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# PHA 5127

## Final Exam
## Fall 2000

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

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Name

Question/Points

1. _____ /15 pts
2. _____ /15 pts
3. _____ /15 pts
4. _____ /20 pts
5. _____ /15 pts
6. _____ /15 pts
7. _____ /45 pts
8. _____ /15 pts
9. _____ /15 pts
10. _____ /15 pts
11. _____ /15 pts
12. _____ /15 pts (Bonus)

TOTAL _____/200 (215)

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1. The terminal half-life after i.v. administration of the opioid peptide dynorphin is less than one minute. When inhaled the terminal half-life is 5 minutes. When given intramuscularly the terminal half-life is 25 minutes. Explain! (15 points)

2.) Explain why for a two-compartmental model, the $Vd_{area} = Vd_{\beta}$ depends on clearance (15 points): $Vd_{area} = CL/\beta$

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3. (15 points)

Explain the meaning of the blocked parts of the equation.

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

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

$$\frac{1}{1 - e^{-k_e \bullet t}}$$

$$e^{-k_e \bullet t}$$

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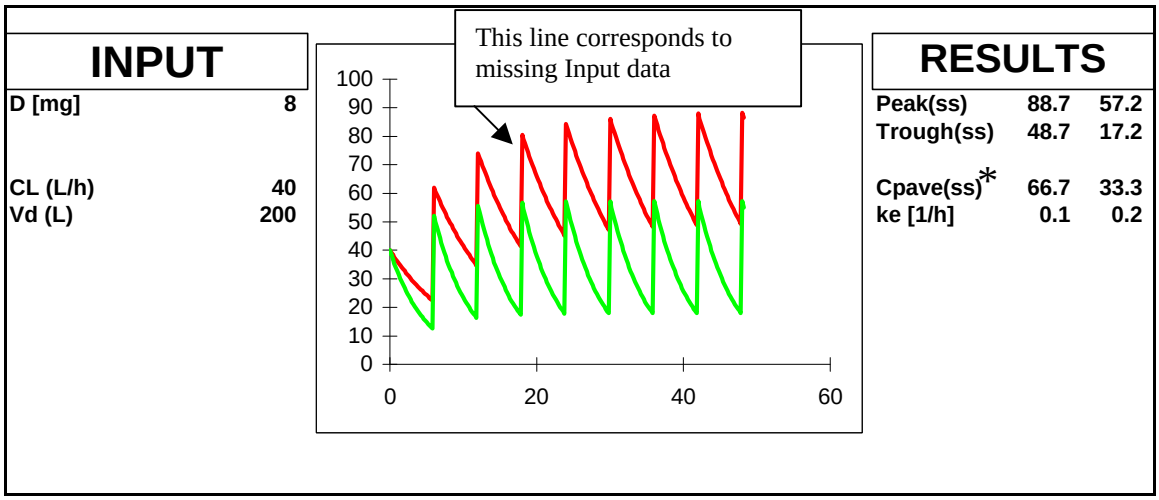
4. The following concentration time profiles were observed after multiple bolus injections of a drug. The two curves differ in one of the input parameters (Dose, CL or Vd). (20 pts).




*Average steady-state concentration

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

plasma level 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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6. 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 (fu = 0.8). Patient 2 shows a plasma protein binding of 60% for this drug (fu = 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", faster than, later than**):

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 patient 1 will result in a steady steady state

plasma level in Patient 1that is _____ that in patient 2

d) Applying the same dose to patient 1 and 2 will result in a 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 $k_o$ in

patient 1 should be _____ that in patient 2.

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7.) A 24-year-old female patient Noel Christmas (72 kg), is admitted to the hospital after sustaining multiple traumatic injuries. Her recovery is complicated by the onset of acute renal failure one-week after admission. During the second week she experienced a spiking fever, gram-positive bacill, resistant to methicillin but susceptible to vancomycin. The physician decides to begin a course of vancomycin. (45 points)

Assume a creatinine clearance of 125 ml/min.

The average Vd for Vancomycin is about 0.9 L/kg (based on total body weight).

K= 0.00083 [CrCL(in ml/min)]+0.0044 (units of $K_e$: 1/hr)

a) Calculate an intravenous vancomycin loading dose to achieve a concentration of 20 mg/L achieved 2 hr after the end of a 1-hr infusion

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7-b) The calculated loading dose was consequently administered to the patient. Two hours after the end of the loading dose, the vancomycin concentration was 29 mg/L; it is 17.5 mg/L at 37 hr after the end of this infusion. Assume that the plasma vancomycin concentration should decline to 10.0 mg/L before another dose is given and that the steady state plasma concentration desired 2 hr after the infusion is 20 mg/L. What would be the dosing interval tau (from start of an infusion to the next start of the infusion) and the dose to achieve these levels at steady state?

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

A the liver blood flow

B the dose

C the plasma protein binding

D the color of the tablet

E the pH of the G.I. tract.

F the dissolution rate

G none of the above

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

9. Which of the following factors significantly affect the renal clearance of an 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-live.

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 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 an drug X is 500 L. 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): _____

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12) The Daily Crossword Puzzle for all you students who like puzzles and some more points (15 points). ☺
Fill in the puzzle by completing the following statements:

DOWN

1. In the kidney, a drug may be either _____, secreted, or reabsorbed.
2. _____ is "Father Christmas" in French. (optional)
3. A two-compartment body model is required to describe the pharmacokinetic profile of a drug if the drug exhibits a pronounced _____ (α) phase.
4. A number between eight and ten; Sounds like "no" in German (optional).
5. Together, _____ and volume of distribution determine the elimination rate constant of a drug.
6. If $k_a << k_e$ for a drug administered orally (typical of a sustained release formulation), the drug is said to follow " _____-_____" kinetics.

ACROSS

1. The method of residuals, also known as "_____", is means by which $k_e$ and $k_a$ may be separated and calculated when oral data is analyzed.
7. _____ clearance may be calculated to estimate the GFR of a patient.
8. A measure of enzyme activity in the liver is _____ clearance.
9. The _____ is the fraction of an oral dose that enters systemic circulation after administration.
10. A _____ dose is often used to reach desired steady state levels more quickly at the beginning of a multiple dosing regimen.
11. Once a constant rate infusion is started, the time required to reach steady state levels is dependent on the _____ (multiplied by 5) of the drug.