1. LÉKAŘSKÁ FAKULTA
Univerzita Karlova

VFN PRAHA
VŠEOBECNÁ FAKULTNÍ NEMOCNICE

Farmakokinetika/farmakodynamika

Ondřej Slanař

Farmakologický ústav 1. LF UK a VFN

Univerzita Karlova

Farmakokinetika/farmakodynamika PK/PD

farmakodynamika (FD):

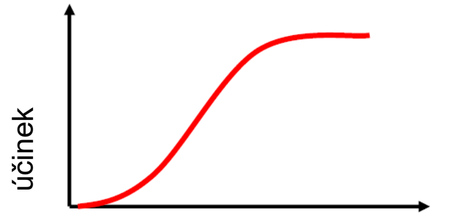
popisuje mechanismus účinku farmak, v širším smyslu veškeré jejich účinky;

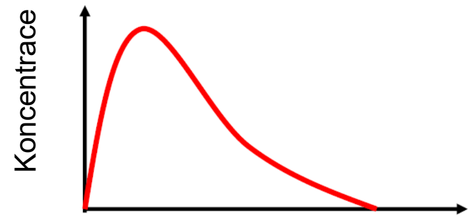
působení farmaka na organismus

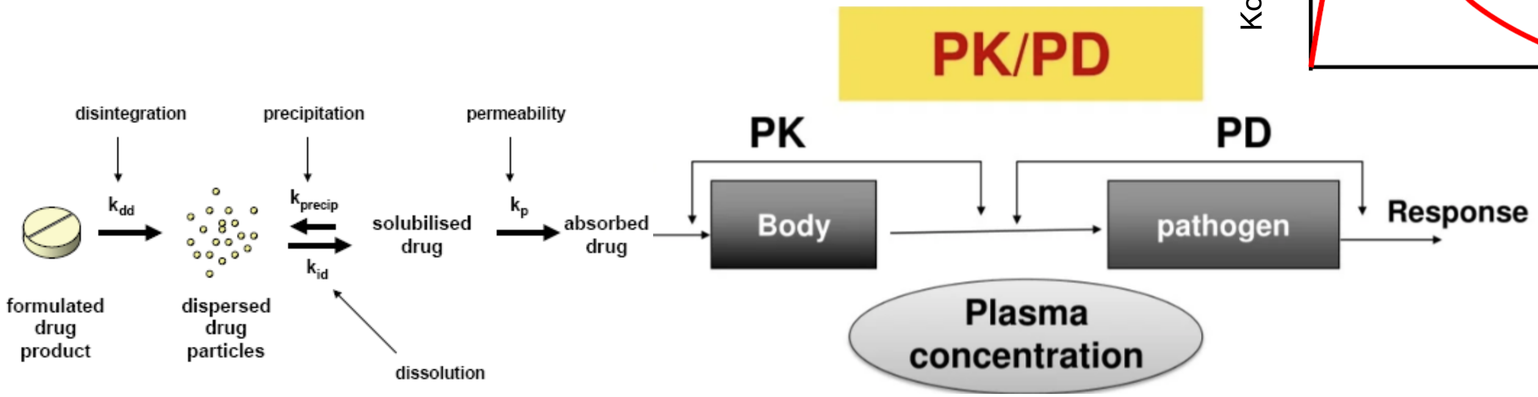
farmakokinetika (FK):

popisuje pohyb léčiva v organizmu;

působení organismu na farmakum







Farmakokinetika/farmakodynamika PK/PD

$$Vd = \frac{D}{k_e \cdot T} \cdot \frac{\left(1 - e^{-k_e \cdot T}\right)}{C_{max} - C_{min} \cdot e^{-k_e \cdot T}}$$

$$CL = \frac{2 \cdot k_0}{(C_1 + C_2)} + \frac{2 \cdot Vd \cdot (C_1 - C_2)}{(C_1 + C_2) \cdot (t_2 - t_1)}$$

$$Cn(t) = \frac{D}{V} \cdot \frac{\left(1 - e^{-nk_e\tau}\right)}{\left(1 - e^{-k_e\tau}\right)} \cdot e^{-k_e t}$$

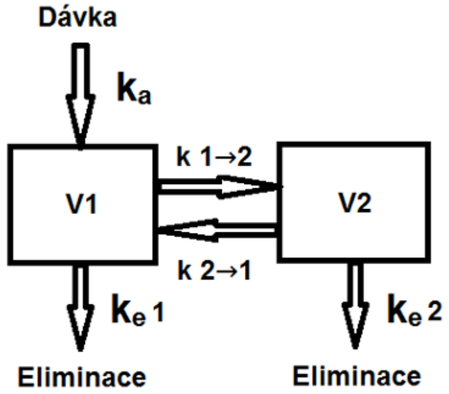
$$C = \frac{F \cdot D \cdot k_a}{Vd(k_a - k_e)} \cdot \left(\frac{e^{-k_e \cdot t}}{\left(1 - e^{-k_e \cdot \tau}\right)} - \frac{e^{-k_a \cdot t}}{\left(1 - e^{-k_a \cdot \tau}\right)} \right)$$

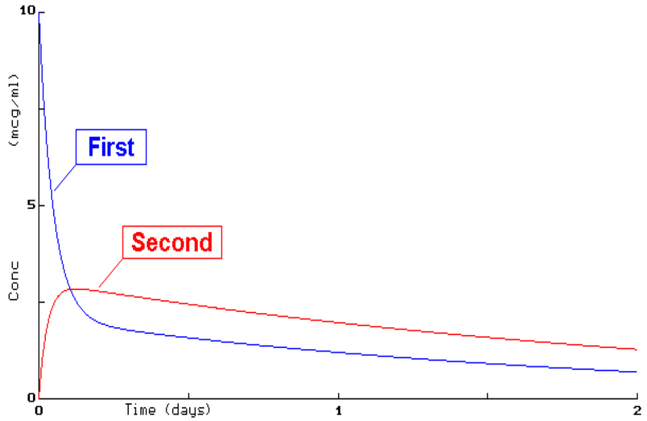
$$Cpss = \frac{D}{Vk_eT} = \frac{k_0}{Vk_e} = \frac{k_0}{CL}$$

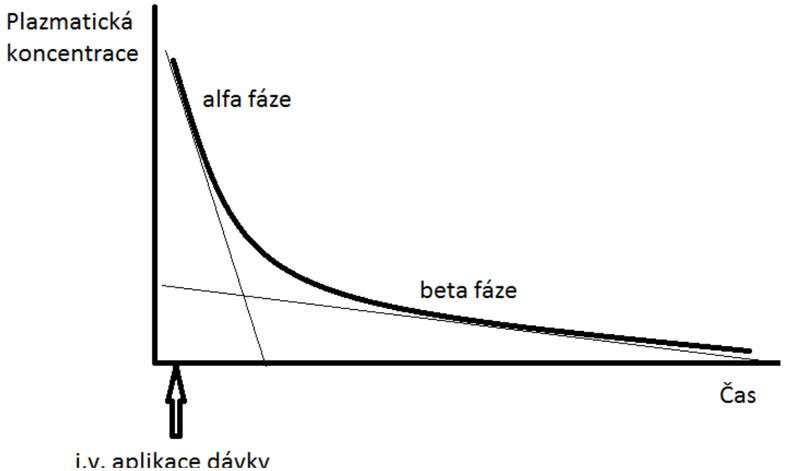
$$C = \frac{F \cdot D \cdot k_a}{V(k_a - k_e)} \cdot \left[\frac{e^{-k_e t}}{\left(1 - e^{-k_e\tau}\right)} - \frac{e^{-k_a t}}{\left(1 - e^{-k_a\tau}\right)} \right]$$

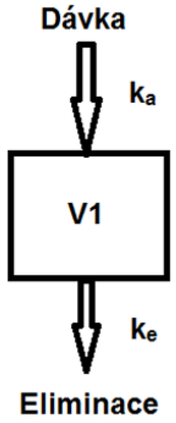
$$t_{max} = \ln\left[\frac{k_a \cdot \left(1 - e^{-k_e\tau}\right)}{k_e \cdot \left(1 - e^{-k_a\tau}\right)} \right] \cdot \frac{1}{(k_a - k_e)}$$

