Chapter-3

Learning questions

Assis. Prof. Dr. Wedad Kamal Ali

LEARNING QUESTIONS

1. A 70-kg volunteer is given an intravenous dose of an antibiotic, and serum drug concentrations were determined at 2 hours and 5 hours after administration. The drug concentrations were 1.2 and 0.3 µg/mL, respectively.

   What is the biologic half-life for this drug, assuming first-order elimination kinetics?

Solution

The Cp decreased from 1.2 to 0.3 ug/mL in 3 hours.

t (hr)	C_P (ug/mL)
2	1.2
5	0.3

$$\log C_P = -\frac{kt}{2.3} + \log C_P^0$$

$$\log 0.3 = -\frac{k(3)}{2.3} + \log 1.2$$

$$k = 0.462 \text{ hr}^{-1}$$

$$t_{1/2} = \frac{0.693}{k} = \frac{0.693}{0.462}$$

$$t_{1/2} = 1.5 \text{ hr}$$

Since:

log 0.3 = - 0.522

log 1.2 = 0.079

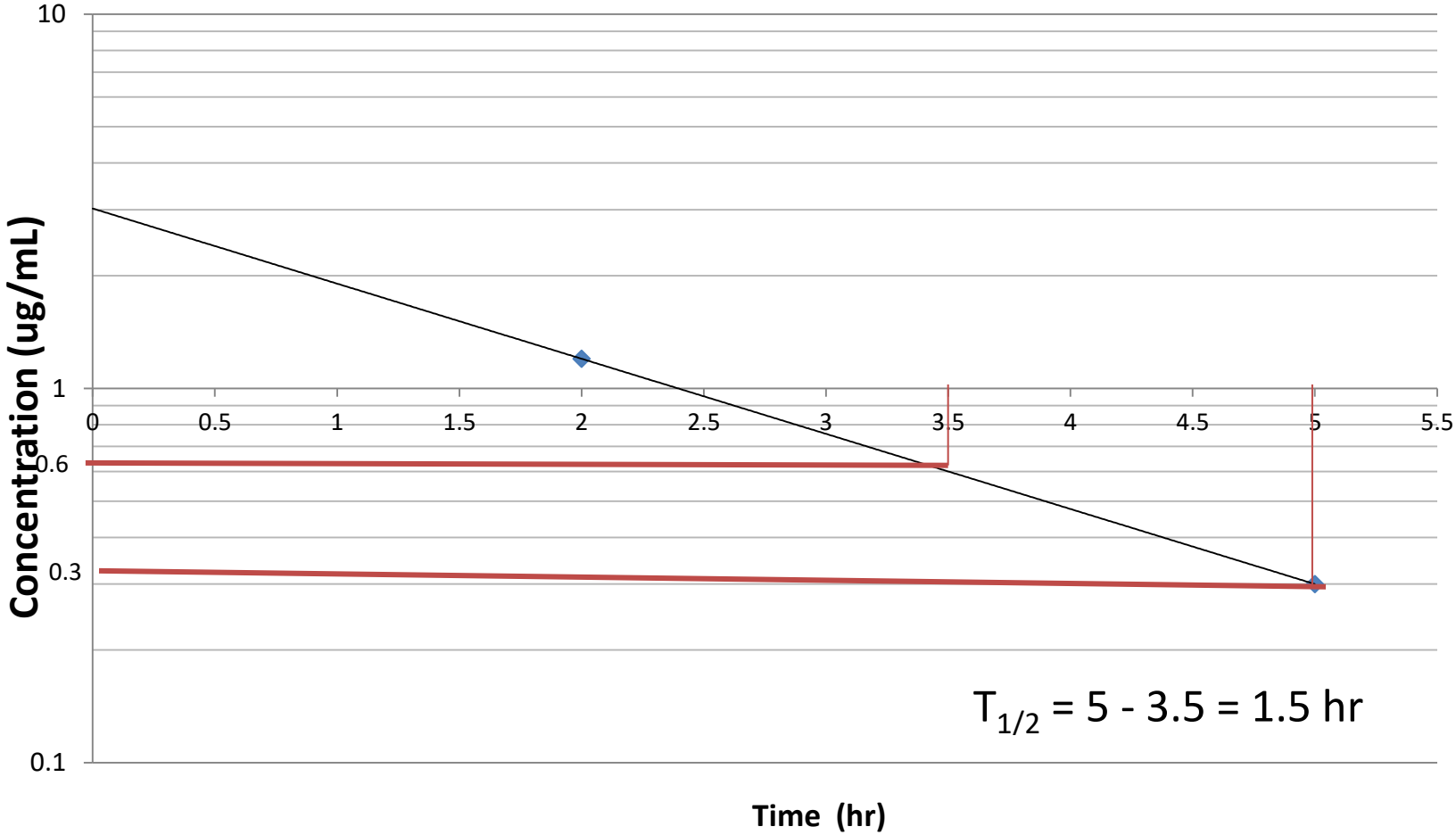
