

Name: _____

UFID #: _____

PHA 5127

Second Exam

Fall 2007

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

Name

Put all answers on the bubble sheet

TOTAL _____/130 pts

Name: _____

UFID #: _____

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 as true (A) or false (B). Drug A is cleared only by hepatic metabolism and has an intrinsic clearance of 80,000 L/h

Looking at intrinsic clearance you can tell this is a high extraction drug.

- 1: T F The oral bioavailability of this drug will be larger than 80%.
- 2: T F Plasma protein binding will affect the oral bioavailability of this drug.
- 3: T F The hepatic clearance of this drug is 1333 L/min
- 4: T F Plasma protein binding will affect the hepatic clearance of this drug.
- 5: T F Drug B, known to induce enzymes also responsible for metabolism of Drug A, will significantly affect the clearance of Drug A if given together.

Name: _____

UFID #: _____

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 A with a volume of distribution of 108 L. When given by an iv bolus injection, the a peak concentration of 0.18 μg is observed (C_o). When given orally, the oral bioavailability is 99.9 %. Plasma Protein Binding is 50% ($f_u=0.5$).

Peak [$\mu\text{g}/\text{ml}$]	0.18
V [L]	108
F (%)	99.9
f_u	0.5

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

This drug is a low extraction drug. $E=0.001$

- 6: T F The drug is highly metabolized in the liver.
- 7: T F Plasma protein binding will affect the oral bioavailability of this drug.
- 8: T F The hepatic clearance of this drug will be smaller than the Cl_{ren}
- 9: T F Plasma protein binding will affect the hepatic clearance of this drug
- 10: T F Drug B, known to induce enzymes also responsible for metabolism of Drug A will significantly affect the clearance of Drug A
- 11: T F Drug B, known to induce enzymes that are also responsible for metabolism of Drug A is likely to decrease the clearance of A

Name: _____

UFID #: _____

Question Set III (Matching)

(20 points)

For the physiological changes listed below, select the induced changes on the pharmacokinetic parameters for a **hydrophilic strong acid, protein bound drug that is only eliminated through the kidneys** (some answers may be used more than once).

Select the effect on kinetics

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

“Strong acid” indicates that this drug will be mostly ionized at physiological pH.

Physiological change

12: Decrease in plasma protein binding (C)

13: Decrease in tissue binding (E)

14: Decrease in GFR (B)

15: Increase in urine flow (E)

Name: _____

UFID #: _____

Question Set IV

(20 points)

A lipophilic acidic drug (pK_a of 7) is eliminated only by the kidney. **Plasma protein binding is 90%**. 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**.

16: What value describes best the clearance? (10 points)

- A: 0.15 mL/min
- B: 13 mL/min
- C: 130 mL/min
- D: 6.6 mL/min**
- E: none of the above

$F_u=0.1$ $GRF \cdot f_u=13\text{mL/min}$ this drug has a significant portion unionized at physiological pH and therefore will undergo some reabsorption. If it were totally reabsorbed the clearance would be $\text{urine flow} \cdot f_u=0.2$ mL/min. However since our drug is ~50% ionized, only the unionized half can be reabsorbed. So the clearance will be 6.5 ml/min which represents the 50% of the drug which undergoes filtration and is then trapped in the tubule (the ionized portion) plus a small amount which has the ability to be reabsorbed and is eliminated by urine flow. So the clearance will be a little bit higher than 6.5mL/min.

17: 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 90 %.

- A: 58.5 ml/min
- B: 130 ml/min
- C: 65 ml/min
- D: 6.5 ml/min**
- E: 35.8 ml/min

$Cl_{ren}=GRF \cdot F_u=65 \text{ mL/min} \cdot 0.1=6.5 \text{ mL/min}$. Aminoglycosides do not undergo reabsorption.