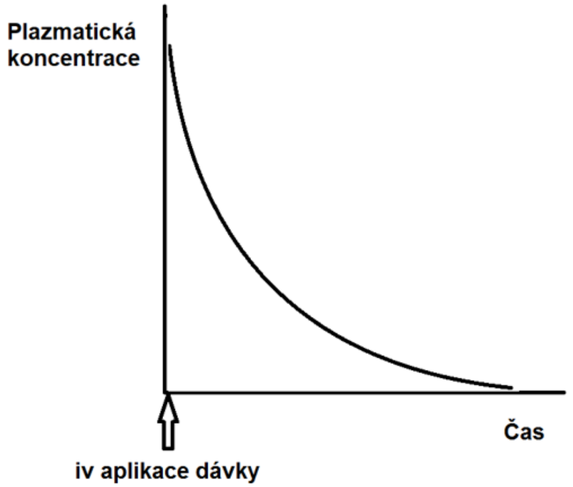
FK principy


Dávka
ka
V1
k 1→2
k 2→1
V2
ke 1
ke 2
Eliminace
Eliminace

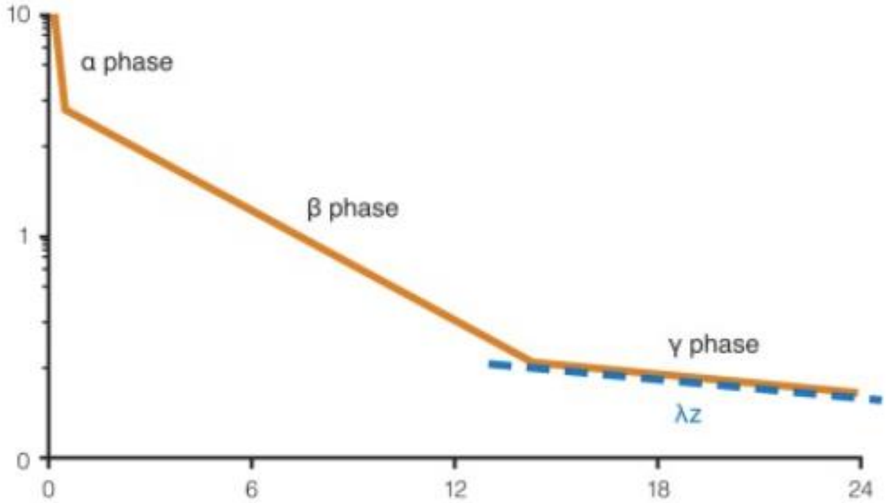

10
5
0
(mcg/ml)
Conc
First
Second
0
Time (days)
1
2

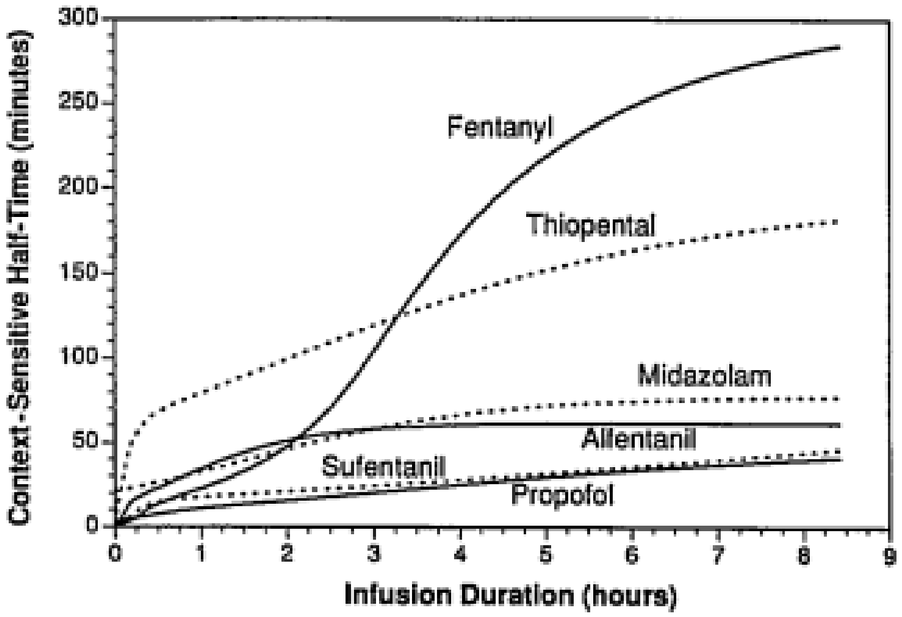

Plazmatická koncentrace
alfa fáze
beta fáze
Čas
i.v. aplikace dávky

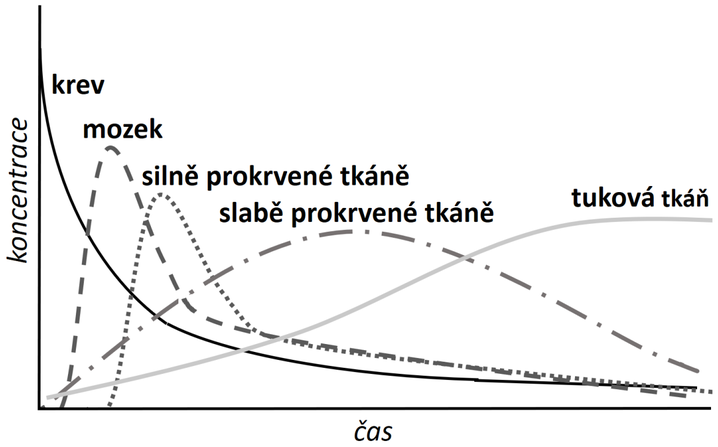

Dávka
ka
V1
ke
Eliminace


Plazmatická koncentrace
Čas
iv aplikace dávky

Context-sensitive half-life