log 1.2 + log 0.3 = 3k/2.3

0.61 =3k/2.3

0.61 x 2.3 /3 = k

K = 0.46

- Alternative method: by plotting the data on a semilog graph and $t_{1/2}$ obtained from the graph. As shown below



2. A 50-kg woman was given a single IV dose of an antibacterial drug at a dose level of 6 mg/kg. Blood samples were taken at various time intervals. The concentration of the drug (*Cp)* was determined in the plasma fraction of each blood sample and the following data were obtained:

Time (hr)	Cp (ug/mL)
0.25	8.21
0.5	7.87
1	7.23
3	5.15
6	3.09
12	1.11
18	0.4

a. What are the values for V_D, *k, and* $t_{1/2}$ *for this drug?*

Answer: To calculate V_D

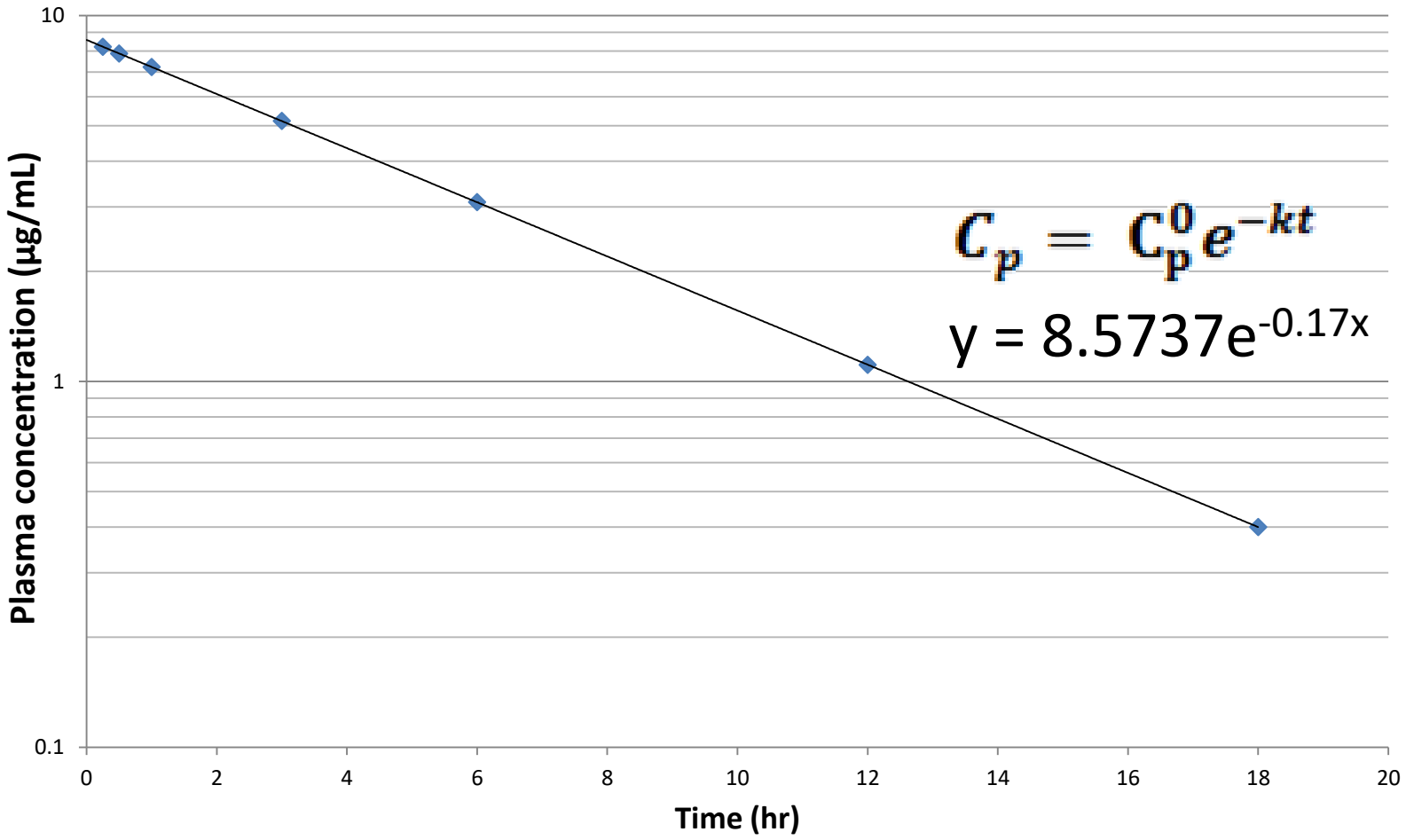
1. plot the data on semilog paper and then find the value of Cp^0 by extrapolation (see the equation in the next slide)

