Please contact Benjamin Weber (benjaminweber@ufl.edu) if there are any questions regarding this homework assignment.

1. TRUE (T) or FALSE (F) [4 points, 0.5 each]

The total body water (in % of body weight) in neonates is usually smaller than in adults

FALSE

The glomerular filtration rate (GFR) in neonates is usually smaller than in adults

TRUE

Patients with an increased body weight tend to have a larger volume of distribution

TRUE

The effect of body weight on volume of distribution does not depend on the lipophilicity of the drug

FALSE

Drugs with a high octanol/water lipid partition coefficient (LPD) usually show a larger volume of distribution in obese patients

TRUE

The allometric body weight model can be used to convert body surface area (BSA) into total body weight (TBW)

FALSE

The terminal half-life of aminoglycosides is approximately 2 hours

FALSE

Aminoglycosides cannot pass membranes very well because of their low protein binding

FALSE
2. Calculate the ideal body weight (IBW) of a female person who is 168 cm tall. Which body weight (IBW, TBW (total body weight), or ABW (adjusted body weight)) would you use in the Cockcroft-Gault equation if the person weighs 60 kg? [0.5 points]

\[
IBW_{female} = 45.5 + 0.9(168 - 150) = 61.7 \text{ kg}
\]

IBW does not exceed 120% of IBW. Thus, TBW needs to be used in Cockcroft-Gault equation.

3. F.G. (female, 32 years, 68 kg, 175cm, serum creatinine = 1.2 mg/dL) is hospitalized with a severe urinary infection. The physician decides to treat the infection with gentamicin (target “true” \( c_{\text{max}} \) at steady state = 4.5 mg/L) and asks you to come up with a once-a-day dosing regimen for F.G.

a. Comment on the once-a-day dosing regimen for gentamicin. What is the rationale for once-a-day dosing regimen for gentamicin? [1 point, 0.25 each]
  
  - Post Antibiotic Effect
  - Toxicity
  - Adaptive Resistance
  - Cost Effective

b. Comment on the choice of 4.5 mg/L as target \( c_{\text{max}} \). Do you support the decision? [0.5 points]

Recommend peak levels for gentamicin to treat urinary infections are > 4 mg/L. Thus, we support the physician’s decision.

c. Which gentamicin dose would you recommend for F.G. assuming drug administration via IV infusion for 30 minutes? [1 point]

\[
Dose = C_{\text{max,desired}} \times k \times V_d \times T \times \left( \frac{1 - e^{-k \tau}}{1 - e^{-kT}} \right)
\]

\[
C_{\text{max,desired}} = 4.5 \frac{mg}{L}
\]

\[
IBW_{female} = 45.5 + 0.9(175 - 150) = 68 \text{ kg}
\]

TBW does not exceed 120% of IBW. Thus, TBW needs to be used in Cockcroft-Gault equation. F.G. is not obese.

\[
V_d = 0.25 \frac{L}{kg} \times 68 kg = 17 L
\]

\[
CL = CL_{Cr} = \frac{(140 - 32) \times 68}{1.2 \times 85} = 72 \frac{mL}{min} = 4.32 \frac{L}{h}
\]

\[
k = \frac{CL}{V_d} = \frac{4.32 L}{17 L} = 0.254 \frac{1}{h}
\]
\[ \tau = 24\text{h (once – daily – dosing)} \]
\[ T = 0.5\text{h} \]
\[ Dose = 4.5 \frac{mg}{L} * 0.254 \frac{1}{h} * 17L * 0.5h * \left( \frac{1 - e^{-0.254\frac{1}{h} * 24h}}{1 - e^{-0.254\frac{1}{h} * 0.5h}} \right) \]
\[ = 9.7155mg * \left( \frac{0.9977}{0.1193} \right) = 81.25mg \]

d. Calculate the “clinical” peak concentration at steady state (30 min before next infusion is started) and comment on this concentration regarding to any possible side effects of aminoglycoside therapy. [0.5 points]

\[ C_{\text{min}}^* = C_{\text{max}}^* e^{-k*23h} = 4.5 \frac{mg}{L} * e^{-0.254\frac{1}{h} * 23h} = 0.0131 \frac{mg}{L} \]

Trough concentration is below 2 mg/mL. Thus, side effects are not expected.

4. J.C. a 75 kg, 40-year-old patient with a serum creatinine of 1.8 mg/dL, has been receiving IV tobramycin, 110 mg over one-half hour every 8 hours, for several days. A peak plasma concentration obtained 1 hour after start of an infusion was 8 mg/L, and a trough concentration obtained 30 minutes before initiation of a dose was 3 mg/L. Estimate k, CL, and Vd for tobramycin in J.C. [1.5 points]

\[ C_{\text{max}}^* = \frac{8}{L} \]
\[ C_{\text{min}}^* = \frac{3}{L} \]
\[ k = \frac{\ln \left( \frac{C_{\max}^*}{C_{\min}^*} \right)}{\Delta t} = \frac{\ln \left( \frac{8}{3} \right)}{6.5h} = 0.15 \frac{1}{h} \]
\[ C_{\max} = \frac{C_{\max}^*}{e^{-kt_{\max}}} = \frac{8 \frac{mg}{L}}{e^{-0.15\frac{1}{h} * 0.5h}} = 8.62 \frac{mg}{L} \]
\[ C_{\min} = C_{\min}^* e^{-kt_{\min}} = \frac{3}{L} * e^{-0.15\frac{1}{h} * 0.5h} = 2.78 \frac{mg}{L} \]
\[ Vd = \frac{110mg}{0.15 \frac{1}{h} * 0.5h \left( 8.62 \frac{mg}{L} - 2.78 \frac{mg}{L} * e^{-0.15\frac{1}{h} * 0.5h} \right)} = 1466.67mg \left( \frac{0.0723}{6.041 \frac{mg}{L}} \right) = 17.55 L \]
\[ CL = k \times Vd = 0.15 \frac{1}{h} \times 17.55 \text{ L} = 2.63 \frac{L}{h} \]

5. Which dosing interval would you recommend for amikacin to treat a patient (CL=83.33 mL/min, 80 kg) that suffers from a pulmonary infection if the “true” peak and trough concentrations at steady state are supposed to be 30 mg/L and 5 mg/L, respectively? Assume a short-term infusion over 45 minutes. [1 point]

\[ CL = 83.33 \frac{\text{mL}}{\text{min}} \approx 5 \frac{L}{h} \]

\[ Vd = 0.25 \frac{L}{kg} \times 80 \text{ kg} = 20 \text{ L} \]

\[ k = \frac{CL}{Vd} = \frac{5}{20} = 0.25 \frac{1}{h} \]

\[ \tau = \frac{\ln \left( \frac{C_{\text{max}}}{C_{\text{min}}} \right)}{k} + T = \frac{\ln \left( \frac{30}{5} \right)}{0.25} + 0.75 = 7.91 \text{ h} \approx 8 \text{ h} \]