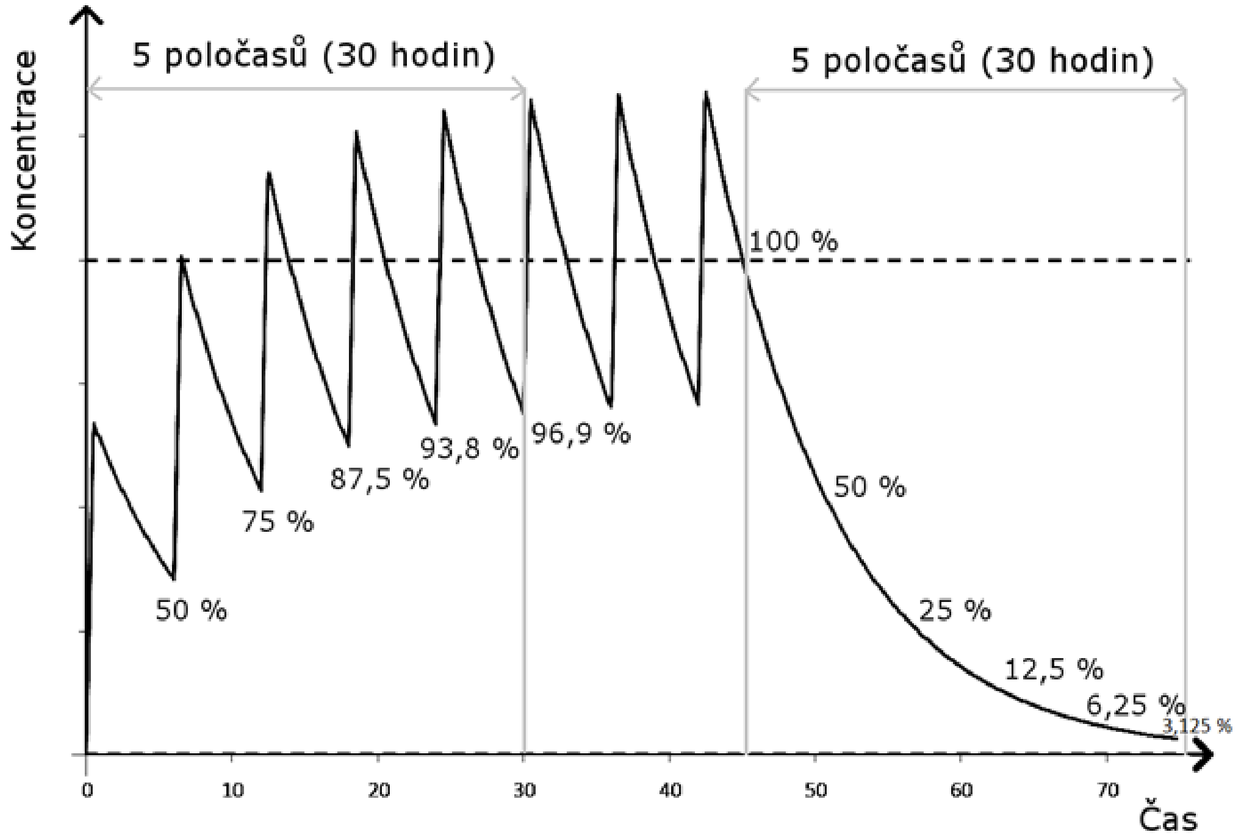




Hartinger, Šíma, Slanař. Grada 2026

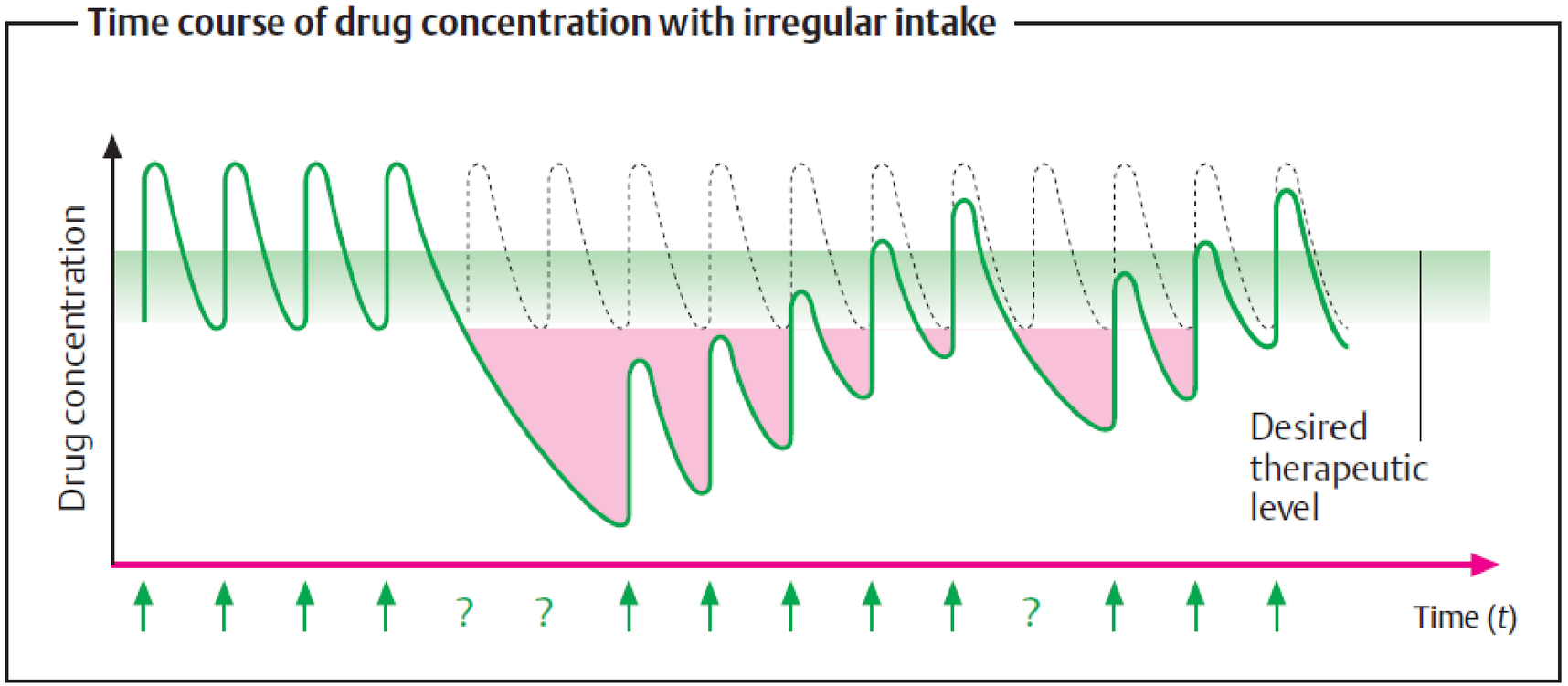
Anesthesiology 76:334-341, 1992

Predikční význam poločasu



Průběh Cpl při vynechání dávky

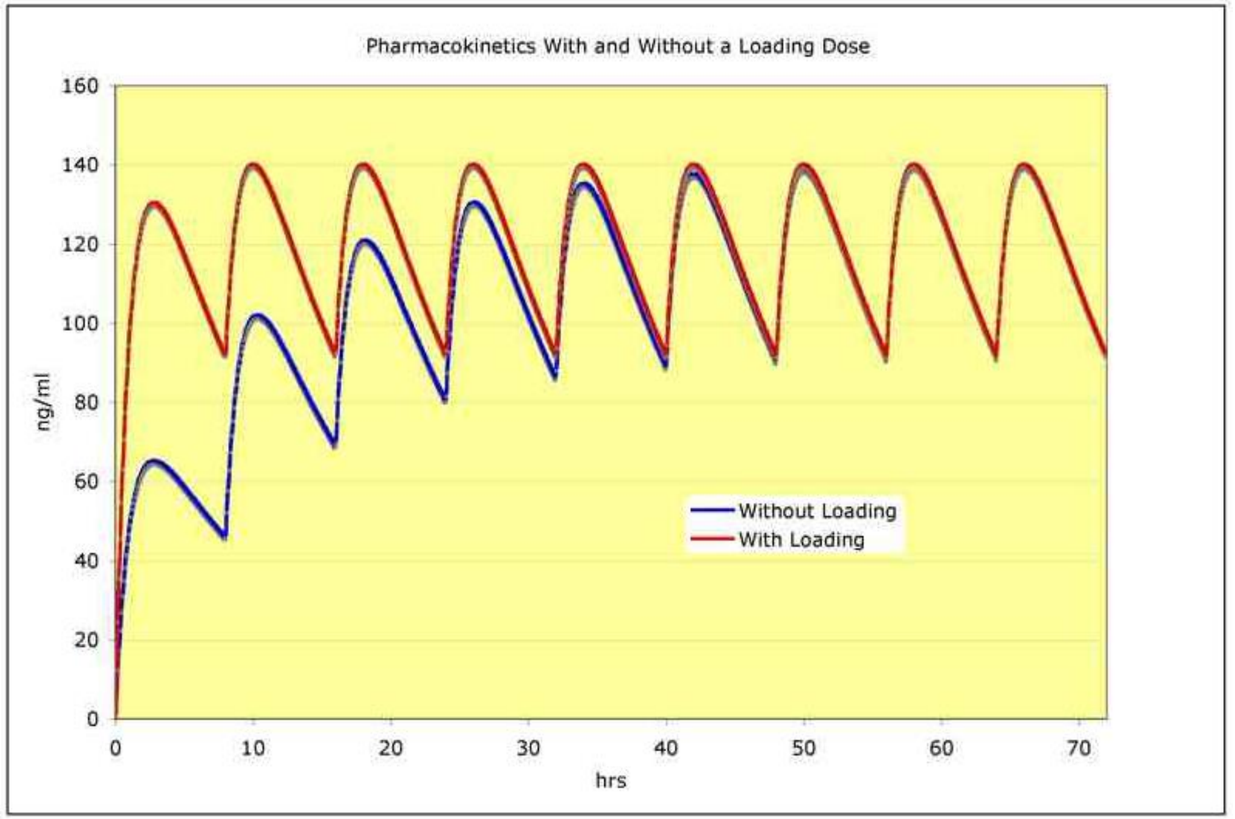
Při vynechání, nebo změně dávky trvá opět 4-5 T1/2 než se navodí Css



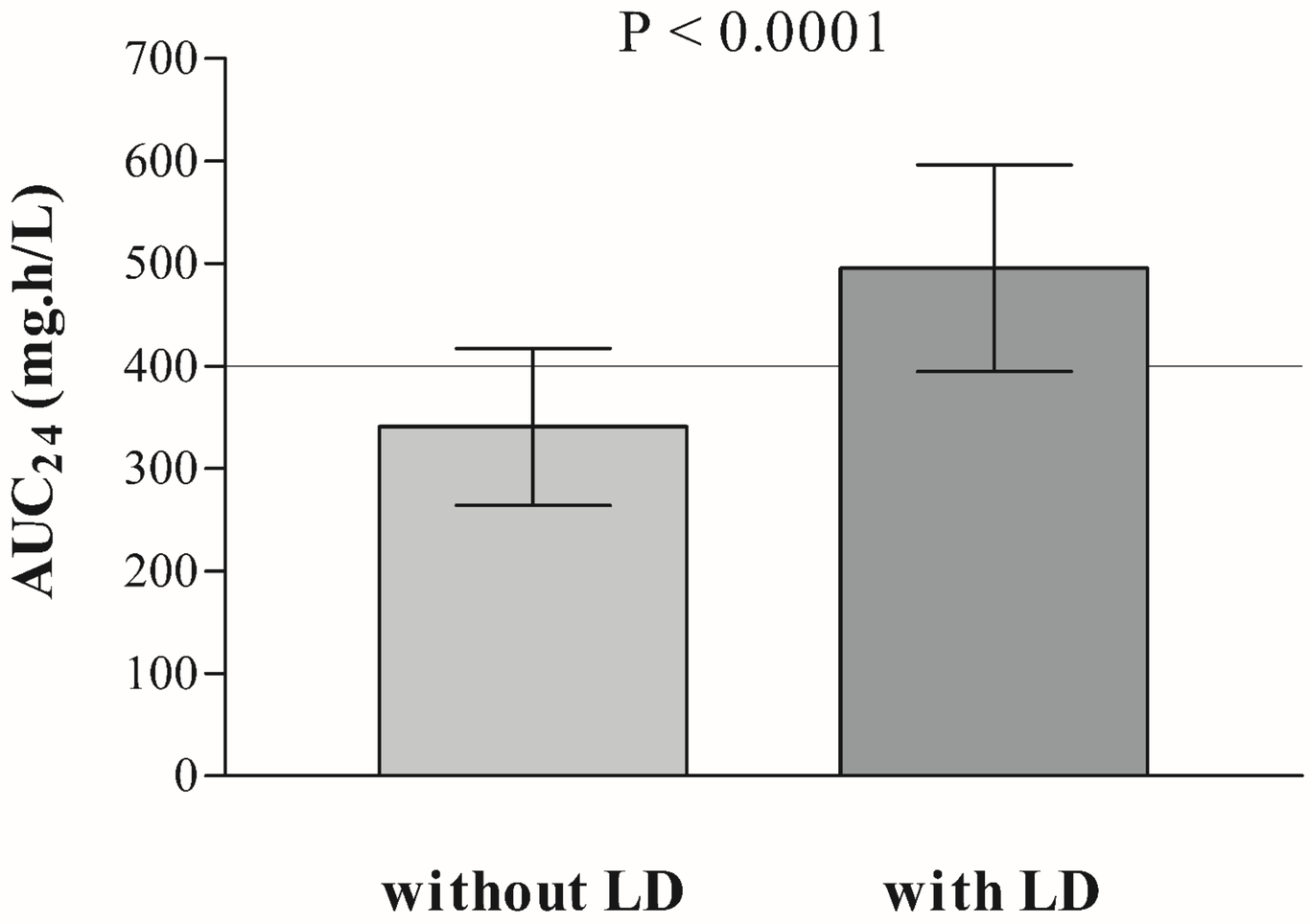
Luellmann, Color Atlas of Pharmacology © 2005 Thieme

Nasycovací dávka

LD (loading dose) = Vd * Cpl (žádaná terapeutická koncentrace)

