

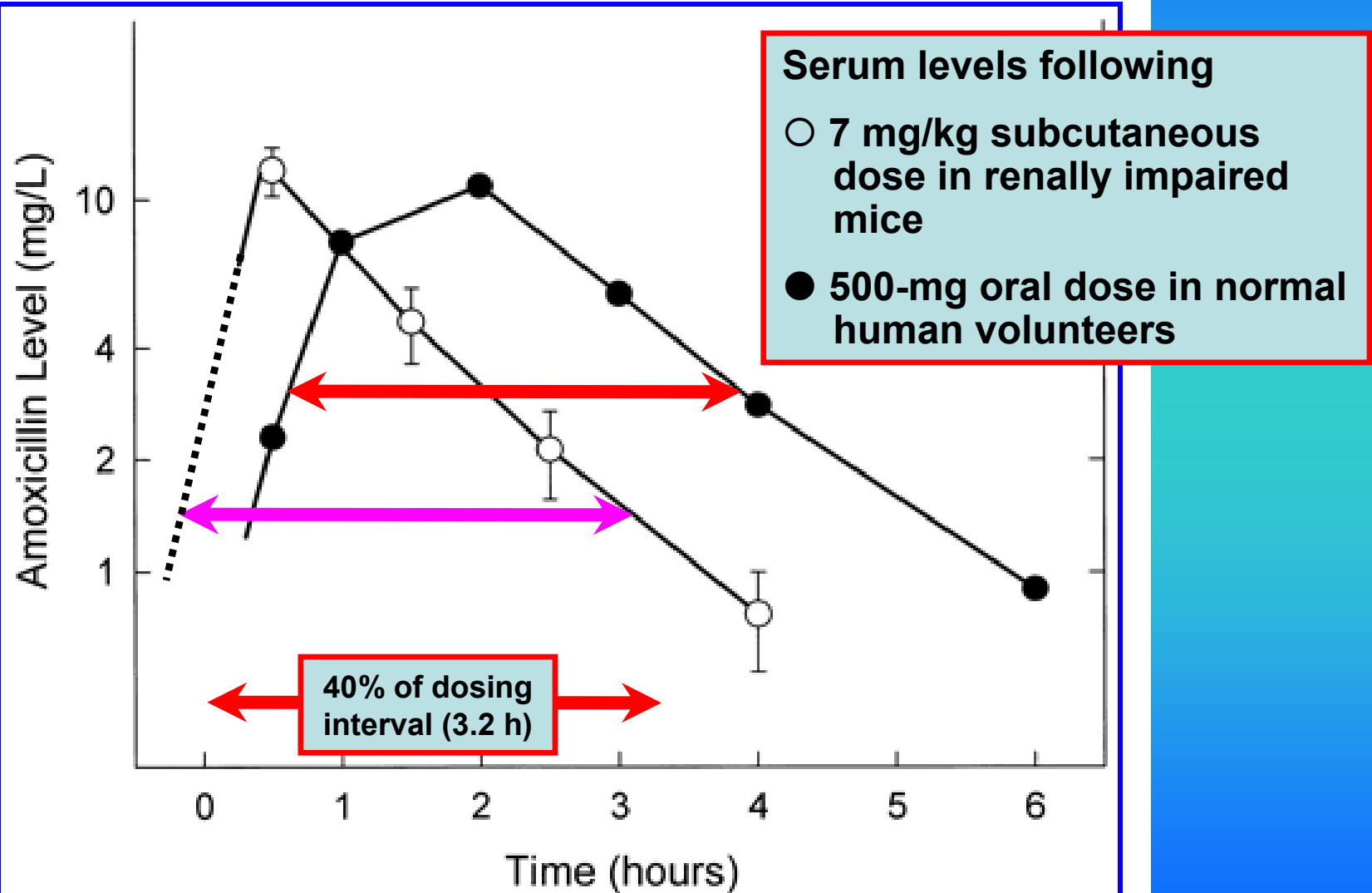
Animal models and PK/PD

**Examples with selected
antibiotics**

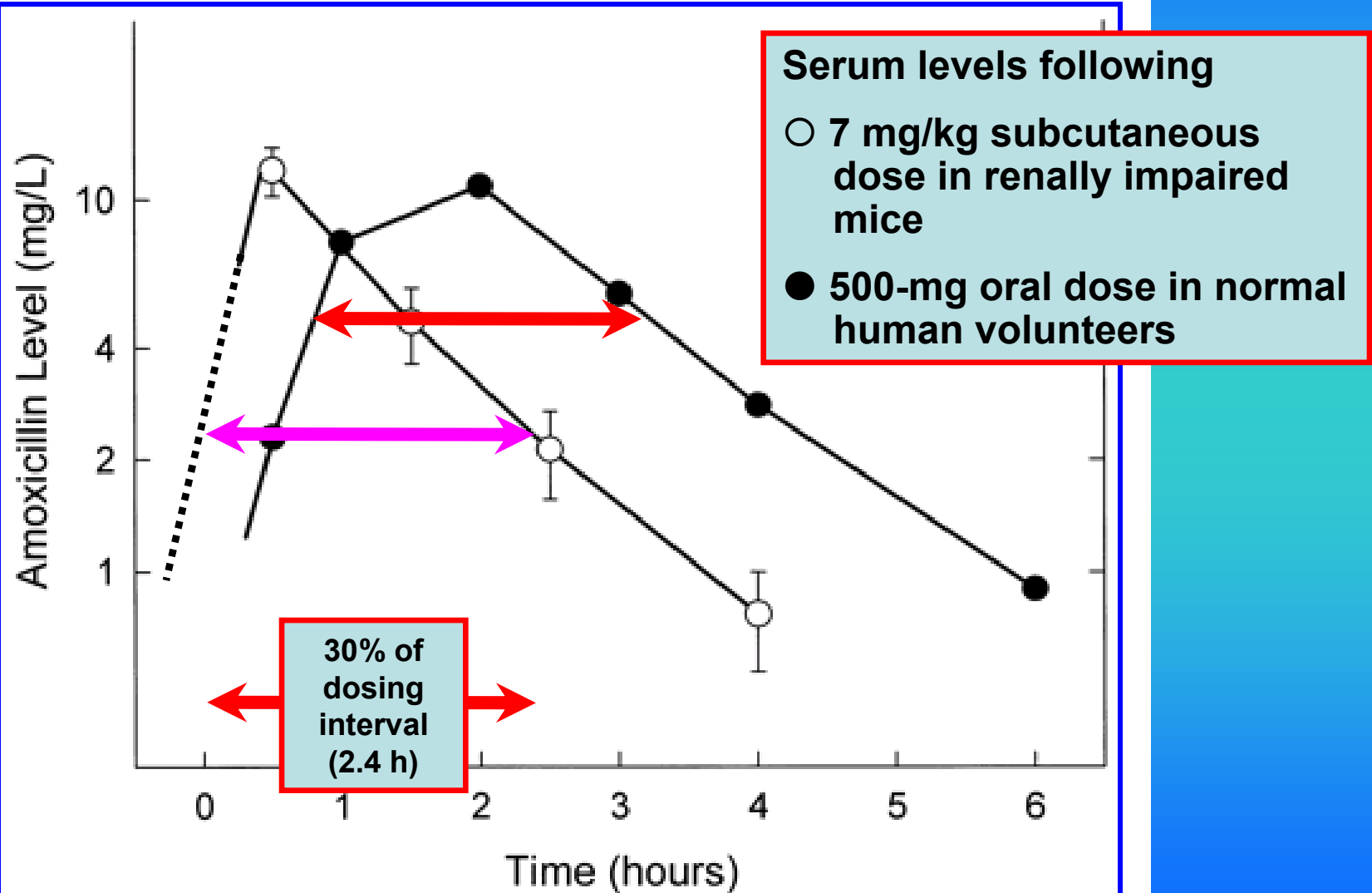
Examples of animal models

- Amoxicillin
- Amoxicillin-clavulanate
- Macrolides
- Quinolones

