

Continuous infusion of beta-lactams: a Belgian experience

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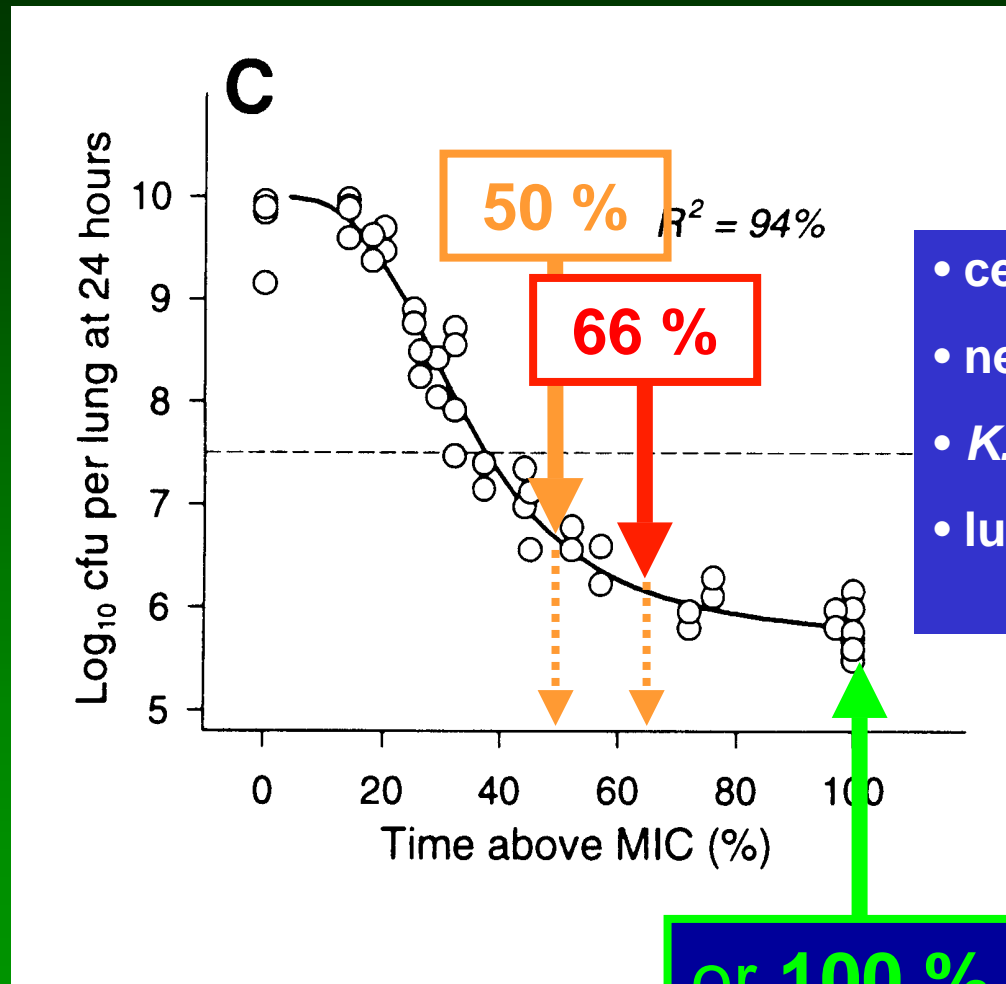
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What did the textbooks say about antibiotic dosages and schedules in the 70's ?

1. Stay above the MIC... **but how much ?**
2. Remain around for a while... **but how long ?**
3. Hope it works... **against everything ?**
4. Hope it is not toxic...

**Sorry, but
I can't do much ...**

How long do you need to remain above the MIC for a beta-lactam ?



- cefotaxime
- neutropenic mice
- *K. pneumoniae*
- lung infection)

W.A. Craig, ECCMID-ISAP workshop 2001

Continuous infusion of ceftazidime in ICU (3 g/day)

	<i>Intermittent</i> <hr/> (n=17)	<i>Continuous</i> <hr/> (n=17)
C max (mg/ml)	106.5 (34.6)	18.2 (6.5)
C min (mg/ml)	10.3 (16.0)	16.5 (5.7)
C mean (mg/ml)		17.4 (6.1)
T_{1/2}(h)	3.2 (2.5)	
AUC_{0-24h}	777.4 (474.6)	419.7 (141.5)
Cl(ml/min)	142.5 (58.7)	133.2 (37.0)

