1. JR is an 80 year old male (86.4 kg, CL\textsubscript{Cr} 42 ml/min) admitted to the hospital with a probable urosepsis in need of parenteral tobramycin. A dose of 600 mg every 36h is administered as a one-hour infusion (from 8-9am). Following the third dose of this regimen the following tobramycin concentrations were determined: 21 µg/ml (11 am) and 4 µg/ml (11 pm). (15pts)

   a) What would be the expected trough concentration before the next dose at 8 pm?

   \[ \frac{\ln 21}{k} = \frac{4}{12} = 0.138 h^{-1} \]

   \[ C_{\text{min}} = 4 \cdot e^{0.138 \cdot 21} = 0.22 \, \mu g/mL \]
1b) Based on the observations, make appropriate changes in this patient's dose regimen of tobramycin.

Measured levels are not on scale.

Calculate at 9h: \[ C = 21 \cdot e^{0.1386} = 9.2 \, \mu g/\text{mL} \]

→ increase \( \tau \) to 48 h

7 mg/kg q48h
2. Mrs D.H., a 53-year-old, 82-kilogram patient with congestive cardiac failure for the past three years, was admitted on April 16 to the hospital at 16:00 because of a worsening of her congestive cardiac failure symptoms. Her admission history indicated that she had taken her digoxin tablet (0.25 mg) that morning at the usual time (8:00-9:00), but had failed to take a tablet on Sunday (April 15). A plasma sample (blood withdrawn at 17:00) was obtained to see if the symptoms were consistent with noncompliance. A plasma digoxin concentration of 0.9 microgram/liter and a serum creatinine of 0.9 milligram/deciliter were reported. (10 pts)

a) Based on population parameters, what concentration would you expect?

\[ CL_{cr} = \frac{(140 - 53) \cdot 82}{85 \cdot 0.9} = 93.3 \text{mL/min} \]

\[ CL = 0.33 \cdot 82 + 0.9 \cdot 93.3 = 111 \text{mL/min} = 6.7 \text{L/h} \]

\[ Cp = \frac{0.7 \cdot 0.25}{6.7 \cdot 24} = 1.1 \mu g/L \]

b) From the information available, conclude if noncompliance is likely.

- Measured level is a little lower than expected level due to the missed dose on the previous day
- No evidence of noncompliance
Show how an increase in tissue binding will affect the clearance, bioavailability and half-life of a high-extraction drug. (10 pts)

\[ V_d = V_B + \frac{f_u}{f_{u_T}} \cdot V_T \uparrow \]

- Clearance and bioavailability are not changed
- Half-life is increased due to increase in \( V_d \)
4. L.E., a 62 kg male patient (53", 52 y.o., SeCr 1.3 mg/dl) received a 30 mg methotrexate loading dose iv followed by a 30 mg/ h infusion over 36 hours. At 36 h, leucovorin rescue (10 mg/ m² q6h ) was started. The following levels were monitored: (15 pts)

<table>
<thead>
<tr>
<th>Time</th>
<th>Methotrexate Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>24h</td>
<td>14 µM</td>
</tr>
<tr>
<td>48 h</td>
<td>0.9 µM</td>
</tr>
<tr>
<td>60 h</td>
<td>0.3 µM</td>
</tr>
</tbody>
</table>

Make a recommendation how to continue therapy. When do you expect the methotrexate level to fall below 0.1 µM?

\[
\frac{\ln 14}{0.9} = 0.229 h^{-1}
\]

\[
t = \frac{\ln 0.5}{0.229} = 2.6 h \Rightarrow 50.6 h
\]

\[
\frac{\ln 0.5}{0.3} = 0.054 h^{-1}
\]

\[
t = \frac{\ln 0.1}{0.054} = 20.3 h \Rightarrow 80.3 h
\]

Continue leucovorin until 108 h
5. The following plasma concentration profile is observed in a patient who received a 24 continuous infusion of quinidine gluconate. (10pts)

Draw the profiles and circle the changes that you would expect in

a. a patient with congestive heart failure

- CL increased
- Vd increased
- T₁/₂ increased
- Cṗ increased

b. a patient with liver disease

- CL decreased
- Vd decreased
- T₁/₂ decreased
- Cṗ decreased
A 5 month old infant, born at full-term gestational age, is admitted to Shands Hospital for possible pneumonia. The infant weighs 6.5 kg. Ampicillin 175 mg iv q6h and Gentamicin 10 mg iv q8h given over 30 minutes is started. On day 3 of therapy, gentamicin serum concentrations are drawn as listed below: (15 pts)

Gentamicin dosing schedule 06-14-22 h.
Gentamicin peak serum conc. 6.4 µg/ml drawn at 0845 on 4/23.
Gentamicin trough serum conc. 2.3 µg/ml drawn at 2130 on 4/23.