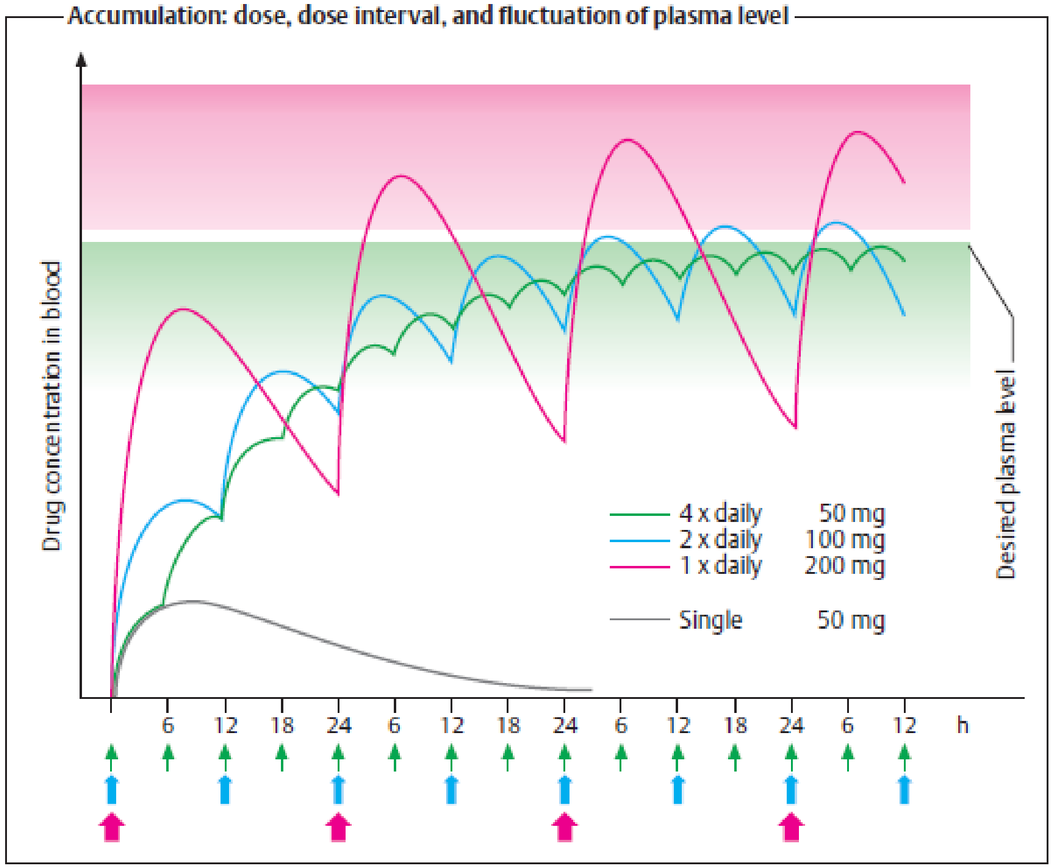


Loading Dose - vancomycin



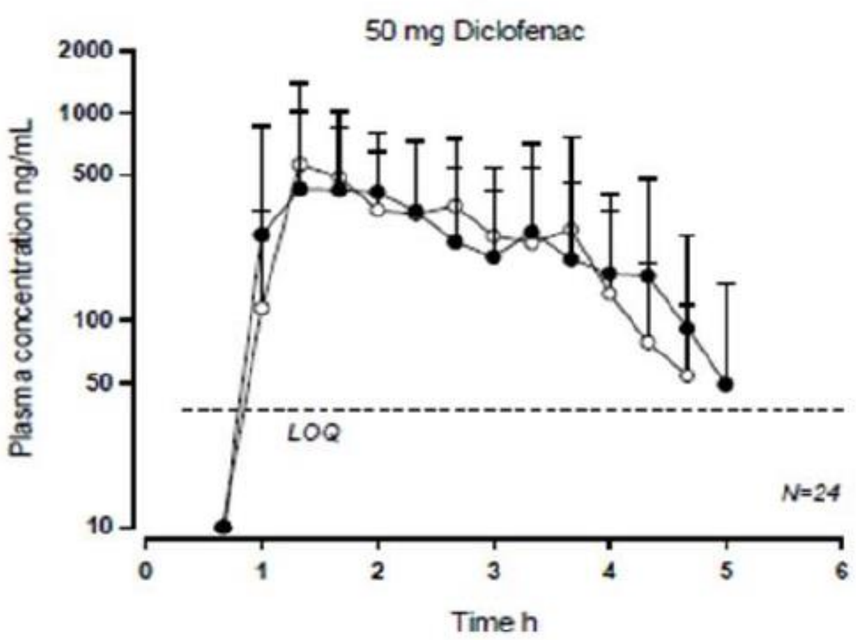
Importance of vancomycin loading doses in intermittent infusion regimens. J Infect Chemother 2018;24(4):247-250.

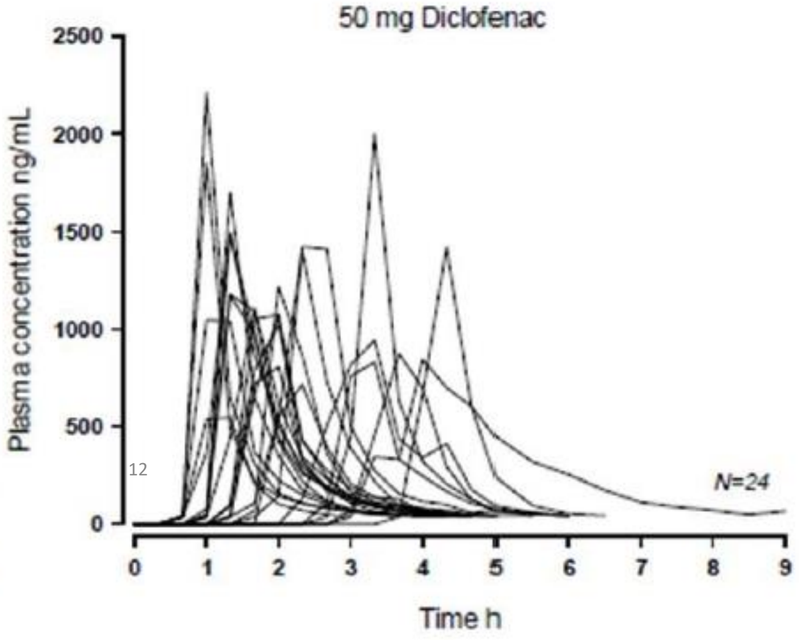
Vliv dávek a dávkovacího intervalu na průběh plazmatických hladin léčiva



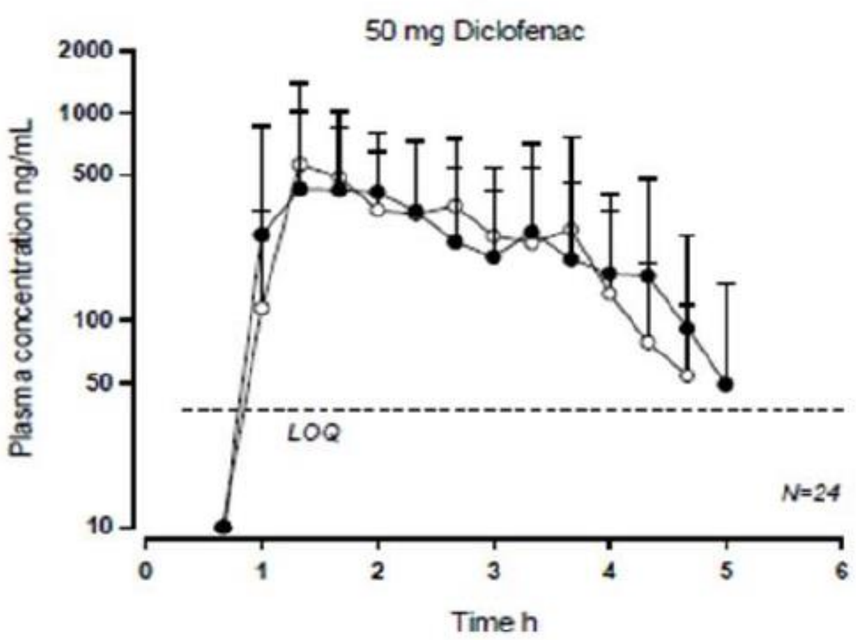
Luellmann, Color Atlas of Pharmacology © 2005 Thieme