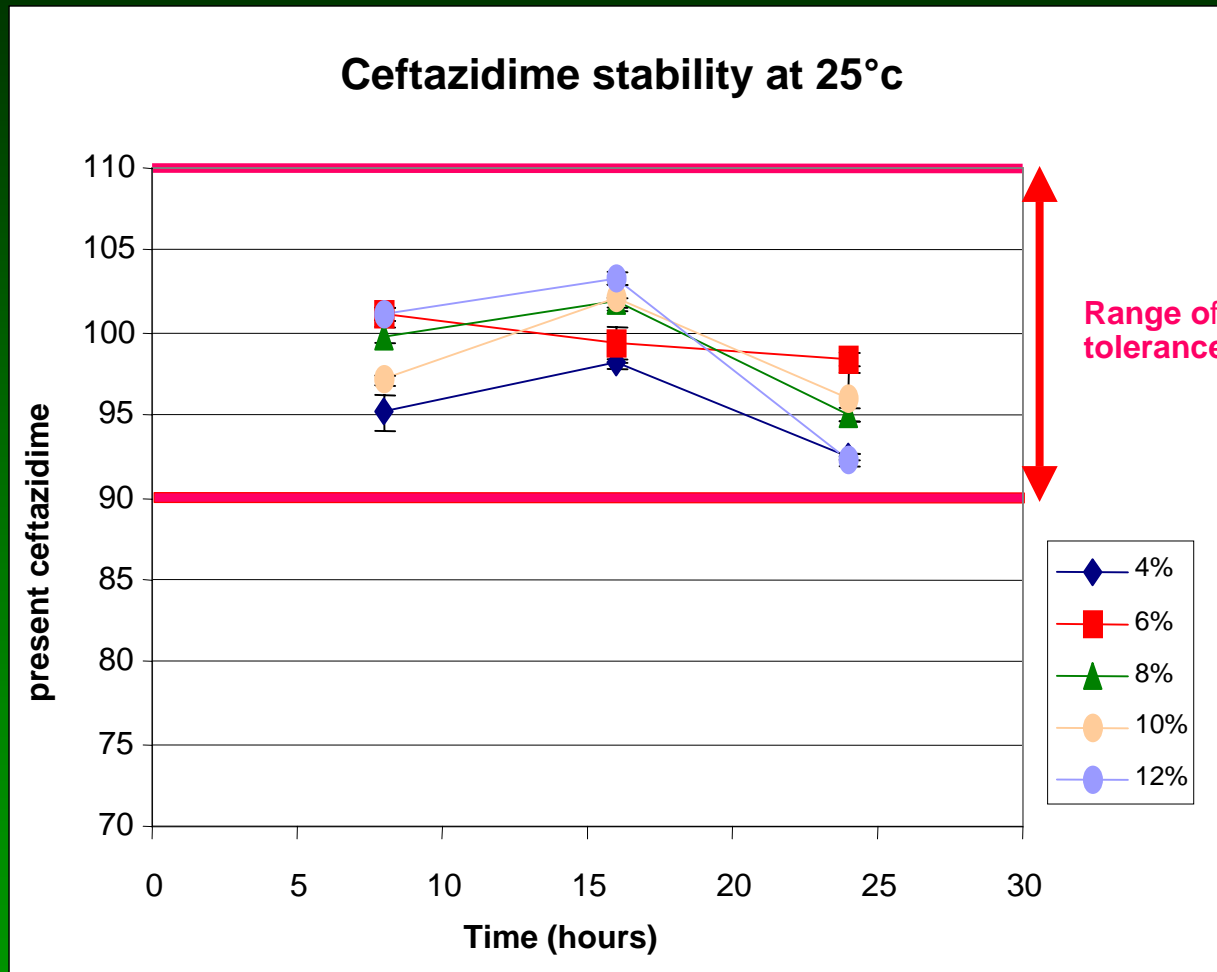
Pharmacokinetics and Pharmacodynamics of continuous and intermittent ceftazidime during the treatment of nosocomial pneumonia. D.P. Nicolau et al. *Clin Drug Invest* 1999;18(2):133-139.

Continuous infusion: a bunch of other studies...

- **suspected Gram (-) infections in critically-ill patients**
Benko et al., AAC 1996
- **severe infections in Intensive Care patients (5 studies)**
Domenig et al., Transplantation, 2000
- **septicemia (2)**
Angus et al., Brit. J. Clin. Pharmacol. 2000
- **severe sepsis**
Leder et al., JAC, 1999
- **cystic Fibrosis (3 25).**
Rapaz et al., Eur. J. Ped. 2000

But is it safe ?

