

Name: _____

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PHA 5127

First Exam

Fall 2005

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

Name

Put all answers on the bubble sheet

TOTAL _____/160 pts

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Question Set I (True or False)
(25 points)

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

For a low extraction drug

- 1: T F Hepatic clearance will be larger than that of a high extraction drug
- 2: T F Hepatic clearance will depend on liver blood flow
- 3: T F Hepatic clearance will depend on tissue protein binding
- 4: T F Oral bioavailability will be below 80%
- 5: T F k_{el} will not be affected by drugs that induce synthesis of the enzyme responsible for the metabolism of the low extraction drug

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Question Set II

(15 points)

Imagine a low extraction drug that is only eliminated via hepatic metabolism. Two patients have been injected with the same dose of this drug. They show the following pharmacokinetic properties

Peak [ug/ml]	1.1	0.4
Ke [1/h]	0.6	0.4
V [L]	38	108
CL [L/h]	22.5	45.0
t _{1/2} [h]	1.17	1.66

6: A list of physiological parameter is shown below. Identify **the one** physiological parameter that would explain **all differences** in above pharmacokinetic parameters

- | | |
|-----------|----------------------|
| | <i>Parameter-</i> |
| A. | GFR |
| B. | f_u |
| C. | f _{ut} |
| D. | Q _{hep} |
| E | Cl _{int} |

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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, unionizable (no acid or basic group in the molecule), protein bound **high extraction** drug **that is also eliminated through the kidneys** (some answers may be used more than once).

Select the effect on kinetics

(A) $Cl_{REN} \uparrow$ (B) $Cl_{HEP} \downarrow$ (C) $V_D \downarrow$ (D) $V_D \uparrow$ (E) oral bioavailability $F \uparrow$

Physiological change

7: Decrease (50%) in metabolic enzymes **E**

8: Increase in tissue binding **D**

9: Decrease in liver blood flow **B**

10: Increase in urine flow **A**

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Question Set IV (Matching)

(20 points)

(Assume GFR is 130 mL min^{-1} , urine flow is 1.5 mL min^{-1}) For the following situations, indicate whether the drug is:

Select from the following choices:

(A) *filtered* (B) *reabsorbed* (C) *actively secreted* (D) *reabsorbed through transporters*

11: A drug with $f_u = 0.02$ and a $\text{Cl}_{\text{REN}} = 20 \text{ mL min}^{-1}$ is **C**

12: A drug with $f_u = 0.40$ and a $\text{Cl}_{\text{REN}} = 52 \text{ mL min}^{-1}$ is **A**

13: A drug with $f_u = 0.60$ and a $\text{Cl}_{\text{REN}} = 0.9 \text{ mL min}^{-1}$ is **B**

14: A drug with $f_u = 1.0$ and a $\text{Cl}_{\text{REN}} = 0.3 \text{ mL min}^{-1}$ is **D**

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Question Set V

(20 points)

A lipophilic drug (not an acid or base, that easily passes membranes) is eliminated only by the kidney. **Plasma protein binding is 50%**. Glomerular filtration rate is normal (**130 ml/min**). Urine flow is 2ml/min. No **active** renal secretion and **active** reabsorption after renal filtration is observed. The volume of distribution is **40 L**.

15: What is the clearance? (10 points)

- A: **1.0 mL/min**
- B: 2.0 mL/min
- C: 4.0 mL/min
- D: 8.0 mL/min

16: What is the k_e of the drug that has a volume of distribution of 100L and a clearance of 600 ml/min? (10 points)

- A: 6 min⁻¹
- B: 0.17 h⁻¹
- C: 27 h⁻¹
- D: 0.36 min⁻¹
- E: **0.36 h⁻¹**

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Question Set VI

(10 points)

