

# Kinetik vid intravenös infusion

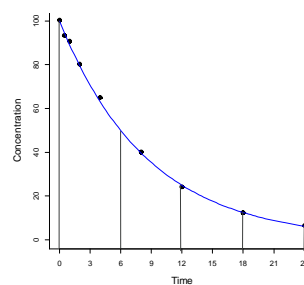
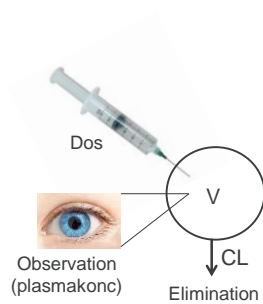
Olof Breuer



Karolinska  
Institutet

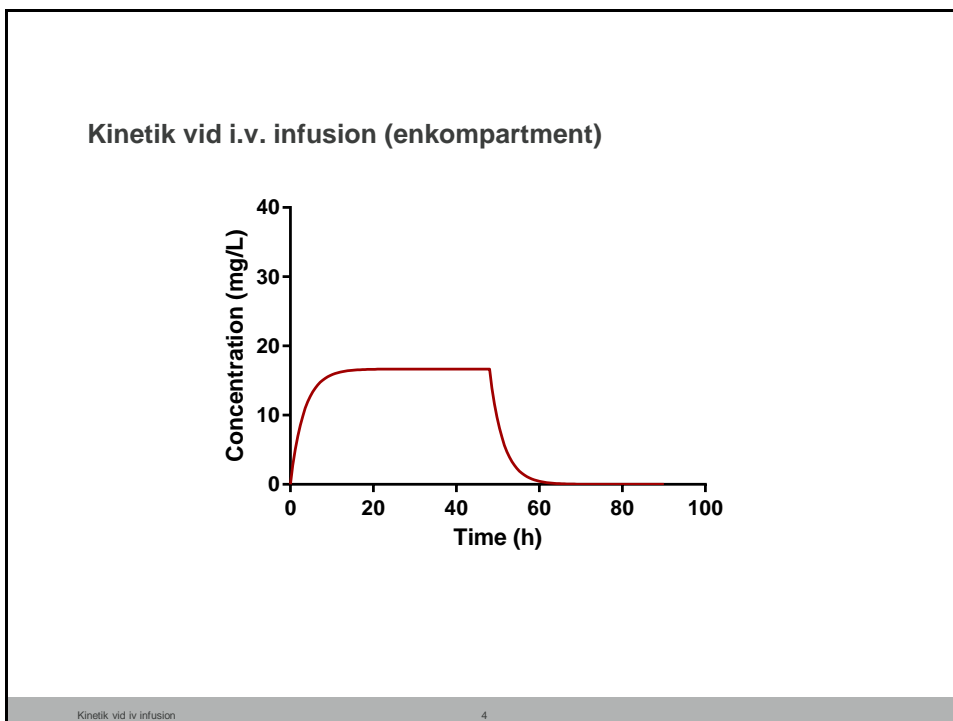
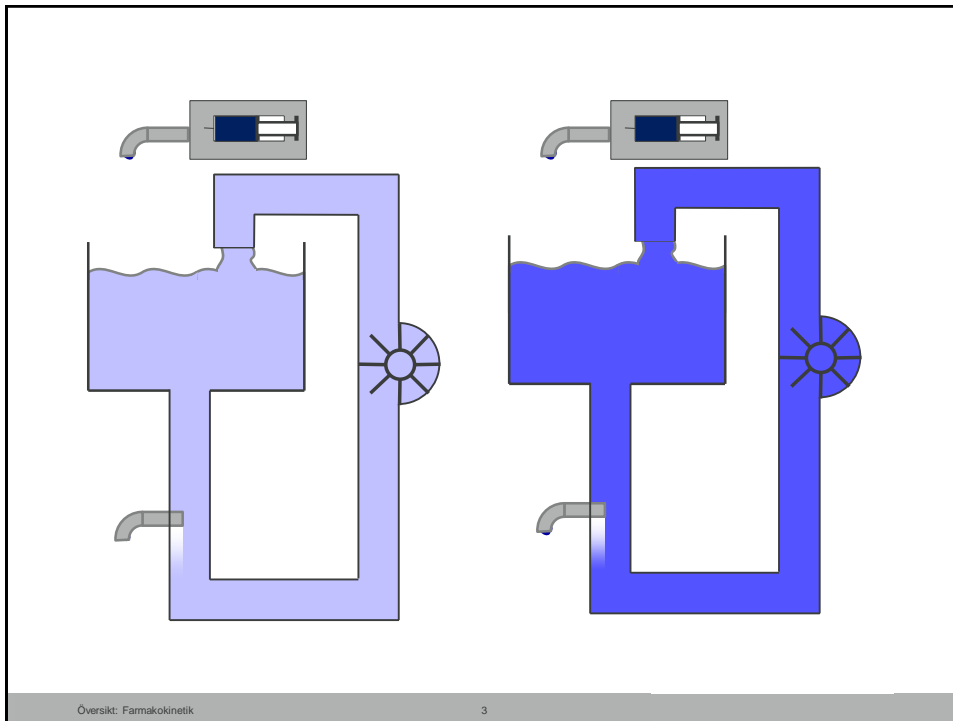
KAROLINSKA  
Universitetssjukhuset

