Homework #3
PHA 5127 2007

1. a. Estimate the volume of distribution if the volume of plasma is 3L, the volume of tissue is 20L, and the fraction unbound in plasma is twice as much as the fraction unbound in tissue (2pts).

$Vd=Vp+Vt*(f_u/f_{ut})$ $Vd=3L+20L*(2x/x)=3L+20L*2=43L$

b. What will the effect be on the volume of distribution if the patient has a decrease in albumin in the plasma(1pt)?

In this scenario if fu↑, then the equation will look like the following
VD?=Vp↔+Vt↔(fu↑/fut↔) and we can see that Vd must increase (Vd↑).

C. Predict the starting concentration if a 500 mg dose were given (1pt).

$Vd=D/Co$ $Co=D/Vd$ $Co=500mg/43L=11.6mg/L$

D. How long would it take for the drug concentration to drop out of therapeutic range if the therapeutic window was 15-5mg/L, and the ke is 0.2 hr^{-1}?(2pts)

$C=C_o*e^{-ke*t}$ $LnC=LnC_o-k_e*t$ $Ln(C/C_o)/-k_e=t$ $Ln(5mg/L/11.6mg/L)/-0.2hr^{-1}=4.2hr$

2. Please state whether the following drugs are likely to displya permability limited distribution, perfusion limited distribution, limited by both, or have the ability to freely distribute. (1pt each)

a. Drug B is a lipophilic base with a pka of 3, which exerts its effect on the heart. Freely distributes.

b. Drug X is not an acid or base, has a partition coefficient of 12, and displays its effect in the brain. Perfusion limited.

3. Please state whether the following statement is true of false. (1pt)
a. If a drug displays a high amount of tissue binding the volume of distribution will be very large. False, the volume of distribution is also dependent on the degree of plasma protein binding. If the plasma protein binding is equal to the tissue binding and subsequently the fraction unbound in plasma is equal to the fraction unbound in tissue than the volume of distribution will range from 18L for a hydrophilic drug to 41L for a lipophilic drug.

b. Drug B is lipophilic, displays 98% plasma protein binding, and a fut of 0.02. This drug has a therapeutic window of 0.3-0.5 mg/L for free drug. A patient who is taking 800 mg of Drug B daily also starting taking Drug X which competes with Drug B for binding sites in plasma. The plasma protein binding for Drug B is now 96%. Calculate the

pharmacologically active concentration of drug B in plasma. With the administration of drug X is a dose adjustment needed for drug B (2pts)?

For Drug B Vd=Vp+Vt(fu/fut) Vd=3L+38L(0.02/0.02)=41L
Co=D/Vd=800mg/41L=19.5mg/L=0.39mg/L free fraction Drug B
For Drub B with Drug X Vd=3L+38L(0.04/0.02)=79L
Co=D/Vd=800mg/79L=10.1mg/L=0.4 mg/L free fraction Drug B
No dose adjustment is needed.