# PHA 5127 Dose Optimization I
# Case Study 2

1. Drug A and drug B are both lipophilic drugs and of low molecular weight. The plasma protein binding for drug A is 95% and for drug B is 5%. Both drug A and drug B have a tissue binding 75%. The same doses (200mg) of the two drugs are given to a healthy volunteer through i.v bolus at two different times (2 weeks of wash out period in between), assume $V_p$ =3L, $V_T$ =38L for both drugs.

1.1 Calculate the volume of distribution and initial free drug concentration of drug A and drug B.

1.2 Suppose the healthy volunteer got liver disease, which results in a two-fold decrease in plasma protein binding for both drug A and drug B (assume tissue binding remains the same), recalculate the volume of distribution and initial free drug concentration of drug A and drug B. What conclusions could you make?

2. TRUE (T) or FALSE (F)

T F Volume of distribution decreases with time because there will be less and less drug remaining in the body.

T F Lipophilic drugs will be able to distribute throughout the body, so their volume of distribution cannot be smaller than total body water volume (41L).

T F A water-soluble drug will pass across muscle membranes faster than across brain membranes (assume permeability-rate limitations).

T F Low molecular weight, lipophilic drugs are generally taken up fast by highly perfused organs.

T F A weak acid, whose unionized form shows a high partition coefficient, is likely to cross most membrane barriers.

T F Assume a drug is substrate of a specific transport protein. Transporters only eliminate drugs from the body.

T F Assume a drug is substrate of a specific transport protein. Transporters do not use energy.

T F If two patients differ in the $V_d$ (volume of distribution), the patient with the smaller $V_d$ will show a higher starting concentration $C_0$ after i.v bolus injection (the same dose for both patients).

T F Consider a patient with myocardial infarction. The increase in plasma alpha-1- glycoprotein will result in movement of free drug to plasma and an increase in $fu_T$ and a decrease in the fu in plasma.

T F Assuming that a protein drug does not bind to plasma and tissue component, the volume of distribution is likely to be 41 liters.