Case Study 5

1. A 500 mg IV dose of getamicin is given as a short-term IV infusion to an 80kg, 52 year old, 5'5" male patient. He has a serum creatinine of 0.8mg/dL. The clearance of this drug is equivalent to creatinine clearance.

   A. Calculate the clearance.

   IBW=50+2.3*5=61.5
   Is he obese? TBW/IBW*100=80kg/61.5kg*100%~130%. Yes, he is clinically obese.
   Therefore use ABW in CLcr calculation.

   ABW=IBW+0.4*(TBW-IBW)=68.9kg

   Clcr=(140-52)*68.9/(72*0.8)=105mL/min

   B. Assuming this drug is only distibutes into extracellular fluid (assume the volume of an average person). What is the half-life?

   Volume of distribution(Vd)=18L
   Half-life=0.693/(Cl/Vd)=0.693/(105mL/min*60/100)/18L=1.98hours~2hours

2. Drug X has a narrow therapeutic window (~5-40mg/L). Two plasma samples are drawn for monitoring; one at 2 hours after the first iv bolus administration and one at 12 hours. The concentrations are 33mg/L and 8mg/L, respectively. This drug displays a one compartment body model and 1g was administered.

   A. Calculate the following: Vd, Cl, and half-life.

      Ke=Ln(C1/C2)/(t2-t1)=Ln(33mg/L/8mg/L)/(12hr-2hr)=0.1417hr^{-1}

      After Ke is know we can back calculate the concentration to find Cmax and calculate the Vd.

      C=C0*e^(-ke*t) C0=C/e^(-ke*t) C0=33mg/L/e^(-0.14*2)=43.66mg/L

      Vd=Dose/C0=1000mg/43.66mg/L=22.9~23L

      Cl=Ke*Vd=0.1417*22.9L=3.24L/hr

      Half-life=0.693/ke=0.693/0.1417hr^{-1}=4.89hr

   B. Assumuing linear kinetics what would the effect be on clearance, volume of distribution, half-life, AUC, and Cmax if the dose were decreased by 25%.

Cl↔
Vd↔
Half-life↔
AUC↓by 25%
Cmax↓by 25%

3. Patient AB and Patient CD are on a multiple IV bolus regimen of the same drug and steady state has been reached. This drug is cleared only by glomerular filtration and is not bound to plasma proteins. Both patients have a CLcr of 130mL/min.

   A. Patient AB has a longer half-life. Explain.

   Because both patients have the same clearance value patient AB must have a larger volume of distribution.

   B. Would you expect the Cmax to be higher for patient AB or CD.

   CD would have a higher Cmax because at steady state

$$C_{\max ss} = \frac{D}{V} \cdot \frac{1}{(1 - e^{-k_e \tau})}$$

   and this patient has a smaller Vd (represented by V in this equation).

   C. Which patient would have more fluctuation in plasma concentration between each dose?

   Patient CD because this patient has a shorter half-life.

   D. Which patient has a higher average steady state concentration.

   The average concentration is the same for both patients at steady state. Based on the formula Css=Dose/(CL*Tau), where tau is the dosing interval.

True or False
State if the following are True or False

1. If the volume of distribution increases the clearance can remain the same. (T)

2. At steady state (equal dose, equal interval multiple IV) accumulation stops because the amount of drug eliminated during the dosing interval is more than the dose given at each dose time. (F)

3. The time it takes for plasma concentrations to reach steady state after repeated IV doses is dependent on the elimination rate constant. (T)