

PHA 5128

Homework I

1. Hydrocortisone (20 mg) was given by an intravenous bolus injection and the following plasma concentrations were measured:

time [h]	C _p [ng/ml]
1	315
2	212
3	136
4	89
6	38
8	15

- a. Prepare a semilogarithmic plot of the plasma concentration of hydrocortisone versus time. Determine the elimination rate constant and the half-life of the drug.
 - b. Using the trapezoidal rule, estimate the total area under the curve of hydrocortisone.
 - c. Calculate total clearance.
 - d. Calculate volume of distribution.
 - e. Assuming that hydrocortisone is eliminated by metabolism, calculate the hepatic extraction ratio.
2. A patient is admitted with an acute theophylline overdose. A serum level is measured at 45 $\mu\text{g}/\text{ml}$. Assuming an 8 hour half-life and no further drug absorption, how long does it take for the serum level to drop to the upper limit of the therapeutic range (20 $\mu\text{g}/\text{ml}$)?
3. A patient was given 80 mg gentamicin over 30 minutes (i.v.) from 9:30 to 10:00 am. The following two serum levels were measured: 6.5 $\mu\text{g}/\text{ml}$ at 10:30 am and 1.2 $\mu\text{g}/\text{ml}$ at 5:00 pm. Calculate:
- a. the elimination rate constant k
 - b. the elimination half-life
 - c. the peak concentration at 10:00 am
 - d. the trough concentration at 5:30 pm
 - e. the volume of distribution
 - f. the clearance

4. Show for both high and low extraction drugs, how doubling the protein binding will affect the resulting unbound and total serum levels. What recommendations would you make for dose adjustments? Assume constant rate infusion and steady state.

5. K.L., a 75 kg male smoker with chronic obstructive pulmonary disease, is to be started on an oral regimen of aminophylline (85% of which is theophylline). The pharmacokinetic parameters for this patient are V_d (0.5 L/kg), CL (80 mL/h/kg) and F (1.0).
 - a. Design an oral dosage regimen of aminophylline (100- and 200 mg tablets are marketed) for this patient to attain and maintain a plasma concentration within the therapeutic range (10-20 $\mu\text{g}/\text{ml}$). The absorption of theophylline is complete and rapid.
 - b. Discuss the result and make a dosing recommendation.