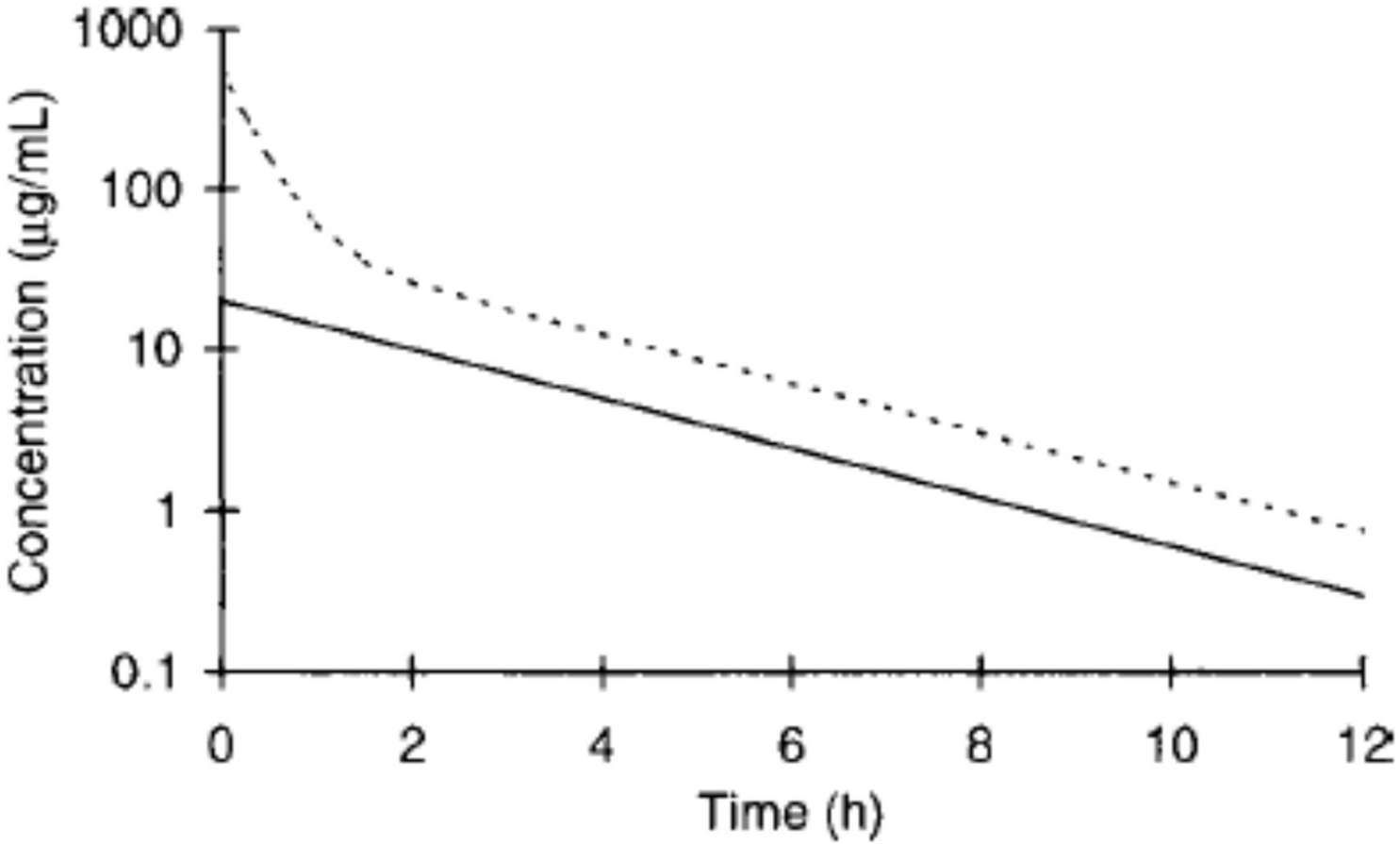
# LEC 2

**Clinical Pharmacokinetic Equations and Calculations**

- *One-compartment model equations for linear pharmacokinetics*
- ***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.


