UWTASP
tele-antimicrobial stewardship program

June 15, 2021

Agenda

- Didactic: PK/PD

Agenda

- Defining Terms
- PK/PD Dosing Principles
- Application: Obesity
- Application: Prolonged Infusion

Defining Terms: Pharmacokinetics

What the body does (in relation to the drug)

ABSORPTION:

gut function, PO surrogates

DISTRIBUTION:

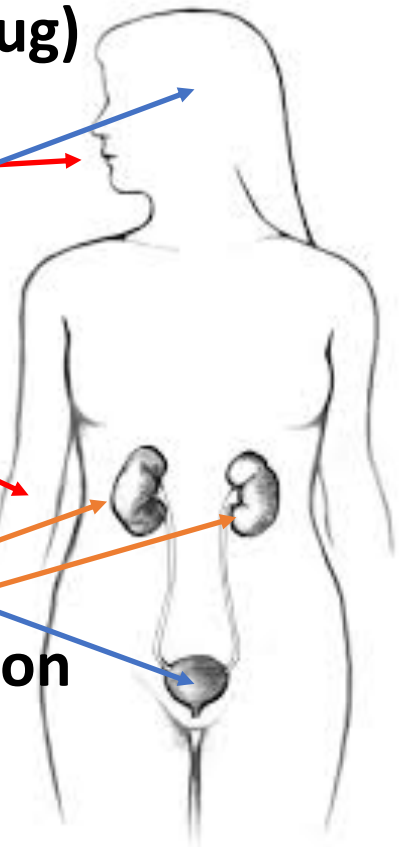
How well does drug go to where the source of infection is

METABOLISM: Enzyme, Genetic variation

Drug-drug interactions!!

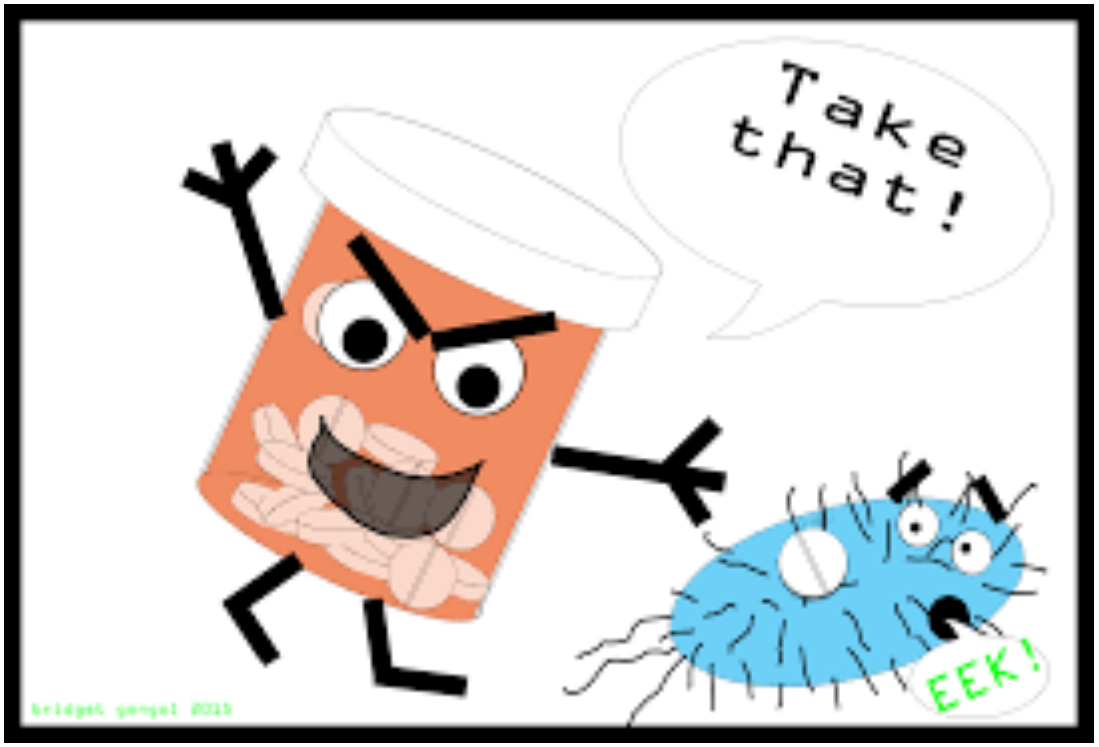
ELIMINATION:

