PHA 4123

2nd EXAM

NAME: _____

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Question	Points
1.	_____/10
2.	_____/5
3.	_____/5
4.	_____/25
5.	_____/10
6.	_____/5
7.	_____/5
8.	_____/10
9.	_____/10
10	_____/15

TOTAL _____/100

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1. Discuss how the following co-treatments will alter the oral bioavailability of cyclosporine:

a.	__↑___	ketoconazole	inhibition
b.	___↓__	rifampin	induction
c.	___↑__	grapefruit juice	inhibition
d.	__-__	orange juice	-

2. The plasma clearance of FK506 is reported to be 1.8 L/h/kg. Determine if FK506 is a high or low extraction drug.

$$\frac{C_B}{Cp} = 30 = \frac{AUC_B}{AUCp}$$

Blood clearance only 0.06L/h/kg (much smaller)

For 70 kg $\Rightarrow$ 4 L/h $\Rightarrow$ <u>low</u> extraction

3. For FK506, the recommended therapeutic range is 10-20 ng/mL blood. Discuss this recommendation.

- not validated yet

- free fraction is active, is very small, highly variable

$$\frac{C_B}{C_p = 30, \quad f_b = 77}$$

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4. A 55 year old, 60 kg female patient SeCr = 1.4 mg/dL is to be treated with methotrexate. The target concentration is 16 μM.

   a. Calculate an appropriate loading dose.

LD = 0.2·60·16 = 192μM = 87 mg ~ <u>90 mg</u>

   b. Calculate an appropriate maintenance dose.

CL_{MTX} = 68.6 mL/min = 4.12 L/h

$$CL_{cr} = \frac{(140-55)\cdot 60}{85\cdot 1.4} = 42.9 mL/min$$

MD = 4.12 ·16 = 65.9 μM/h = <u>30 mg/h</u>

   c. How long would you administer the maintenance dose?

36 h

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4. d. Recommend a time schedule for drug level monitoring. Recommend a dosing regimen.

Samples 24h
48 h
60 h
if above 0.1 μM, more samples

dosing regimen: leucovorin after 36 h for 3 days
10 mg/m^2 Q6h
if after 48 h > 1 μM, then 50-100 mg/m^2 Q6h

e. For an infusion rate of 30 mg/h over 36 h, calculate the estimated concentrations:

1. At the end of the infusion

$$Cp_{ss} = \frac{66}{4.12} = 16\mu M$$

2. 12 h after the end of the infusion

$Cp = 16 \cdot e^{-k \cdot 12} = 1\mu M$

$$k_{\alpha} = \frac{0.693}{3} = 0.231$$

3. 36 h after the end of the infusion

time to reach 0.5 μM: $$t = \frac{ln\frac{16}{0.5}}{0.231} = 15h$$

$$k_{\beta} = \frac{0.693}{10} = 0.0693$$

$Cp = 0.5 \cdot e^{-0.0693 \cdot 21} = 0.12\ \mu M$

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5. Explain why the term "biological half-life" frequently is not appropriate.

Effects usually do not follow first-order kinetics, but rather zero-order kinetics.

Answers not supplied for following questions

6. List four explanations for delayed drug absorption associated with overdose.
7. Describe the mechanism of activated charcoal use in the treatment of overdose and the rationale(s) for administering it on a repeated basis. (Example 1 gm/kg every 6 hours).
8. A 37 year old, 60 kg woman arrived in the Emergency Department 2 hours after ingestion of thirty 200-mg aminophylline tablets. No theophylline plasma concentration was available. The patient had sinus tachycardia of 100 beats/min and was agitated. Predict the maximum theophylline concentration for this patient. (Theophylline volume of distribution = 0.45 L/kg).
9. Describe the changes in the maturation process for the premature neonate, infant/toddler through adolescent, compared to adults for the pharmacokinetic parameters of distribution and elimination and its effect on drug concentration. Assume in this example the drug is primarily water soluble, and is 5% metabolized by the liver, and 90% eliminated unchanged in the urine. (Suggestion: put your answer in the form of a table to make it easier.
10. A 2 week old, 30 week gestional age, 1.3 kg, infant has been hospitalized since birth for prematurity. The infant now appears to be septic, and has some chest x-ray changes possible indicating pneumonia. A previous trach culture from 5 days ago was growing enterobacter cloacae sensitive to tobramycin and is now felt this organism may be causing the infant's current problems.

    Tobramycin is started at 3.6 mg iv q 12 hr on 4/14/96 at 0800 and remains on a 0800 and 2000 schedule with serum samples drawn on 4/17/96. The following tobramycin serum samples are drawn:

    Tobramycin peak concentration 6.3 mcg/ml drawn on 4/17/96 at 0930. Tobramycin trough concentration 1.4 mcg/ml drawn on 4/17/96 at 1930.

    The tobramycin is sent to the floor in syringes, with 3.6 mg in a volume of 0.36 ml.

    A. What intravenous delivery factors are important in the delivery of this small volume of Tobramycin?
    B. Determine the ke and $t_{1/2}$ of tobramycin in this patient. You need to show work to receive full credit.
    C. Calculate the tobramycin "post-distribution" peak which would have occurred at 0900.
    D. Calculate the dose and dosage schedule to achieve a peak serum tobramycin concentration of at least 8 mcg/ml, using your answer in C above for this determination.