On my honor, I have neither given nor received unauthorized aid in doing this assignment.

Please transfer the answers onto the bubble sheet. The question number refers to the number on the bubble sheet. Please fill in all the information necessary to identify yourself. The proctors will also collect your exams.

Good LUCK.

TOTAL _____120 /pts
Question set I (10 pts): Select whether the following statements are True (A) or False (B) concerning a drug that is absorbed by a first order process and eliminated by a first order process.

1:  T  F  The faster the absorption, the shorter will be t_{max}.

2:  T  F  The faster the absorption, the lower will be C_{max}.

3:  T  F  The smaller k_{a}, the smaller the fluctuation between peak and trough concentration when given twice daily.

4:  T  F  Assume that all the drug will dissolve in time to enter the portal vein. For a high extraction drug, an increase in k_{a} tends to decrease the oral bioavailability.

5:  T  F  Assume that all the drug will dissolve in time to enter the portal vein. For a low extraction drug, the oral bioavailability will increase with increasing k_{a}.
**Question set II (6 pts):** Select from the following statements whether the statements are True (A) or False (B).

6: T  F  Assume steady state has been reached after having started a constant rate infusion. At steady state, $k_0$ will equal clearance.

7: T  F  The time to reach steady state after an constant rate infusion is affected by the clearance and volume of distribution of the drug.

8: T  F  Drugs showing a high degree of accumulation after multiple iv bolus injections will need a long time to reach steady state when the drug is given as a constant rate infusion (no loading dose is given)

**Question set III (4 pts):**

Select from the following statements whether the statements are True (A) or False (B).

Assume a multiple dosing situation.

9: T  F  For a lipophilic drug whose clearance is constant under the given conditions, the following statement can be made: The stronger the tissue binding the more pronounced the degree of accumulation.

10: T  F  For a lipophilic drug whose clearance is constant under the given conditions, the following statement can be made: The stronger the tissue binding the more pronounced the fluctuation between peak and trough concentration.
Question set IV (20 pts):

The following applies to questions 11-14: A 60-kg patient is to be started on a continuous intravenous infusion. From a previous regimen of the same drug, you estimate the patient’s $k_e$ is 0.07 h$^{-1}$ and the $V_d$ is 40 L. Assume that none of this drug has been administered this month.

Question 11: What rate of infusion ($k_0$ for the following constant rate infusion) should result in a $C_{pss}$ of 20 mg/L. Round appropriately. (5 pts)

A: 56 mg/0.5 hours
B: 28 mg/0.5 hours
C: 28 mg/hr
D: 28 mg
E: none of the above
A 60-kg patient is to be started on a **continuous intravenous infusion**. From a previous regimen of the same drug, you estimate the patient’s $k_e$ is 0.07 h$^{-1}$ and the $V_d$ is 40 L. Assume that none of this drug has been administered this month.

**Question 12:** If the $C_{pss}$ is to be 20 mg/L, what should be the loading dose (mg) given as intravenous bolus injection? **Round appropriately.** (5 pts)

A: 400 mg  
B: 800 mg  
C: 1200 mg  
D: 1220 mg  
E: none of the above
A 60-kg patient is to be started on a continuous intravenous infusion. From a previous regimen of the same drug, you estimate the patient’s $k_e$ is 0.07 h$^{-1}$ and the $V_d$ is 40 L. Assume that none of this drug has been administered this month.

**Question 13:** What will be the plasma concentration 1 hour after start of the continuous infusion (remember a loading dose was given). **Round appropriately.** (5 pts)

A: 3.9 mg/L
B: 4.0 mg/L
C: 3.6 mg/L
D: 20 mg/L
E: None of the above.
A 60-kg patient is to be started on a continuous intravenous infusion. From a previous regimen of the same drug, you estimate the patient’s $k_e$ is 0.07 h$^{-1}$ and the $V_d$ is 40 L. Assume that none of this drug has been administered this month.