## En-kompartiment-modellen

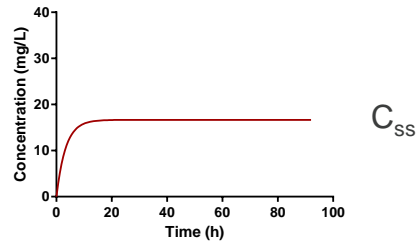


Eliminationshastighet (mg/h) beror av koncentrationen

$$R_{\text{elim}} = CL \times C$$



### Kinetik vid i.v. infusion - jämvikt



Jämvikt: tillförelshastighet = eliminationshastighet

$$R_{inf} = R_{elim}$$

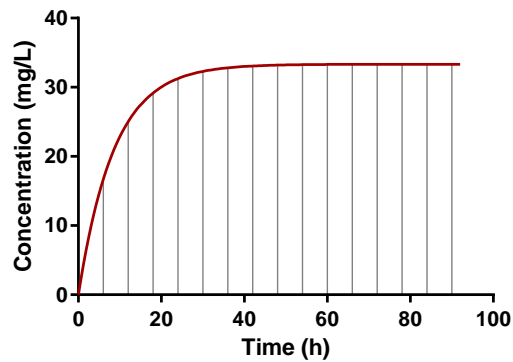
$$R_{inf} = CL \times C_{ss}$$

$$\Leftrightarrow C_{ss} = R_{inf} / CL$$

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### Kinetik vid i.v. infusion – tid till jämvikt är 4 till 5 gånger $t_{1/2}$



$$t_{1/2} \approx 0,693 \times \frac{V_d}{CL}$$

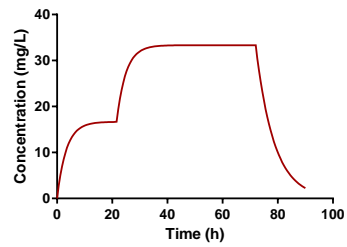
$$t_{ss} \approx 4 \times t_{1/2}$$

Tid till jämvikt ( $t_{ss}$ ) bestäms av både CL och  $V_d$

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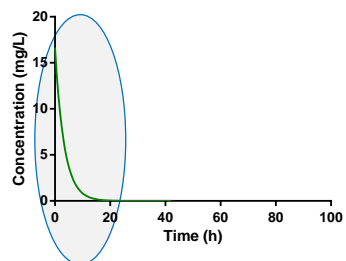
### Vid i.v. infusion – ändrad infusionshastighet



