1. Which combination of the following pharmacokinetic characteristics best describes the neonates compared to Adults?

1) Less total body water (% of body weight)
2) Decreased protein binding
3) Lower renal clearance
4) Longer gastric emptying time

A) 2&3&4  
B) 2&4  
C) 4 only  
D) All of the statements are right
2. Calculate the creatinine clearance of following patients using Cockcroft-Gault equation.

(1) A female, 40 years old, 160 cm, 60 kg, has a concentration of serum creatinine of 1.2 mg/dL.

First to decide which body weight (IBW, TBW or ABW) would be used in the equation.

\[
\text{IBW} = 45 + 0.9(\text{height in cm} - 150) = 45 + 0.9(160 - 150) = 45 + 9 = 54 \text{ kg}
\]

\[
\frac{\text{TBW}}{\text{IBW}} = \frac{60}{54} \times 100\% = 111.1\% < 120\%
\]

Since TBW is less than 120% of IBW, we should use TBW as dosing weight to calculate creatinine clearance

\[
\text{CL}_{cr} = \frac{(140 - \text{age}) \times \text{BW}}{\text{Cp}_{cr} \times 85} = \frac{(140 - 40) \times 60}{1.2 \times 85} = 58.8 \text{ ml/min}
\]

(2) A male, 30 years old, 180 cm, 110 kg, has a concentration of serum creatinine of 2.5 mg/dL.

\[
\text{IBW} = 50 + 0.9(\text{height in cm} - 150) = 50 + 0.9(180 - 150) = 77 \text{ kg}
\]

\[
\frac{\text{TBW}}{\text{IBW}} = \frac{110}{77} \times 100\% = 142.9\% > 120\%
\]

Since TBW is more than 120% of IBW, ABW is used

\[
\text{ABW} = \text{IBW} + 0.4(\text{TBW} - \text{IBW}) = 77 + 0.4(110 - 77) = 90.2 \text{ kg}
\]

\[
\text{CL}_{cr} = \frac{(140 - \text{age}) \times \text{BW}}{\text{Cp}_{cr} \times 72} = \frac{(140 - 30) \times 90.2}{2.5 \times 72} = 55.1 \text{ ml/min}
\]
3. J. J. is a 55 years old male person with 75 kg weight and 176 cm height. He suffers from a severe urinary infection and the treatment suggested by the physician is 7 mg/kg gentamicin once daily IV infused over 30 minutes. Assuming his serum creatinine is 1.1 mg/dL and Vd=0.25L/kg, what is the measured peak gentamicin concentration 30 minutes after the infusion was ended and the measured trough gentamicin concentration 30 minutes before the new infusion at steady state?

\[ \text{IBW}=50+0.9(\text{height in cm}-150)=50+0.9(176-150)=50+23.4=73.4 \text{ kg} \]

\[ \frac{\text{TBW}}{\text{IBW}} = \frac{75}{73.4} \times 100\% = 102.2\% < 120\% \]

So the TBW is used to calculate the creatinine clearance.

\[ CL \approx CL_{cr} = \frac{(140-\text{age}) \times BW}{Cp_{cr} \times 72} = \frac{(140-55) \times 75}{1.1 \times 72} = 80.5 \text{ ml/min} = 4.8 \text{ L/h} \]

\[ Vd = 0.25 \text{ L/kg} \times 75 \text{ kg} = 18.75 \text{ L} \]

\[ k_e = \frac{CL}{Vd} = \frac{4.8}{18.75} = 0.256 \text{ h}^{-1} \]

\( \tau=24 \text{ h} \) and \( T=0.5 \text{ h} \)

\[ C_{\text{max}} = \frac{\text{Dose}}{Vd \times k_e \times T \times (\frac{1-e^{-k_e T}}{1-e^{-k_e \tau}})} = \frac{7 \times 75}{18.75 \times 0.256 \times 0.5 \times (\frac{1-e^{-0.256 \times 24}}{1-e^{-0.256 \times 0.5}})} = 26.3 \text{ mg/L} \]

\( t_1=0.5 \text{ h}, t_2=24-0.5-0.5=23 \text{ h} \)

\[ C_{\text{max}}^* = C_{\text{max}} \times e^{-k_e t_1} = 26.3 \times e^{-0.256 \times 0.5} = 23.1 \text{ mg/L} \]

\[ C_{\text{min}}^* = C_{\text{max}} \times e^{-k_e t_2} = 26.3 \times e^{-0.256 \times 23} = 0.073 \text{ mg/L} \]
4. T.C. is a 64 kg, 169 cm, 35 years old female patient with a serum creatinine of 0.8 mg/dL. She is going to receive IV infusion of vancomycin over 1 hour for several days. After achieving steady state, the peak concentration obtained 30 minutes after the end of the infusion was 20 mg/L and a trough concentration obtained 30 minutes before the next dosing was 0.5 mg/L. What is the “true” peak and trough concentration at steady state? What dose and dosing interval would you recommend for her (Assume Vd=0.25 L/kg)?