How fast does it go out



Defining Terms: Pharmacodynamics

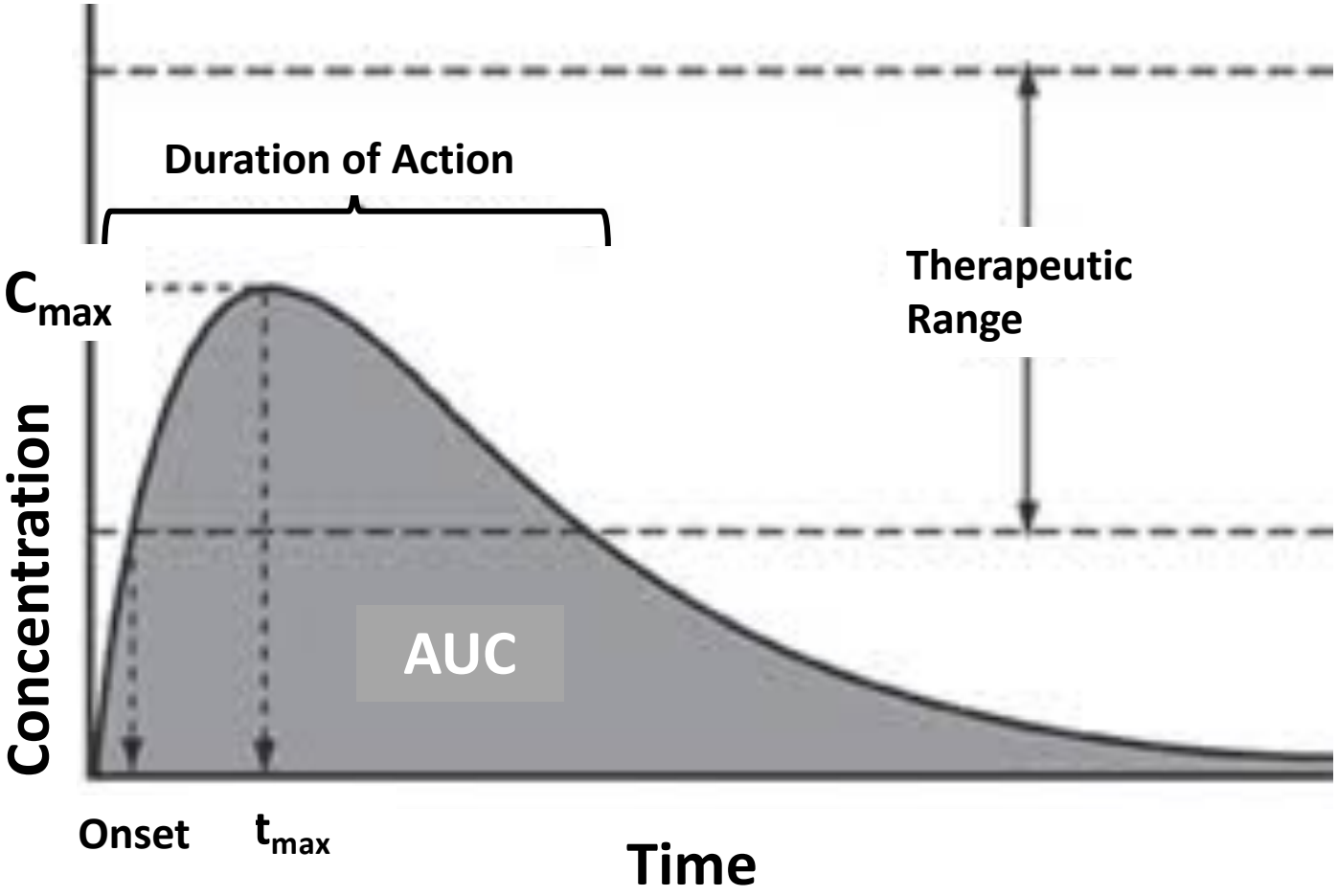
What the drug does (in relation to the body)