Name: _____

UFID #: _____

Question Set V

(10 points)

18: 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: 70 ml/min

D: 103 ml/min

E: none of the above

280 lbs/2.2=127.3 kg IBW=50+2.3*10=73 kg This patient is obese must use adjusted body weight in Creatinine clearance equation. ABW=73kg+0.4*(127.3-73)=94.7kg

Clcr=(140-34)*94.7kg/(72*1.5 mg/dl)=92.9 mL/min

Name: _____

UFID #: _____

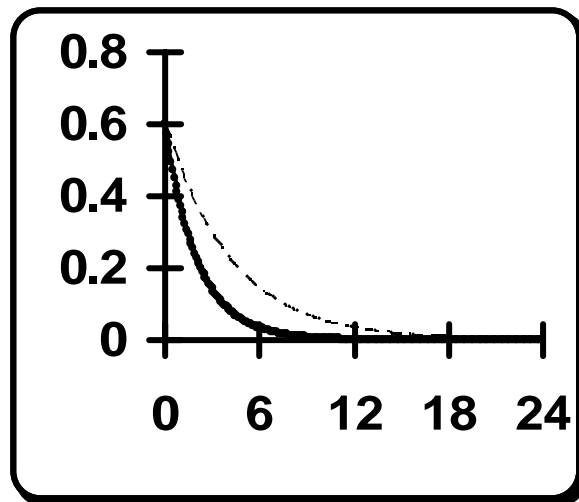
Question Set VI

(5 points)

19: The following patients differ in the

- (A) dose received
- (B) clearance**
- (C) volume of distribution

Peak (mg/L)	0.60	0.60
Ke (1/h)	0.2	0.5
t1/2 (h)	2.9	1.4
AUC (mg/L*h)	2.50	1.25



The peak concentration is the same, which means that these patients were given the same dose and have the same V_d . Clearance must be different because the elimination rate is different.

Name: _____

UFID #: _____

Question Set VII (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)

- 20: T **F** The renal clearance of a drug (as determined by filtration and reabsorption) always depends on the tissue binding of the drug. No, Protein 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. False, it is possible to use noncompartmental models.
- 22: T **F** Drinking a lot of water (urine flow is doubled) will increase significantly the renal clearance of aminoglycosides. False, these drugs do not undergo reabsorption.
- 23: T **F** For an acidic drug with a pK_a of 1.0, adjustment of the urine pH within physiological ranges will significantly change the renal clearance. False, the pK_a will always be outside physiological range.
- 24: T **F** Hepatic clearance depends on the drug plasma concentration, as the rate of metabolism increases with increasing drug concentrations in the blood. False, clearance is set for a certain drug.

Name: _____

UFID #: _____

Question Set VIII (True or False)

(12 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 that is mainly eliminated through hepatic metabolism.

- 25: T F The larger the volume of distribution, the smaller the AUC of a given drug. AUC relates to CL, which is independent of Vd.
- 26: T F Doubling the dose will generally double the AUC of a drug after iv bolus injection. Yes, this is due to dose dependent or linear pharmacokinetics.
- 27: T F An increase in plasma protein binding will always result in a decrease of the drug's hepatic clearance. Not for a high extraction drug.
- 28: T F An increase in plasma protein binding will under no circumstances result in a decrease of the drug's hepatic clearance. It would for a low extraction drug.

Name: _____

UFID #: _____

Question Set IX (5 points)

29. Which of the following statements are correct?

- 1) We can roughly assume that a change in clearance will result in a change in volume of distribution. These are independent parameters.
- 2) Drug A is 40% protein bound, drug B 98% protein bound. A two percent decrease in plasma protein binding will be most significant for drug A. When looking at clearance of a low extraction drug a two percent change in f_u will give a clearance twice as large.
- 3) Genetic variability in metabolizing enzymes always alters hepatic clearance. Not for high extraction drugs.
- 4) In general, we should always use IBW for drug recommendations for calculating creatinine clearance (CL_{cr}). Not if TBW is $<120\%$ IBW, then we use TBW.

- A) 2, 3, 4
- B) 1, 3 & 4
- C) 2, 3
- D) 3, 4

E) None of the above

Name: _____

UFID #: _____

Question Set X (10 points)

30. 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) 1.10L/min
 - B) 1.50L/min
 - C) 1.18L/min
 - D) 0.99L/min**
 - E) Cannot be determined because the dose is not given.

Since this drug is entirely eliminated by the liver you can set up a simple ratio. $1.35\text{L}/\text{min}/1.50\text{L}/\text{min} = X/1.10\text{L}/\text{min}$ $X = 0.99\text{L}/\text{min}$