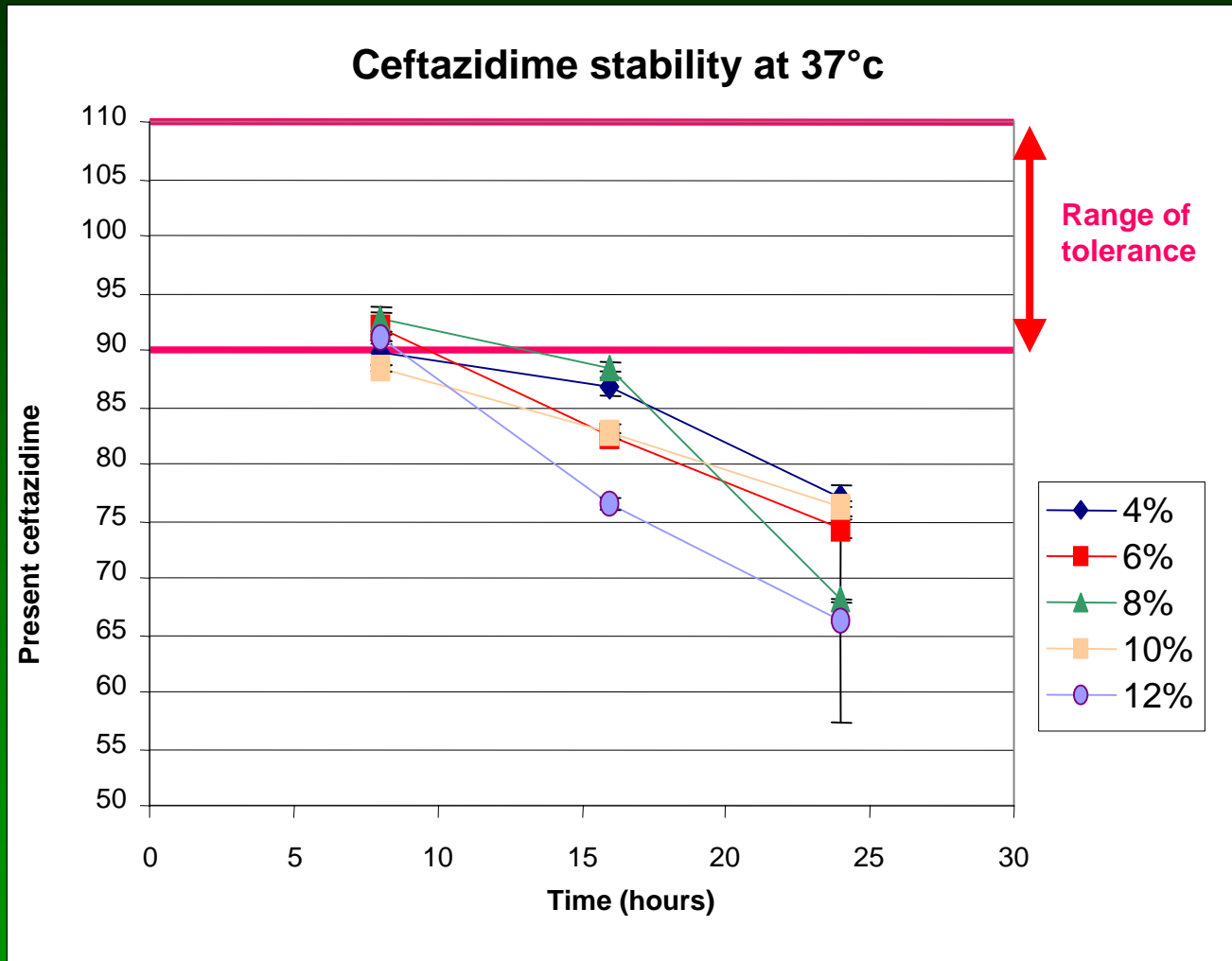
Ceftazidime stability studies ... 25°C



Servais & Tulkens, AAC, 2001

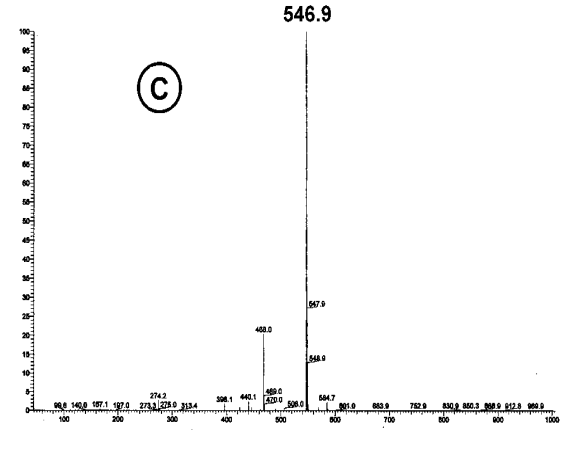