Cp^0 = 8.57 µg/mL = 8.5 mg/ L

2. Dose = 6mg/Kg X 50 = 300mg

3. V_D = Dose/ Cp^0

V_D = 300 mg / 8.57 mg/L = 35 L


10
1
0.1
Plasma concentration (µg/mL)
0
2
4
6
8
10
12
14
16
18
20
Time (hr)
$C_p = C_p^0 e^{-kt}$
y = 8.5737e^-0.17x

$$C_p = C_p^0 e^{-kt}$$

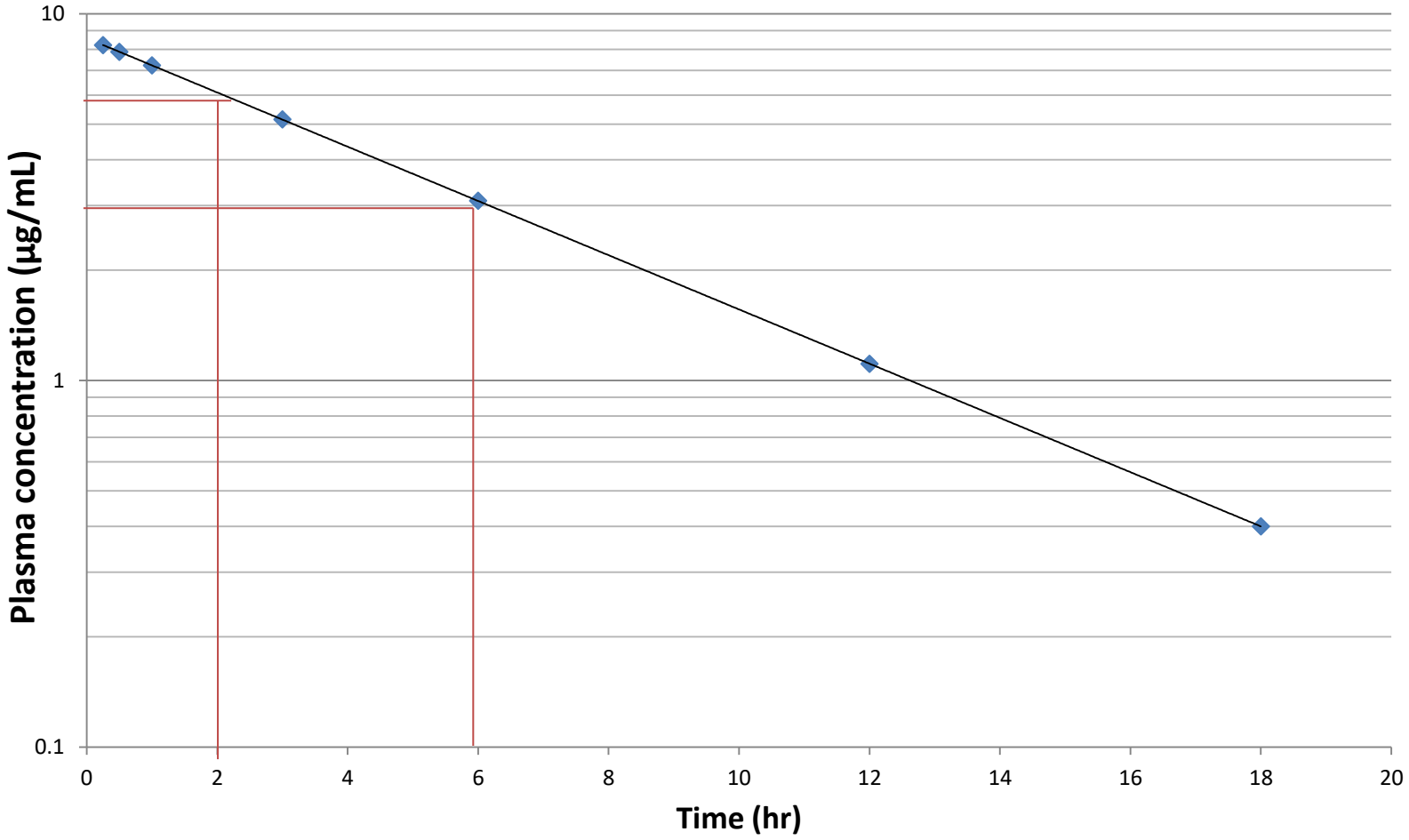
(1) From the equation of best fit line shown within the figure: first find k then $t_{1/2}$
The value of rate constant k is equal to 0.17 hr^{-1} (from the equation)
$t_{1/2}$ = 0.693/ 0.17 = 4.07 hr