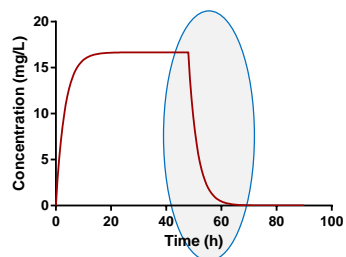
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### Kinetik vid i.v. enkeldos (enkompartiment) - repetition



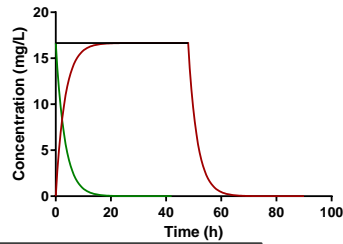
### Kinetik vid i.v. stoppad infusion (enkompartiment)



Kinetik vid iv infusion

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#### Iv. infusion (enkompartiment) – underhålls & laddningsdos



$$R_{inf} = C_{ss} \times CL$$

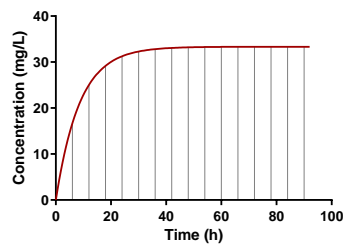
Vi vill nå  $C_{ss}$  från början dvs  $C_0 = C_{ss}$

$$C_0 = D_{bolus} / V_d$$

$$C_0 = C_{ss}$$

$$D_{bolus} = C_{ss} \times V_d$$

#### Kinetik vid i.v. infusion - sammanfattning



Underhållsdos

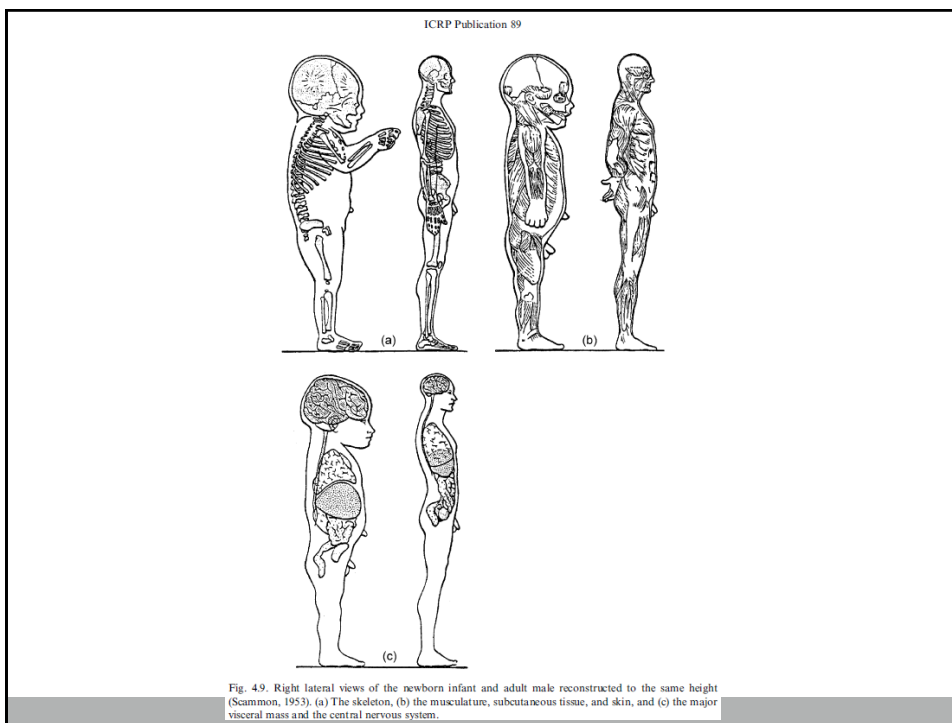
$$R_{inf} = C_{ss} \times CL \quad \text{OBS! } V_d \text{ spelar ingen roll}$$