Efficacy of Antibiotics is directly related to how we dose them

Defining Terms: Pharmacodynamics

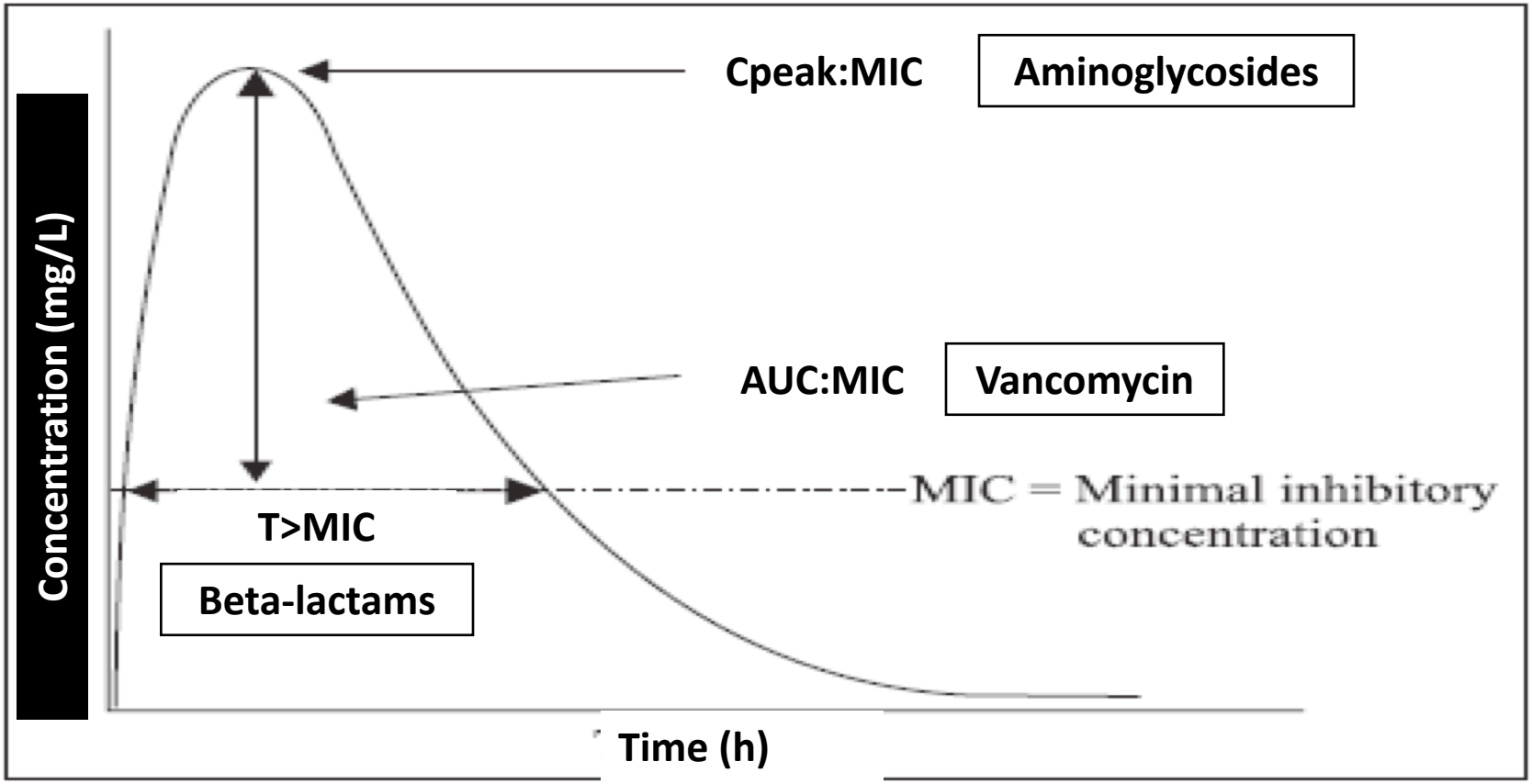
What the drug does (in relation to the body)



PK/PD Dosing Principles:

Managing antibiotic dose in relation to bacteria

What the drug does (in relation to the body)



