1. An investigational new drug is eliminated entirely by liver (hepatic) metabolism, with a clearance of 1.40 L/min in subjects with an average liver blood flow of 1.50 L/min. What would be its expected clearance in a congestive heart failure patient with a liver blood flow of 1.10 L/min but no change in hepatic extraction ratio? (5 pts)

A) 1.10 L/min  
B) 1.50 L/min  
C) 1.18 L/min  
D) **1.03 L/min**  
E) Cannot be determined because the dose is not given.

\[ \text{CL}_H = Q_H \times E \]

\[ E = \frac{\text{CL}_H}{Q_H} = \frac{1.4 \text{ L/min}}{1.5 \text{ L/min}} = 0.933 \]

For CHF patient: \( Q_H = 1.1 \text{ L/min} \)

\[ \text{CL}_H = Q_H \times E = 1.10 \text{ L/min} \times 0.933 = 1.03 \text{ L/min} \]

2.) How will an increase in tissue binding affect the clearance, bioavailability and half-life of a high-extraction drug? (5 pts)

A. Clearance is decreased, bioavailability is not changed, Half-life is increased  
B. Clearance is decreased, bioavailability is not changed, Half-life is not changed  
C. Clearance is not changed, bioavailability is not changed, Half-life is not changed  
D. Clearance is decreased, bioavailability is increased, Half-life is increased  
E. Clearance is not changed, bioavailability is not changed, Half-life is increased

Clearance and bioavailability are not changed  
Half-life is increased due to increase in Vd
3.) The dosing interval ($\tau$) can be greater than drug half-life if: (5 pts)

A) the therapeutic index of the drug is high

B) pharmacologically active metabolites of the drug have longer half lives than the drug

C) the therapeutic effect of the drug is unrelated to plasma concentrations

D) both A and B

**E) all of the above**

Answer: E

4. S.T., a 55-year-old, 6’, 65 kg man with serum creatinine of 0.9 mg/dL is to be given gentamicin for septicemia. Calculate a gentamicin dose which will produce a steady-state peak of 8mg/L and a steady-state trough of 1 mg/L. The peak level is obtained one hour after initiating the one-half hour infusion and trough level is obtained just before the initiation of a dose. (10 pts)

IBW = 50 + 2.3(72-60) = 77.6 kg

TBW < 1.2* IBW using TBW

\[
CL_{cr} = \frac{(140 - age) \cdot TBW}{C_{pcr} \cdot 72} = \frac{(140 - 55) \cdot 65}{0.9 \cdot 72} = 85.3 \text{mL/min} = 5.12L/hr
\]

Vd = 25% TBW = 0.25*65 = 16.25 L

Ke = CL/Vd = 5.12/16.25 = 0.315 h⁻¹

Cmax = \(8 / e^{-0.315 \cdot 0.5} = 9.37 \text{mg/L}\)

\[
\elln \left( \frac{C_{\text{max}}}{C_{\text{min}}} \right) / k + \elln \left( \frac{9.37}{1} \right) / 0.315 + 0.5 = 7.6hr \approx 8hr
\]

\[
\tau = \left( \frac{1 - e^{-kT}}{k} \right) \cdot \left( \frac{1 - e^{-0.315 \cdot 5.0}}{0.315} \right) = 9.37 \cdot 0.315 \cdot 16.25 \cdot 0.5 \cdot \left( \frac{1 - e^{-0.315 \cdot 0.5}}{1 - e^{-0.315 \cdot 0.5}} \right) = 151.12 \text{mg}
\]

Version B 2
5. What is the pharmacokinetic parameter that should be monitored for vancomycin therapy to achieve the desired efficacy? (5 pts)

A. Clearance  
B. AUC  
C. Peak concentration  
D. Trough concentration  
E. Vd

6. A.B., a 50-year-old, 6’, 65kg man with a serum creatinine concentration 1.6mg/dL is given vancomycin for MRSA. Use the nomogram to make a dose recommendation. (5 pts)

A. 1g q12h  
B. **1g q24h**  
C. 0.5g q24h  
D. 0.5g q 12h

IBW = 50 + 2.3*(72-60) = 77.6kg  
TBW < 1.2* IBW, using TBW  

\[
CL_{cr} = \frac{(140 - \text{age}) \cdot TBW}{C_{pcr} \cdot 72} = \frac{(140 - 50) \cdot 65}{1.6 \cdot 72} = 50.78 \text{mL/min}
\]

From Nomogram : 1g q24h
7. Which combination of data below would be consistent with the conclusion that product A and product B are bioequivalent? (5 pts)

