

Name: _____

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PHA 5127

**Final Exam
Fall 1999**

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

Name

Question/Points

1. _____ /15 pts

2. _____ /15 pts

3. _____ /20 pts

4. _____ /15 pts

5. _____ /15 pts

6. _____ /45 pts

7. _____ /15 pts

8. _____ /15 pts

9. _____ /15 pts

10. _____ /15 pts

11. _____ /15 pts

TOTAL _____ /200

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1. The terminal half-life of a drug when given after i.m. administration was longer than that of the same drug given intravenously. Explain! (15 points)

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2. (15 points)

$$Cp_{\min} = \frac{D}{V_d} \cdot \frac{1}{1 - e^{-k_e \cdot \tau}} \cdot e^{-k_e \cdot \tau}$$

For which dosage regimen would you use the above equation.

Explain the meaning of the blocked parts of the equation.

$$Cp_{\min} = \boxed{\frac{D}{V_d}} \cdot \boxed{\frac{1}{1 - e^{-k_e \cdot \tau}}} \cdot \boxed{e^{-k_e \cdot \tau}}$$

$$\frac{D}{V_d}$$

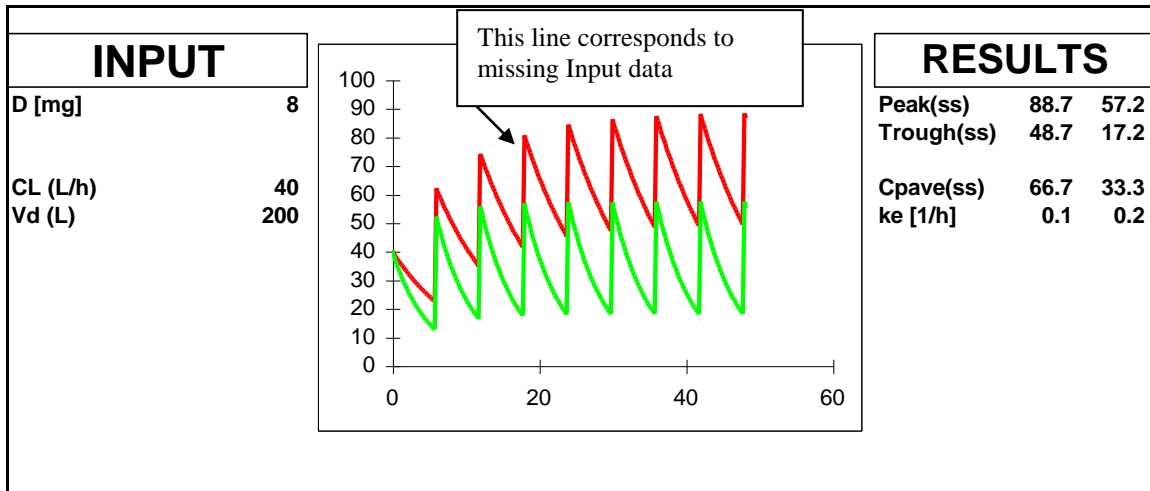
$$\frac{1}{1 - e^{-k_e \cdot \tau}}$$

$$e^{-k_e \cdot \tau}$$

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3. The following concentration time profiles were observed after multiple bolus injections of a drug. The two curves differ in one of the input parameters (Dose, CL or Vd). (20 pts).



Identify the input parameter that differs.

Explain in one or two sentences your reasoning.

What is the numeric value of this parameter?

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4. A lipophilic, neutral, **high** extraction drug (cleared only by the liver) is given to two patients by constant rate infusion (not multiple short term infusions). Steady state has been reached. Patient 1 shows a plasma protein binding of 20% for this drug ($f_u = 0.8$). Patient 2 shows a plasma protein binding of 60% for this drug ($f_u = 0.4$). (15 pts)

Fill in the blanks for the following statements (**always compare patient 1 and 2, you might want to use the terms “larger than”, “smaller than”, “the same as”**):

- a) The volume of distribution of drug A in patient 1 is _____ the volume of distribution in patient 2.
- b) The clearance of drug A in patient 1 is _____ the clearance in patient 2.
- c) Applying the same dose to patient 1 and 2 will result in a steady state plasma level in Patient 1 that is _____ that in patient 2
- d) Applying the same dose to patient 1 and 2 will result in free steady-state plasma levels in Patient 1 that is _____ that in patient 2.
- e) To achieve the same **free** plasma steady state concentrations the daily dose in patient 1 should be _____ that in patient 2.

