Clinical Pharmacokinetic Equations and Calculations

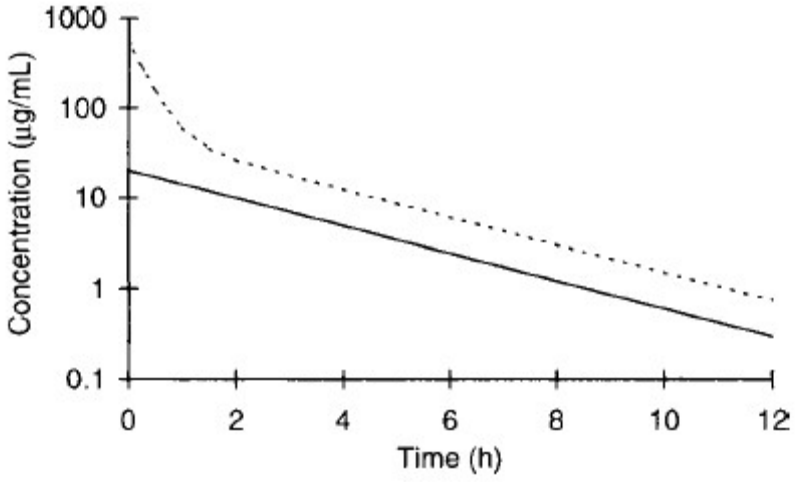
One-compartment model equations for linear pharmacokinetics

1. *Intravenous Bolus Equation*

- When a drug is given as an intravenous bolus and the drug distributes from the blood into the tissues quickly, the serum concentrations often decline in a straight line when plotted on semilogarithmic axes.

$$C = (D/V)e^{-k_e t}$$

- Most drugs given intravenously cannot be given as an actual intravenous bolus because of side effects related to rapid injection. A short infusion of 5–30 minutes can avoid these types of adverse effects, and if the intravenous infusion time is very short compared to the half-life of the drug so that a large amount of drug is not eliminated during the infusion time, intravenous bolus equations can still be used.



- Pharmacokinetic parameters for patients can also be computed for use in the equations. If two or more serum concentrations are obtained after an intravenous bolus dose, the ***elimination rate constant***, ***half-life*** and ***volume of distribution*** can be calculated.

$$k_e = 0.693/t_{1/2}$$

- The elimination rate constant can be computed using the following equation:

$$k_e = -(\ln C_1 - \ln C_2)/(t_1 - t_2)$$

where t1 and C1 are the first time/concentration pair and t2 and C2 are the second time/concentration pair

- The volume of distribution can be calculated by dividing the dose by the serum concentration at time = 0.

$$V = D/C_0$$

2. *Continuous and Intermittent Intravenous Infusion Equations*

- Some drugs are administered using a continuous intravenous infusion, and if the infusion is discontinued the serum concentration/time profile decreases in a straight line when graphed on a semilogarithmic axes.
- one compartment model intravenous infusion equation can be used to compute concentrations (C) while the infusion is running:

$$C = (k_0/Cl)(1 - e^{-k_e t}) = [k_0/(k_e V)](1 - e^{-k_e t})$$

where k_0 is the drug infusion rate (in amount per unit time, such as mg/h or μg/min), Cl is the drug clearance (since $Cl = k_e V$, this substitution was made in the second version of the equation), k_e is the elimination rate constant, and t is the time that the infusion has been running.

- If the infusion is allowed to continue until steady state is achieved, the steady-state concentration (Css) can be calculated easily:

$$Css = k_0/Cl = k_0/(k_e V)$$

- If the infusion is stopped, postinfusion serum concentrations ($C_{postinfusion}$) can be computed by calculating the concentration when the infusion ended (C_{end}) using the appropriate equation in the preceding paragraph, and the following equation:

$$C_{postinfusion} = C_{end} e^{-k_e t_{postinfusion}},$$

$t_{postinfusion}$ is the postinfusion time ($t_{postinfusion} = 0$ at end of infusion and increases from that point).

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- The volume of distribution (V) can be computed using the following equation:

$$V = \frac{k_0(1 - e^{-k_e t'})}{k_e[C_{max} - (C_{predose} e^{-k_e t'})]}$$

where k_0 is the infusion rate, ke is the elimination rate constant, t′ = infusion time, Cmax is the maximum concentration at the end of infusion, and Cpredose is the predose concentration.

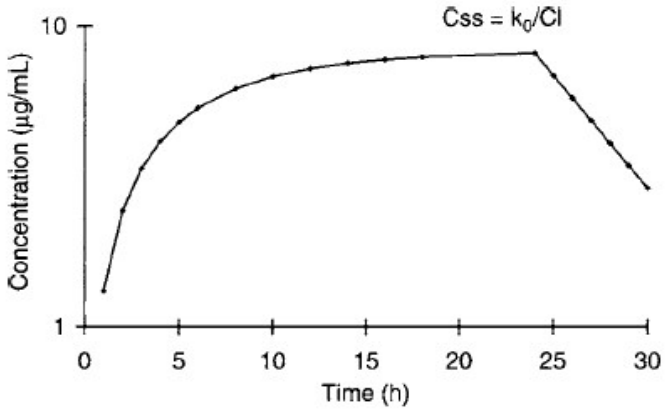

FIGURE 2-5 If a drug is given as a continuous intravenous infusion, serum concentrations increase until a steady-state concentration *(Css)* is achieved in 5–7 half-lives. The steady-state concentration is determined by the quotient of the infusion rate *(k_0)* and drug clearance *(Cl):* Css = k_0/Cl. When the infusion is discontinued, serum concentrations decline in a straight line if the graph is plotted on semilogarithmic axes. When using $\log_{10}$ graph paper, the elimination rate constant (k_e) can be computed using the following formula: slope = $-k_e/2.303$.