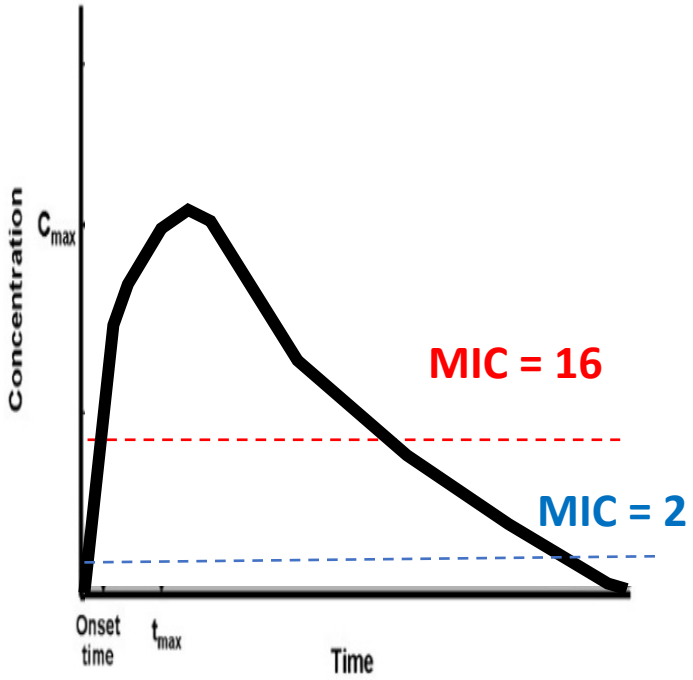
AUC = Area under the curve, MIC = Minimal inhibitory concentration, T = Time

Santos Filho L et al. Braz J Microbiol. 2007 Apr/June;38(2):183-193.
Meagher AK et al. Antimicrob Agents Chemother. 2007 Jun;51(6):1939-45.
Craig WA. Infect Dis Clin North Am. 2003 Sep;17(3):479-501.

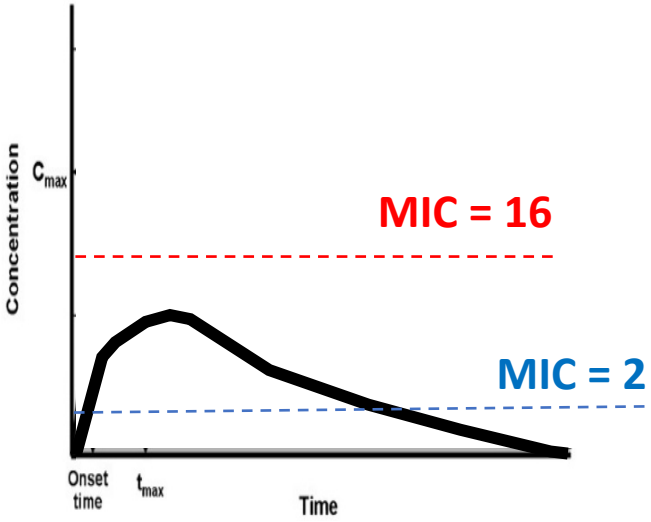
PK Practical Applications:

