

Name: \_\_\_\_\_

SS#: \_\_\_\_\_

## PHA 5127

### First Exam Fall 2000

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

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Name \_\_\_\_\_

#### Question/Points

1. \_\_\_\_\_/ 7.5pts

2. \_\_\_\_\_/7.5 pts

3. \_\_\_\_\_/5 pts

4. \_\_\_\_\_/10 pts

5. \_\_\_\_\_/10 pts

6. \_\_\_\_\_/10 pts

7. \_\_\_\_\_/10 pts

8. \_\_\_\_\_/10 pts

9. \_\_\_\_\_/10 pts

10. \_\_\_\_\_/20 pts

TOTAL \_\_\_\_\_/100 pts

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1.) Forced diuresis is likely to significantly enhance the clearance of...  
(7.5 points)

- a) a drug which is both polar and slowly removed from the body.
- b) a drug mainly cleared via metabolism.
- c) a drug for which most of the filtered and secreted drug is reabsorbed
- d) a drug for which the ratio of its renal clearance to creatinine clearance is 1.0

List correct answer(s):

2.) Pharmacokinetic studies have shown that a new centrally active drug entity (works in the brain) designed for headaches has a very slow onset of action when compared to other headache drugs. Indicate what possible statements might agree with this observation.(7.5 points)

- a) The drug is hydrophilic
- b) The plasma protein binding is too low.
- c) Distribution is controlled by perfusion rate limitations
- d) Distribution into the brain shows permeability-rate limitations
- e) The drug is a strong base.

List correct statement(s):

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- 3.) Two patients receive the **high extraction drug Anonymous** which is mainly metabolized by the P450 system. One patient also takes a drug which is an enzyme inducer of the P450 system. As a result, the intrinsic clearances between the patients differ by a factor of 10. What of the following statements is/are correct (5 points).
- a) Differences in the total clearance observed for the two patients will be clinically relevant
  - b) The oral bioavailability of this drug in the two patients will be different and this difference will be of clinical relevance.
  - c) Assume that the plasma protein binding in both patients increases, the  $t_{1/2}$  of the of the drug will be reduced in both patients.
  - d) Assuming that the plasma protein binding in both patients increases during treatment, the  $t_{1/2}$  of the drug will be increased in both patients.

List the correct answer(s)

- 4.) For the physiological changes listed below, select the induced change on the pharmacokinetic parameters for a lipophilic, protein bound, low extraction drug cleared by liver and kidney. (10 points)

Physiological change	Effect on kinetics
1. Increase in plasma protein binding _____	a. $Cl_{tot}$ ↑
2. Increase in liver blood flow _____	b. $V_d$ ↓
3. Decrease in metabolic liver enzymes _____	c. $V_d$ ↑
4. Decrease in creatinine clearance _____	d. $GFR$ ↓
5. Increase in the number of fat cells _____	e. $Cl_{int}$ ↓
	f. $Cl_{hep}$ ↑
	g. none of the above effect

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- 5.) An aminoglycoside has a normal elimination half-life of 100 minutes in young adults. In patients 70-90 years old, the elimination half-life of this aminoglycoside is 300 minutes. The normal dose of the aminoglycoside is 15 mg/kg per day divided into two doses. Assume that the volume of distribution per body weight is not changed by the patient's age. What should be the daily dose for a 75-year-old patient when the dosing frequency is unchanged (10 points).

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- 6.) A drug was given as an i.v. bolus twice a day. Steady state was reached.  
6 hours after the last dose a serum concentration of 10.5  $\mu\text{g/ml}$  was measured.  
12 hours after the last dose a concentration of 6.4  $\mu\text{g/ml}$  was observed (10 points).

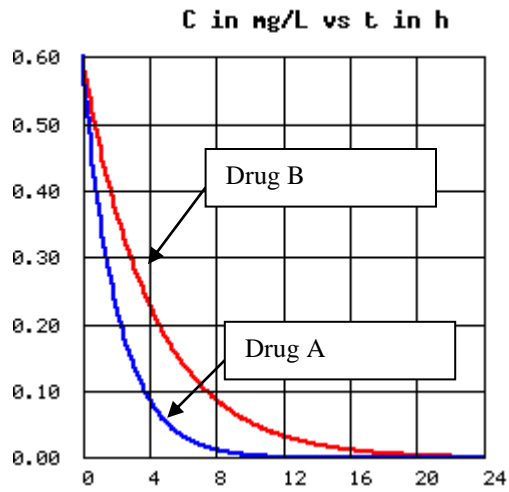
Calculate  $C_{\text{max}}$ ?

What will be the  $C_{\text{min}}$ ?

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- 7.) The concentration time profiles of a certain drug differ in two patients, as shown in the graph. The dose was the same. What is the reason for this difference? (10 points)



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8.) Assume a drug is predominantly cleared via the kidney. What factors (**drug properties**) determine its renal clearance (10 points)

9.) How is the volume of distribution of digoxin likely to change if a patient who is on digoxin also gets started on quinidine. Assume that plasma volume, tissue volume and unbound fraction of drug in plasma are unchanged. Brief explanation! (10 points)

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- 10.) Peter Pan is a non-smoker (60 kg) asthmatic. He is to be started on an oral regimen of aminophylline (85% of which is theophylline). The population pharmacokinetic parameters for theophylline are:  $F$  (bioavailability)=1,  $V=0.5$  L/kg,  $Cl=40$ ml/hr/kg).

Assume that the absorption of this tablet is so fast, so that we can use i.v. model for describing plasma levels. Design an oral dosage form of aminophylline (100 mg or 200 mg tablets are available) to maintain a plasma concentration between 10 and 20 mg/L at steady state. (20 points)