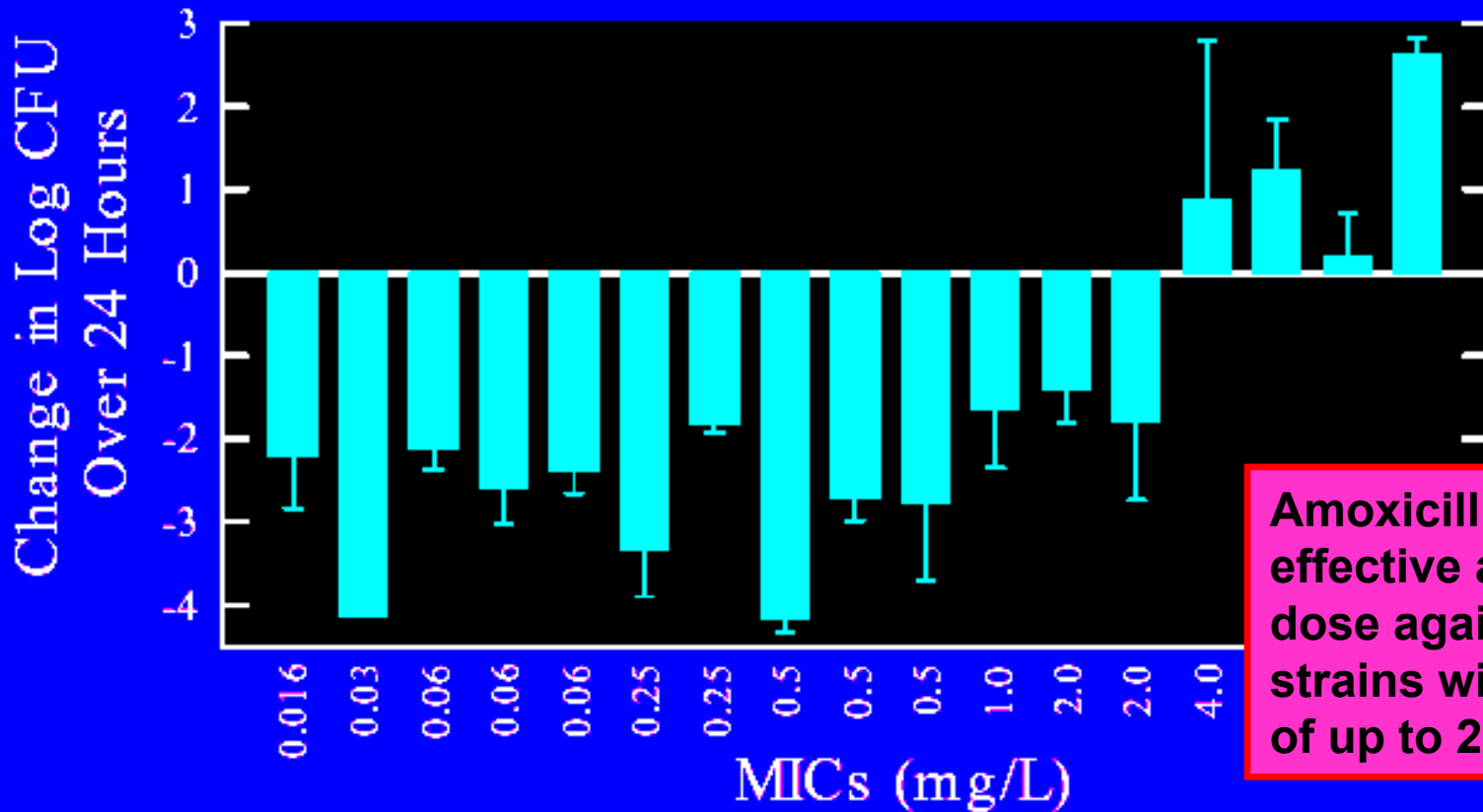
Amoxicillin in mouse thigh infection model



Amoxicillin in mouse thigh infection model



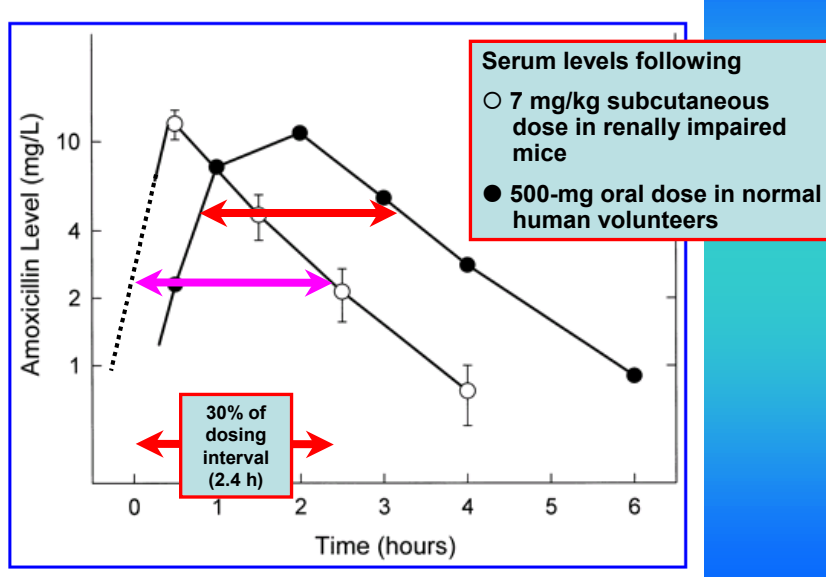
Effect of Amoxicillin (7 mg/kg) on 17 Strains of *S. pneumoniae* in Thighs of Neutropenic Mice