Cefazolin concentration in blood vs. urine

URINE Concentrations of Cefazolin

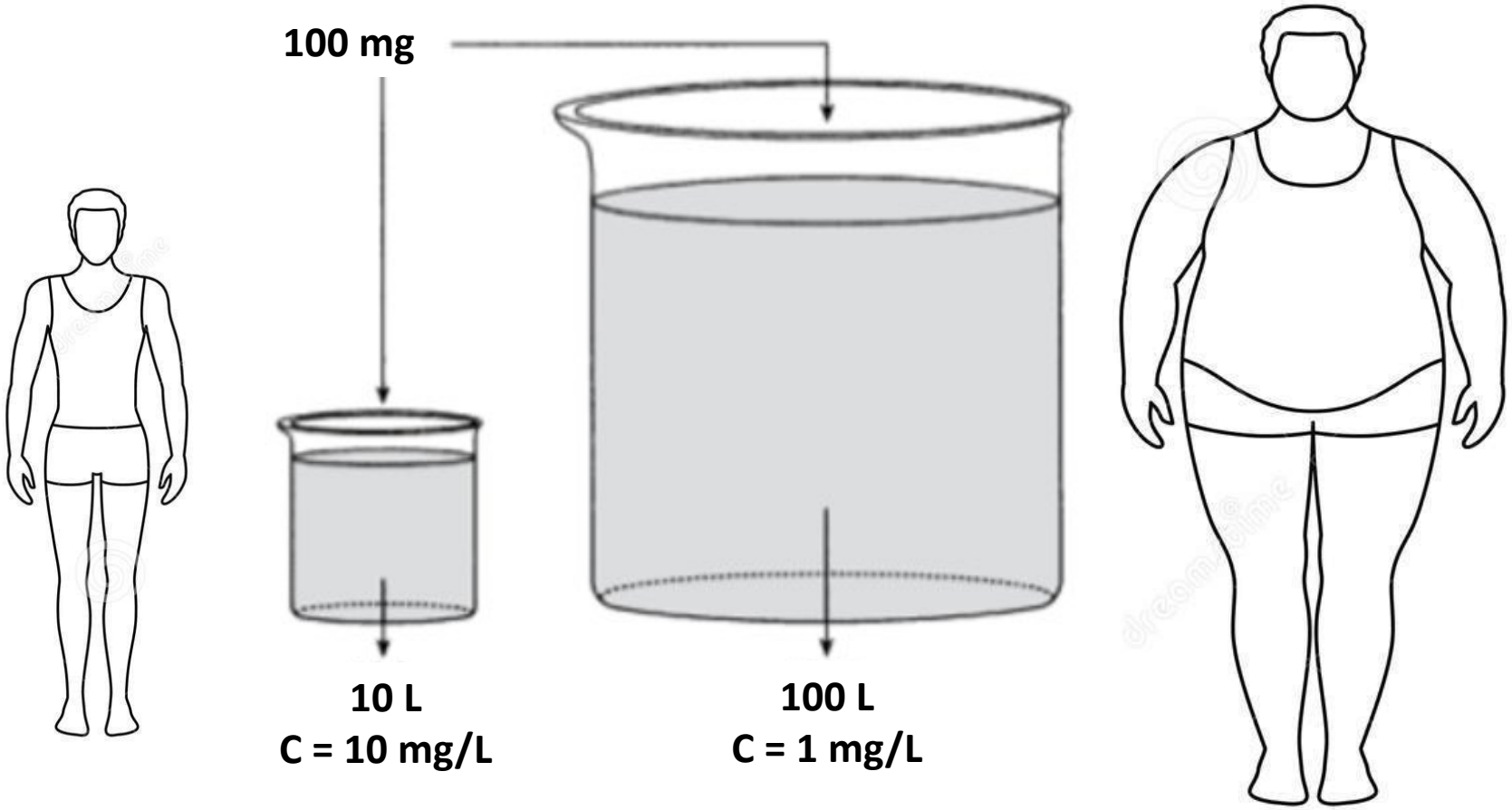


BLOOD Concentrations of Cefazolin



Clinical Infectious Diseases 2011;52(7):917–924

PK Practical Applications:
Dosing in Obese Patients



Bauer LA, Applied Clinical Pharmacokinetics 2nd Edition

PK Practical Applications:

Obese Patients: PK Altered due to Extra Adipose Tissue

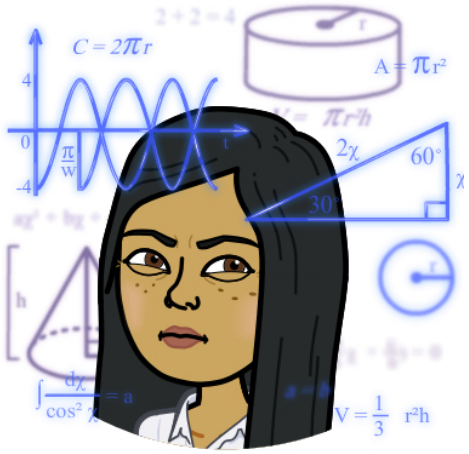
Total Body Weight

Ideal Body Weight

Hydrophilic Drug

Adipose is 30-40% water

Ex: Gentamicin



Hydrophobic Drug

(Lipophilic)

Drug accumulation

Ex: Amphotericin B

Adjusted Body Weight

PK Practical Applications:

