Case Study # 2 (Fall 2008)

Q1) A 80 kg male patient was given a single i.v. dose of 45 mg cocaine which is known to have a half-life of 0.693 hr and a volume distribution of 2 L/kg.

(1) What is the clearance of cocaine? Is it solely metabolized by liver? Why?
(2) Predict AUC$_{0-\infty}$.

Q2) A patient is to be started on two medications (A and B) administered by IV bolus injections. Blood samples were taken at 1 and 4 hours following the first injections of drug A or B alone in order to determine whether concentrations were in an appropriate range for each drug. See table below for these levels and additional information.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg)</th>
<th>Cp at 1h (mg/L)</th>
<th>Cp at 4h (mg/L)</th>
<th>Eh</th>
<th>fu</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>400</td>
<td>1.22</td>
<td>0.76</td>
<td>0.8</td>
<td>0.1</td>
</tr>
<tr>
<td>B</td>
<td>1200</td>
<td>0.92</td>
<td>0.51</td>
<td>0.1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Assume liver blood flow of 90 L/h, where Eh is the extraction ratio and fu is the fraction unbound. Both drugs are metabolized by CYP 3A4. Is it possible to calculate the AUC$_{0-\infty}$, for drug B, if yes how much is it? if no, why not?

**Say True or False**

T  F  For a drug with high tissue binding, the volume of distribution will be very low.

T  F  Volume of distribution is not important to determine what loading dose is required.

T  F  Drug A has 98% protein binding and has a narrow therapeutic index. Any change in the protein binding is not of significant consequence since already 98% drug is bound and very less is available for receptors

T  F  If volume of distribution changes, this will affect the drug clearance as well since this means less volume of drug to be cleared.

T  F  If Drug A and Drug B are being administered at the same time then dose adjustment may be needed if there are drug interactions between A and B

T  F  Clearance and Volume of distribution are independent parameters.
T F If the drug clearance changes then the volume of distribution changes since 
\[ ke = \frac{Cl}{Vd} \]

T F If Drug A is cleared only by hepatic metabolism only, then the clearance of drug A cannot be greater than liver blood flow.

T F If Drug A and Drug B are being administered at the same time then dose adjustment may be needed if there are drug interactions between A and B

T F For a low extraction drug, the lower the protein binding the higher will be the clearance