**Question #1** (10 points)

A 30 mg dose of a drug is given as an i.v. bolus injection. The starting concentration is 750 µg/L and the AUC is 1500 µg/L*hr. Calculate the \( k_e \), half-life, \( V_d \), and \( CL \).

**A)** \( k_e = 0.5 h^{-1}, \quad t_{1/2} = 1.39 h, \quad V_d = 40 L, \quad CL = 20 L/h \)

**B)** \( k_e = 0.4 h^{-1}, \quad t_{1/2} = 1.39 h, \quad V_d = 80 L, \quad CL = 20 L/h \)

**C)** \( k_e = 0.4 h^{-1}, \quad t_{1/2} = 1.39 h, \quad V_d = 40 L, \quad CL = 20 L/h \)

**D)** \( k_e = 0.5 h^{-1}, \quad t_{1/2} = 3.45 h, \quad V_d = 20 L, \quad CL = 20 L/h \)

**E)** \( k_e = 0.5 h^{-1}, \quad t_{1/2} = 1.39 h, \quad V_d = 40 L, \quad CL = 40 L/h \)

\[
V_d = \frac{D}{C_0} = \frac{30000 \mu g}{750 \mu g/L} = 40 L
\]

\[
CL = \frac{D}{AUC} = \frac{30000 \mu g}{1500 \mu g \cdot h/L} = 20 \frac{L}{h}
\]

\[
k_e = \frac{CL}{V_d} = \frac{20 \frac{L}{h}}{40 L} = 0.5 h^{-1}
\]

\[
\frac{t_{1/2}}{k_e} = \frac{\ln 2}{0.5 h^{-1}} = 1.39 h
\]
Question #2 (10 points)

How will an increase in tissue binding affect the following properties of a high-extraction drug administrated through an intravenous injection? (Please note that $\leftrightarrow$ means no change)

\[ \text{high extraction drug } \Rightarrow CL = Q_H \leftrightarrow \]
\[ V_d = V_p + V_T \cdot \frac{f_u}{f_{u,T}} \& f_{u,T} \downarrow \Rightarrow V_d \uparrow \]
\[ AUC_{0-\infty} = \frac{D}{CL} \Rightarrow AUC_{0-\infty} \leftrightarrow \]
\[ C_{\text{max}} = C_0 = \frac{D}{V_d} \Rightarrow C_{\text{max}} \downarrow \]
\[ T_{1/2} = \frac{\ln 2}{ke} = \frac{\ln 2}{CL/V_d} = \frac{\ln 2 \cdot V_d}{CL} \Rightarrow T_{1/2} \uparrow \]

A) \hspace{1cm} \uparrow \ AUC, \downarrow \ C_{\text{max}}, \downarrow \ t_{1/2}

B) \hspace{1cm} \leftrightarrow \ AUC, \uparrow \ C_{\text{max}}, \leftrightarrow \ t_{1/2}

C) \hspace{1cm} \leftrightarrow \ AUC, \downarrow \ C_{\text{max}}, \uparrow \ t_{1/2}

D) \hspace{1cm} \downarrow \ AUC, \leftrightarrow \ C_{\text{max}}, \uparrow \ t_{1/2}

E) \hspace{1cm} \uparrow \ AUC, \uparrow \ C_{\text{max}}, \downarrow \ t_{1/2}
Which combination of the following factors makes the serum creatinine level a good choice to estimate renal function?

1) Creatinine is endogenous
2) Creatinine is only eliminated by kidney
3) Creatinine is not binding to protein in plasma
4) Creatinine urinary excretion rate is not affected by diseases
5) Creatinine is constantly formed by muscle

A) all of the above
B) 1, 2, & 4
C) 1, 2, 3, & 5
D) 1, 3, 4, & 5
E) 2, 3, 4 & 5
Question #4 (10 points)

JM is an 80-year-old, 87 kg, 5’7’’ man with gram-negative sepsis. His serum creatinine is 1.5mg/dL and has been stable since hospital admission. Compute a gentamicin dose to provide a steady-state peak concentration of 9μg/mL and a steady-state trough concentration of 1.5μg/mL after short-term infusion (30min).

(Please use the aminoglycoside $k_e$ equation from the equation sheet.)