Total Body Weight Overestimates Vanco Dose in Obese Patients

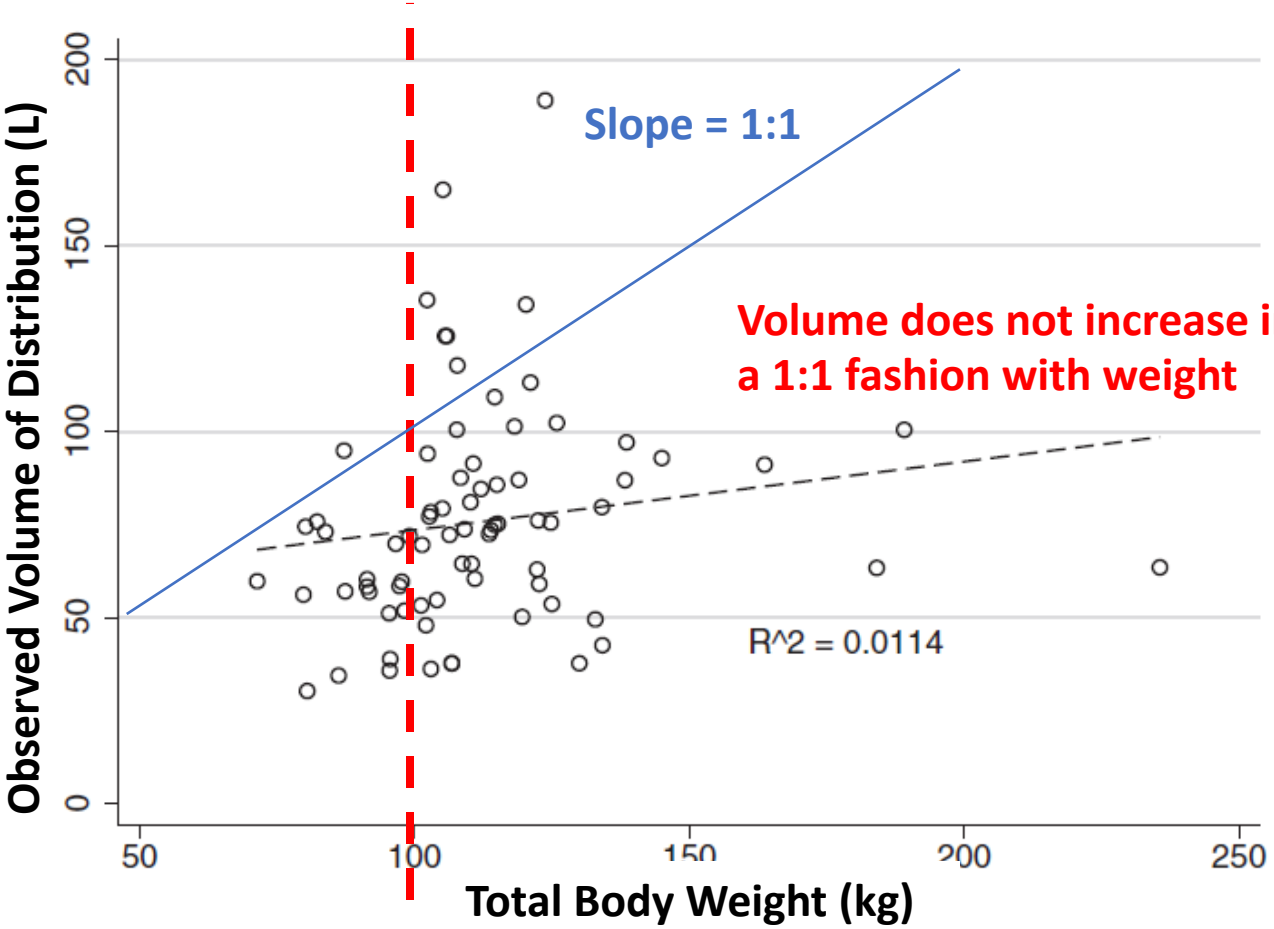
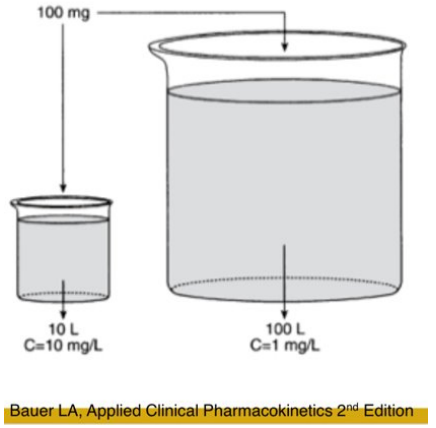