Laddningsdos

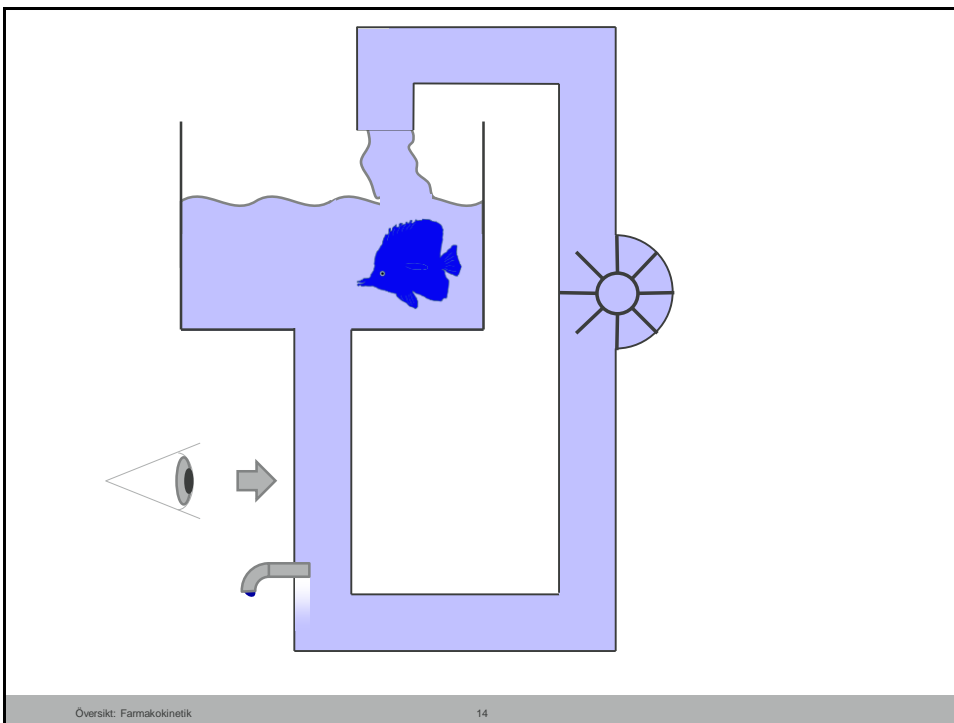
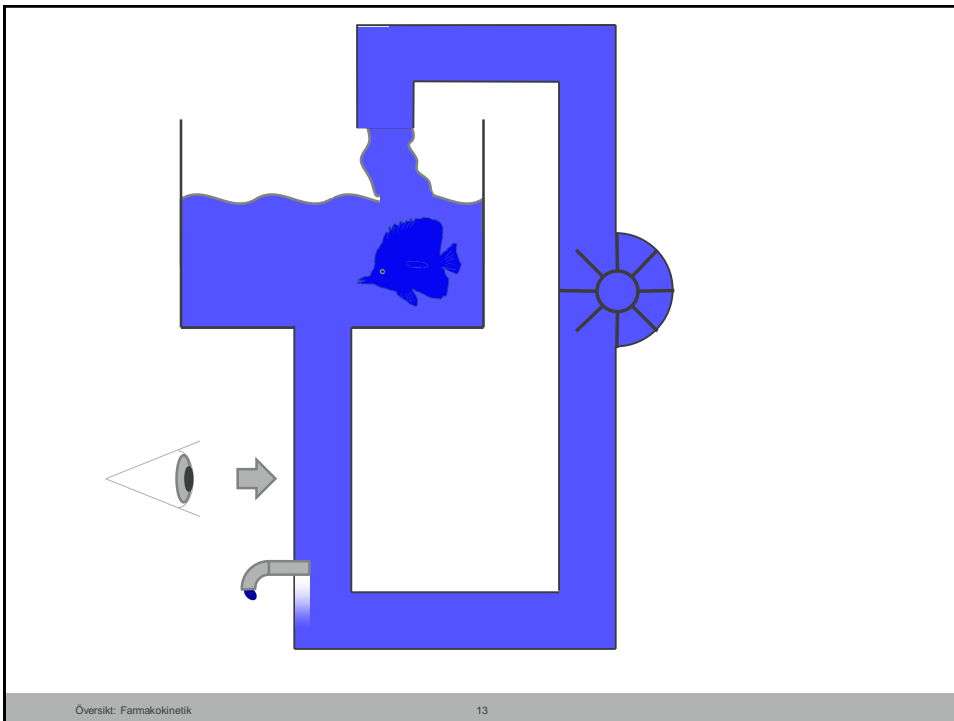
$$D_{bolus} = C_{ss} \times V_d \quad \text{OBS! } CL \text{ spelar ingen roll}$$