Alternative method if the equation is not written within the equation then
first find $t_{1/2}$ from graph the then calculate k
from the data plotted on semilog graph paper use two points from the line of best fit

t (hr)	C_p (μg/mL)
2	6
6	3

(2) $t_{1/2}$ (from graph) = 4 hr $\qquad k = \frac{0.693}{4} = 0.173\ \text{hr}^{-1}$

To find $t_{1/2}$ from the graph



3. A new drug was given in a single intravenous dose of 200 mg to an 80-kg adult male patient. After 6 hours, the plasma drug concentration of drug was 1.5 mg/100 mL of plasma. Assuming that the apparent V_D is 10% of body weight, compute the total amount of drug in the body fluids after 6 hours. What is the half-life of this drug?

3. $D_0 = 200$ mg

$V_D = 10\%$ of body weight $= 0.1\ (80\ \text{kg}) = 8000\ \text{mL} = 8\ \text{L}$

At 6 hours:

$$C_P = 1.5\ \text{mg}/100\ \text{mL}$$

$$V_D = \frac{\text{drug in body } (D_B)}{C_P}$$

$$D_B = C_P V_D = \frac{1.5\ \text{mg}}{100\ \text{mL}}\ (8000\ \text{mL}) = 120\ \text{mg}$$

$$\log D_B = -\frac{kt}{2.3} + \log D_B^0$$

$$\log 120 = -\frac{k(6)}{2.3} + \log 200$$

$$k = 0.085\ \text{hr}^{-1}$$

$$t_{1/2} = \frac{0.693}{k} = \frac{0.693}{0.085} = 8.1\ \text{hr}$$

4. A new antibiotic drug was given in a single intravenous bolus of 4 mg/kg to five healthy male adults ranging in age from 23 to 38 years (average weight 75 kg). The pharmacokinetics of the plasma drug concentration-time curve for this drug fits a one-compartment model. The equation of the curve that best fits the data is

$$Cp = 78\ e^{-0.46t}$$

Determine the following (assume units of ug/mL for *C p and hr for t):*

a. What is the $t_{1/2}$

b. What is the V_D

c. What is the plasma level of the drug after 4 hours?