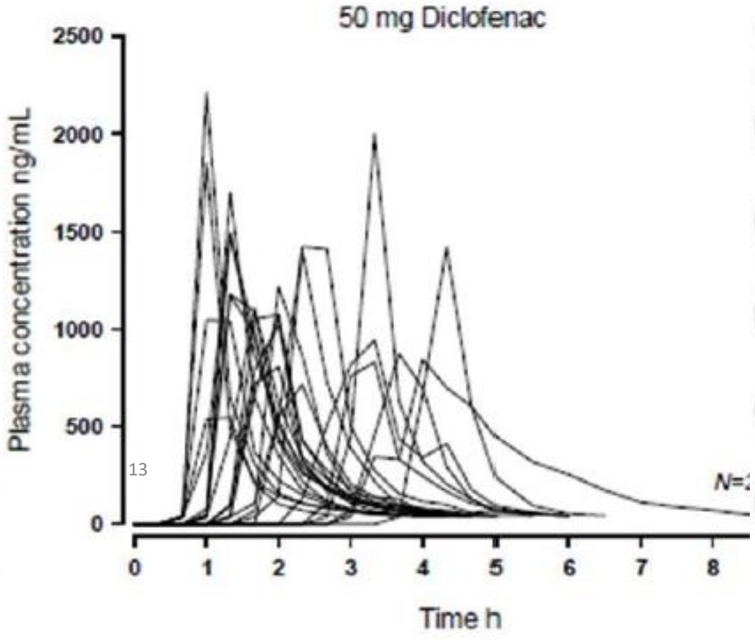
Variabilita PK – absorpce

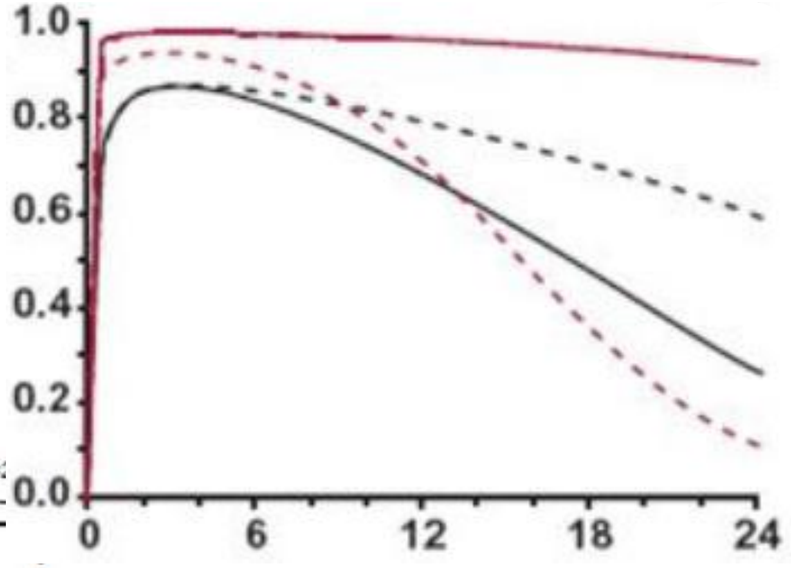




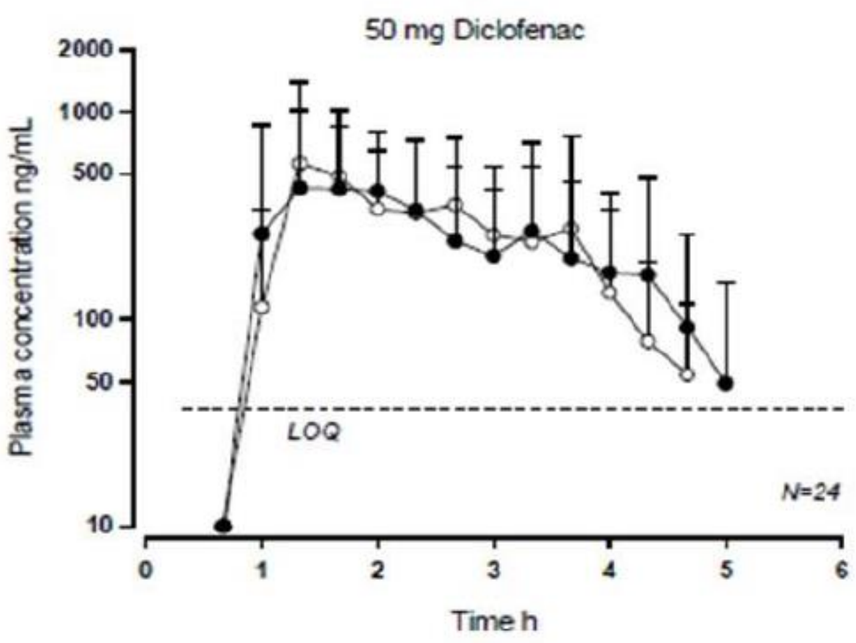
Variabilita PK – absorpce - eliminace

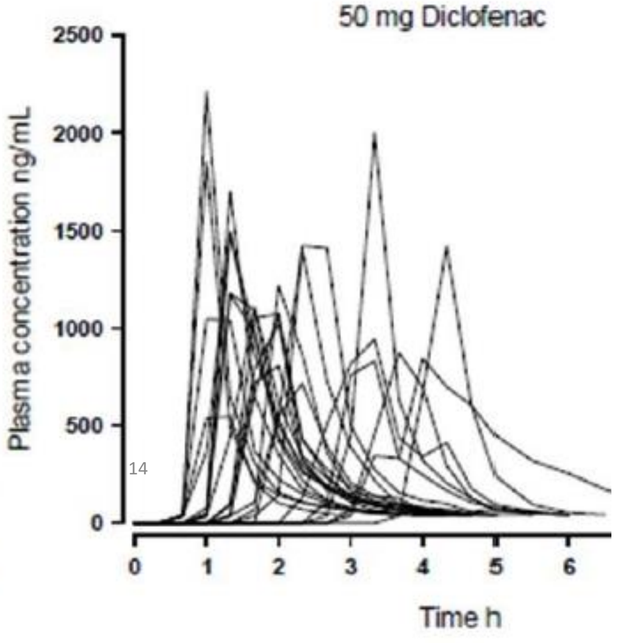


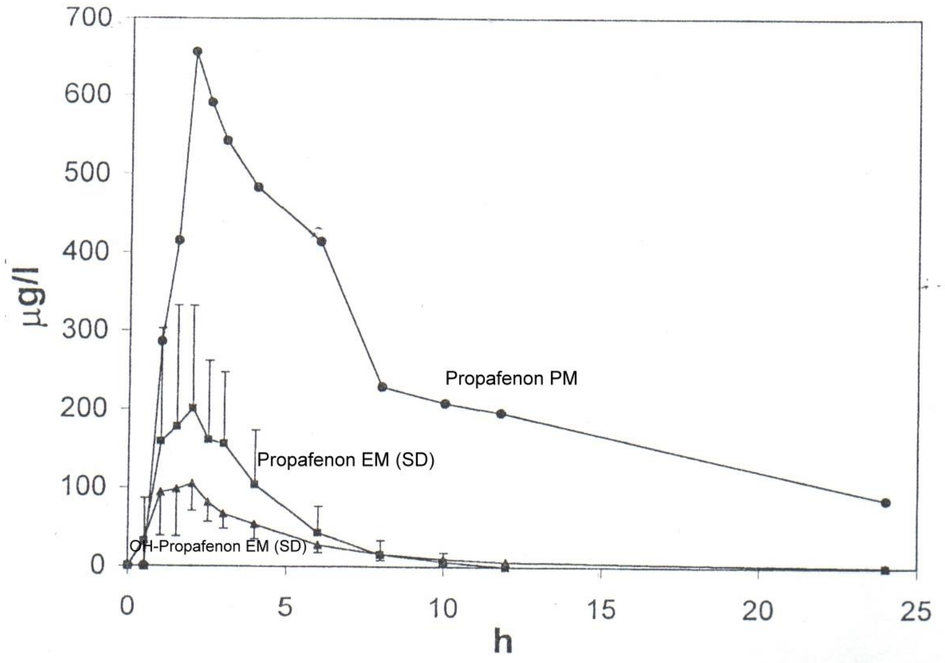




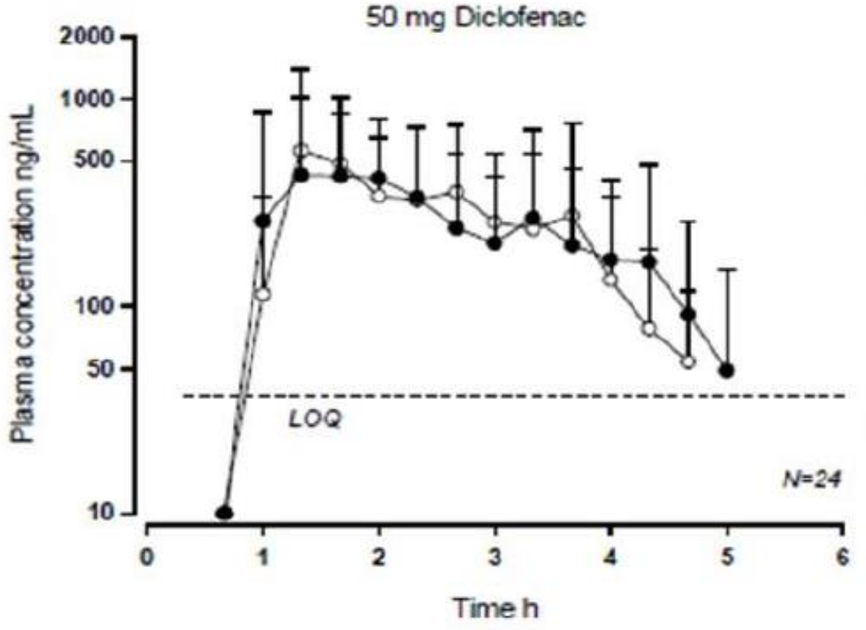