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5. A lipophilic, neutral, **low** extraction drug (cleared only by the liver) is given to two patients by constant rate infusion (not multiple short term infusions). Steady state has been reached. Patient 1 shows a plasma protein binding of 20% for this drug ($f_u = 0.8$). Patient 2 shows a plasma protein binding of 60% for this drug ($f_u = 0.4$). (15 pts)

Fill in the blanks for the following statements (**always compare patient 1 and 2, you might want to use the terms “larger than”, “smaller than”, “the same as”**):

- a) The volume of distribution of drug A in patient 1 is _____ the volume of distribution in patient 2.
- b) The clearance of drug A in patient 1 is _____ the clearance in patient 2.
- c) Applying the same dose to patient 1 and 2 will result in a steady state plasma level in Patient 1 that is _____ that in patient 2
- d) Applying the same dose to patient 1 and 2 will result in free steady state plasma levels in Patient 1 that is _____ that in patient 2.
- e) To achieve the same **free** plasma steady state concentrations the k_0 in patient 1 should be _____ that in patient 2.

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- 6.) A 59 year-old white female, patient CS, is admitted to the intensive care unit with a ruptured duodenal diverticulum that was surgically repaired. Before surgery you are asked to begin the patient on aminoglycosides. Other pertinent patient data include: height, 5 ft, 1 in.; weight, 55 kg; and serum creatinine, 1.3 mg/dl. (45 points)

You should assume that this aminoglycoside is given as intermittent intravenous infusion. The infusion time of a single infusion is 1 hour.

To calculate an initial maintenance dose and dosing interval, we shall use the population estimates for k_e and V_d :

$$K_e = 0.000293 \text{ hr}^{-1} \times \text{creatinine clearance (in ml/min)} + 0.014 \text{ (units of } K_e: 1/\text{hr)}$$

$$V_d = 0.24 \text{ L/kg} \times \text{IBW}$$

a) Calculate the IBW for this patient:

b) Estimate the creatinine clearance for this patient.

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6-c) Estimate k_e (see above relationship)

6-d) Estimate the volume of distribution (see above relationship)

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6-e) Calculate most appropriate dosing interval (τ) for patient CS. Assume a desired C_{peak} of 6 mg/L and a C_{trough} of 1 mg/L and an infusion time of 1 hr.

6-f) Calculate the necessary maintenance dose for the selected dosing interval to achieve the selected peak and trough concentrations.

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7.) Anti-asthma drugs are often administered via inhalation. This form of administration should induce distinct pulmonary effects and reduced systemic side effects. Please select the **2** most important properties to achieve this goal from the list below (15 points):

- | | |
|-----------------------------------|----------------------------------|
| 1. low pulmonary drug deposition, | 4. high oral bioavailability |
| 2. high systemic clearance, | 5. low oral bioavailability, |
| 3. low systemic clearance, | 6. large volume of distribution. |

Choice 1: _____

Choice 2: _____

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8. The oral bioavailability of a **very lipophilic**, neutral, **low extraction** drug after oral administration of a tablet is significantly affected by: (15 pts)

- | | | | |
|---|----------------------------|---|---------------------------|
| A | the liver blood flow | E | the pH of the G.I. tract. |
| B | the dose | F | the dissolution rate |
| C | the plasma protein binding | G | none of the above |
| D | the color of the tablet | | |

Select the correct answer(s) from the list above: _____

9. Which of the following factors significantly affect the renal clearance of a unionized drug that shows complete passive renal reabsorption from the “urine” back into the blood: (15 pts)

- a) plasma protein binding
- b) activity of cationic transporters in the tubuli.
- c) urine flow
- d) pH of urine
- e) liver blood flow

List the correct answer(s): _____

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10. Mark whether the following statements are true (T) or false (F). (15 pts)

T F Loading doses are mainly given for drugs with short half-life.

T F A high volume of distribution will result in a high clearance

T F If Drug A is excreted by glomerular filtration as well as by hepatic metabolism and Drug B is cleared only by hepatic clearance, then in a patient with total renal failure, total body clearance of drug A and B will be affected.

T F The oral bioavailability of a drug is determined significantly by the extraction ratio E .

T F The distribution of highly lipophilic small drug molecule is perfusion rate limited.

11. The volume of distribution of a drug X is 500 L. Mark the following statements. Select which statement(s) is (are) consistent with this observation (15 pts)

A. plasma protein binding is more pronounced than tissue binding

B. tissue protein binding is more pronounced than plasma protein binding

C. the drug is able to cross membranes

D. drug X can not be an acid or base as drug X is able to cross membranes

E. the clearance of the drug has to be high, as the plasma protein binding is low

Answer(s): _____