Estimate the creatinine clearance:

$$IBW = 50kg + 2.3kg \cdot 7 = 66.1kg \rightarrow \text{obese patient, therefore, use ABW}$$

$$ABW = IBW + 0.4 \times (TBW - IBW) =$$

$$= 66.1kg + 0.4 \times (87kg - 66.1kg) \sim 74.5kg$$

$$Cl_{creat} = \frac{(140 - \text{age}) \cdot ABW}{72 \cdot Cp_{creat}} = \frac{(140 - 80) \cdot 74.5kg}{72 \cdot 1.5mg/dL} \sim 41.4mL/min = 2.48L/h$$

Estimate the elimination rate constant ($k_e$) and half-life ($t_{1/2}$):

$$k_e = 0.00293(Cl_{creat}) + 0.014 = 0.135 h^{-1}$$

Estimate the volume of distribution ($V_d$):

$$V_d = 0.25L/kg \times 74.5kg = 18.63L$$

Calculate the dosing interval:

$$\tau = \frac{\ln\left(\frac{C_{\text{max}}(\text{desired})}{C_{\text{min}}(\text{desired})}\right)}{k_e} + T = \frac{\ln\left(\frac{9\mu g/mL}{1.5\mu g/mL}\right)}{0.135 h^{-1}} + 0.5h = 13.27h \sim 12h$$

Calculate the dose:
\[
D = C_{\text{max (desired)}} \cdot k_e \cdot V_d \cdot T \cdot \frac{\left(1 - e^{-k_e T}\right)}{\left(1 - e^{-\frac{T}{\tau}}\right)} = \\
= 9 \mu g / mL \cdot 0.135 h^{-1} \cdot 18.63 L \cdot 0.5 h \cdot \frac{\left(1 - e^{-0.135 h^{-1} \cdot 12 h}\right)}{\left(1 - e^{-0.135 h^{-1} \cdot 0.5 h}\right)} = 139.3 mg
\]

A) 158mg every 12 hours
B) 115mg every 8 hours
C) 180mg every 12 hours
D) 180mg every 24 hours
E) 130mg every 12 hours
Question #5 (10 points)

Tobramycin has been used in the treatment of Cystic Fibrosis (CF). In a recent study, the reported parameters in CF patients are listed in the table:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Population Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume of Distribution (Central) (L)</td>
<td>15</td>
</tr>
<tr>
<td>Creatinine Clearance (ml/min)</td>
<td>105</td>
</tr>
</tbody>
</table>

A male CF patient is 60 kg, 40 year-old, and receives 7 mg/kg tobramycin via a 30 min infusion. (Assume tobramycin clearance equals to creatinine clearance, and use total body weight for calculation.) Calculate tobramycin $AUC_{x_0}$ and creatinine plasma concentration ($Cp_{Creat}$) for this patient.

$$CL_{cr} = CL = 105\,(mL / min) = 6.3\,(L / hr)$$

$$AUC_{x_0} = \frac{DOSE}{CL} = \frac{60\,kg \cdot 7\,mg / kg}{6.3\,L / hr} = 66.7\,(mg \cdot hr / L) = 4\,(mg \cdot min / mL)$$

$$CL_{cr} = \frac{(140 - age) \cdot TBW}{72 \cdot Cp_{creat}}$$

$$105\,ml / min = \frac{(140 - 40) \cdot 60\,kg}{72 \cdot Cp_{creat}}$$

$$Cp_{creat} = 0.79\,(mg / dL)$$

A) 4 mg•min/mL  7.9 mg/dL
B) 66.7 mg•hr/L  7.9 mg/dL
C) 4 mg•hr/L  0.79 mg/dL
D) 66.7 mg•min/mL  0.79 mg/dL
E) 4 mg•min/mL  0.79 mg/dL
**Question #6** (5 points)

The patient is currently on a 7mg/kg QD gentamicin dosing regimen. Based on the observations, is this treatment schedule appropriate or is a change in dosing regimen necessary?

A) 14mg/kg q12h  
B) 7mg/kg q24h  
**C)** 7mg/kg q36h  
D) 7mg/kg q48h  
E) No change needed
Question #7 (5 points)

Which statement is wrong?
A) Creatinine clearance is a measurement for kidney function.
B) Bioavailability of high extraction drugs is dependent on plasma protein binding.
C) Clearance and volume of distribution determine the half-life of a drug.
D) A multi-compartment-body model has only one volume of distribution.
E) Clearance determines steady-state plasma levels
Question #8 (5 points)

Which statement is wrong?