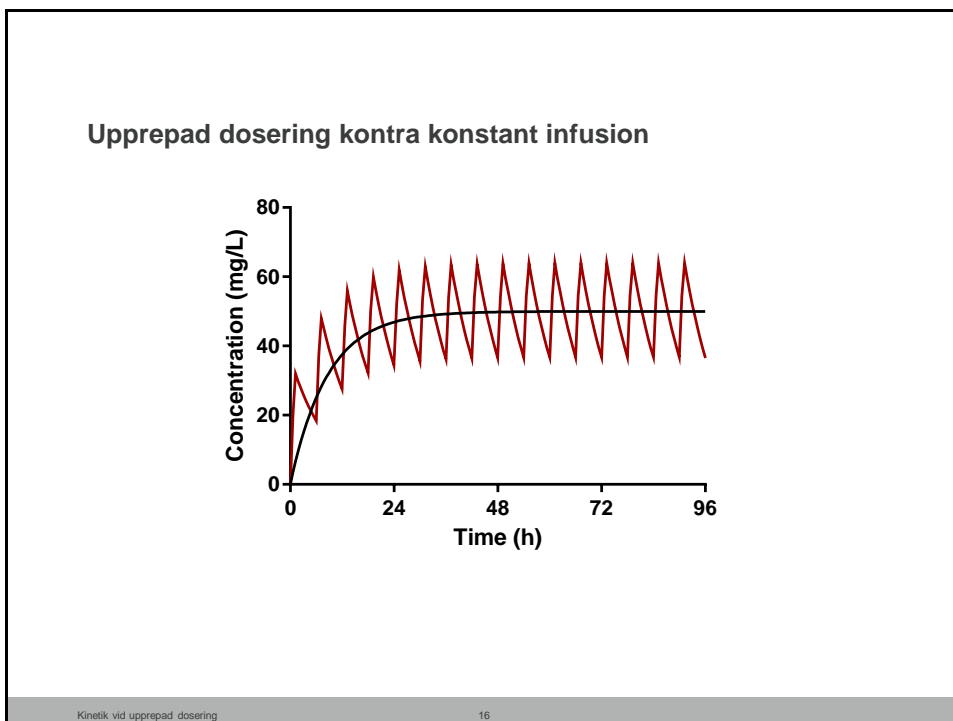
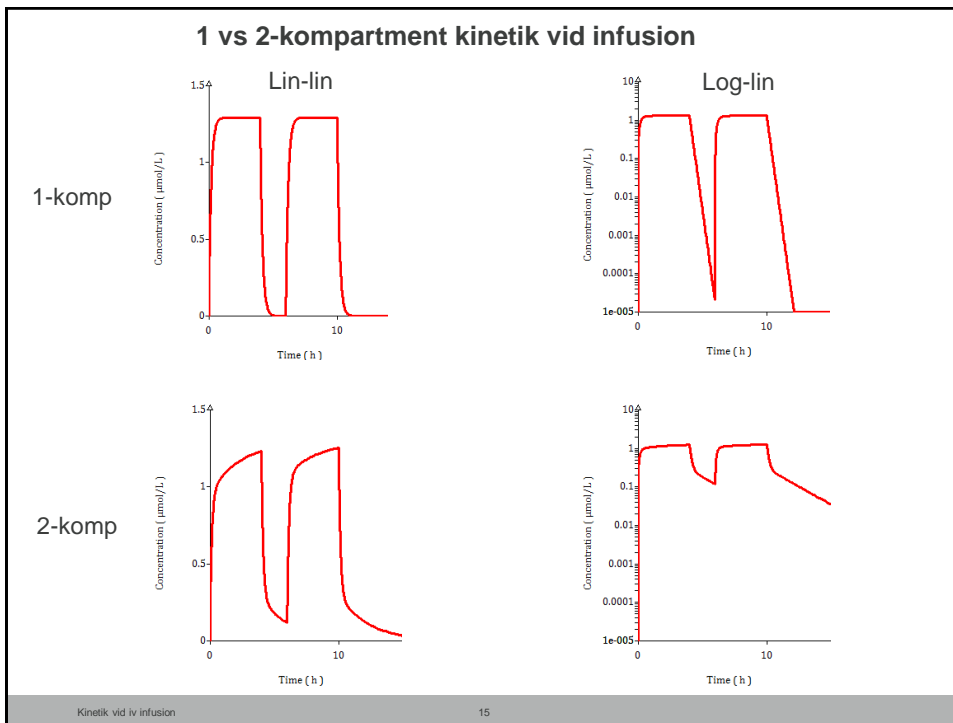
Tid till jämvikt

