1. True or False (0.25 each, total 1 point)

(1) The effect of body weight on volume of distribution does not depend on the lipophilicity of the drug. (False)

(2) There are two methods for interspecies scaling, physiological models are always less complicated than allometric method. (False)

(3) The extracellular water (in % of body weight) in neonates is usually bigger than that in adults. (True)

(4) Based on the figure below, we could read tobramycin is time-dependent antimicrobial agent and ticarcillin is concentration-dependent antimicrobial agent against this isolate. (False)
2. Please calculate the body surface area for the following patients, as well as their creatinine clearance using Cockcroft-Gault equation. (2 each, total 4 points)

(1) Patient A: male, 40 years old, 175 cm, 80 kg, serum creatinine is 1.3 mg/dL

The body surface area can be calculated by:

$$BSA[m^2] = \left(\frac{TBW[kg]}{70[kg]}\right)^{0.7} \times 1.73[m^2] = \left(\frac{80}{70}\right)^{0.7} \times 1.73 = 1.90m^2$$

Or

$$BSA[m^2] = TBW[kg]^{0.425} \times H[cm]^{0.725} \times 0.007184 = 80^{0.425} \times 175^{0.725} \times 0.007184 = 1.96m^2$$

IBW = 50 + 0.9(Height in cm - 150) = 50 + 0.9(175 - 150) = 72.5 kg

$$\frac{TBW}{IBW} = \frac{80}{72.5} \times 100\% = 110.3\% < 120\%$$

$$CL_{cr} = \frac{(140 - age) \times BW}{Cp_{cr} \times 72} = \frac{(140 - 40) \times 80}{1.3 \times 72} = 85.5 ml/min$$

(2) Patient B: female, 52 years old, 155 cm, 66 kg, serum creatinine is 1.9 mg/dL

The body surface area can be calculated by:

$$BSA[m^2] = \left(\frac{TBW[kg]}{70[kg]}\right)^{0.7} \times 1.73[m^2] = \left(\frac{66}{70}\right)^{0.7} \times 1.73 = 1.66m^2$$

Or

$$BSA[m^2] = TBW[kg]^{0.425} \times H[cm]^{0.725} \times 0.007184 = 66^{0.425} \times 155^{0.725} \times 0.007184 = 1.65m^2$$

IBW = 45 + 0.9(Height in cm - 150) = 45 + 0.9(155 - 150) = 49.5 kg

$$\frac{TBW}{IBW} = \frac{66}{49.5} \times 100\% = 133.3\% > 120\%$$

ABW = IBW + 0.4(TBW - IBW) = 49.5 + 0.4(66 - 49.5) = 56.1 kg

$$CL_{cr} = \frac{(140 - age) \times BW}{Cp_{cr} \times 85} = \frac{(140 - 52) \times 56.1}{1.9 \times 85} = 30.6 ml/min$$
3. C.F. is a 65 years old female who suffers post-surgical wound infection and has been treated with gentamicin for several days. She is 5’6” tall and 133 lbs weight. Her serum creatinine is 1.2 mg/dL and Vd=0.25L/kg. The gentamycin is given by IV infusion over 45 min with dose of 5mg/kg once daily. Predict the measure peak concentration one hour after the infusion was started and the measured trough concentration one and half hours before the next infusion. (2 points)

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

IBW=45+2.3(height in inches-60)=45+2.3(66-60)=45+13.8=58.8 kg

\[
\frac{TBW}{IBW} = \frac{133/2.2 \times 100\%}{58.8} = 102.8\% < 120\%
\]