1000
100
10
1
0.1
Concentration (µg/mL)
0
2
4
6
8
10
12
Time (h)

- 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.

- The elimination rate constant can be computed using the following equation: $k_e = 0.693/t_{1/2}$

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

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.

$$V = D/C_0$$

- ***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

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

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

$$Css = k_0 / Cl$$

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

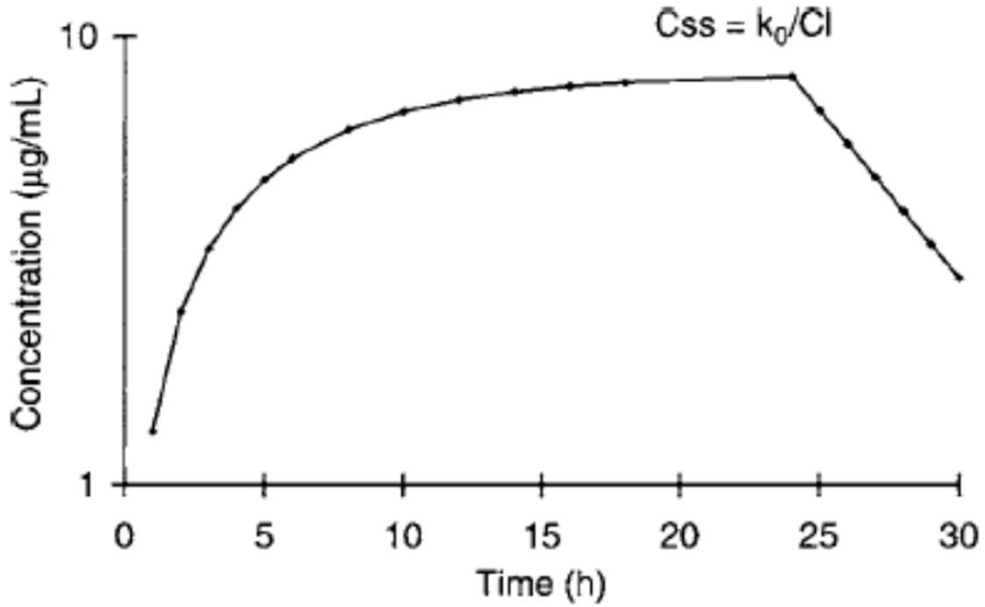



**FIGURE 2-5** If a drug is given as a continuous intravenous infusion, serum concentrations increase until a steady-state concentration *(Css)* is achieved in 5–7 half-lives. The steady-state concentration is determined by the quotient of the infusion rate *($k_0$)* and drug clearance *(Cl):* Css = $k_0$/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 = $-k_e/2.303$.

7. Table 3–2 summarizes plasma data obtained after a bolus dose of ceftriaxone, a semisynthetic cephalosporin antibiotic, in a newborn infant. (Adapted from Schaad, U.B., Hayton, W.L., and Stoeckel, K.: Single-dose ceftriaxone kinetics in the newborn. Clin. Pharmacol. Ther., 37:522–528, 1985.)

**Table 3–2. Plasma Concentrations of Ceftriaxone After i.v. Administration of a 184 mg (50 mg/kg) Dose**

| Time (hr) | 1 | 6 | 12 | 24 | 48 | 72 | 96 | 144 |
|---|---|---|---|---|---|---|---|---|
| Concentration (mg/l) | 137 | 120 | 103 | 76 | 42 | 23 | 12 | 3.7 |

a. Prepare a semilogarithmic plot of the plasma concentration of ceftriaxone versus time. Estimate the half-life of the drug.
b. Estimate the total *AUC* of ceftriaxone.
c. Calculate total clearance.
d. Calculate the volume of distribution.