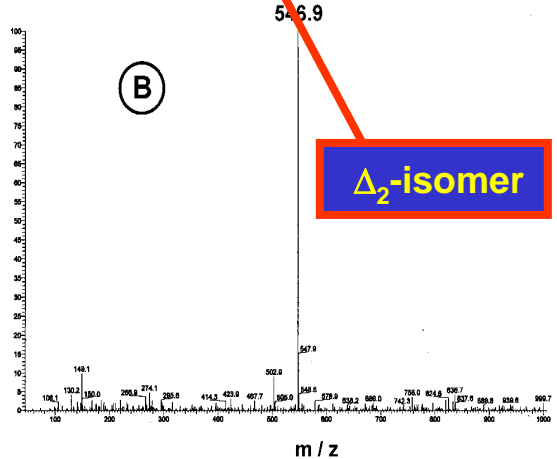
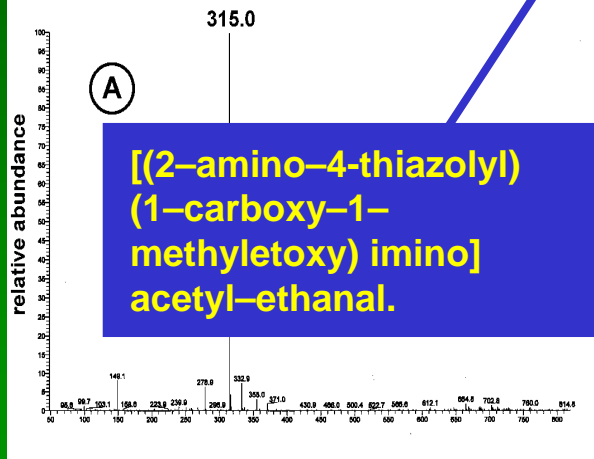
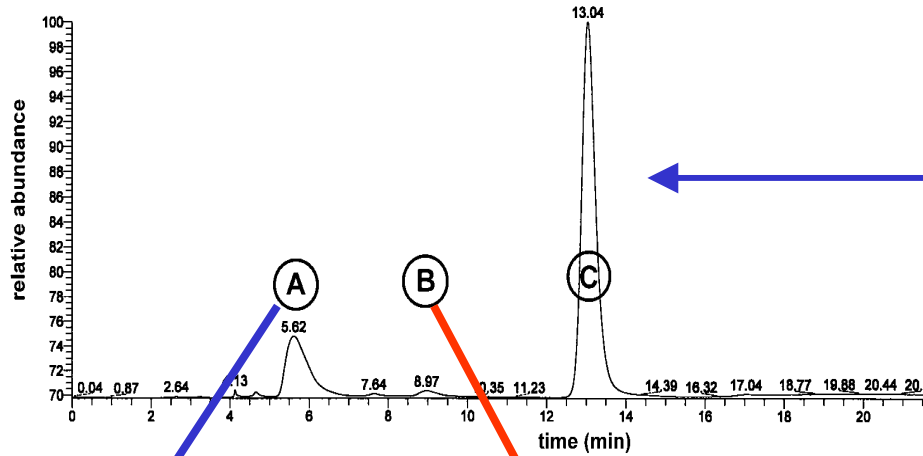
But is it safe ?

Ceftazidime stability studies ... 37°C ...