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

\[
CL \approx CL_{cr} = \frac{(140 – age) \times BW}{C_p \times 85} = \frac{(140 – 65) \times 133/2.2}{1.2 \times 85} = 44.5 \text{ ml/min} = 2.7 \text{ L/h}
\]

\[
Vd = 0.25 \text{ L/kg} \times \frac{133}{2.2} \text{ kg} = 15.1 \text{ L}
\]

\[
k_e = \frac{CL}{Vd} = \frac{2.7}{15.1} = 0.179 \text{ h}^{-1}
\]

\[
\tau = 24 \text{ h and } T = 0.75 \text{ h}
\]

\[
C_{\text{max}} = \frac{Dose}{Vd \times k_e \times T \times \left(1 - e^{-k_e \tau}ight)} = \frac{5 \times 133/2.2}{15.1 \times 0.179 \times 0.75 \times \left(1 - e^{-0.179 \times 24}ight)} = 19.0 \text{ mg/L}
\]

\[
t_1 = 0.25 \text{ h, } t_2 = 24 - 0.75 - 1.5 = 21.75 \text{ h}
\]

\[
C_{\text{max}}^* = C_{\text{max}} \times e^{-k_e t_1} = 19.0 \times e^{-0.179 \times 0.25} = 18.2 \text{ mg/L}
\]

\[
C_{\text{min}}^* = C_{\text{min}} \times e^{-k_e t_2} = 19.0 \times e^{-0.179 \times 21.75} = 0.4 \text{ mg/L}
\]
4. A male patient has been treated with 1200 mg amikacin (IV infusion for 45 min, BID) for several days. His plasma samples at steady state were analyzed and result shows the plasma concentration is 25 µg/ml at 1 hour after the beginning of the infusion and 5 µg/ml at 1 hour before the new infusion. Please predict the apparent volume of distribution of amikacin in this patient. (2 points)

\[ C_{\text{max}}^+ = 25 \, \mu g/ml \]

\[ C_{\text{min}}^+ = 5 \, \mu g/ml \]

\[ k_e = \frac{\ln C_{\text{max}}^+}{\Delta t} = \frac{\ln 25}{5} = 0.161 \, h^{-1} \]

\[ t_1=0.25h, \ t_2=1h \]

\[ C_{\text{max}} = C_{\text{max}}^+ e^{-k_e t_1} = \frac{25}{e^{-0.161 \times 0.25}} = 26.0 \, \mu g/ml \]

\[ C_{\text{min}} = C_{\text{min}}^+ e^{-k_e t_2} = 5 \times e^{-0.161 \times 1} = 4.3 \, \mu g/mL \]

\[ V_d = \frac{Dose}{k_e \times T} \times \frac{(1-e^{-k_e T})}{(C_{\text{max}} - C_{\text{min}} \times e^{-k_e T})} = \frac{1200}{0.161 \times 0.75} \times \frac{(1-e^{-0.161 \times 0.75})}{(26.0-4.3 \times e^{-0.161 \times 0.75})} = 50.9 \, L \]
5. Which dosing interval of gentamicin will you pick if the patient has the clinical peak concentration (30 min after the infusion started) of 30 µg/ml and the clinical trough concentration (30 min before the next infusion) of 2.5 µg/ml at steady state? (Infusion time is 15 min and half-life is 2 hours) (1 points)

\[ k_e = \frac{0.693}{t_{1/2}} = \frac{0.693}{2} = 0.3465 \text{ hr}^{-1} \]

\[ \tau = \frac{\ln(C_{max}^*)}{k_e} + T + t_{max}^* + t_{min}^* = \frac{\ln(30/2.5)}{0.3465} + 0.25 + 0.25 + 0.5 \approx 8.2 \text{ hr} \approx 8 \text{ h} \]

Or

\[ C_{max} = C_{max}^* e^{-k_e T} = \frac{30}{e^{0.3465 \times 0.25}} = 32.7 \mu g/ml \]

\[ C_{min} = C_{max}^* e^{-k_e t_{1/2}} = 2.5 \times e^{-0.3465 \times 0.5} = 2.1 \mu g/ml \]

\[ \tau = \frac{\ln(C_{max}^*)}{k_e} + T = \frac{\ln(32.7/2.1)}{0.3465} + 0.25 \approx 8.2 \text{ hr} \approx 8 \text{ h} \]

Thus the dosing strategy is TID.