$$C_P = 78e^{-0.46t} \text{ (the equation is in the form } C_P = C_P^0 e^{-kt})$$

$$\ln C_P = \text{In}\,78 - 0.46t$$

$$\log C_P = -\frac{0.46t}{2.3} + \log 78$$

Thus, $k = 0.46\ \text{hr}^{-1}$, $C_P^0 = 78\ \mu\text{g/mL}$.

a. $$t_{1/2} = \frac{0.693}{k} = \frac{0.693}{0.46} = 1.5\ \text{hr}$$

b. $$V_D = \frac{\text{dose}}{C_P^0} = \frac{300{,}000\ \mu\text{g}}{78\ \mu\text{g/mL}} = 3846\ \text{mL}$$

$$\text{Dose} = 4\ \text{mg/kg} \times 75\ \text{kg} = 300\ \text{mg}$$

c. (1) $$\log C_P = -\frac{0.46(4)}{2.3} + \log 78 = 1.092$$

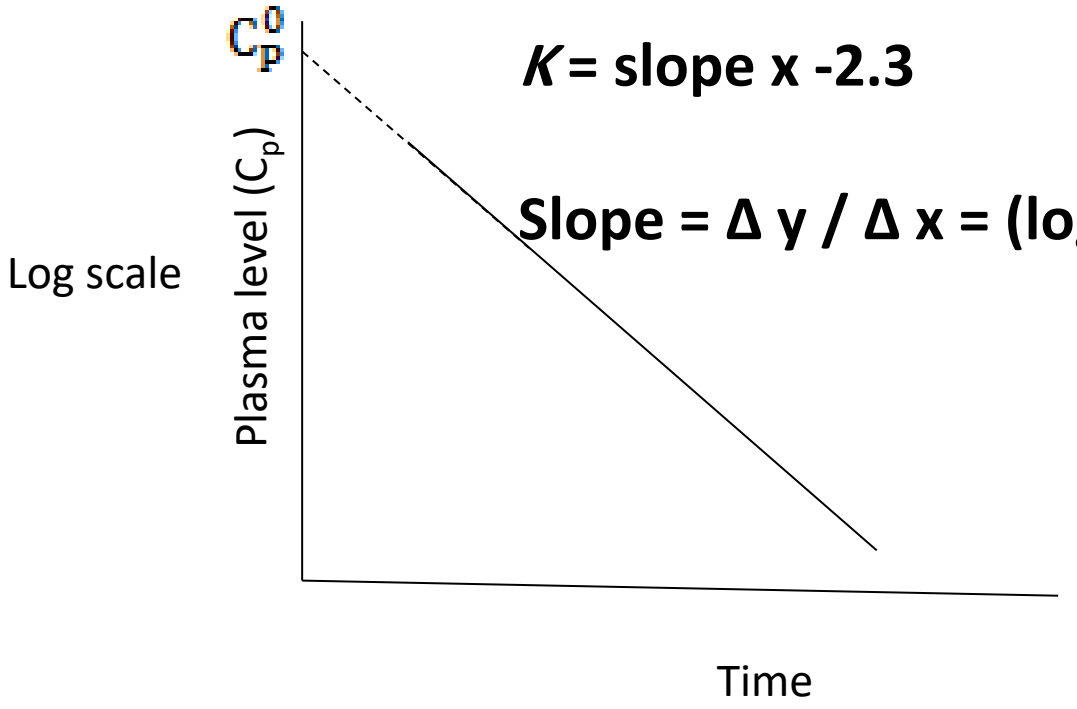
$$C_P = 12.4\ \mu\text{g/mL}$$

(2) $$C_P = 78e^{-0.46(4)} = 78e^{-1.84} = 78(0.165)$$

$$C_P = 12.9\ \mu\text{g/mL}$$

Residual method to calculate area under the curve

For iv one compartment model $[AUC]_0^\infty = \frac{cp_0}{k}$



K **= slope x -2.3**

Slope = Δ y / Δ x = (log Cp_2 – log Cp_1) / (t_2 – t_1)