

NAME: _____

UFID: _____

PHA 5127

Second Exam

Fall 2006

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

Mark whether the following statements as true or false for **drug A**, which is cleared only by hepatic metabolism and has a CL_{tot} of 80 L/h

- 1: T **F** This drug is a low extraction drug
- 2: **T** F The clearance of another drug eliminated only by the kidney (only filtered not re-absorbed) will be smaller than that of Drug A
- 3: **T** F The oral bioavailability of this drug will be significantly smaller than 80%
- 4: **T** F The oral bioavailability will depend on liver blood flow
- 5: T **F** Drug C, known to induce enzymes also responsible for metabolism of Drug A will significantly affect the clearance of Drug A

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Question Set II

(15 points)

Imagine a high 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

C_{\max} [$\mu\text{g/ml}$]	0.18	0.18
K_e [1/h]	0.55	0.73
V_d [L]	108	108
CL [L/h]	56	80
F (%)	6	1

- 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 drug **that is eliminated only 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) $V_D \uparrow$ (D) oral bioavailability $F \uparrow$ (E) factor not listed in A-D

Physiological change

7: Decrease in plasma protein binding **A or C**

8: Increase in tissue binding **C**

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

10: Increase in urine flow **A**

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 $Cl_{REN} = 20 \text{ mL min}^{-1}$ is **C**

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

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

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

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Question Set V

(10 points)

A hydrophilic drug (predominantly ionized at $\text{pH}=7.4$) is eliminated only by the kidney. **Plasma protein binding is 90%**. Glomerular filtration rate is normal (**130 ml/min**). Urine flow is 2ml/min. No **active** renal secretion or **active** reabsorption after renal filtration is observed. The volume of distribution is **40 L**.

15: What is the clearance? (10 points)

- A. 0.15 mL/min
- B. 13 mL/min**
- C. 1 mL/min
- D. 130 mL/min

16: Assume a one compartment body model? What is the renal clearance of a typical aminoglycoside in a patient showing a creatinine clearance of 65 ml/min (10 points). The plasma protein binding for this aminoglycoside is 55 %.

- A. 58.5 ml/min
- B. 130 ml/min
- C. 65 ml/min
- D. 29.3 ml/min**
- E. 35.8 ml/min

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Question Set VI

(20 points)

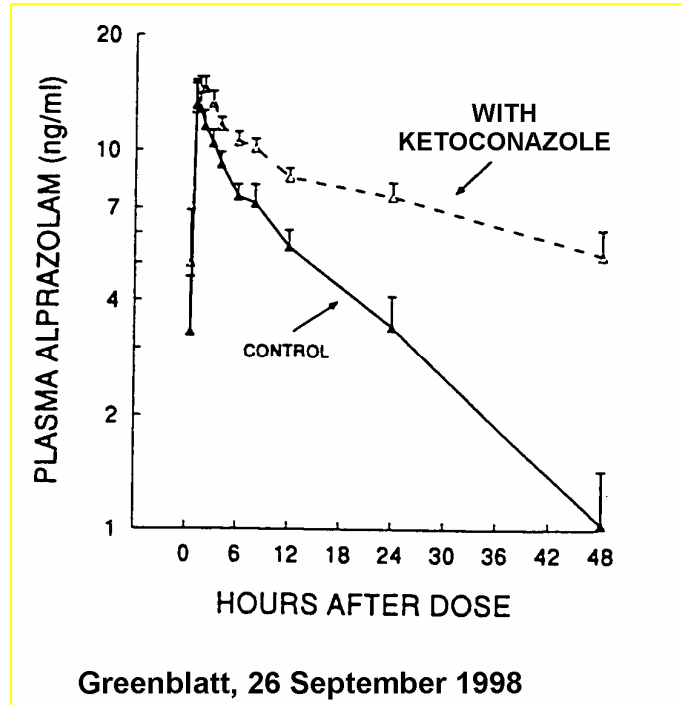
- 17: Robert is very sick and needs treatment with an aminoglycoside. In order to start him on the aminoglycoside an iv bolus loading dose shall be given. Your responsibility is to give him the first dose. In order to do so, you have to estimate Robert's creatinine clearance. Robert is 5 ft 10 inches tall, 34 years old, male, and weights 280 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. 93 ml/min**
 - D. 103 ml/min
 - E. none of the above

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Question Set VII

The same dose of Alprazolam was given either alone or with ketoconazole. 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 Ketoconazole.
- 2: Alprazolam is likely to be a low extraction drug.
- 3: Ketoconazole decreases the volume of distribution of Alprazolam, thereby increasing the half-life of the drug
- 4: Ketoconazole is likely to increase liver blood flow.

18. The correct answer is: _____

- A. 1
- B. 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

Mark whether the following statements are true (A) or False (B)

- 19: T **F** The renal clearance of a drug depends the tissue binding of the drug.
- 20: **T** F The half-life of a drug increases with increasing tissue binding.
- 21: T **F** To determine the clearance of a drug, one needs to know whether the drug is a one or two compartment drug.
- 22: T **F** Drinking a lot of water (urine flow is doubled) will increase the renal clearance of aminoglycosides
- 23: T **F** For an acidic drug with a pka of 2.0, adjustment of the urine pH within physiological ranges will significantly change the renal clearance.
- 24: T **F** For a drug with linear pharmacokinetics, hepatic clearance depends on the drug plasma concentration, as the rate of metabolism increases with increasing drug concentrations in the blood.

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). Assume linear pharmacokinetics for all questions.

- 25: T **F** The larger the volume of distribution, the smaller the AUC of a given drug.
- 26: **T** F Doubling the dose will double the AUC of a drug
- 27: **T** F An increase in f_u will decrease AUC of a high-extraction drug given orally.