**Question 14:** The infusion is continued for 3 days and the steady state concentration has been maintained at 20 mg/L. The physician wants to change the drug delivery to multiple short term infusions with a $C_{\text{max}}$ of 20 mg/L and a trough of 10 mg/L. (Hint: The first short-term infusions should be administered when the remaining plasma concentration reaches 10 mg/L). How many hours after the continuous infusion has been stopped should the first short-term infusion be given. Round appropriately. (5 points)

A: 1 h  
B: 2 h  
C: 8 h  
D: 10 h  
E: None of the above.
Question set V (5 pts)

**Question 15:** A 60 kg patient is started on 80 mg of gentamicin, every 6 hr given as a one-hour infusion. Assume that steady state has been reached for this multiple dosing situation. If this patient is assumed to have an “average” volume of distribution (value of the population mean) of 0.25 L/kg and a normal half-life of 3 hr, what would be the plasma concentration 1 hour before the start of the next infusion? *Round appropriately.* (5 points)

A: 3.2 mg/L  
B: 2.5 mg/L  
C: 0.8 mg/L  
D: 1.2 mg/L  
E: None of the above
Question set VI (5 points)

**Question 16:** A 60 kg patient is started on 80 mg of drug X, every 6 hr given as a one-hour infusion. The half-life of this drug is 4 hours. If the infusion is given the first time, how much lower is the first peak when compared to the $C_{\text{max},\text{ss}}$.

A: 30-40% of $C_{\text{max},\text{ss}}$
B: 41-50% of $C_{\text{max},\text{ss}}$
C: 61-75% of $C_{\text{max},\text{ss}}$
D: None of the above
E: Don’t have enough information to provide this information.
Consider the following equation:

\[ Cp_{\text{min}} = \frac{k_o}{CL} \bullet \frac{1-e^{-k_e \bullet T}}{1-e^{-k_e \bullet \tau}} \bullet e^{-k_e \bullet t'} \]

Select the true statements concerning the following part of the equation: (10 points)

17: T F  This part provides information on how much the first \( C_{\text{max}} \) (after the first short term infusion) is away from the steady level of a continuous infusion using the same \( k_o \).

18: T F  This part allows the calculation of the trough concentration after the stop of the infusion, as it converts the peak levels into the trough value.

19: T F  This part makes sure that the calculated plasma concentrations will increase with increasing infusion time.

20: T F  Is a number between 0 and 1.

21: T F  Will give, when multiplied with the \( k_o/CL \) term, the peak concentration after the first dose.
Consider the following relationship.

\[ \tau = \frac{Vd \times \ln F}{Cl} \]

22: T F F stands for oral bioavailability

23: T F This term indicates that the higher the clearance and/or the smaller VD of a drug, the shorter will be the dosing interval necessary to maintain a given \( \frac{C_{\text{max}}}{C_{\text{min}}} \) ratio

24: T F This relationship can be used to calculate the dosing interval for multiple short-term infusions if one adds the infusion time to the above expression.

25: T F This term should only be used for a drug after oral administration
Question Set IX (15 points)

Question 26-30: Two patients received a **low extraction drug, which is only cleared by the liver**, as an iv bolus injection. Pharmacokinetic and physiological characteristics, such as dose, fraction of the drug unbound in plasma (fu), volume of plasma (Vp) and volume of the tissue water (VTW) in both patients are shown below. Assume that both patients show the same tissue protein binding.

**TABLE 1: INPUT PARAMETERS**

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>D [mg]</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Clint</td>
<td>0.8</td>
<td>1.6</td>
</tr>
<tr>
<td>fu</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Vp [L]</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>VTW [L]</td>
<td>38</td>
<td>38</td>
</tr>
</tbody>
</table>

Indicate which of the following parameters (questions 27-31) in patient 2 will be clearly larger (A), be ABOUT the same (B), or will be clearly smaller (C) than those in **Patient 1**.