<table>
<thead>
<tr>
<th></th>
<th>Product A</th>
<th>Product B</th>
<th>Ratio (%) A/B</th>
<th>90% Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AUC₀₋∞ (µg min/mL)</td>
<td>204.5</td>
<td>216</td>
<td>94.7</td>
</tr>
<tr>
<td>2</td>
<td>AUC₀₋∞ (µg min/mL)</td>
<td>220.9</td>
<td>222</td>
<td>99.5</td>
</tr>
<tr>
<td>3</td>
<td>Cₘₐₓ (ng/mL)</td>
<td>1020</td>
<td>1053</td>
<td>96.9</td>
</tr>
<tr>
<td>4</td>
<td>Tₘₐₓ (h)</td>
<td>56.0</td>
<td>52.8</td>
<td>106.1</td>
</tr>
<tr>
<td>5</td>
<td>T₁/₂ (min)</td>
<td>186.2</td>
<td>170.4</td>
<td>109.3</td>
</tr>
<tr>
<td>6</td>
<td>AUC₀₋∞ (µg min/mL)</td>
<td>189.8</td>
<td>222</td>
<td>85.5</td>
</tr>
<tr>
<td>7</td>
<td>Cₘₐₓ (ng/mL)</td>
<td>1106</td>
<td>1053</td>
<td>105.0</td>
</tr>
<tr>
<td>8</td>
<td>Tₘₐₓ (h)</td>
<td>51.7</td>
<td>52.8</td>
<td>97.9</td>
</tr>
</tbody>
</table>

A. 1, 2, & 4.
B. 1, 2, & 3.
C. 1, 3, & 6.
D. 1, 6, & 7.
E. 1, 6, & 8.

C is correct, for bioequivalence the 90% confidence limit for AUC and Cₘₐₓ must fall between 80-125%.
8. L.J. is a 30 year old male 5 foot 10 inch 110kg patient a doctor has ordered to be given a dose of the new drug Alenpromycin. Alenpromycin is an antibiotic that 80% of is excreted in the urine. A patient with normal kidney function would be given 1000mg of Alenpromycin. However L.J. is suffering from kidney failure (\(C_{p\text{creat}} = 5.4\text{mg/dl}\)). What dose would you recommend for L.J.? (Normal \(\text{CL}_{\text{creat}} = 125\text{mg/min}\)) (10 pts)

A. 400 mg  
B. 360 mg  
C. 250 mg  
D. 200 mg  
E. 280 mg

To solve this we must first calculate L.J.’s IBW

\[
IBW = 50 + 2.3 \cdot (\text{Height in inches} - 60)\text{kg} = 50 + 2.3(70 - 60)\text{kg} = 73\text{kg}
\]

Is L.J.’s total body weight more than 120% of his ideal?

\[
IBW = 73\text{kg} \quad 73 \cdot 1.2 = 87.6\text{kg} < 110\text{kg} = \text{total body weight}
\]

It is so we will need to use the adjusted body weight to find \(\text{CL}_{\text{creat}}\).

\[
ABW = IBW + 0.4 \cdot (TBW - IBW) = 73 + 0.4(110 - 73) = 87.8\text{kg}
\]

Now we can calculate \(\text{CL}_{\text{creat}}\).

\[
\text{CL}_{\text{creat}}(\text{male}) = \frac{(140 - \text{age}) \cdot \text{weight}}{72 \cdot Cp_{\text{creat}}} = \frac{(140 - 30) \cdot 87.8}{72 \cdot 5.4} = 25\text{ml/min}
\]

Now lets determine his renal function

\[
RF = \frac{\text{CL}_{\text{creat}}}{\text{CL}_{\text{creat normal}}} = \frac{25\text{ml/min}}{125\text{ml/min}} = 0.2
\]

Now we can calculate the dose for L.J.

\[
D_{\text{pat}} = D_{\text{norm}} \cdot [1 - f_{\text{rev}} \cdot (1 - RF)] = 1000\text{mg} \cdot [1 - 0.8 \cdot (1 - 0.2)] = 360\text{mg}
\]
9. Based on the table of pharmacokinetic parameters obtained after a 10 mg dose of felodipine, calculate the oral bioavailability of felodipine for the three age groups. (5 pts)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>CL (L/h)</th>
<th>$T_{1/2}$ (h)</th>
<th>Oral AUC (mg·h/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-39</td>
<td>49.2</td>
<td>18</td>
<td>0.028</td>
</tr>
<tr>
<td>40-59</td>
<td>38.4</td>
<td>24</td>
<td>0.041</td>
</tr>
<tr>
<td>60-80</td>
<td>27.0</td>
<td>29</td>
<td>0.082</td>
</tr>
</tbody>
</table>