Amox dosed at 7 mg/kg/8 h

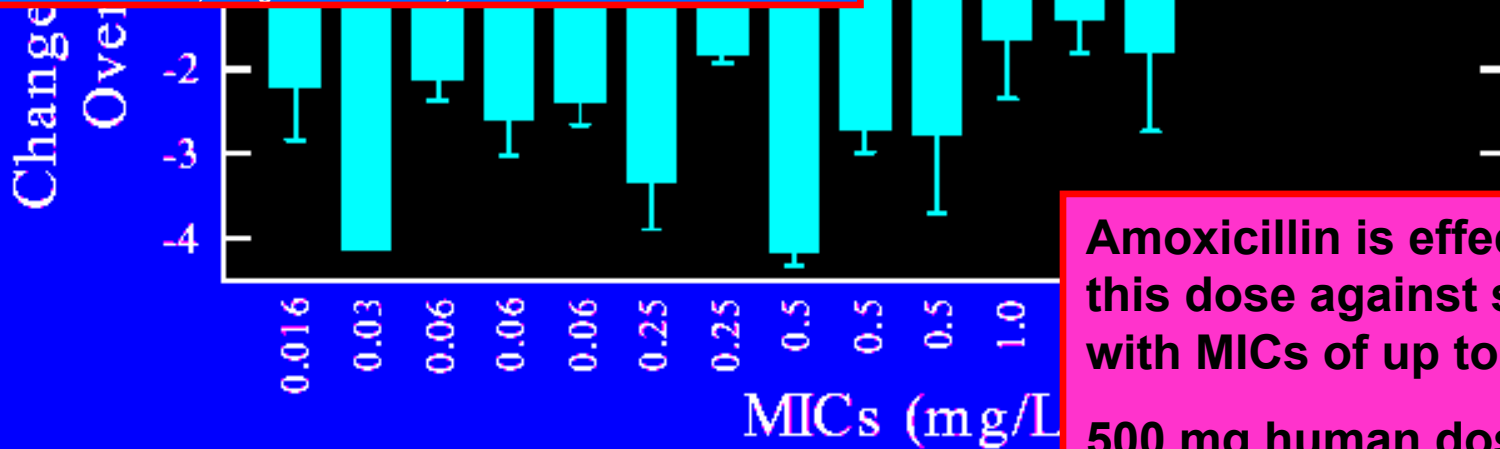
Amoxicillin is effective at this dose against strains with MICs of up to 2 mg/L