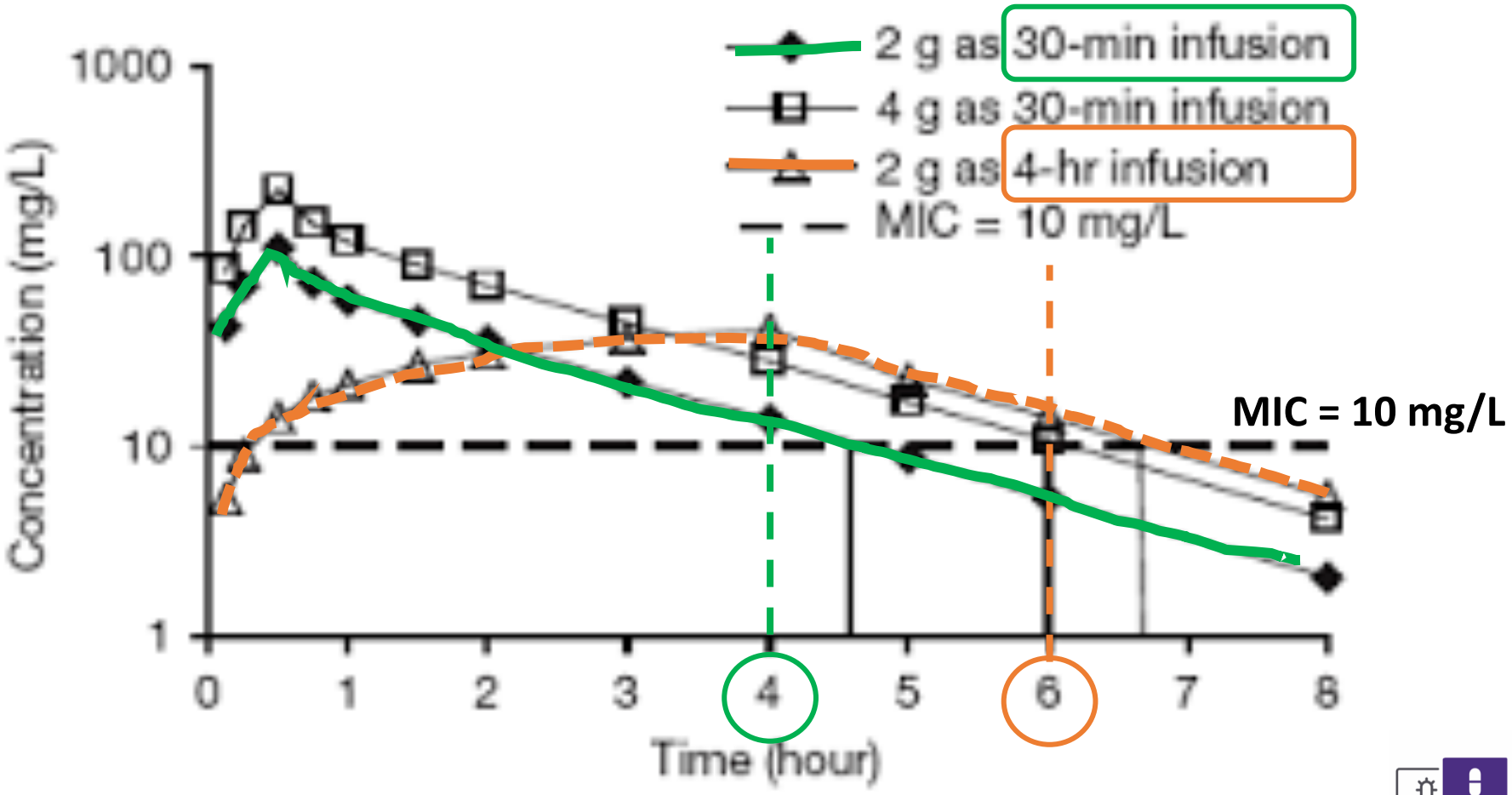
Figure 2. Scatterplot and linear fit plot of the observed vancomycin volume of distribution based on two-sample estimation compared to total body weight.