A. $F_{20-39}=0.05$, $F_{40-59}=0.10$, $F_{60-80}=0.24$
B. $F_{20-39}=0.14$, $F_{40-59}=0.16$, $F_{60-80}=0.22$
C. $F_{20-39}=0.86$, $F_{40-59}=0.84$, $F_{60-80}=0.78$
D. $F_{20-39}=0.95$, $F_{40-59}=0.90$, $F_{60-80}=0.76$
E. $F_{20-39}=0.08$, $F_{40-59}=0.07$, $F_{60-80}=0.08$

We can solve for the bioavailability by rearranging the following equation:

$$\frac{Dose \cdot F}{AUC} \quad \text{to} \quad F = \frac{AUC \cdot Cl}{Dose}$$

Now we can solve for $F$ for each of the age groups

$$F_{20-39} = \frac{AUC \cdot Cl}{Dose} = \frac{0.028\text{mg/hr/L} \cdot 49.2\text{L/hr}}{10\text{mg}} = 0.14$$

$$F_{40-59} = \frac{AUC \cdot Cl}{Dose} = \frac{0.041\text{mg/hr/L} \cdot 38.4\text{L/hr}}{10\text{mg}} = 0.16$$

$$F_{60-80} = \frac{AUC \cdot Cl}{Dose} = \frac{0.082\text{mg/hr/L} \cdot 27.0\text{L/hr}}{10\text{mg}} = 0.22$$

So B is correct.
10. A patient was given 80 mg gentamicin over 30 minutes (i.v.) from 8:00 to 8:30 am. The following two serum levels were measured: 7.5 µg/ml at 9:00 am and 0.9 µg/ml at 3:30 pm. Calculate the peak concentration at 8:30 AM and the trough concentration at 4 PM. (5 pts)

**the elimination rate constant:**

\[
\ln \frac{7.5}{0.9} = \frac{6.5}{5.7} = 0.33 h^{-1}
\]

**the peak concentration at 8:30 AM:**

\[
C_{\text{max}} = \frac{7.5}{e^{-0.33 \times 8.5}} = 8.85 \mu g / mL
\]

**the trough concentration at 4 PM:**

\[
C_{\text{min}} = 8.85 \cdot e^{-0.33 \times 7.5} = 0.74 \mu g / mL
\]

a. Cmax = 8.85 µg/mL; Cmin = 1.06 µg/mL
b. Cmax = 8.62 mg/L; Cmin = 1.06 mg/L
c. **Cmax = 8.85 µg/mL; Cmin = 0.74 µg/mL**
d. Cmax = 6.55 µg/mL; Cmin = 0.74 µg/mL
e. Cmax = 8.85 mg/mL; Cmin = 1.06 mg/mL
11. Given the data below for two drug X tablet formulations, are these products bioequivalent? Based on what criteria? (5 pts)

<table>
<thead>
<tr>
<th>Parameter Estimates</th>
<th>Product A</th>
<th>Product B</th>
<th>Ratio (%)</th>
<th>A/B 90% Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC&lt;sub&gt;0-15&lt;/sub&gt; (µg·min/mL)</td>
<td>204.5</td>
<td>216</td>
<td>94.7</td>
<td>81.2-108.2</td>
</tr>
<tr>
<td>AUC&lt;sub&gt;0-∞&lt;/sub&gt; (µg·min/mL)</td>
<td>212</td>
<td>222</td>
<td>95.5</td>
<td>78.6-112.4</td>
</tr>
<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt; (µg/mL)</td>
<td>102</td>
<td>105</td>
<td>96.9</td>
<td>90.8-103.0</td>
</tr>
<tr>
<td>T&lt;sub&gt;max&lt;/sub&gt; (h)</td>
<td>39.6</td>
<td>52.8</td>
<td>75.0</td>
<td></td>
</tr>
<tr>
<td>T&lt;sub&gt;1/2&lt;/sub&gt; (min)</td>
<td>186.2</td>
<td>170.4</td>
<td>109.3</td>
<td></td>
</tr>
</tbody>
</table>

- a. Yes, A/B ratio for AUC<sub>0-∞</sub> and C<sub>max</sub> are within the acceptance range
- b. No, A/B ratio for AUC<sub>0-∞</sub> are out of the acceptance range
- c. No, A/B confidence limits for C<sub>max</sub> are out of the acceptance range
- d. Yes, A/B ratio for AUC<sub>0-∞</sub> and C<sub>max</sub> are within the acceptance range
- e. No, A/B confidence limits for AUC<sub>0-∞</sub> are out of the acceptance range