$$t_{ss} = 4 \text{ till } 5 \times t_{1/2} \quad \text{där } t_{1/2} = 0,693 \times V_d / CL$$



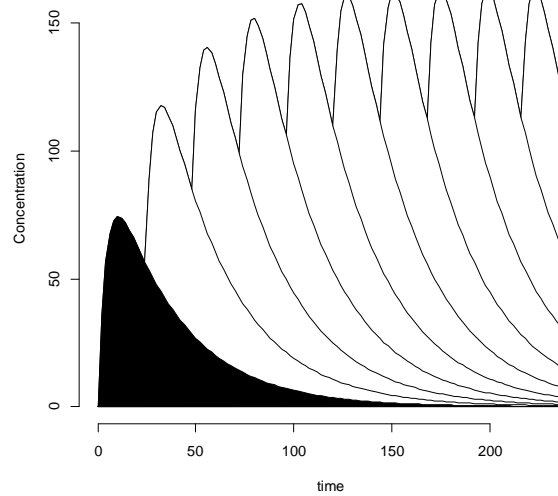
Drug	Average Dose				Primary Determinants of Difference in Age-Related Doses
	Neonates	Infants	Children	Adults	
Gentamicin	2.5 mg/kg every 12 hr	2.5 mg/kg every 6–8 hr	2.5 mg/kg every 8 hr	1–2 mg/kg every 8 hr	Pharmacokinetic: apparent renal clearance and apparent volume of distribution
Ceftazidime	50 mg/kg every 12 hr	50 mg/kg every 8 hr	50 mg/kg every 8 hr	14–28 mg/kg every 8–12 hr	Pharmacokinetic: apparent renal clearance and apparent volume of distribution
Clindamycin	15 mg/kg every 8 hr	10 mg/kg every 6–8 hr	10 mg/kg every 6–8 hr	8–12 mg/kg every 8–12 hr	Pharmacokinetic: apparent hepatic clearance
Carbamazepine	Not established	3–10 mg/kg every 8 hr	3–10 mg/kg every 8 hr	5–8 mg/kg every 12 hr	Pharmacokinetic: apparent hepatic clearance
Phenytoin	2.5–4.0 mg/kg every 12 hr	2–3 mg/kg every 8 hr	2.3–2.6 mg/kg every 8 hr	2 mg/kg every 12 hr	Pharmacokinetic: apparent hepatic clearance
Phenobarbital	3–4 mg/kg every 24 hr	2.5–3.0 mg/kg every 12 hr	2–4 mg/kg every 12 hr	0.5–1.0 mg/kg every 12 hr	Pharmacokinetic: apparent hepatic clearance, followed by apparent volume of distribution
Theophylline	0.5 mg/kg/hr	0.6–0.7 mg/kg/hr	1.0–1.2 mg/kg/hr	0.5–0.7 mg/kg/hr	Pharmacokinetic: apparent hepatic clearance
Digoxin	4–8 μg/kg every 24 hr	7.5–12.0 μg/kg every 24 hr	3–8 μg/kg every 24 hr	1.4–4.0 μg/kg every 24 hr	Pharmacokinetic (apparent renal clearance followed by apparent volume of distribution) and pharmacodynamic
Captopril†	0.01–0.05 mg/kg every 8–12 hr	0.15–0.3 mg/kg every 8–12 hr	0.2–0.4 mg/kg every 12–24 hr	0.2–0.4 mg/kg every 8–12 hr	Pharmacokinetic: apparent hepatic clearance
Ranitidine	0.75–1.0 mg/kg every 12 hr	0.75–1.0 mg/kg every 12 hr	1 mg/kg every 6–12 hr	0.7 mg/kg every 6–8 hr	Pharmacokinetic: apparent renal clearance, followed by apparent volume of distribution







