**Answer to case study 1**

1. You can use Excel or graph paper to plot the Ln(concentration) vs Time, then add the trendline. The slope of the trendline will be \(-Ke\).
   Or, you can use any of the two time points to determine Ke by the equation below:
   \[ Ke = \frac{-(\ln C_1 - \ln C_2)}{(t_1 - t_2)} = 0.004153 /\text{min} \]

   \[ Cp(t) = Cp(0) \cdot \exp(-Ke \cdot t) \]
   \[ Cp(0) = Cp(5) \cdot \exp(Ke \cdot 5) = 32.7 \cdot \exp(0.004153 \cdot 5) = 33.39 \text{mg/L} \]

   By trapezoidal rule,
   \[ AUC(0-5) = \frac{(C_0 + C_5)}{2} \cdot 5 = 165.25 \text{mg min/L} \]
   \[ AUC(5-10) = 161.75 \text{mg min/L} \]
   \[ AUC(10-15) = 158.25 \text{mg min/L} \]
   \[ AUC(15-25) = 306.5 \text{mg min/L} \]
   \[ AUC(25-50) = 713.75 \text{mg min/L} \]
   \[ AUC(50-100) = 1227.5 \text{mg min/L} \]
   \[ AUC(100-150) = 995 \text{mg min/L} \]
   \[ AUC(150-200) = 807.5 \text{mg min/L} \]
   \[ AUC(200-250) = 657.5 \text{mg min/L} \]
   \[ AUC(250-300) = 533.75 \text{mg min/L} \]
   \[ AUC(300-355) = 481.25 \text{mg min/L} \]
   \[ AUC(355-400) = 320.625 \text{mg min/L} \]
   \[ AUC(400-500) = 522.5 \text{mg min/L} \]
   \[ AUC(500-600) = 344.5 \text{mg min/L} \]
   \[ AUC(600-800) = 393 \text{mg min/L} \]
   \[ AUC(800-1000) = 171 \text{mg min/L} \]
   \[ AUC(1000-\text{inf}) = \frac{C_{1000}}{Ke} = 125.2172 \text{mg min/L} \]
   \[ AUC(\text{total}) = 8084.84 \text{mg min/L} \]

2. Small \(V_d\) is due to very large plasma protein binding compared to tissue binding or the inability of a drug to cross membranes. The smallest (theoretical) \(V_d\) is 3L, the volume of plasma in the body.

3. 80\% of plasma protein binding is used for calculation of \(V_d\) of normal people
   \[ V_d = V_p + V_t \cdot Fu/Fu_t \]
   \[ V_d = 3 + 38 \times 0.2/0.7 = 13.86 \text{L (normal patient)} \]
   In patients with chronic liver disease,
   \[ Fu = 1 - 0.8 \times 0.8 = 0.36 \]
   \[ V_d = 3 + 38 \times 0.36/0.7 = 22.54 \text{L} \]