12. J. T., a 55-year old, 5’4” tall, 75-kg woman with a serum creatinine of 1 mg/dL, has been started on 500 mg of vancomycin every 8 hours for the treatment of staphylococcal infection. What is the expected trough vancomycin concentrations for her at steady state? (10 pts)

A. 8.7 mg/L  
B. 11.13 mg/L  
C. 9.2 mg/L  
D. 9.2 mg/dL  
E. 23.24 mg/L

V<sub>d</sub> = 0.178(55)+0.22(75)+15=10.54+13.2+15=41.3 L  
IBW=45.5+2.3(4)=54.7, so use ABW  
ABW=54.7+0.4(75-54.7)=62.82  
CL ≅ Cl<sub>cr</sub> ≅ 0.85 · (140 - 55) · 62.8 / 72 · 1 = 63 mL/ min = 3.78L/hr  
ke = CL / V<sub>d</sub> = 3.78 / 41.3 = 0.092 hr<sup>-1</sup>
\[
C_{ss,max} = \frac{S \cdot F \cdot Dose}{V_d} = \frac{1 \cdot 1 \cdot 500}{41.3} = 23.24 \text{mg/L}
\]
\[
C_{ss,max} = C_{min} \cdot e^{-k_e \cdot \tau} = 23.24 \cdot e^{-0.0928} = 11.13 \text{mg/L}
\]

13. The extent to which a drug is absorbed partially determines its: (5 pts)

A: elimination rate
B: clearance
C: half-life
D: volume of distribution
E: bioavailability

14. You wish to begin a patient on a sustained release preparation of drug X and to maintain average plasma drug concentration of 20 mg/L. From published data, you estimate V and k_e for this drug to 10 L and 0.3 hr\(^{-1}\) in this patient, respectively. If the fraction of drug absorbed is assumed to be 1.0 and the drug is to be given every 12 hours what dose should be administered? (10 pts)

A: 500 mg
B: 360 mg
C: 2400 mg
D: 720 mg
E: 150 mg

Clearance = k_e \cdot V = 0.3 \text{ hr}^{-1} \cdot 10 \text{ L} = 3.0 \text{ L/hr}

\[
C_{avg} = \frac{(\text{Dose} \cdot F)}{(\text{Cl} \cdot \text{Tau})}
\]

Dose = (C_{avg} \cdot \text{Cl} \cdot \text{Tau})/F = (20 \text{ mg/L} \cdot 3.0 \text{ L/hr} \cdot 12 \text{ hr})/1.0 = 720 \text{ mg every 12 hours}
15. A 3 month old infant, born at full-term gestational age, is admitted to Shands Hospital for possible pneumonia. The infant weighs 3.5 kg. On 4/21 Ampicillin 175 mg iv q6h and Gentamicin 5 mg iv q8h (30 min infusion) is started. On day 3 of therapy, gentamicin serum concentrations are drawn as listed below:

(10 pts)

The gentamicin dosing schedule is 6AM, 2 PM and 10 PM.

Gentamicin peak serum conc. 6.2 µg/ml drawn at 7 AM on 4/23.
Gentamicin trough serum conc. 1.3 µg/ml drawn at 1:30 PM on 4/23.

Design a dosing regimen to produce a true peak of 6 µg/mL and a trough of 1 µg/mL.

A. 10mg q12h
B. 10mg q6h
C. 2 mg q8h
D. 4 mg q8h
E. 5mg q4h

\[ K_e = \ln\left(\frac{6.2}{1.3}\right)/6.5 = 0.24 \text{ hr}^{-1} \]

\[ C_{\text{max}} = \frac{6.2}{e^{-0.24*0.5}} = 6.99 \mu\text{g/ml} \]

\[ C_{\text{min}} = 1.3 * e^{-0.24*0.5} = 1.15 \mu\text{g/ml} \]

\[ V_d = \frac{5 * (1 - e^{-0.24*0.5})}{0.24 * 0.5 * 6.99 - 1.15 * e^{-0.24*0.5}} = 41.67 * \frac{0.113}{5.97} = 0.79L \]

true peak and troughs are used.

\[ \text{Tau} = \ln \left(\frac{6}{1}\right)/k + 0.5 = 7.96 \text{ hrs approx 8 hours} \]

\[ \text{Dose} = 6*0.24*0.79*0.5* (1-e^{-0.24*0})/(1-e^{-0.24*0.5}) = 4.3 \text{ mg approx 4 mg} \]

\[ \text{Dose} = 4 \text{ mg q 8 hours.} \]