 \text{ L}
\]

\[
k = \frac{6}{37.5} = 0.16 \text{ h}^{-1}
\]

\[
\tau = \frac{\ln \left( \frac{20}{10} \right)}{0.16} = 4.3 \text{ h} \rightarrow 4 \text{ h}
\]

\[
D = \frac{C \cdot CL \cdot \tau}{F} = \frac{15 \cdot 6 \cdot 4}{0.85} = 424 \text{ mg} \rightarrow 400 \text{ mg}
\]

5. Propranolol, a high-extraction drug, is combined with phenobarbital. What is your expectation for a potential change in propranolol half-life (show evidence).

\[
CL = Q
\]

\[
t_{1/2} = \frac{0.693 \cdot V_d}{Q} \rightarrow \text{ independent of } CL_{\text{int}}
\]

\[\Rightarrow \text{ no change}\]