Amoxicillin in mouse thigh infection model



Andes D, Craig WA. AAC 1998, 42:2375

(mg/kg) on 17 Strains of Neutropenic Mice

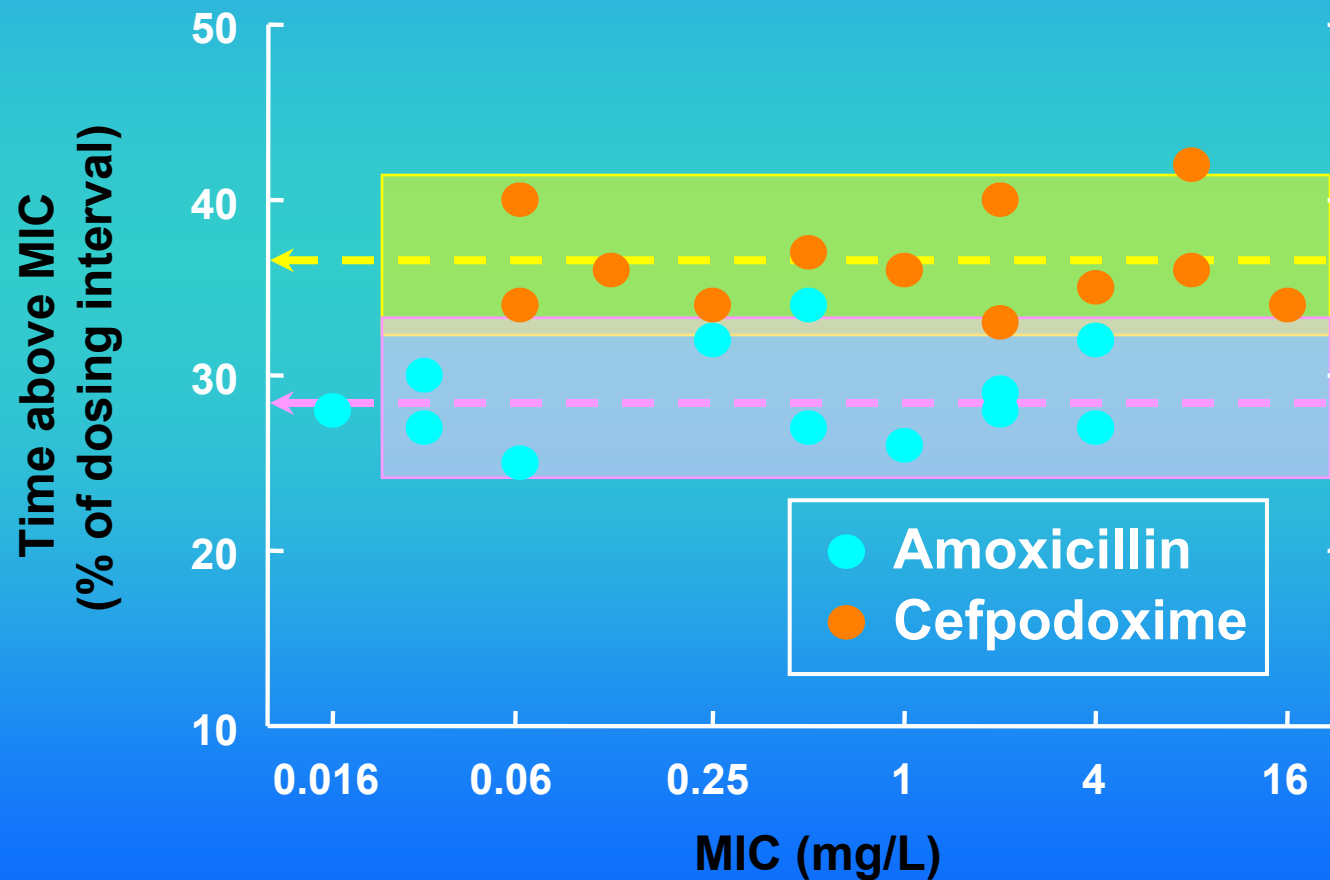


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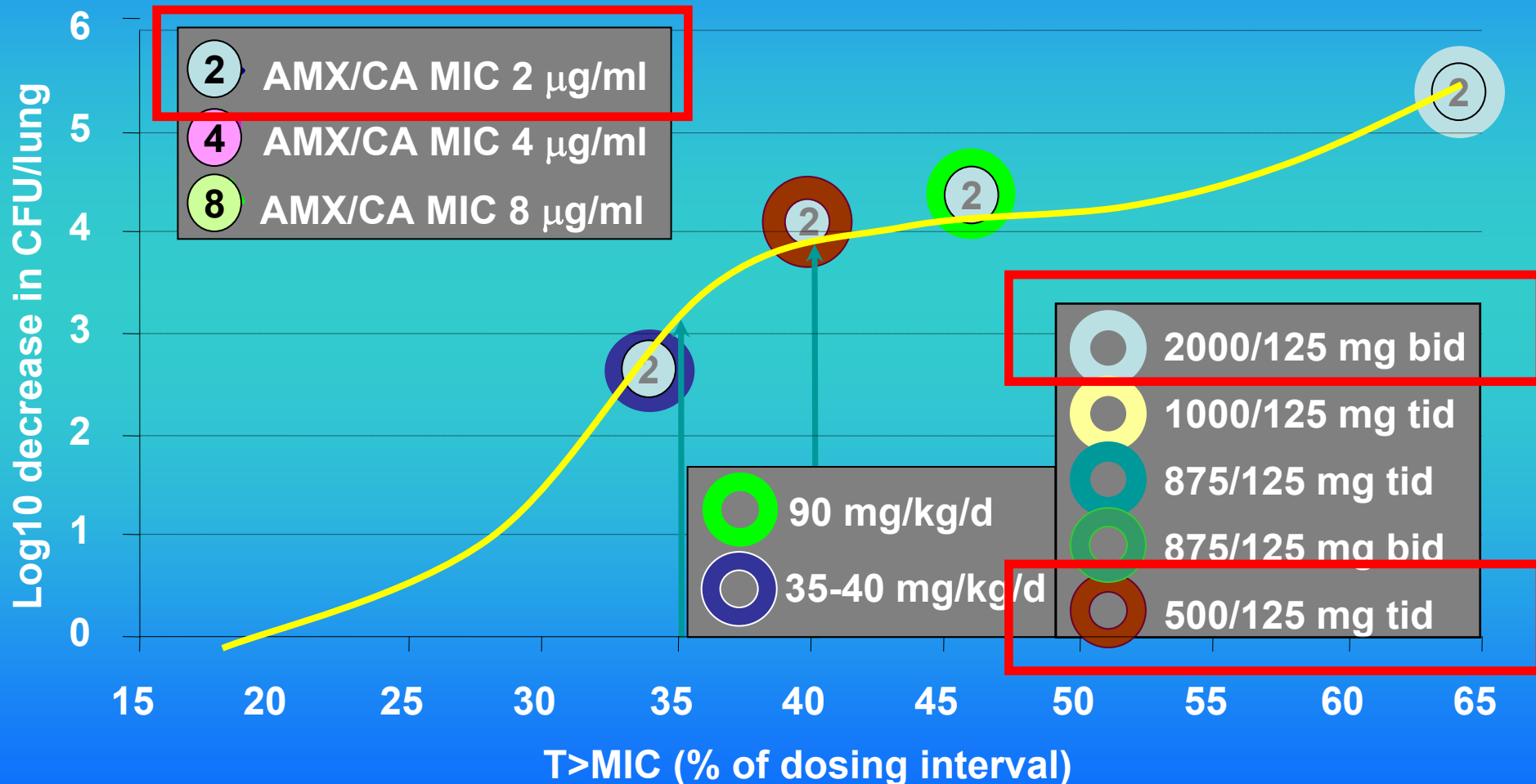
500 mg human dose tid therefore expected to be as effective or more effective

Maximal bactericidal activity of amoxicillin and cefpodoxime with strains of *S. pneumoniae* in mouse thigh model



