PHA 5127
Answers Case Study 5
Fall 2007

Set I:
True or False

T F 1: A one compartment model means that drug in the blood is in rapid equilibration with drug in extravascular tissues. ***(T)***

T F 2: For a linear model, the rate constant for elimination is not proportional to the amount of drug remaining to be eliminated. ***(T)***

T F 3: Clearance and volume of distribution are independent each other, but both of them are dependent of dose. ***(F)***

T F 4: A drug with a linear protein binding has linear pharmacokinetics. ***(F)***
can have nonlinear elimination

T F 5: In a linear one-compartmental model, lower dose and lower volume of distribution result in a lower initial drug concentration after a single IV bolus**.** ***(F)***
C(0)=Dose/Vd

T F 6: In a linear one-compartmental model, any two concentration points in concentration-time profile can determine drug half-life after a single IV bolus. ***(T)***

$$t_{1/2} = \frac{0.693 \cdot (t_2 - t_1)}{\ln\left(\frac{C_1}{C_2}\right)}$$

T F 7: Total clearance is always greater or equal to renal clearance**.** ***(T)***
$CL_{tot} = CL_{ren} + CL_{bil} + CL_{met}$

Set II:

Jane, 5'8", 35-year-old, is being treated with the new drug for an infection disease. Jane weights 64.4 kg. Cp_{creat} in Jane is 0.8 mg/dL Assume a Vd of 0.24 L/kg*(TBW), and clearance of this drug is equal to creatinine clearance, and this drug follows a linear one compartment model.

1. In order to achieve initial concentration 6 mg/L, please calculate this IV bolus dose.

   V_d = 0.24 L/kg

   $$V_d = \frac{0.24L}{kg} x 64.4kg = 15.5L$$

   Initial Cp = 6 mg/L

   To determine the correct dose, we may use: $Cp_0 = \frac{Dose}{V_d} \rightarrow D = Cp_0 \cdot V_d$

   D = (6mg/L)(15.5 L) = 93 mg

2. Calculate half-life of this drug, and how many half-lives will it take to drop concentration from 6 mg/L to 750 µg/mL

   IBW= 45.5 kg + 2.3 kg for each inch over 5 ft in height

   *=45.5+2.3*8=63.9 (kg)→TBW<1.2 IBW*

   $$CL_{creat}(female) = \frac{(140 - age) \cdot weight}{85 \cdot Cp_{creat}} = \frac{(140-35) \cdot 64.4}{85 \cdot 0.8} = 99.44ml/\min = 5.97L/hr$$

   $$k_e = \frac{Cl}{Vd} = 5.97/15.5 = 0.385hr^{-1}$$

   $$t_{1/2} = \frac{0.693}{k_e} = 0.693/0.385 = 1.8hr$$

   6 mg/L →3mg/L →1.5mg/L →0.75mg/L=750 µg/mL (3 half-lives)

   OR:

   Assume 6mg/L is initial concentration:

   *0.75mg/L=6mg/L*EXP(-0.385*t) →t=5.4 hr →5.4/1.8=3 half-lives*

SET III:

Drug-Y is mainly eliminated by liver and kidney. Renal elimination is only by glomerula filtration. Mike with liver failure was given 70mg of this drug via IV bolus. Two plasma concentrations at 3 hours and 8 hours after dose were 1.31mg/L and 0.65mg/L, respectively. The plasma protein binding for the drug is 90%. Calculate the hepatic clearance and the volume of distribution of this drug in Mike? (Use 130ml/min for glomerula filtration rate).

k_e=-log(0.65/1.31)/5=0.14/hr
*C_0 = 1.31*exp(0.14*3)=1.99 mg/L*
Vd = Dose/C0=70/1.99=35.2L
*Cl = ke*Vd=0.14*35.2=4.93L/hr*
*Cl_{ren} = GFR*fu=130*60*(1-0.9)/1000=0.78L/hr*
Cl_{hep} = 4.93-0.78=4.15L/hr

SET IV:

The renal clearances, the fractions of unbound in plasma and the molecular weights of four drugs in a 75 kg subject are as follows:

	CL_{renal} (mL/min)	**fu**	**MW**
A	20	0.5	500
B	0.10	0.5	200
C	20	0.1	800
D	50	0.9	100

Which of following statement is true? (GFR is 130 mL/min and urine flow is 1.5mL/min.)

A: Drug A has renal secretion.
B: Drug B has renal secretion.
C: Drug C has renal secretion.
D: Drug D has renal secretion.
E: None of above

Answer: C

	Filtration	Secretion	Reabsorption
A	√ MW<20000		√ 20<130*0.5=65
B	√ MW<20000		√ 0.1<130*0.5=65
C	√ MW<20000	√ 20>130*0.1=13	
D	√ MW<20000		√ 50<130*0.9=117