1.1. General Pharmacokinetic Applications

Self-Assessment Problems

Half-Life

Knowledge of a drug's half-life (t½) is useful in pharmacokinetic monitoring of patients as it gives information on: (1) how long it would take for a drug to be eliminated from the body (e.g., cases of drug overdose) or how long a dose must be held to reach a certain concentration, (2) the length of a dosage interval if a desired therapeutic range is known, and (3) how long a drug must be given before steady state is reached, since approximately five half-lives must elapse before steady state has been achieved.

1. After five half-lives of a drug, how much of a 1000-mg dose remains in the body (in mg)?

Determining the Half-Life of a Drug Based on Measured Concentrations

Assume first-order elimination, one compartment distribution, and that concentrations are in the elimination phase for all of the following problems.

2. The following two concentrations were determined after administration of an IV bolus dose of a drug at time zero. Determine the half-life without using a calculator.

C (mg/L)	8	4
t (hours)	3	9

3. Determine the half-life from this concentration versus time data without using a calculator.

C (mg/L)	12	3
t (hours)	8	12

4. If the lower concentration is not exactly ½, ¼, 1/8, etc., of the original concentration, the half-life can still be estimated, but with slightly reduced accuracy. Estimate the approximate t½ from the following concentration versus time data without using a calculator.

C (mcg/mL)	10	2
t (hours)	3	11

Determining Elimination Rate Constant (k) and Half-Life Using Appropriate Equations

5. Determine the elimination rate constant k and then the half-life of the drug based on the following concentration versus time data.

C (mcg/mL)	32	8
t (hours)	3	10

6. Determine the elimination rate constant k and then the half-life of the drug based on the following concentration versus time data.

C (mg/L)	6.8	3.5
t	1 p.m.	11 p.m.

7. The following concentrations versus time were obtained after a 500-mg IV bolus dose of amikacin at 8 a.m. What is the half-life of amikacin in the patient?

C (mg/L)	22	4.5
t	10 a.m.	8:15 p.m.

Using Half-Life (Elimination Rate Constant) to Solve for the Time That Must Elapse for One Concentration to Decrease to a Lower Concentration

8. A patient received an excessive dose of digoxin and a digoxin concentration was reported as 5 mcg/L. The patient's digoxin half-life was estimated to be 2 days. Assume that the measured concentration is post-absorption and post-distribution. How long (in days) would it be estimated to take for the digoxin concentration to decrease to 1 mcg/L?

Using Half-Life (Elimination Rate Constant) to Determine a Dosage Interval

Equation 1* can be used to determine a dosage interval, which is, of course, simply a time change.

9. The therapeutic range for a new drug has been determined to be 4–13 mg/L. The average half-life in patients with normal hepatic and renal function is 8 hours.
   A. Based on the half-life, what is the maximum dosage interval that might be used?
   B. What is a logical interval that would be used?

Volume of Distribution

The apparent volume of distribution is the theoretical volume that would have to be available for a drug to disperse in if the concentration everywhere in the body were the same as that in the plasma or serum, the place where drug concentration sampling generally occurs. **Equation 6** provides three useful values: D (dose), C_{Δ} (the desired concentration change after the dose), and V (the apparent volume of distribution) that can each be solved if the other two are known or can be estimated.

Using Volume of Distribution to Determine a Loading Dose

10. The estimated volume of distribution of phenytoin in a female patient is 36 L. Estimate a loading dose of IV fosphenytoin sodium (S = 0.92, F = 1) to produce an estimated concentration after the dose (C_0) of 20 mg/L. Although the dose would generally be given over a short period of time, treat as if given IV bolus.

11. A 70-kg patient is to receive an IV bolus dose of a drug (S = 1). The population average weighted volume of distribution is 0.3 L/kg. The desired concentration immediately after the dose is 10 mg/L. Calculate the dose (in mg).

* For Equation 1 and other numbered equations mentioned in this text, see ***Select Pharmacokinetic Equations,*** p xix.