AMX/CA efficacy against *S. pneumoniae*

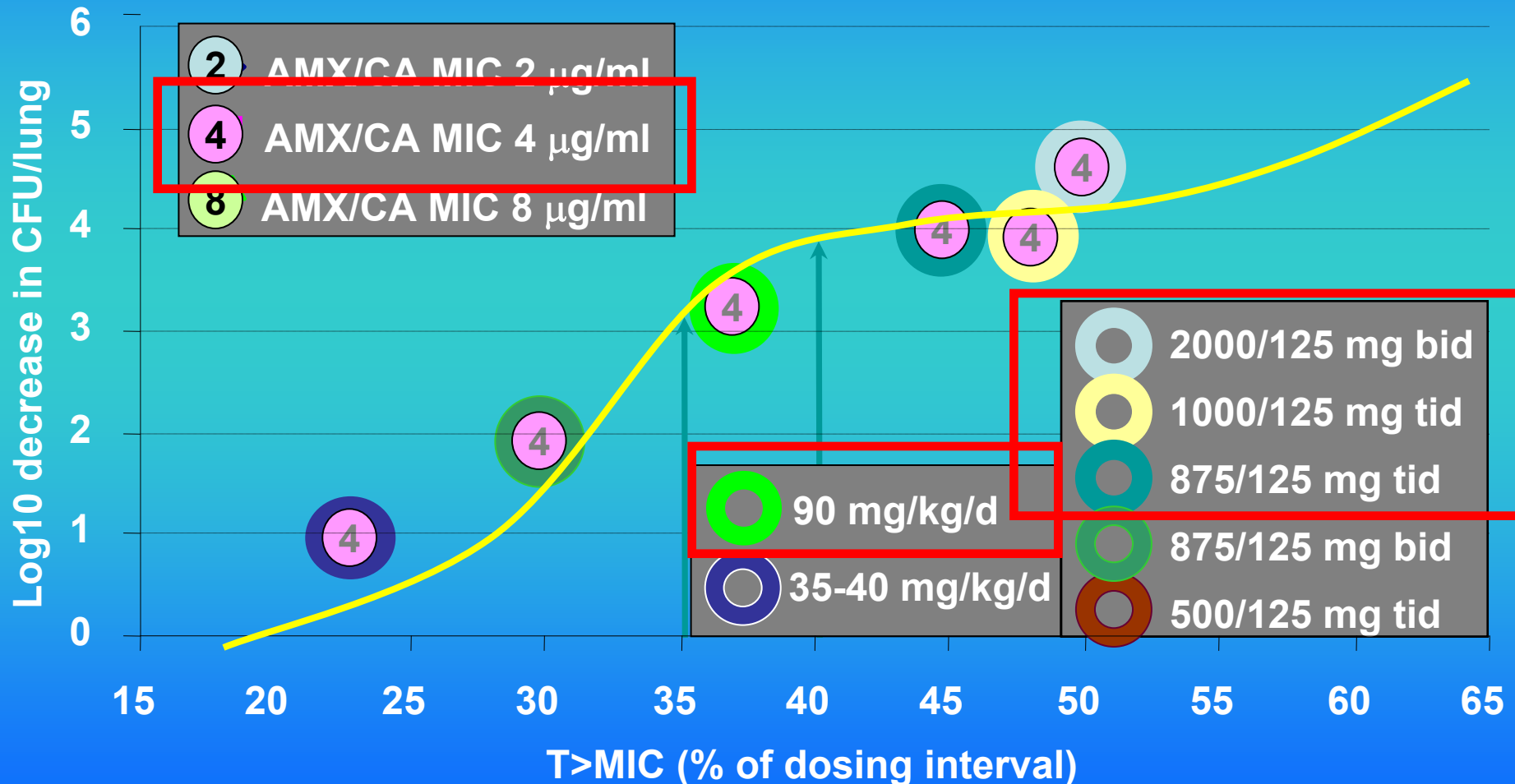
Rat *S. pneumoniae* pneumonia model



Adapted from Berry et al. ICAAC 2001, abstract B-988 and Woodnutt & Berry. Antimicrob Agents Chemother 1999;43:35-40