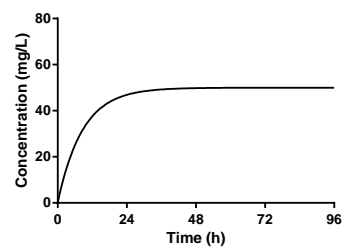
## Superpositionsprincipen (summering)



NCA-lathund

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## Kinetik vid konstant infusion – jämviktskoncentration

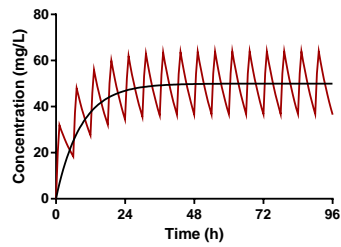


$$C_{ss} = R_{inf} / CL$$

Kinetik vid upprepad dosering

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### Kinetik vid upprepad dosering – jämviktskoncentration

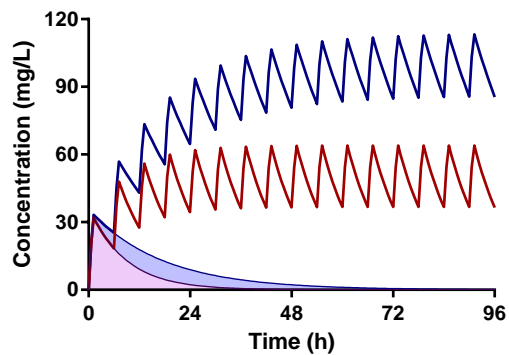


$$(C_{ss} = R_{inf} / CL)$$

$$C_{medel, ss} = \frac{D}{\tau \times CL}$$

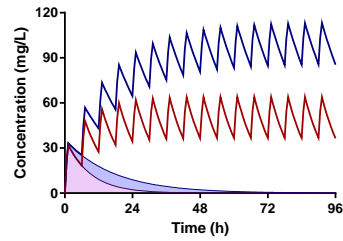
där  $\tau$  är dosintervall

### Upprepad dosering vid olika clearance men samma $V_d$



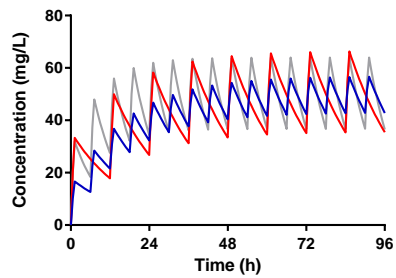
Olika  $C_{medel, ss}$

### Dosanpassning vid förändrat clearance



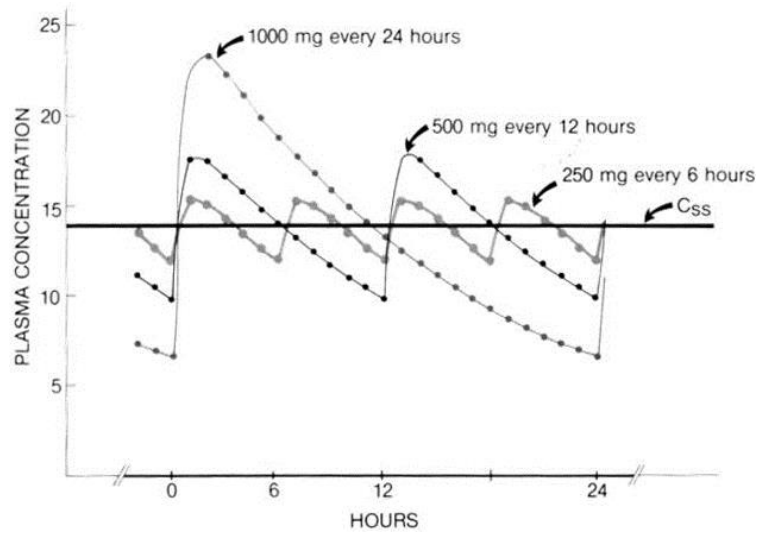
$$C_{medel, ss} = \frac{D}{\tau \times CL}$$