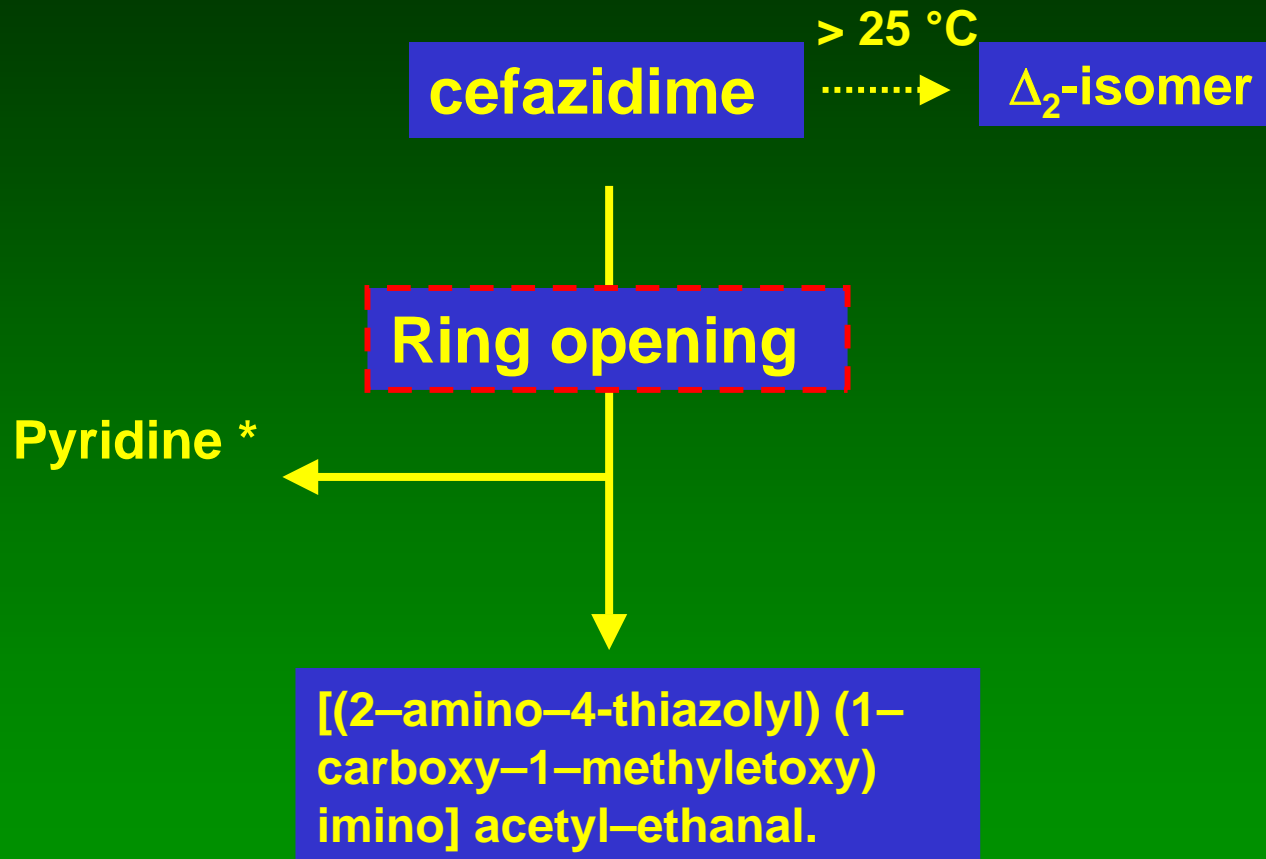
Servais & Tulkens, AAC, 2001

Degradation products of ceftazidime



Servais & Tulkens, 11th ECCMID, 2001

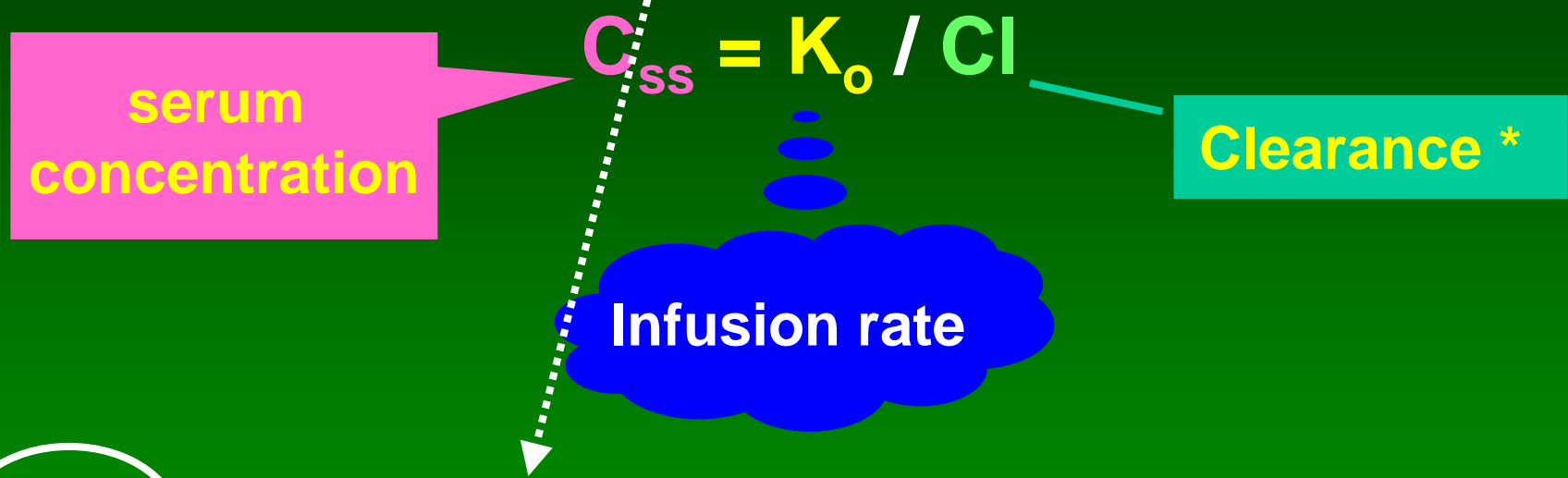
Degradation pathways of ceftazidime (24h in aqueous media)



* < 50 mg from an amount of 4 g in 24h at temp < 25°C

PK / PD in action ...

continuous infusion of β -lactams:
the case of ceftazidime (4g / day) in Intensive Care Units



