

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

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**PHA 5127**

**Second Exam**

**Fall 2009**

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

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Name

Put all answers on the bubble sheet

TOTAL \_\_\_\_\_/150pts

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**Question Set I (True or False)**

(15 points)

**True (A) or False (B). On the bubble sheet mark A for true or B for false**

Mark whether the following statements are true (A) or false (B). Mark **false** if there is not sufficient information given to provide answer.

The lipophilic drug A is not an acid or a base, is cleared only by renal elimination, crosses membranes quite easily, and dissolves in the GI tract.

- 1:    T    F    The oral bioavailability of this drug is likely to be large. **TRUE**
  
- 2:    T    F    Plasma protein binding will affect the oral bioavailability of this drug. **FALSE**
  
- 3:    T    F    A one compartment body model is likely to be able to describe the concentration time profiles after iv bolus injection. **TRUE**
  
- 4:    T    F    This drug will have a smaller clearance than creatinine. **TRUE**
  
- 5:    T    F    It is unlikely that the renal clearance of this drug is affected by drug-drug interactions **TRUE**

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### Question Set II

(18 points)

**True (A) or False (B). On the bubble sheet mark A for true or B for false**

Imagine a lipophilic unionized drug X that is eliminated through renal and hepatic mechanisms and easily crosses membranes. When given by an iv bolus injection to patient A, a peak concentration of 0.18  $\mu\text{g/mL}$  is observed ( $C_{p_0}$ ). The  $V_d$  in patient A is 108 L. When given orally, the oral bioavailability in patient A is 99.0 %. Plasma Protein Binding is 50% ( $f_u=0.5$ ) in patient A. The drug shows in a second patient (patient B) a plasma protein binding of 25%. This is the only difference in physiological conditions between patient A and B. Both patients have a liver blood flow of 80 L/h (1333 ml/min) and an urine flow of 2 ml/min.

Peak [ $\mu\text{g/ml}$ ]	0.18	?
V [L]	108	?
F (%)	99.0	?
$f_u$	0.5	0.75

Mark whether the following statements are true (A) or false (B). Mark FALSE if not sufficient information was provided for making a proper decision.

- 6: T F The oral bioavailability in Patient B is similar to that of patient A **TRUE**
- 7: T F The renal clearance of this drug in patient A is larger than that of patient B **FALSE**
- 8: T F For both patients, the hepatic clearance of this drug will be smaller than the renal clearance. **FALSE**
- 9: T F Plasma protein binding will affect the hepatic clearance of this drug **TRUE**
- 10: T F The volume of distribution in Patient A is larger than that in Patient B **FALSE**
- 11: T F The half-life of this drug will be similar in patient A and B **TRUE**

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### Question Set III (Matching)

(20 points)

For the physiological changes listed below, select the induced changes on the pharmacokinetic parameters for a **lipophilic, protein bound drug that is only eliminated through hepatic metabolism**. The oral bioavailability of this drug in an “average” patient is generally around 3%. Some answers may be used more than once.

*Select the effect on pharmacokinetic parameters*

(A)  $Cl_{hep} \uparrow$  (B)  $Cl_{hep} \downarrow$  (C)  $V_D \downarrow$  (D) oral bioavailability  $F \downarrow$  (E) *nothing happens or effect is not listed*

Physiological change

- |     |   |              |
|-----|---|--------------|
| 12: | Decrease in plasma protein binding      | <u>  D  </u> |
| 13: | Increase in tissue binding              | <u>  E  </u> |
| 14: | Increase in liver blood flow            | <u>  A  </u> |
| 15: | Enzyme induction of the relevant enzyme | <u>  D  </u> |

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**Question set IV (20point)**

A drug (not an acid, not a base) is cleared through renal and hepatic clearance. Plasma protein binding suddenly increases.

Indicate for this situation whether the following parameters increase (A), decrease (B), stay unchanged (C) or not sufficient information is provided (D)

16: oral bioavailability **D**

17: hepatic clearance **D**

18: renal clearance **B**

19:  $k_e$  **D**

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### Question Set V

(20 points)

20. A lipophilic drug (not an acid, not a base, easily crosses membranes) is eliminated only by the kidney. **Plasma protein binding is 80%**. Glomerular filtration rate is normal (**130 ml/min**). Urine flow is 2ml/min. Urine pH is similar to that of blood (about 7). The volume of distribution is **40L**. Urine flow is 2ml/min. Urine pH is similar to that of blood (about 7).

What value describes best the clearance? (10 points)

- A: 0.4 mL/min**
- B: 13 mL/min
- C: 130 mL/min
- D: 6.6 mL/min
- E: none of the above

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21: A new aminoglycoside is given to a patient showing a creatinine clearance of 65 ml /min (10 points). The plasma protein binding for this new aminoglycoside is 80 %. Urine flow is 2 ml.

What value describes best the clearance? (10 points)

A: 0.4 ml/min

**B: 13 ml/min**

C: 65 ml/min

D: 6.5 ml/min

E: 35.8 ml/min

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### Question Set VI

(10 points)

Robert is very sick and needs treatment with an aminoglycoside. In order to start him on the aminoglycoside you have to estimate Robert's creatinine clearance. Robert is 5 ft 10 inches tall, 34 years old, male, and weights 82 kg. His serum creatinine is 1.5 mg/dl.