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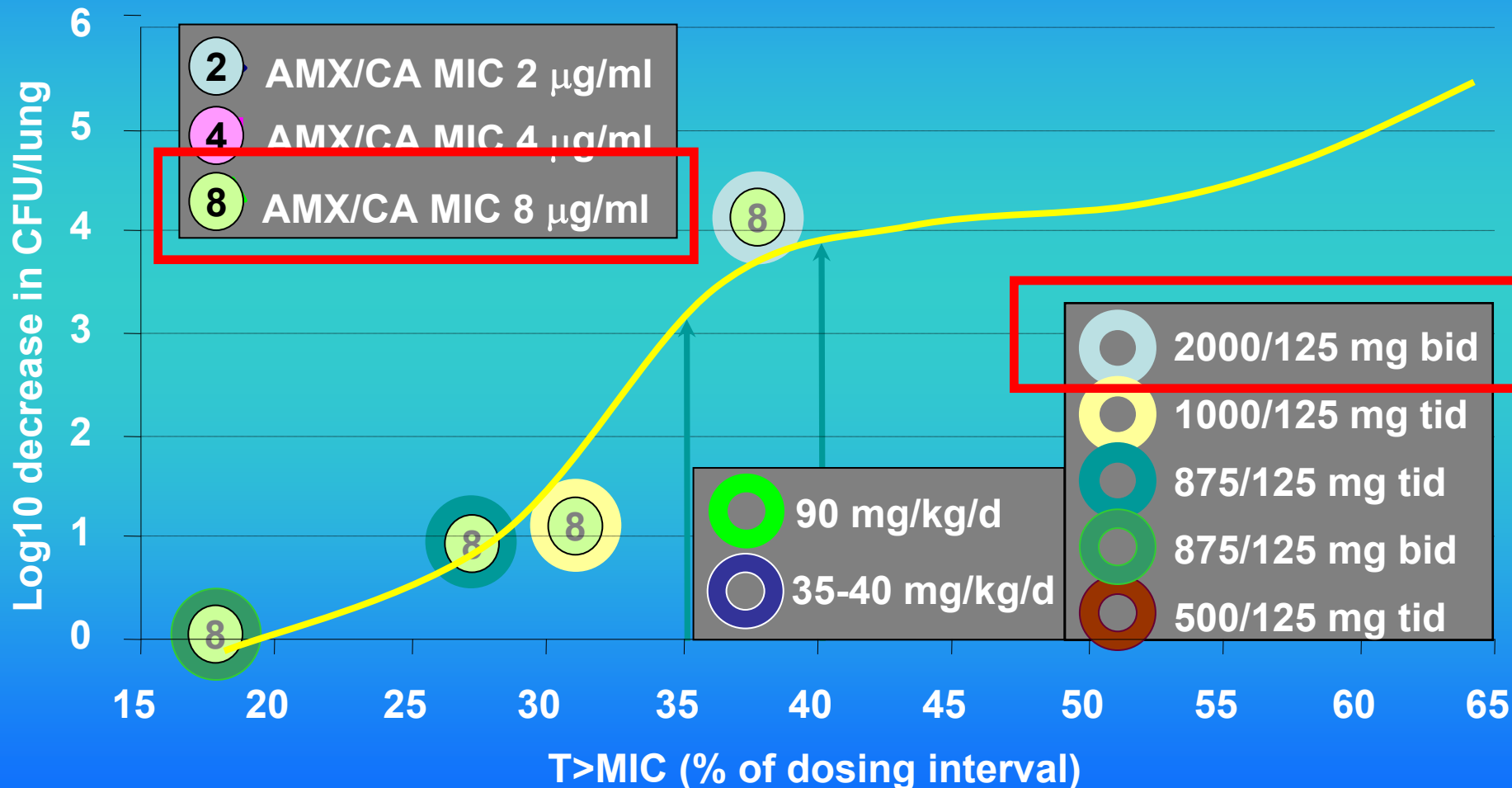
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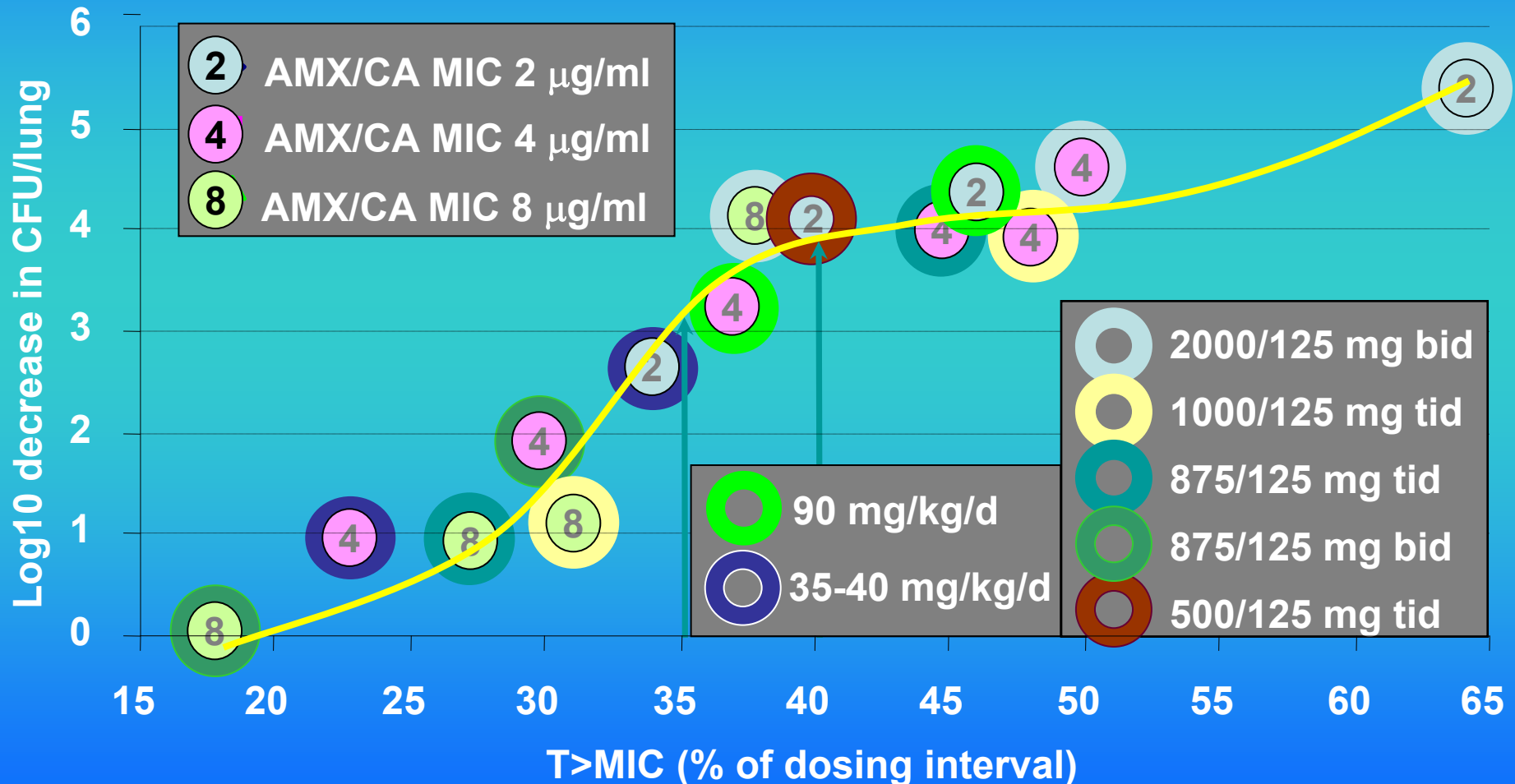