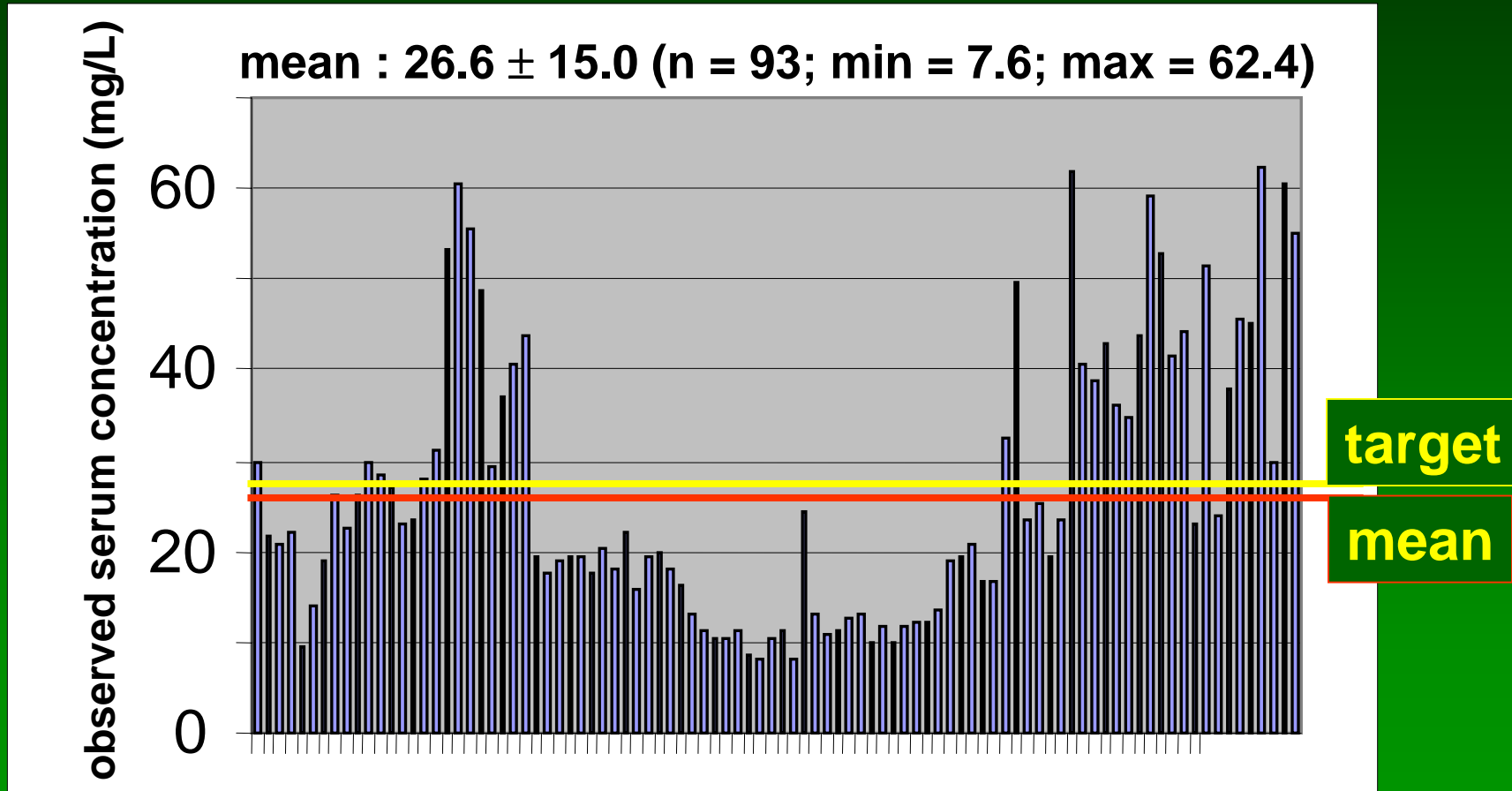
$$27 \text{ } [\mu\text{g/ml}] = \left\{ 2.77 \text{ } [\text{mg/min}] / 102 \text{ } [\text{ml/min}] \right\} \times 10^3$$

Targeted level for MIC's up to 6-8 mg/L ...

PK / PD in action ...