**Table 2: OUTPUT PARAMETERS**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>26. (3 points)</td>
<td>Larger (A), same (B), Smaller (C) than in Patient 1</td>
<td>Larger (A), same (B), Smaller (C) than in Patient 1</td>
<td>Larger (A), same (B), Smaller (C) than in Patient 1</td>
<td>Larger (A), same (B), Smaller (C) than in Patient 1</td>
<td>Larger (A), same (B), Smaller (C) than in Patient 1</td>
</tr>
</tbody>
</table>
Question Set X (6 points)

Question 31:

The following concentration time profiles were observed after multiple iv bolus injections of a drug. The two curves differ in one of the input parameters (Dose, tau, CL or Vd).

<table>
<thead>
<tr>
<th>INPUT</th>
<th>OUTPUT</th>
</tr>
</thead>
<tbody>
<tr>
<td>D [mg] 8</td>
<td>Peak(ss) 89</td>
</tr>
<tr>
<td>tau [h] 4</td>
<td>Trough(ss) 49</td>
</tr>
<tr>
<td>n 12</td>
<td>r(ss) 2.2</td>
</tr>
<tr>
<td>CL 30</td>
<td>Cpave(ss) 67</td>
</tr>
<tr>
<td>Vd 200</td>
<td>ke [1/h] 0.2</td>
</tr>
</tbody>
</table>

Identify the one input parameter that differs (question 32)

A: Dose
B: Clearance
C: Volume of distribution
D: tau
E: none of the above
Question Set XI (10 pts)

Question 32: Which of the following factors significantly affect(s) the renal clearance of an aminoglycoside:

1. plasma protein binding.
2. activity of cationic transporters in the tubuli.
3. urine flow.
4. pH of urine.
5. GFR.

A: 1, 2, 3, 5
B: 1, 2
C: 1, 5
D: 1, 3, 4, 5
E: none of the above combinations
Questions 33-36

Assume first-order processes. Mark whether the following statements are true (A) or false (B).

33: T F A drug is eliminated through liver metabolism and renal clearance. The overall elimination rate constant for this drug is 0.5 h\(^{-1}\). The rate constant for metabolism (k\(_{\text{met}}\)) is 0.1. This indicates that 20\% of the dose will be metabolized.

34: T F Assume that a drug is metabolized. The K\(_e^M\) of the metabolite is 20 h\(^{-1}\) while the k\(_e\) of the parent drug is 0.231 h\(^{-1}\). If the plasma concentrations 10 hours after injection of the parent drug are 1 µg/ml for the parent drug and 0.5 µg/ml for the metabolite, the plasma concentrations 13 hours after injection of the parent drug must be 0.5 µg/ml for the parent drug and 0.25µg/ml for the metabolite. (Assume first-order kinetics for all elimination processes.)

35: T F For a two-compartment model drug, the volume of distribution just after administration of the drug is larger than that observed some time later.

36: T F Clearance and volume of distribution are always independent parameters.
Question Set XIV

Questions 37-39 (9 points)

Select the most appropriate differential equation for the following situations. A given differential equation might have to be used more than once. Assume “X” is the amount of drug in the body (drug that has been absorbed and has not yet been eliminated) and “A” is the amount left at the absorption site.

A: \( \frac{dx}{dt} = k_a - k_e \)

B: \( \frac{dx}{dt} = -k_a - k_e \times X \)

C: \( \frac{dx}{dt} = k_a \times A - k_e \times X \)

D: \( \frac{dx}{dt} = -k_e \)

E: none of the above

37: A drug that is absorbed and eliminated through active transport. Both transporter systems are saturated (Select from A-E)

38: An immediate release tablet of a drug able to cross membranes easily and eliminated through renal filtration. (Select from A-E)

39: A high extraction drug given as an iv bolus injection showing linear pharmacokinetics (Select from A-E)
Question Set XV

**Question 41-43 (2 points) (Bonus Question)**

40:  T  F  I think the case studies are a waste of time

41:  T  F  I do not benefit from the home works.

42:  T  F  I missed a textbook for this class.