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

\[
\begin{align*}
0845 & \rightarrow t = 2.75 \text{ h} \\
2130 & \rightarrow t = 7.5 \text{ h}
\end{align*}
\]

\[
k = \frac{\ln 6.4}{4.75} = 0.215 h^{-1}
\]

\[
t_{1/2} = \frac{0.693}{0.215} = 3.2 \text{ h}
\]

b. Recommend a dose and dosage schedule necessary to achieve a peak serum gentamicin concentration of 8 µg/ml and a trough of 1 µg/ml.

\[
C_{\text{max}} = \frac{6.4}{e^{-0.215 \cdot 2.25}} = 10.4 \mu\text{g/mL}
\]

\[
C_{\text{min}} = 2.3 \cdot e^{-0.215 \cdot 0.5} = 2.1 \mu\text{g/mL}
\]

\[
V_d = \frac{10}{0.215 \cdot 0.5} \cdot \frac{(1 - e^{-0.125 \cdot 0.5})}{(10.4 - 2.1 \cdot e^{-0.215 \cdot 0.5})} = 93 \cdot \frac{0.102}{8.51} = 1.1 \text{L}
\]

\[
\tau = \frac{\ln \frac{8}{1}}{0.215} + 0.5 = 10.2 \text{h} \Rightarrow 12 \text{h}
\]

\[
D = 8 \cdot 0.215 \cdot 1.1 \cdot 0.5 \cdot \frac{(1 - e^{-0.215 \cdot 12})}{(1 - e^{-0.215 \cdot 0.5})} = 0.946 \cdot \frac{0.924}{0.102} = 8.6 \text{mg} \Rightarrow 10 \text{mg}
\]

Give 10 mg q12 h
7. A patient (65kg) is treated with 300 mg q6h using immediate-release quinidine sulfate product. The trough level is found to be 1.0 µg/mL. (15 pts)

a) What is the expected trough level based on population pharmacokinetic parameters?

\[ V_d = 2.7 \cdot 65 = 176 \text{ L} \]
\[ CL = 0.28 \cdot 65 = 18.2 \text{ L/h} \]
\[ k = 0.1 \text{ h}^{-1} \]

\[
C_{\text{min}} = \frac{0.7 \cdot 0.82 \cdot 300}{176} \cdot \frac{e^{-0.16}}{1 - e^{-0.16}} = 0.978 \cdot \frac{0.549}{0.451} = 1.2 \mu g / mL
\]

b) Assuming a volume of distribution of 2.7 L/kg, what is the clearance and the half-life in our patient?

\[ C_{\text{max}} = 1.0 + \frac{0.7 \cdot 0.82 \cdot 300}{176} = 1.98 \mu g / mL \]

\[ k = \frac{\ln 1.98}{6} = 0.114 \text{ h}^{-1} \]

\[ t_{1/2} = \frac{0.693}{0.114} = 6.1 \text{ h} \]

CL = 0.114 \cdot 176 = 20.1 \text{ L/h}

C) Make a dose recommendation to increase the trough to 1.5 µg/mL.

Increase by 50% → 450 mg q6h

\[
D = \frac{C_{\text{min}} \cdot V_d}{F \cdot S} \cdot \frac{(1-e^{-kt})}{e^{-kt}} = 1.5 \cdot 176 \cdot \frac{(1-e^{-0.114 \cdot 6})}{0.7 \cdot 0.82 \cdot e^{-0.114 \cdot 6}} = 460 \cdot \frac{0.495}{0.505} = 450
\]
8. Gertrude Magilicutty is a frail 68 year old lady with atrial flutter secondary to hyperthyroidism. Design a loading and maintenance dosage regimen of Lanoxin tablets. What would you do as a pharmacist when she becomes euthyroid? Mrs. Magilicutty is 5'8", 95 lbs. She has a serum creatinine of 0.5mg%. (10 pts)

\[
\text{IBW} = 45 + 2.3 \cdot 8 = 63.4 \text{ kg}
\]

\[
CL_{cr} = \frac{(140 - 68) \cdot 63.4}{85 \cdot 0.5} = 107 \text{ mL/min}
\]

\[
V_d = 3.8 \cdot 63.4 + 3.1 \cdot 107 = 573 \text{ L}
\]

Hyperthy. : \( V_d = 1.3 \cdot 573 = 745 \text{ L} \)

\[
CL = 0.8 \cdot 6.34 + 107 = 158 \text{ mL/min} = 9.5 \text{ L/h}
\]

Hyperthy.: \( CL = 1.3 \cdot 9.5 \text{ L/h} = 12.3 \text{ L/h} \)

\[
LD = \frac{1.5 \cdot 745}{0.7} = 1596 \to 1.5 \text{ mg in divided doses}
\]

\[
MD = \frac{1.5 \cdot 12.3 \cdot 24}{0.7} = 632 \mu g \to 625 \mu g / \text{day}
\]

If patient becomes euthyroid:

\[
\text{New } CL = 9.5 \text{ L/h}
\]
\[
\text{New } V_d = 573 \text{ L}
\]

\[
\text{New } MD = \frac{1.5 \cdot 9.5 \cdot 24}{0.7} = 489 \mu g \to 500 \mu g / \text{day}
\]