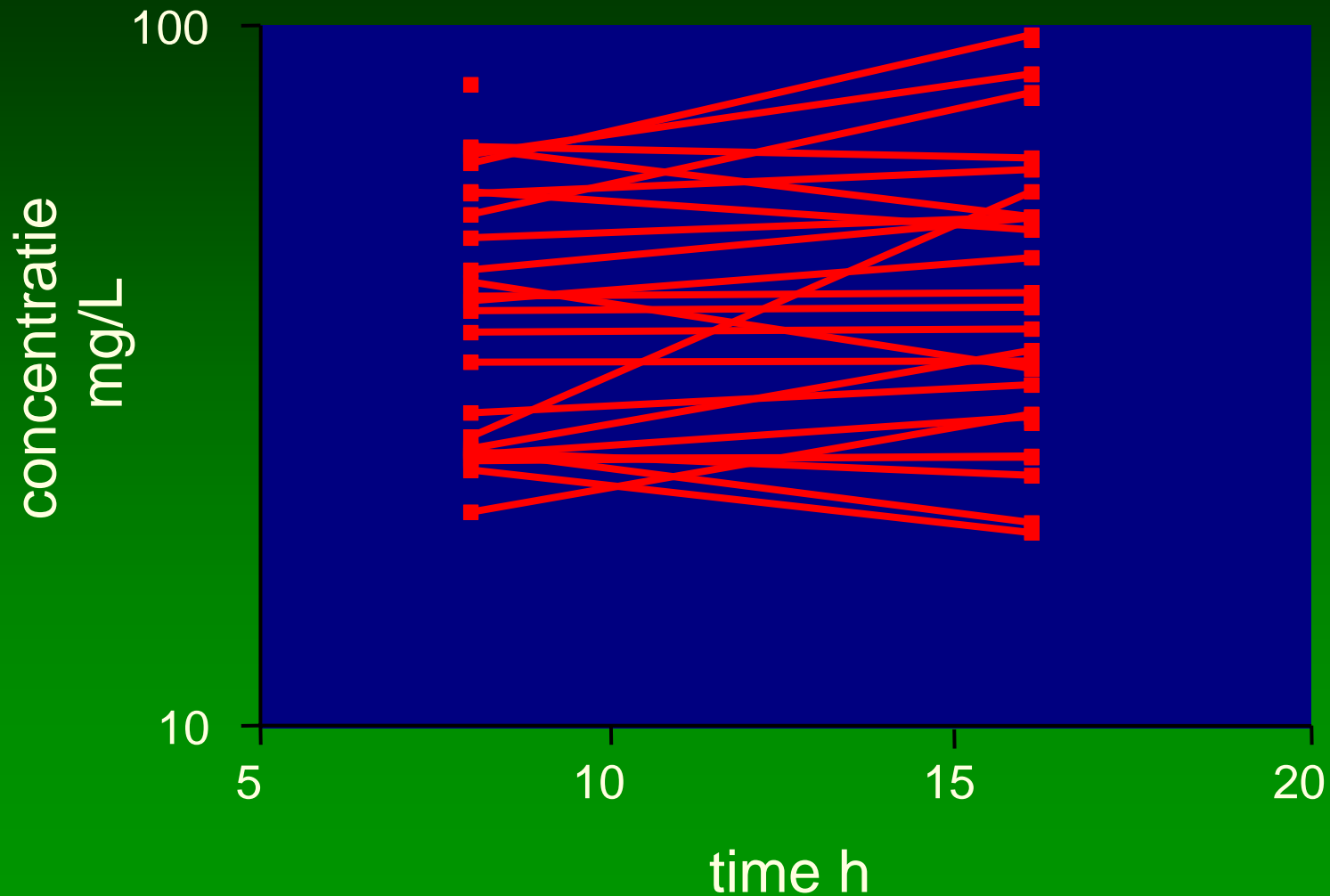
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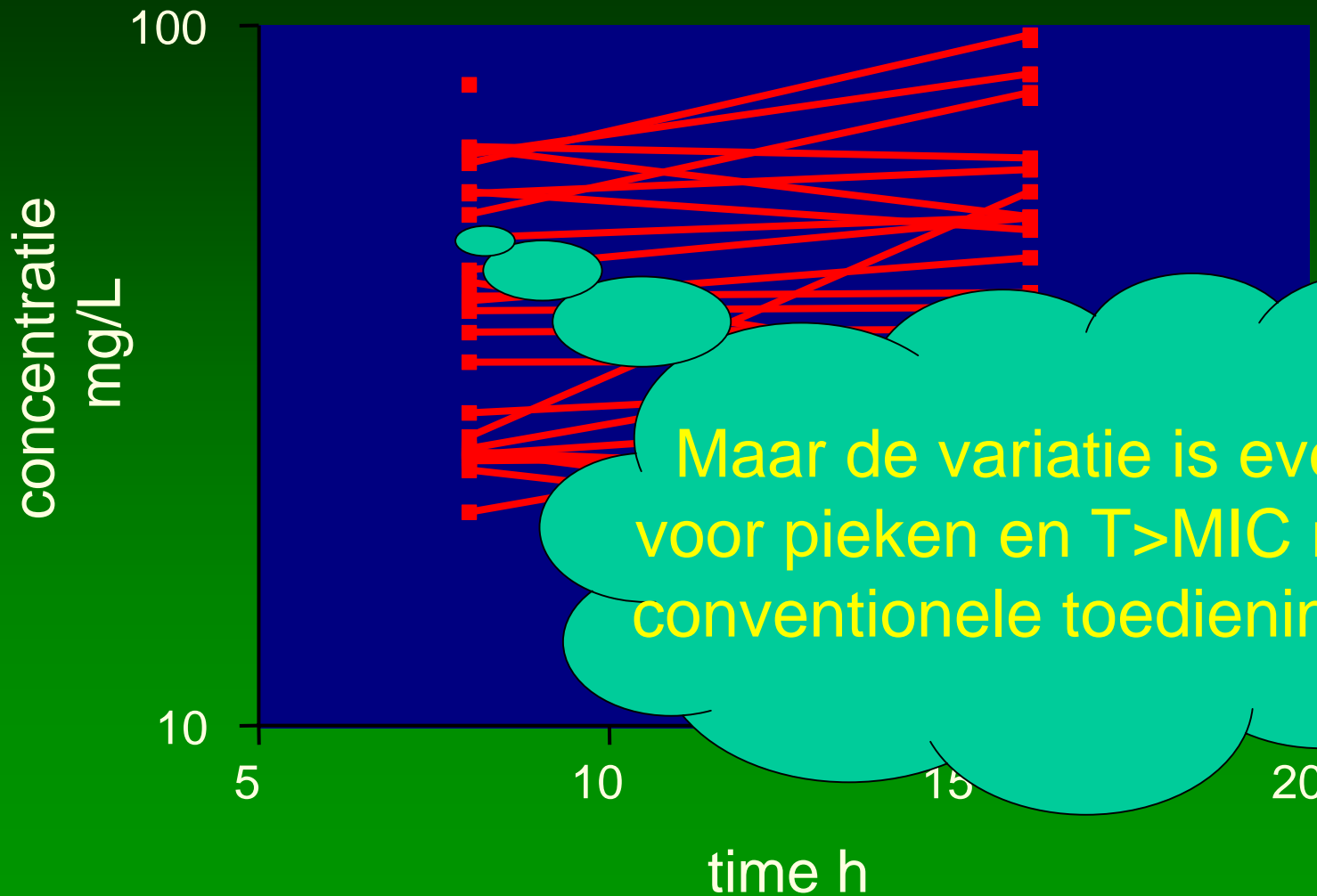
Servais, Laterre & Tulkens, unpublished

Variaties in ceftazidime concentraties bij ICU-patiënten werden niet alleen in Brussel waargenomen ...