A) Renal clearance can vary with age.
B) Heart failure can have an impact on clearance.
C) Aminoglycosides are used to treat infections with both gram-positive and gram-negative pathogens.
D) Given linear pharmacokinetics, a plot of average steady-state concentration vs. dose results in a straight line.
E) $AUC, C_{\text{max}}$ and $t_{\text{max}}$ are used to evaluate bioequivalence.
Question #9 (10 points)

A female patient (50yr, 75 kg), has MRSA infection. The plasma creatinine concentration was 1.1 mg/dL when she was admitted into hospital.

After the patient received 5 days of treatment, plasma creatinine concentration was measured again (2 mg/dL). What was the starting dose based on nomogram if vancomycin was used? What is the possible reason for the increase of creatinine plasma concentration? What should be the adjusted dose? (use total body weight (TBW) for question.)

\[
CL_{cr} = \frac{(140 - \text{age}) \cdot TBW}{85 \cdot Cp_{creat}}
\]

\[
CL_{cr} = \frac{(140 - 50) \cdot 75kg}{85 \cdot 1.1mg/dL}
\]

\[
CL_{cr} = 72.19 \frac{mL}{min} \approx 70 \frac{mL}{min}
\]

\[
CL_{cr} = \frac{(140 - \text{age}) \cdot TBW}{85 \cdot 2mg/dL}
\]

\[
CL_{cr} = \frac{(140 - 50) \cdot 75kg}{85 \cdot 2mg/dL}
\]

\[
CL_{cr} = 39.7 \frac{mL}{min} \approx 40 \frac{mL}{min}
\]

75kg, 70 mL/min → 1000 q24h
75kg, 40 mL/min → 1000 q12h
Creatinine is eliminated via kidney, and renal impairment will increase plasma creatinine concentration.

A) 1000 q24h, Renal impairment, 1000 q12h.
B) 1000 q24h, Liver failure, 1000 q12h
C) 1000 q12h, Renal impairment, 1000 q24h
D) 1000 q12h, Liver failure, 1000 q12h.
E) 1000 q24h, Renal impairment, 1000 q24h.
Question #10 (10 points)

V.S., a 52-year-old male, was admitted to the hospital following a car accident. He is 5’2” and on admission weighed 60 kg. He was taken for abdominal surgery and post-operatively became hypotensive and required large volumes of fluid to maintain his blood pressure. Currently, he weighs 64 kg and has a serum creatinine of 0.6 mg/dL. V.S. is to receive gentamicin empirically after his abdominal surgery. Estimate the half-life in this patient. (Use the given serum creatinine!)

A) \( t_{1/2} = 1.79 \text{min} \)
B) \( t_{1/2} = 1.79 \text{h} \)
C) \( t_{1/2} = 3.12 \text{h} \)
D) \( t_{1/2} = 0.386 \text{h} \)
E) \( t_{1/2} = 7.33 \text{h} \)

\( IBW = (50 + 2.3 \cdot 3) \text{kg} = 54.6 \text{kg} \)

\( TBW = 60 \text{kg} \)

\( TBW < 120\% \text{IBW} \Rightarrow \text{use } TBW \)

\( V_d = 0.25 \frac{L}{\text{kg}} \cdot 60 \text{kg} + 4L = 19L \)

\[ Cl_{Cr} = \frac{(140 - \text{age}) \cdot TBW}{72 \cdot \text{SeCr}} = \frac{(140 - 52) \cdot 60 \text{kg}}{72 \cdot 0.6 \text{mg/dL}} = 122 \frac{mL}{\text{min}} = 7.33 \frac{L}{\text{hr}} \]

\[ k_e = \frac{Cl}{V_d} = \frac{7.33 \frac{L}{\text{hr}}}{19L} = 0.386 \text{h}^{-1} \]

\[ t_{1/2} = \frac{\ln 2}{k_e} = \frac{\ln 2}{0.386 \text{h}^{-1}} = 1.79 \text{h} \]
**Question #11** (10 points)

Drug A (F = 0.7) follows one-compartmental pharmacokinetics and has a total body clearance of 3L/hr and a volume of distribution of 60L. A 770mg tablet contains 500mg of active drug A. The oral absorption rate constant $k_a$ is 0.5h$^{-1}$.