### Dosanpassning vid förändrat clearance



$$C_{medel, ss} = \frac{D}{\tau \times CL}$$

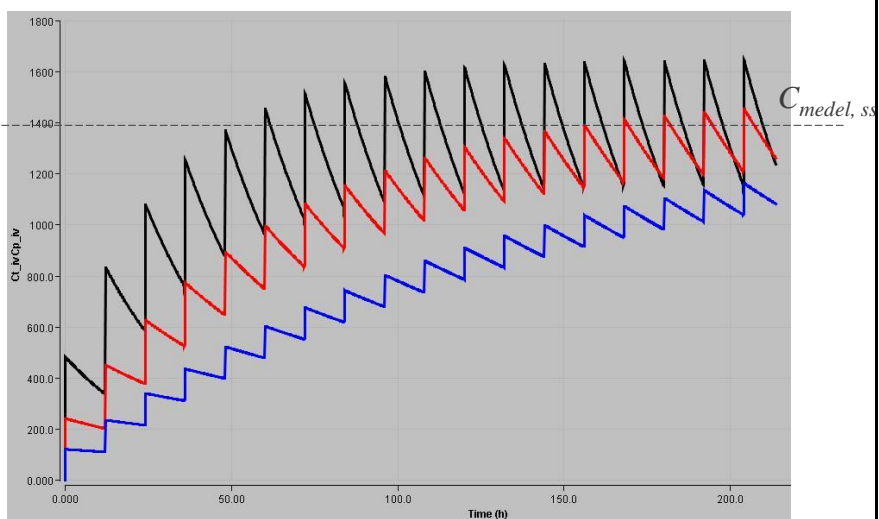
### Farmakokinetiska konsekvenser av olika doseringsregimer



Kinetik vid upprepad dosering

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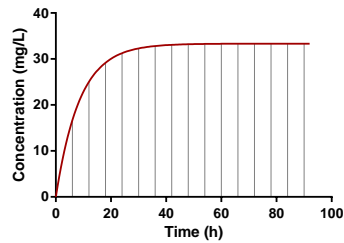
### Olika $V_d$ men samma CL: Amplituden och tid till jämvikt ändras men ej $C_{medel,ss}$



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### Take home message – underhåll och laddning



Underhållsdos

$$R_{inf} = C_{ss} \times CL$$

$$D / \tau = C_{medel,ss} \times CL$$

**OBS!  $V_d$  spelar ingen roll**

Laddningsdos

$$D_{bolus} = C_{ss} \times V_d$$

**OBS!  $CL$  spelar ingen roll**

Tid till jämvikt

$$t_{ss} = 4 \text{ till } 5 \times t_{1/2} \quad \text{där} \quad t_{1/2} = 0,693 \times V_d / CL$$