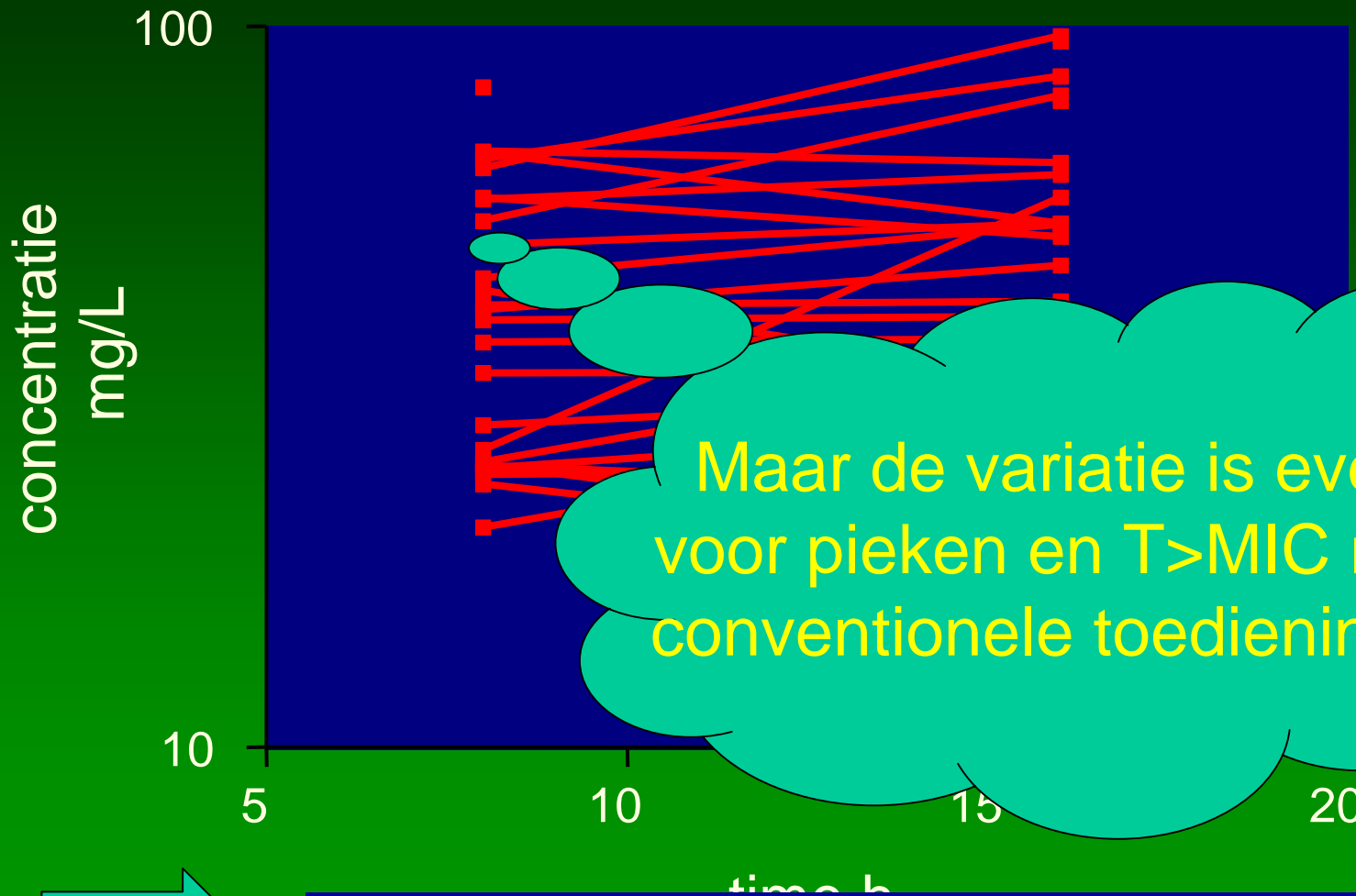
From Mouton, 8th ISAP symposium, Nijmegen, 2001

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Maar de variatie is even groot voor pieken en $T > MIC$ met conventionele toedieningen

β-lactamen bloedspiegels opvolgen ?

n, 2001

And now, en route to the future ...

**Using "old"
drugs for
their best**



... to a bright future !