Calculate $t_{\text{max}}$, $C_{\text{max}}$ and AUC of the active compound.

\[ k_e = \frac{Cl}{Vd} = \frac{3L}{60L} = 0.05h^{-1} \]

\[ t_{\text{max}} = \frac{\ln\left( \frac{k_e}{k_a} \right)}{(k_a - k_e)} = 5.1h \]

\[ C_{\text{max}} = \frac{S \cdot F \cdot D \cdot k_{a} \cdot k_e}{Vd \cdot (k_a - k_e)} \left( e^{-k_e t_{\text{max}}} - e^{-k_a t_{\text{max}}} \right) \]

\[ = \frac{1 \cdot 0.7 \cdot 500mg \cdot 0.5h^{-1}}{60L \cdot (0.5h^{-1} - 0.05h^{-1})} \left( e^{-0.05h^{-1} \cdot 5.1h} - e^{-0.5h^{-1} \cdot 5.1h} \right) = 4.52mg/L \]

\[ AUC = \frac{D \cdot S \cdot F}{Cl} = \frac{500mg \cdot 1 \cdot 0.7}{3L} = 116.7mg \cdot h/L \]

A) $t_{\text{max}} = 5.1h$, $C_{\text{max}} = 2.94\mu g/L$, AUC = 90mg*h/L

B) $t_{\text{max}} = 6.5h$, $C_{\text{max}} = 3.3mg/L$, AUC = 76mg*h/L

C) $t_{\text{max}} = 5.1h$, $C_{\text{max}} = 4.52\mu g/mL$, AUC = 116.7mg*h/L

D) $t_{\text{max}} = 3.7h$, $C_{\text{max}} = 3.3mg/L$, AUC = 90mg*h/L

E) $t_{\text{max}} = 6.5h$, $C_{\text{max}} = 2.5\mu g/mL$, AUC = 50mg*h/L

P.S. There was a mistake on the answer key in the exam. All answers will be given correct
Question #12 (10 points)

H.W., a 65-year-old, 5’4”, 60kg woman with a serum creatinine of 1mg/dL, has been started on 1g of vancomycin over 1 hr infusion q12h for the treatment of staphylococcal. Calculate steady-state peak and trough vancomycin concentration. 

\[ V_d = 0.178 \times \text{age} + 0.22 \times \text{TBW} + 15 \]

\[ \text{TBW} < 120\% IBW, \text{we will stay with TBW} \]

\[ CL \equiv CL_{cr} = \frac{75 \times \text{TBW}}{85 \times 1} = 52.94 \text{ ml/min} = 3.18 \text{ L/hr} \]

\[ V_d = 0.178 \times 65 + 0.22 \times 60 + 15 = 39.77 \text{ L} \]

\[ K = CL/V_d = 0.08 / \text{hr} \]

\[ C_{\text{peak, ss}} = \frac{1000}{3.18 \times 1} (1 - e^{-0.08 \times 11}) = 24.14 \text{ mg/L} \]

\[ C_{\text{trough, ss}} = 24.14 \times e^{-0.08 \times 11} = 10 \text{ mg/L} \]

\[ C_{\text{peak, ss}} = 24.14 / (1 - e^{-0.08 \times 12}) = 39 \text{ mg/L} \]

\[ C_{\text{trough, ss}} = 39 \times e^{-0.08 \times 11} = 16 \text{ mg/L} \]

A) \[ C_{\text{max, ss}} = 24 \text{ µg/mL}; C_{\text{min, ss}} = 8 \text{ µg/mL} \]

B) \[ C_{\text{max, ss}} = 24 \text{ mg/L}; C_{\text{min, ss}} = 10 \text{ mg/L} \]

C) \[ C_{\text{max, ss}} = 32 \text{ µg/mL}; C_{\text{min, ss}} = 16 \text{ µg/mL} \]

D) \[ C_{\text{max, ss}} = 39 \text{ µg/mL}; C_{\text{min, ss}} = 10 \text{ µg/mL} \]

E) \[ C_{\text{max, ss}} = 39 \text{ mg/L}; C_{\text{min, ss}} = 16 \text{ mg/L} \]