Variabilita PK – absorpce - eliminace

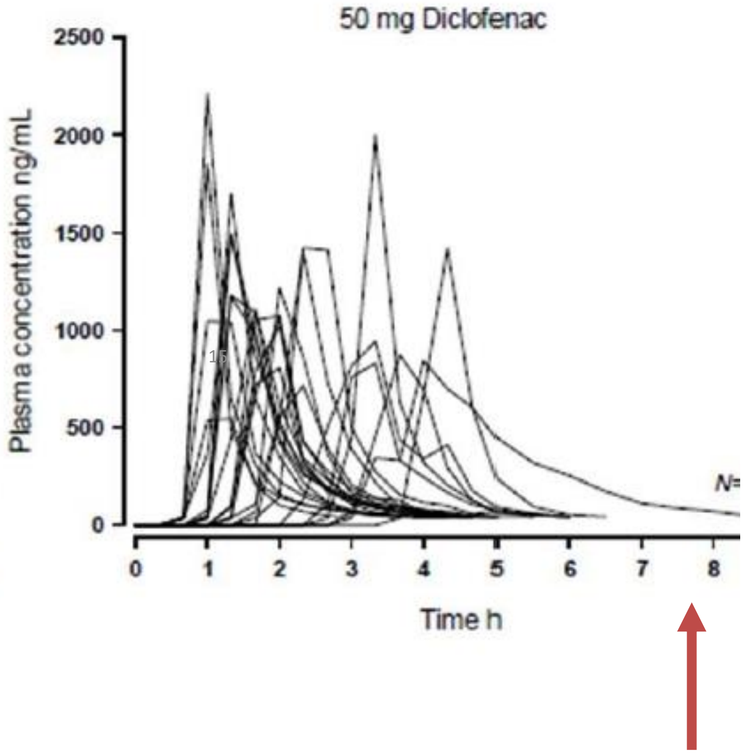


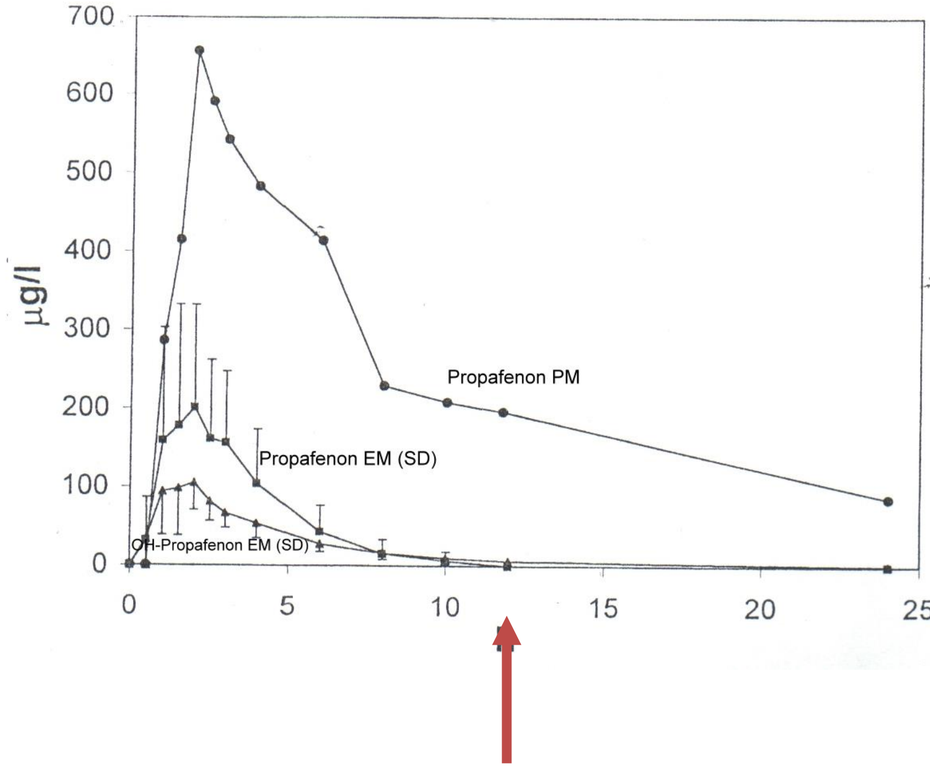




Jaké sledovat hladiny
Variabilita PK – absorpce - eliminace

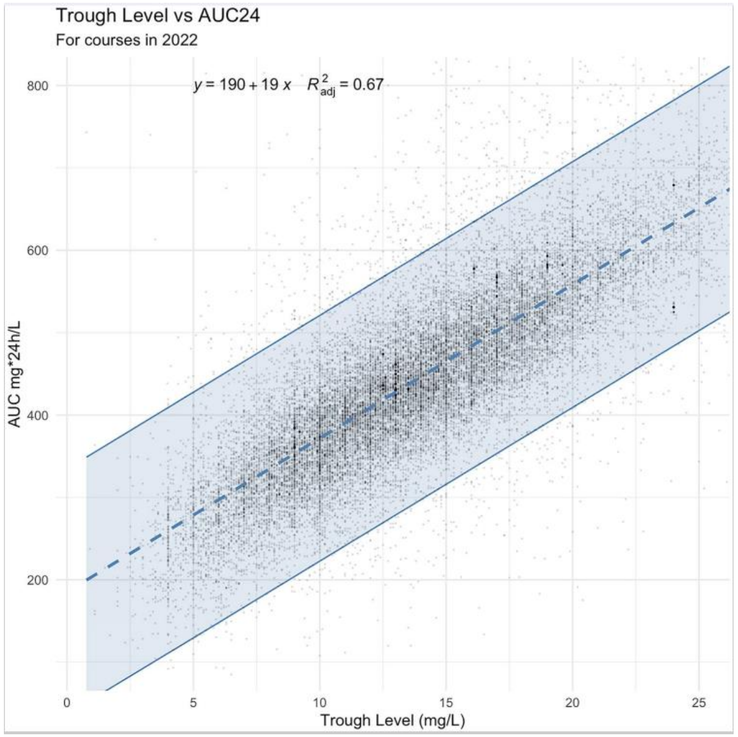






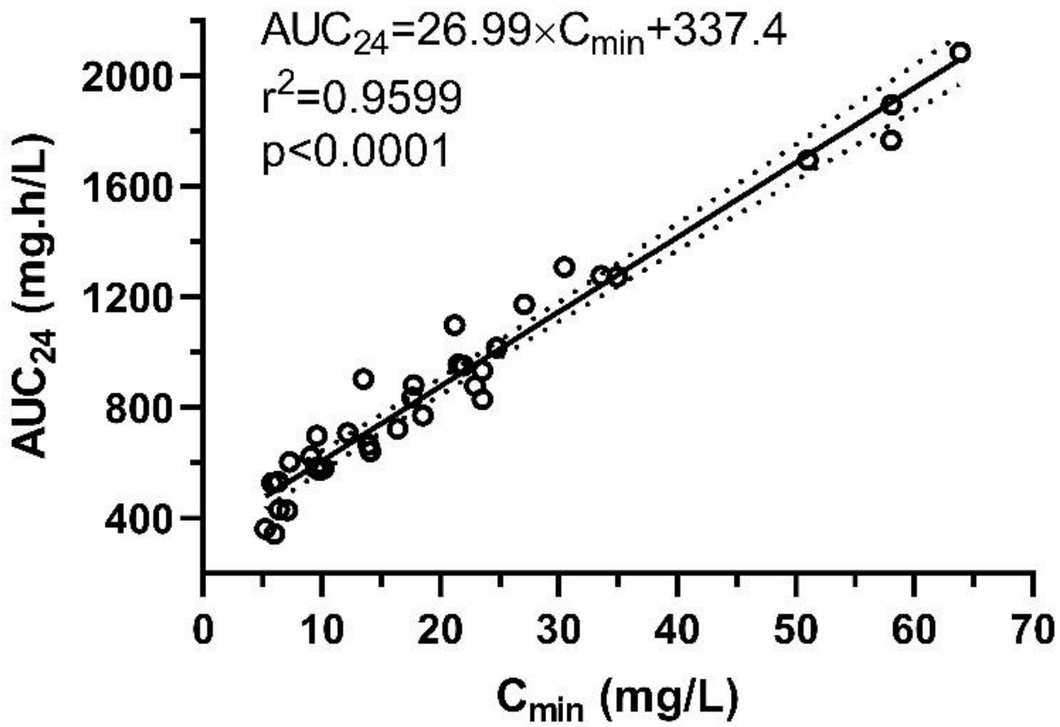
Jaké sledovat hladiny?
Vztah C_{trough} a AUC_{0-24}

