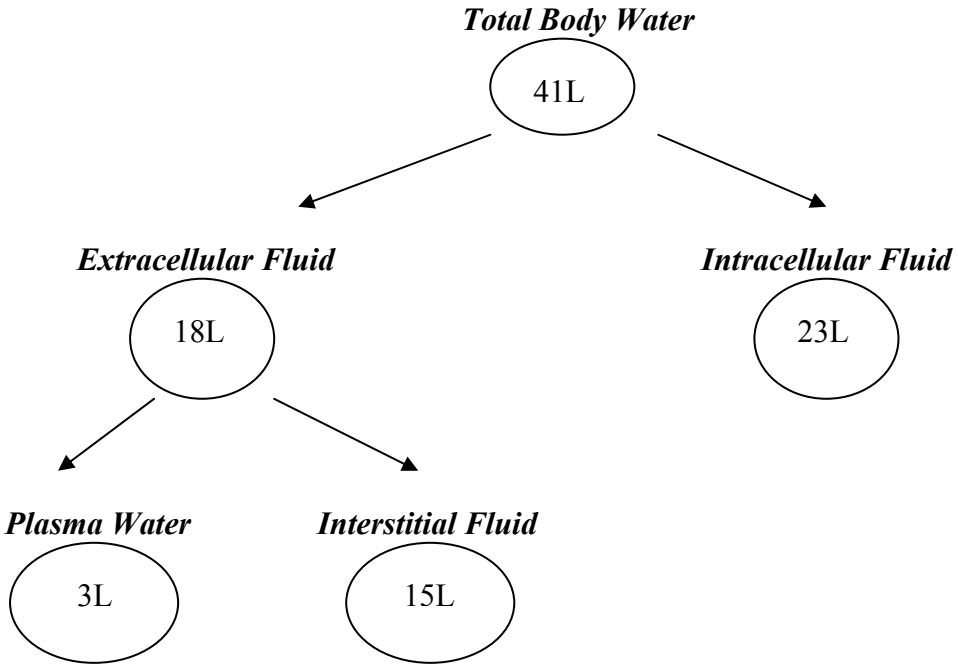
PHA 5127 – Fall 2006
Answers Case Study #2

#1 Please fill in the missing numbers!



#2: The volume of distribution (V_d) of a lipophilic drug A is 800L. Answer the following questions with true or false!

a)	Drug A is able to cross membranes	***TRUE***
b)	Drug A does not show any tissue protein binding	***FALSE***
c)	Plasma protein binding is more pronounced than tissue binding	***FALSE***
d)	V_d indicates that this drug is highly metabolized in the tissue	***FALSE***
e)	Drug A does not leave the plasma	***FALSE***
f)	V_d does reflect a real volume	***FALSE***

#3: Basics and Background of V_d.

a) Give a definition of the Volume of distribution in your own words and give additionally the formula used for calculations.

The volume of distribution (V_d) relates the amount of drug in the body to plasma or serum concentrations.

$$V_d = \frac{\text{Amount in the body}}{\text{Plasma concentration}}$$

b) Patient H. was given 100mg of drug M intravenously. His plasma levels are listed below. Please calculate V_d!

Time (h)	Cp (µg/L)
1.5	171
4	119
6	79.5
7.5	51
10	1

Graphing the data on a linear scale gives a straight line. That means that drug M follows a zero order elimination process in which the same amount of drug M is eliminated per time unit.
Exemplary calculation of the decrease in concentration:

C(4h)-C(6h)=(119-79.5)µg/L=***39.5µg/L in 2 hours***

That means that the plasma concentration drops approximately 20µg/L per hour. Back-extrapolation to time zero gives us a C_0 of 200µg/L = 0.2mg/L.

$$V_d = \frac{Amount\ in\ the\ body}{Plasma\ concentration} = \frac{100mg}{0.2\,mg/L} = 500L$$

#4: Drug C has a plasma protein binding, ranging from 70-90%. In patients with chronic liver disease plasma protein binding is decreased by 20%. How will the volume of distribution change? Use a plasma volume of 3 L and the fraction bound in plasma 85% (for normal patients), a tissue volume of 38 L and the fraction unbound in tissue 30% to calculate the volume of distribution in patients with liver disease.

Answer:

$$V_d = V_p + V_T \frac{fu}{fu_T}$$

For normal patients:

$$V_d = 3L + 38L \frac{0.15}{0.3} = 22L$$

For patients with liver disease:
Plasma protein binding decreases by 20%, all the other parameters remain the same
→ new fraction bound: 0.85 * (1-0.20) = 0.85 * 0.8 = **<u>0.68</u>**
→ fraction unbound for liver patients: fu = 1-0.68= **<u>0.32</u>** (> normal patients')

$$V_d = 3L + 38L \frac{0.32}{0.3} = 43.5L$$