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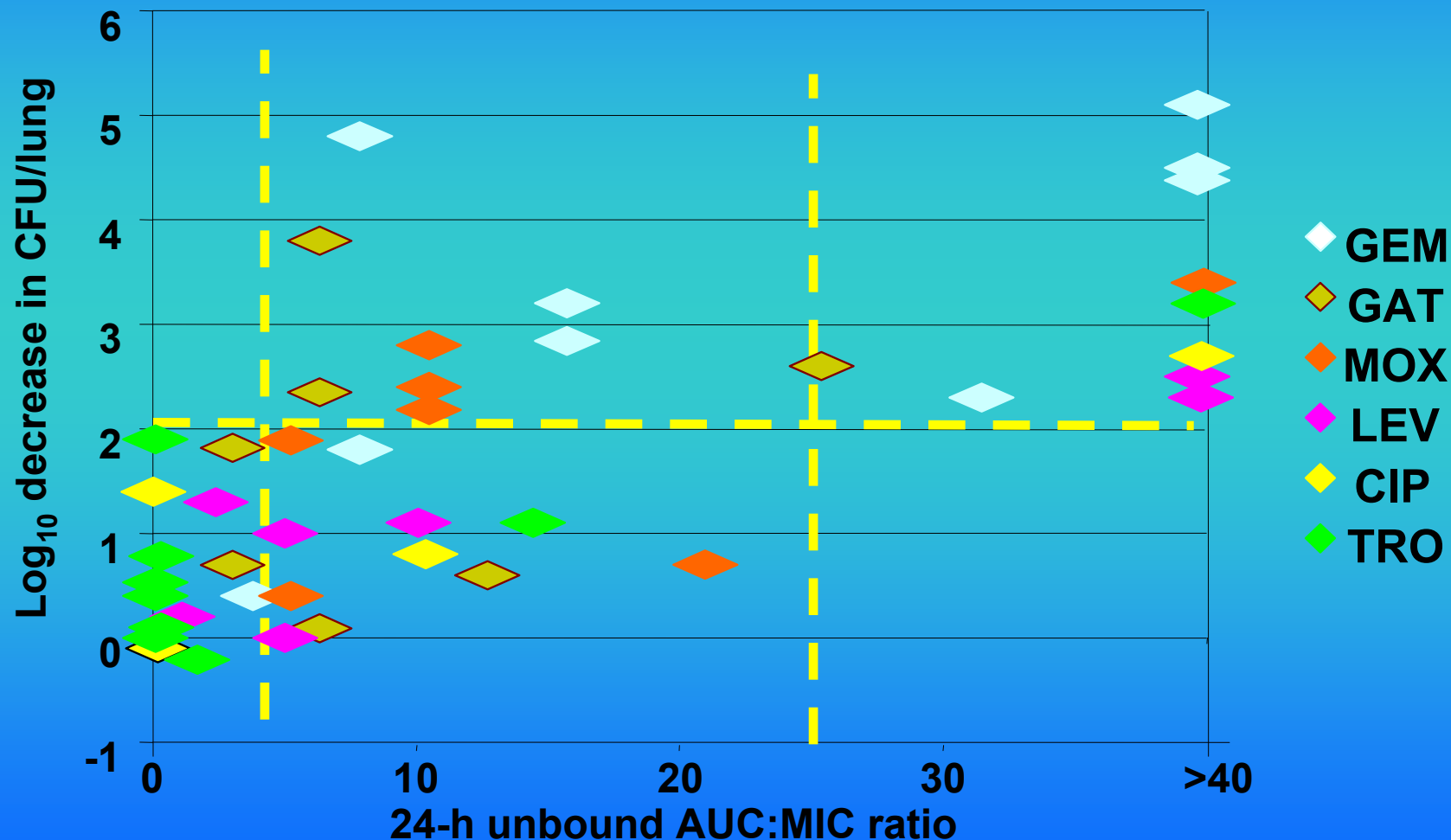
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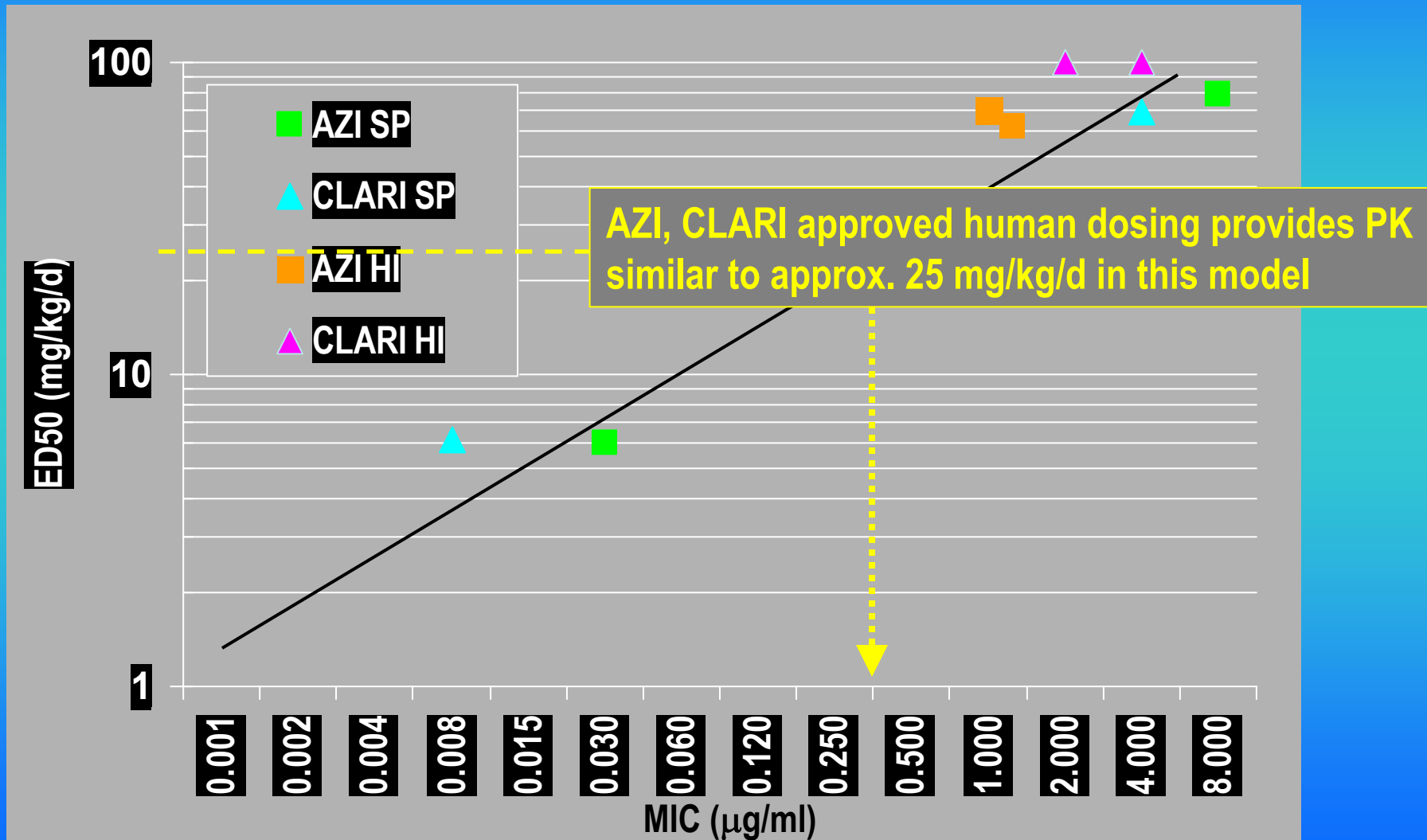
Fluoroquinolone unbound AUC:MIC and bacterial killing