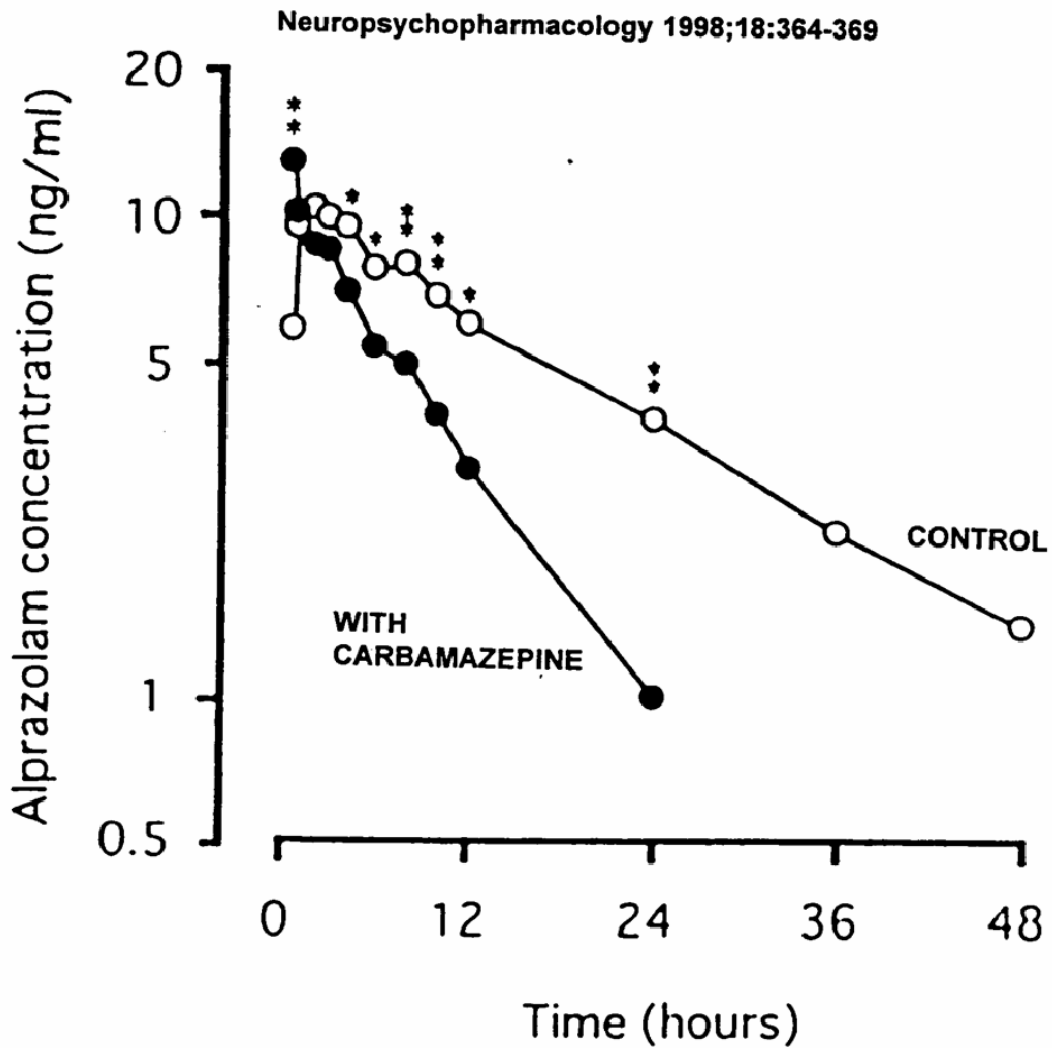
17: Robert is very sick and needs treatment with an aminoglycoside. In order to start him on the aminoglycoside an iv bolus loading dose shall be given. Your responsibility is to give him the first dose. In order to do so, you have to estimate Robert's creatinine clearance. Robert is 5 ft 10 inches tall, 34 years old, male, and weights 230 pounds. His serum creatinine is 1.5 mg/dl. What creatinine clearance do you come up with?

- A 72 ml/min
- B 84 ml/min**
- C 70 ml/min
- D 103 ml/min
- E 61 ml/min

Question Set VII

(5)

The same dose of Alprazolam was given either alone or with carbamazepine. Explain what is going on by selecting the correct answer from the following list. (5 points)



- 1: The clearance of alprazolam is increased in the presence of carbamazepine.
- 2: Alprazolam is likely to be a low extraction drug.
- 3: Carbamazepine is an enzyme inhibitor.
- 4: Carbamazepine decreases liver blood flow.

18. The correct answer is: 1, 2

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A: 1
B: 1, 2
C: 3, 4
D: 2, 3
E: 1, 2, 3, 4

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Question Set VIII (True or False)

(30 points)

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

Assume the pH of urine to be 7, a glomerula filtration rate of 130 ml/min, a urine flow of 1.5 ml/min. For a basic drug (unionized form is very lipophilic, pka of the drug 7, plasma protein binding 50%, lacks affinity to transporters) that is only eliminated by the kidney, mark whether the following statements are true (A) or False (B)

- 19: T F The renal clearance will depend on the tissue binding of the drug.
- 20: T F The renal clearance will be about 35 ml/min (about means +/-10%)
- 21: T F The renal clearance of the drug will be about 65 ml/min
- 22: T F Drinking a lot of water (urine flow is doubled) will increase the renal clearance by a factor of 2
- 23: T F Changing the pH of the urine to 6 will increase the clearance.
- 24: T F Drug/drug interactions are likely for the elimination of this drug

Question Set IX (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)

- 25: T F Lipophilic unionized drugs are likely to enter tissues relatively fast.
- 26: T F The uptake of a hydrophilic drug into tissue can be increased significantly by increasing the blood flow through the tissue.
- 27: T F The volume of distribution will be reduced with increased clearance of a drug.