Vancomycin



Shiau et al 2025

Daptomycin



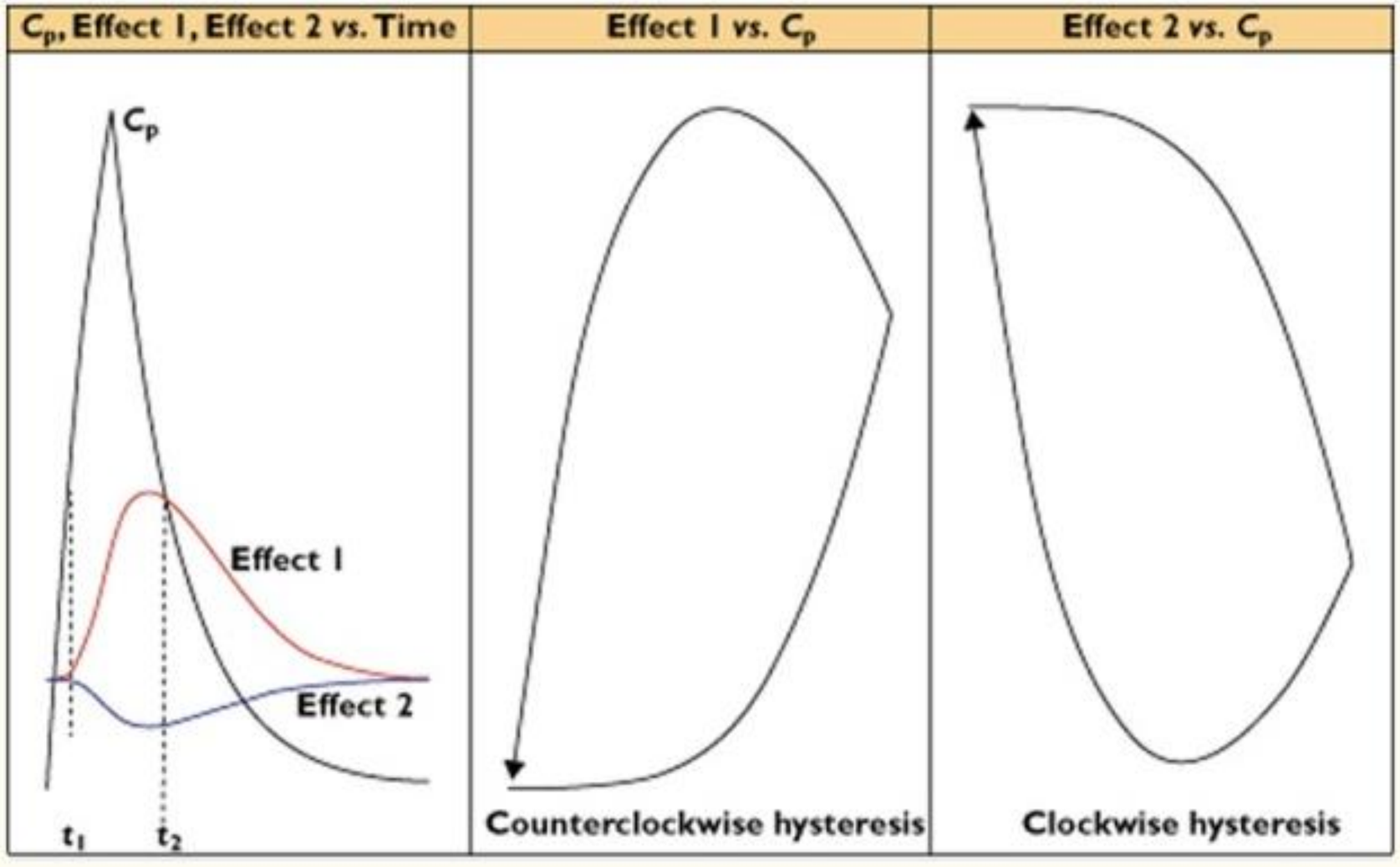
Šubrtová et al. v recenzmím řízení

Populační PK modely

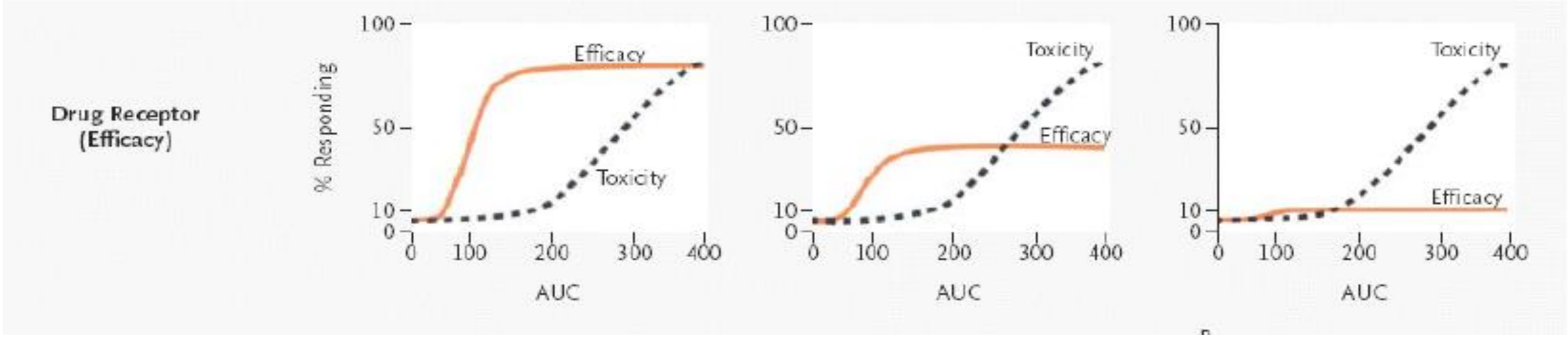
- popisují variabilitu farmakokinetiky léčiva v populaci pacientů
- kvantifikuje různé zdroje variability v koncentracích léčiva
- umožňuje analyzovat řídce vzorkovaná data

- Kvalitně sestavené modely mohou být věrohodnou predikční matricí pro optimalizaci dávkování na podkladě sporadicky ověřených koncentrací

Časový průběh koncentrací a účinku

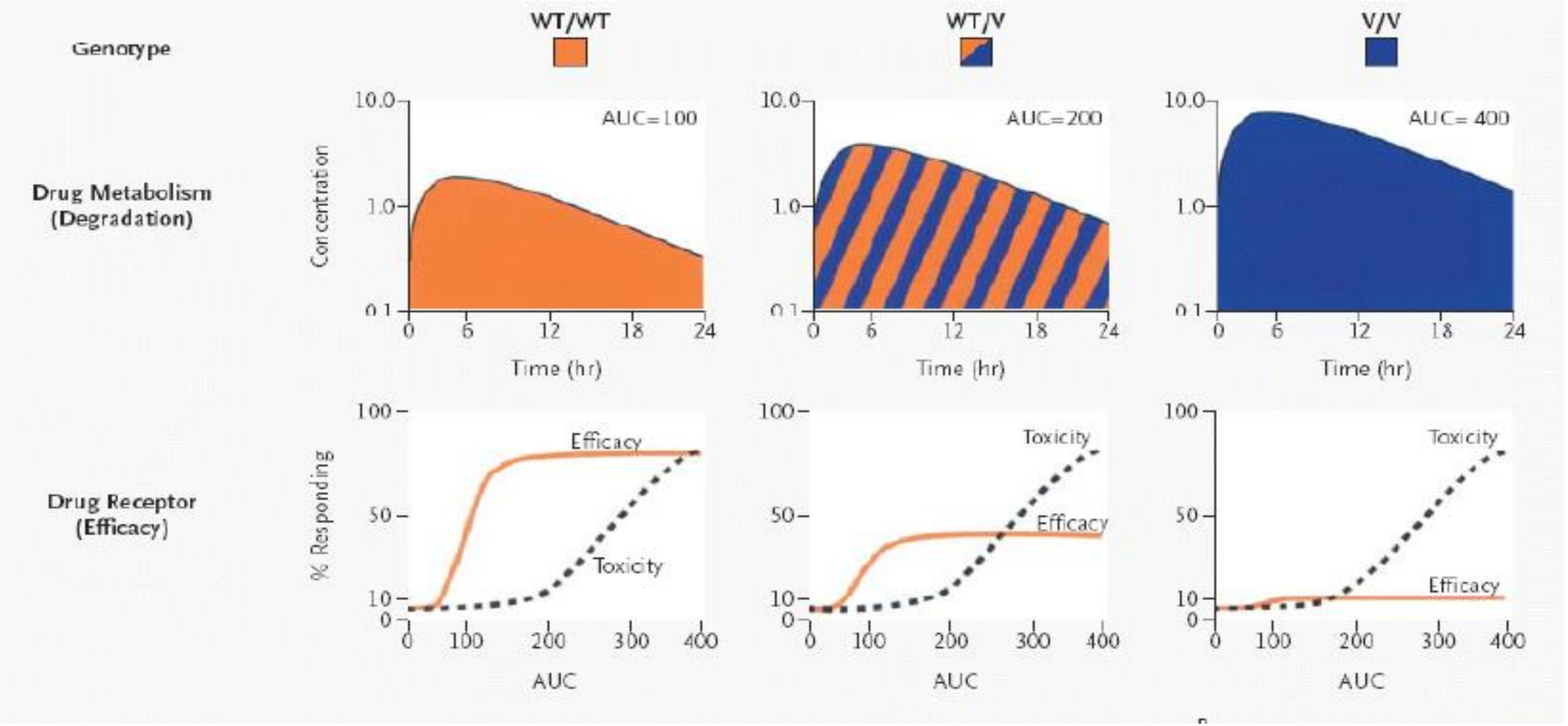


Variabilita PD – senzitivita/rezistence



Evans & McLeod NEJM, 2003;38(6):538-49.