Rat *S. pneumoniae* pneumonia model

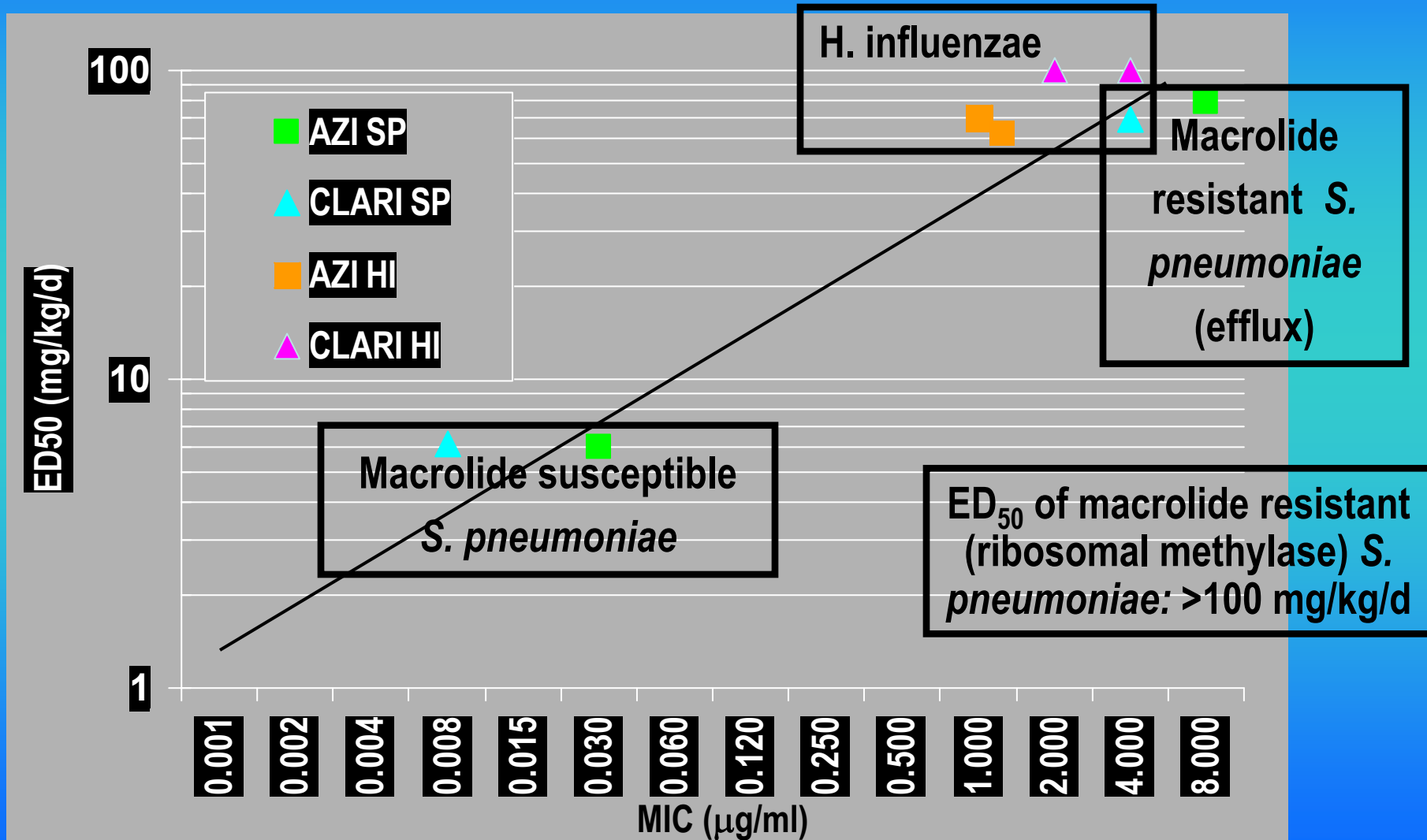


Berry et al. ICAAC 1999, abstract 1548; ICAAC 2001 abstract B-990;
J Antimicrob Chemother 2000;45(Suppl. S1):87-93

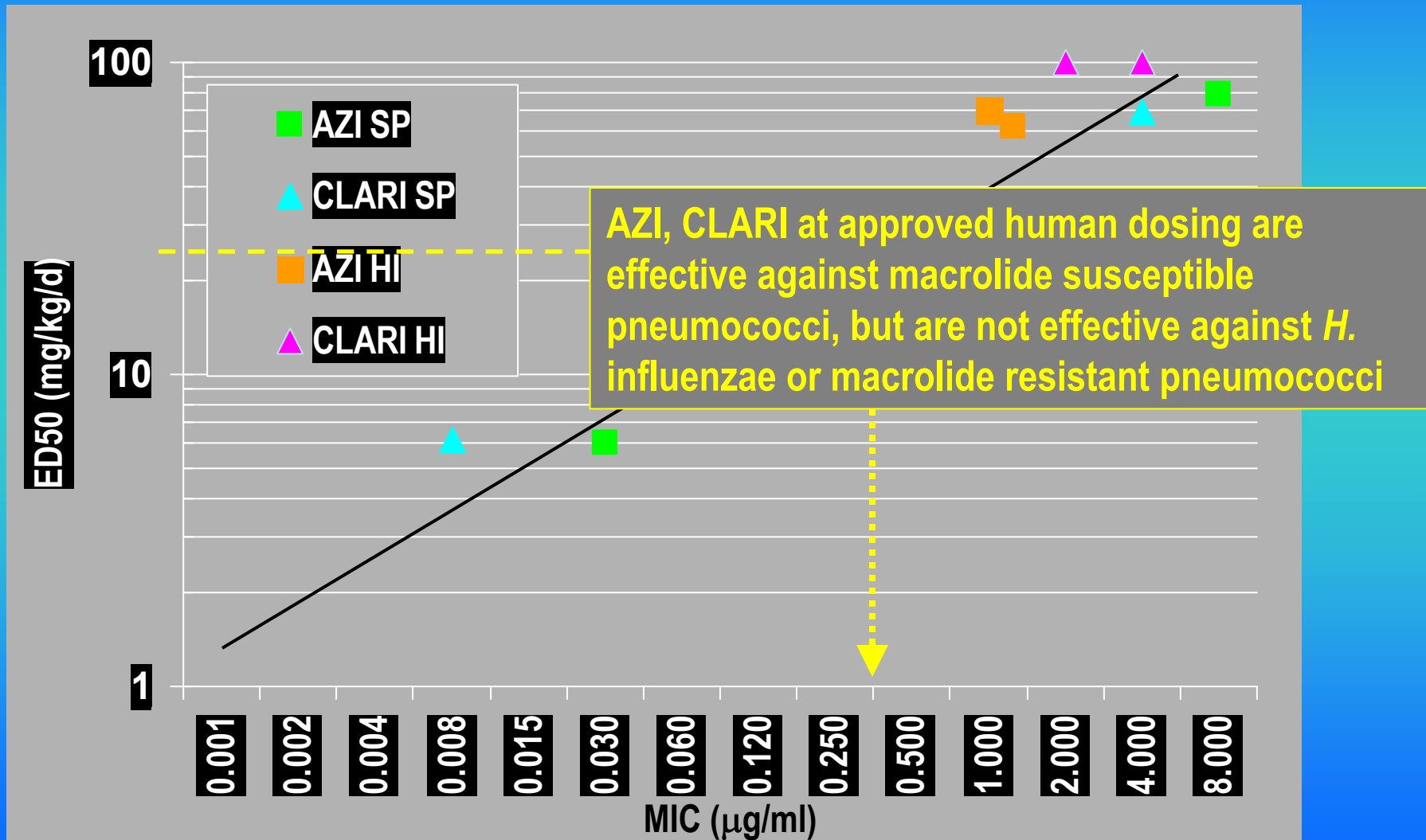
S. pneumoniae and *H. influenzae* pneumonia in rats: ED₅₀ based on $\geq 3 \log_{10}$ reduction in cfu/lung



S. pneumoniae and *H. influenzae* pneumonia in rats: ED₅₀ based on $\geq 3 \log_{10}$ reduction in cfu/lung



S. pneumoniae and *H. influenzae* pneumonia in rats: ED₅₀ based on $\geq 3 \log_{10}$ reduction in cfu/lung



Conclusions

- **In vitro testing provides useful information that can be correlated with results of animal infection models and human infections**
- **Animal models can detect small differences in MICs based on correlations with appropriate PK/PD parameters ($T > MIC$ or AUC:MIC ratio)**