What creatinine clearance do you come up with? **80.48 ml/min**

**Assume that the result will be between 10 and 99 ml/min**

22: Mark A, B, C, or D, if the number in the tens column is 1 (A), 2(B), 3(C), 4(D), 5(E).  
*Leave blank if this is not the case This would be E for 50 ml/min*

23: Mark A, B, C, D, E if the number in the tens column is 6 (A), 7(B), **8(C)**, 9(D), 0(E) *Leave blank if this is not the case. You would leave this blank for 50 ml/min*

24: Mark A, B, C, or D, if the number in the ones column is 1 (A), 2(B), 3(C), 4(D), 5(E).  
*Leave blank if this is not the case . You would leave this blank for 50 ml/min*

25: Mark A, B, C, or D, if the number in the ones column is 6 (A), 7(B), 8(C), 9(D), **0 (E)**  
*Leave blank if this is not the case. This would be E for 50 ml/min*

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### Question Set VII

(5 points)

26: Two patients take a drug as an iv bolus (see graph). The drug is predominantly **cleared through the kidneys**. Peak concentrations and AUC are listed below. The patients differ in one of the following parameters. Select the correct parameter that differs.

A:  $f_u$

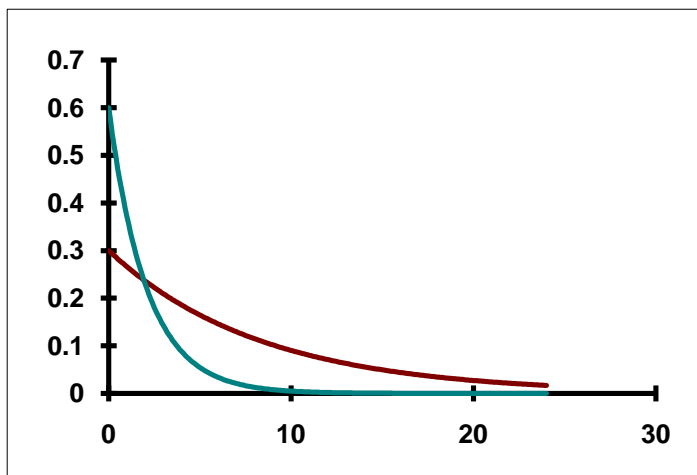
B:  **$f_u T$**

C: GFR

D: Dose

Peak (mg/L)      0.6      0.3

AUC (mg/L\*h)    2.5      2.5



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**Question Set VIII (True or False)**

(15 points)

**True (A) or False (B). On the bubble sheet mark A for true or B for false**

Mark whether the following statements are true (A) or False (B) for a drug given as iv bolus

- 27:    T    F    The renal clearance of a drug is always smaller than the drugs hepatic clearance. **FALSE**
- 28:    T    F    Clearance =  $k_e / C_p$ . **FALSE**
- 29:    T    F    Clearance =  $k_e * \text{dose} / C_{p0}$ . **TRUE**
- 30:    T    F    For an acidic drug with a  $pK_a$  of 7.0, adjustment of the urine pH within physiological ranges will significantly change the renal clearance. **TRUE/FALSE**
- 31:    T    F    For an acidic drug with a  $pK_a$  of 13.0, adjustment of the urine pH within physiological ranges will significantly change the renal clearance. **FALSE**

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### Question Set IX

(12 points)

**True (A) or False (B). On the bubble sheet mark A for true or B for false**

Patient A receives 100 mg of drug A. Patient B 200 mg of drug B. Evaluate the following statements. (Assume IV-bolus administration and linear pharmacokinetics).

- 32: T F The  $AUC_{\infty}$  of patient A must be twice as high as the  $AUC_{\infty}$  of patient B **FALSE**
- 33: T F Both patients must show the same total concentrations at time point zero if the volume of distribution of drug B is twice as high the volume of distribution of drug A **TRUE**
- 34: T F If patient B received 400 mg of drug B instead of 200 mg, his  $AUC_{\infty}$  will be twice as high. **TRUE**

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**Question Set X (5 points)**

35. Which of the following four statements are correct?

- 1) The shorter the half-life of a drug the smaller the AUC
- 2) The oral bioavailability  $F$  of a high extraction drug is not affected by the liver blood flow.
- 3) Genetic variability in metabolizing enzymes does always alter hepatic clearance of a low extraction drug.
- 4) For aminoglycosides,  $k_e$  can be calculated from  $GFR \cdot f_u / V_d$

A: 2, 3, 4

B: 1, 3 & 4

C: 2, 3

**D: 3, 4**

E: None of the above statements are correct

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**Question Set XI (10 points)**

36. An investigational new drug is eliminated entirely by liver (hepatic) metabolism, with a clearance of 1.35L/min in subjects with an average liver blood flow of 1.50L/min. What would be its expected clearance in a congestive heart failure patient with a liver blood flow of 1.10L/min but no change in hepatic extraction ratio?
- A: 1.10 L/min
- B: 1.50 L/min
- C: 1.18 L/min
- D: 0.99 L/min**
- E: Cannot be determined because the  $V_d$  is not given.