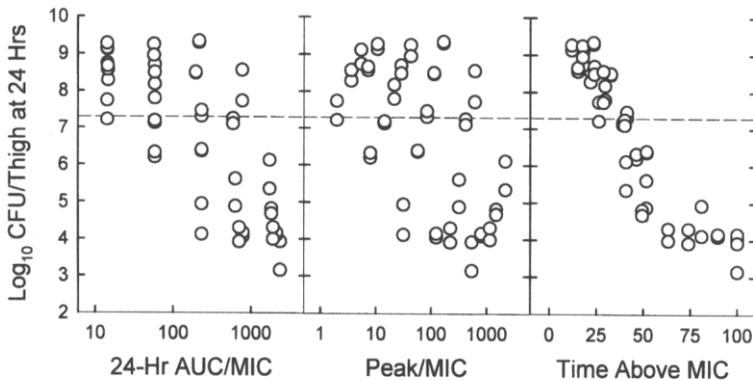


PHA 5128 Dose Optimization II
Spring 2011
Homework 3

1. Which of the following are true about aminoglycosides?
 - a. Approximately 50% of the drugs are excreted in the urine.
 - b. Hepatic metabolism is an important factor in their elimination.
 - c. For gentamicin and tobramycin, the trough concentration should be below 2 $\mu\text{g/mL}$.
 - d. Clinical peak and trough concentrations can be used to compute the volume of distribution.
 - e. Clinical peak and trough concentrations can be used to compute the dosing interval but adjustments are required.
 - i. A, B and C are false
 - ii. D and E are true
 - iii. C and E are true

2. Use the following graph to answer the question regarding ceftazidime:



Explain which parameter(s) you will use to evaluate efficacy of ceftazidime against the infection of *K. pneumonia* in neutropenic mice, based on the graph above. Estimate the value of your selected parameter that is required to achieve a minimum efficacy, if the target is 7.2 Log_{10} CFU/Thigh at 24 hours. Also estimate the minimum value of this parameter that achieves the maximum efficacy. Discuss how the drug relates to bactericidal versus bacteriostatic killing of antibiotics.

3. Gentamicin, after IV bolus administration, exhibits a triphasic disposition that is characterized by the following equation $\text{Conc}(t) = A \exp(-\alpha t) + B \exp(-\beta t) + C \exp(-\gamma t)$.

If the $t_{1/2}$ for the α -, β -, and γ -phases are 10 minutes, 1.5 hours and 125 hours, respectively, estimate the parameter values for α , β , and γ .

Detroit receiving Hospital and University Health Center vancomycin dosing nomogram table

Cl_{cr} (ml/min) →	30	40	50	60	70	80	90	100	≥ 110
Weight (kg) ↓									
50	500 q24h	500 q24h	500 q12h	500 q8h	500 q8h				
55	500 q24h	500 q24h	500 q12h	500 q8h	500 q8h				
60	500 q24h	500 q24h	500 q12h	500 q12h	1000 q12h	1000 q12h	1000 q12h	500 q8h	500 q8h
65	1000 q24h	1000 q24h	1000 q24h	1000 q12h	1000 q8h				
70	1000 q24h	1000 q24h	1000 q24h	1000 q12h	1000 q12h	1000 q12h	1000 q12h	1000 q8h	1000 q8h
75	1000 q24h	1000 q24h	1000 q24h	1000 q12h	1000 q12h	1000 q12h	1000 q12h	1000 q8h	1000 q8h
80	1000 q24h	1000 q24h	1000 q24h	1000 q12h	1000 q12h	1000 q12h	1000 q12h	1000 q8h	1000 q8h
85	1000 q24h	1000 q24h	1000 q24h	1000 q12h	1000 q12h	1000 q12h	1000 q8h	1000 q8h	1000 q8h
90	1000 q24h	1000 q24h	1000 q12h	1000 q12h	1000 q12h	1000 q8h	1000 q8h	1000 q8h	1000 q8h
95	1000 q24h	1000 q24h	1000 q12h	1000 q12h	1000 q12h	1000 q8h	1000 q8h	1000 q8h	1000 q8h
100	1000 q24h	1000 q24h	1000 q12h	1000 q12h	1000 q12h	1000 q8h	1000 q8h	1000 q8h	1000 q8h
105	1000 q24h	1000 q24h	1000 q12h	1000 q12h	1000 q12h	1000 q8h	1000 q8h	1000 q8h	1000 q8h
≥ 110	1000 q24h	1000 q24h	1000 q12h	1000 q12h	1000 q12h	1000 q8h	1000 q8h	1000 q8h	1000 q8h

Figure 1. Detroit Receiving Hospital and University Health Center vancomycin dosing nomogram. (Updated 5/99)

Useful information: 1 kg = 2.2 lbs

- A female patient, 45 years of age, 5'2" in height and 130 lbs in weight acquired S. pneumonia. Her serum creatinine is 0.75 mg/dL. The MIC of vancomycin against her infection was estimated in the laboratory to be 6 $\mu\text{g/mL}$. Compute both $C_{ss, \max}$ and $C_{ss, \min}$ based on IV bolus administration. Do you need to adjust the dosing frequency based on the computation that you have obtained? If so, estimate the next dose based on a desired steady-state trough concentration of 20 $\mu\text{g/L}$.
- An aminoglycoside was administered as an IV infusion over 30 minutes q24h. The "clinical" peak Cp_{\max}^* (measured 30 minutes after the end of the infusion) was reported to be 8.8 $\mu\text{g/mL}$ and "clinical" trough Cp_{\min}^* (measured 30 minutes before the end of the dosing interval) was 0.2 $\mu\text{g/mL}$. Calculate the expected peak and troughs. If the MIC for the specific infection is 1 $\mu\text{g/mL}$, compute the time above MIC after a single infusion dose. Compute the individual's volume of distribution, if the original dose was 180 mg. What is the optimized dosing interval so that the trough concentration is maintained at 1 $\mu\text{g/mL}$?