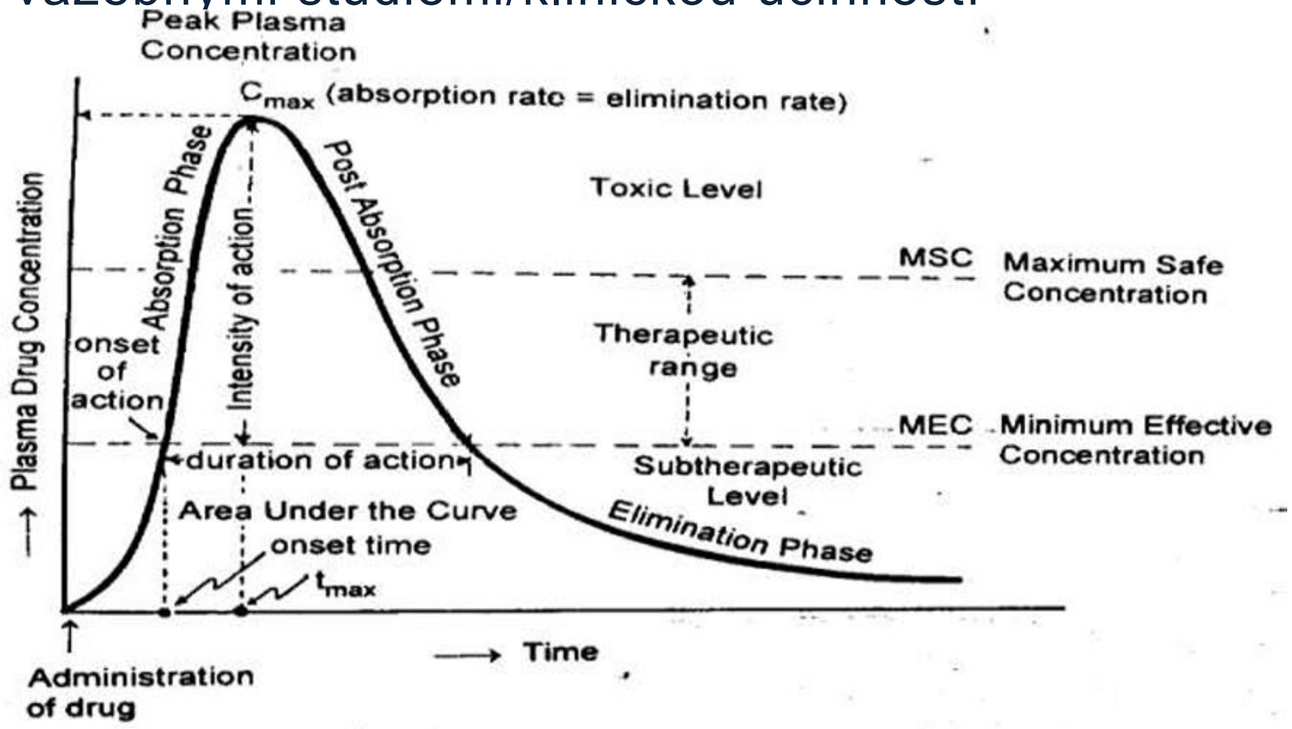
Variabilita PK/PD



Evans & McLeod NEJM, 2003;38(6):538-49.

PK/PD prediktory účinku

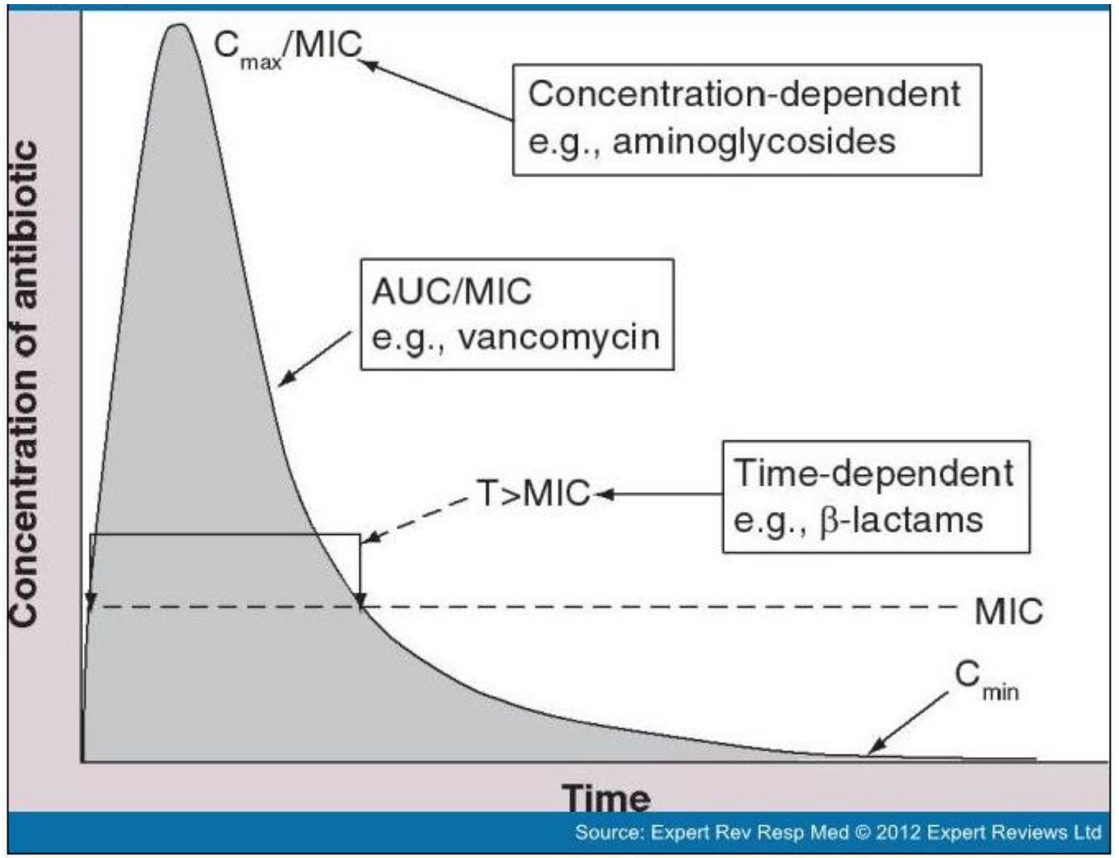
- Cpl jako zástupný parametr pro C v místě účinku
- MEC – minimální efektivní koncentrace/ MEAC – minimální efektivní analgetická koncentrace …
- PD reflektována vazebnými studiemi/klinickou účinností



PK/PD prediktory účinku

- Komplexní – např. ATB

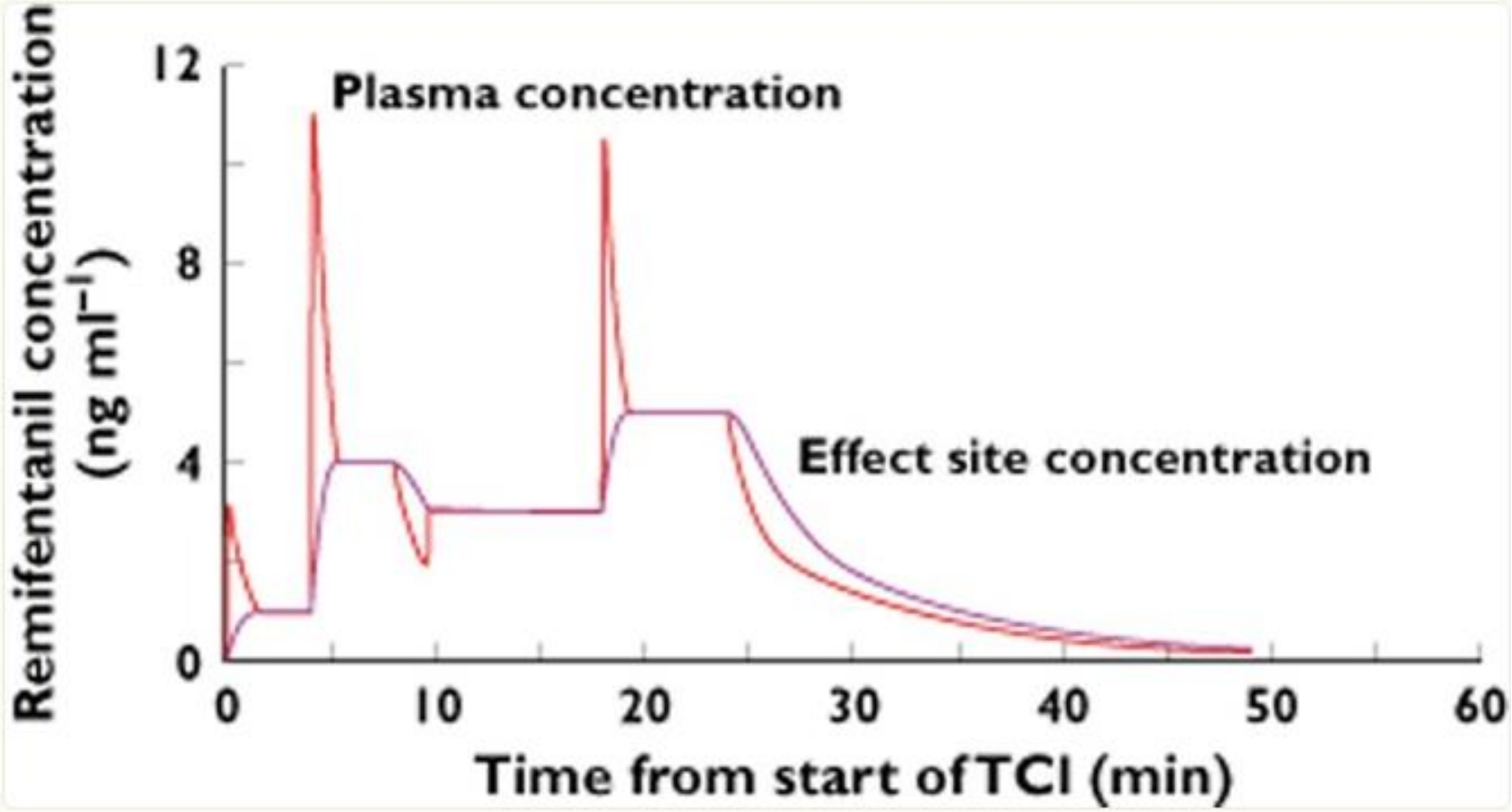
1. C_{max}/MIC
2. AUC_{0-24}/MIC
3. T>MIC



- Nejde o nezávislé PK parametry
- Účinnost volné frakce přesněji odráží např. *f*AUC_{0-24}/MIC

Grgurich PE et al. Management and prevention of ventilator-associated pneumonia caused by multidrug-resistant pathogens. Expert Rev Resp Med 2012;6(5).

PK/PD modely


Remifentanil concentration (ng ml⁻¹)
12
8
4
0
Plasma concentration
Effect site concentration
0
10
20
30
40
50
60
Time from start of TCI (min)

Děkuji Vám za pozornost