\[ C_{\text{max}}^* = 20 \text{mg/L} \]
\[ C_{\text{min}}^* = 0.5 \text{mg/L} \]

So we need to obtain \( k_e \) value to calculate the \( C_{\text{max}} \) and \( C_{\text{min}} \). Before that, we firstly have to decide which dosing weight we have to use.

\[
\text{IBW} = 45 + 0.9(\text{height in cm} - 150) = 45 + 0.9(169 - 150) = 62.1 \text{ kg}
\]

\[
\frac{\text{TBW}}{\text{IBW}} = \frac{64}{62.1} \times 100\% = 103.1\% <120\%
\]

Thus, TBW is used to calculate the Vd
\[
Vd = 0.25 \text{L/kg} \times 64 \text{kg} = 16 \text{L}
\]

\[
CL \approx CL_{cr} = \frac{(140 - \text{age}) \times \text{BW}}{Cp_{cr} \times 85} = \frac{(140 - 35) \times 64}{0.8 \times 85} = 98.8 \text{ml/min} = 5.9 \text{L/h}
\]

\[
k_e = \frac{CL}{Vd} = \frac{5.9}{16} = 0.369 \text{h}^{-1}
\]

\[ t_1 = 0.5 \text{h}, \ t_2 = 0.5 \text{h} \]

\[
C_{\text{max}} = \frac{C_{\text{max}}^*}{e^{-k_e t_1}} = \frac{20}{e^{-0.369 \times 0.5}} = 24.1 \text{mg/L}
\]

\[
C_{\text{min}} = C_{\text{min}}^* \times e^{-k_e t_2} = 0.5 \times e^{-0.369 \times 0.5} = 0.4 \text{mg/L}
\]

\[
\tau = \frac{\ln\left(\frac{C_{\text{max}}}{C_{\text{min}}}\right)}{k_e} + T = \frac{\ln\left(\frac{24.1}{0.4}\right)}{0.369} + 1 \approx 12 \text{h}
\]

\[
\text{Dose} = \frac{C_{\text{max(desired)}}}{k_e} \times Vd \times T \times \frac{(1 - e^{-k_e t\tau})}{(1 - e^{-k_e T})} = 24.1 \times 0.369 \times 16 \times 1 \times \frac{1 - e^{-0.369 \times 12}}{1 - e^{-0.369 \times 1}} = 455.6 \text{mg} \approx 450 \text{mg}
\]

So the recommended dose is 450 mg and dosing interval is 12 hours.
5. A 3 months old infant is hospitalized with possible pneumonia. 3 mg Tobramycin was given every 8 hours with IV infusion over 30 min. The dosing time is 6 am, 2 pm and 10 pm. Several days later, the serum concentrations of tobramycin are tested using HPLC and listed as follows:

<table>
<thead>
<tr>
<th>Time</th>
<th>Point</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 am</td>
<td></td>
<td>6.0 µg/ml</td>
</tr>
<tr>
<td>1 pm</td>
<td></td>
<td>2.0 µg/ml</td>
</tr>
</tbody>
</table>

Determine the half-life and volume distribution of tobramycin in this infant.

\[
\ln \frac{C_{\text{max}}}{C_{\text{min}}} = \frac{\ln 6.0}{2.0} = 0.183h^{-1}
\]

\[
t_{1/2} = \frac{0.693}{k_e} = \frac{0.693}{0.183} = 3.8h
\]

\(t_1=0.5h, \ t_2=1h\)

\[
C_{\text{max}} = \frac{C_{\text{max}}}{e^{-k_e t_1}} = \frac{6.0}{e^{-0.183\times0.5}} = 6.6 \mu g/ml
\]

\[
C_{\text{min}} = C_{\text{min}} \times e^{-k_e t_2} = 2.0 \times e^{-0.183\times1} = 1.7 \mu g/mL
\]

\[
Vd = \frac{Dose \times (1-e^{-k_e T})}{k_e \times T \times (C_{\text{max}} - C_{\text{min}} \times e^{-k_e T})} = \frac{3 \times (1-e^{-0.183\times0.5})}{0.183\times0.5 \times (6.6-1.7 \times e^{-0.183\times0.5})} = 0.57 L
\]