Pharmacotherapy 2015;35(5):455-463

PD Practical Applications:
Prolonged infusion of Piperacillin/Tazobactam

Dosing goal: Drug concentration > MIC for as long as possible



Lodise TP. Pharmacotherapy 2006;26:1320

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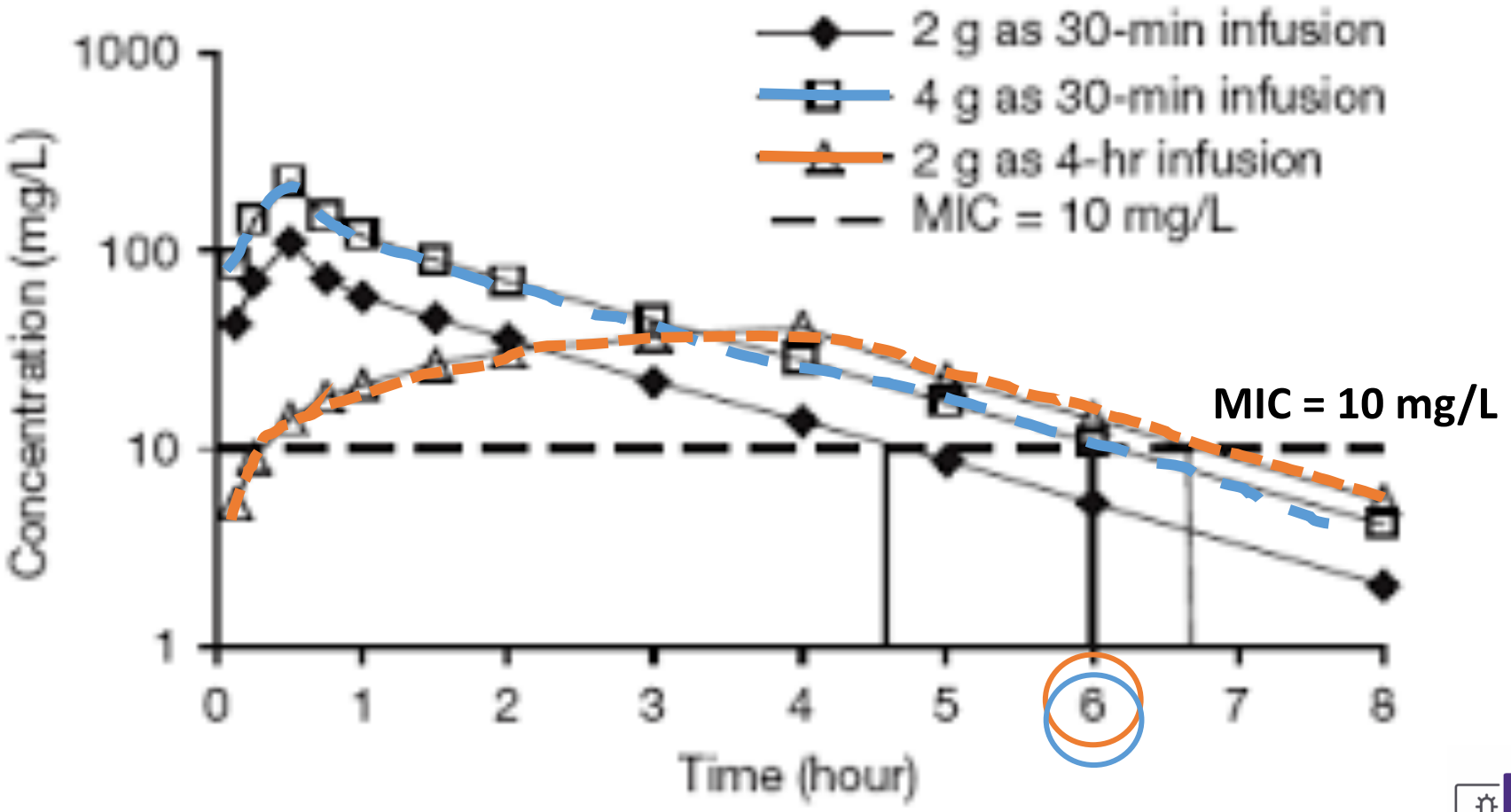

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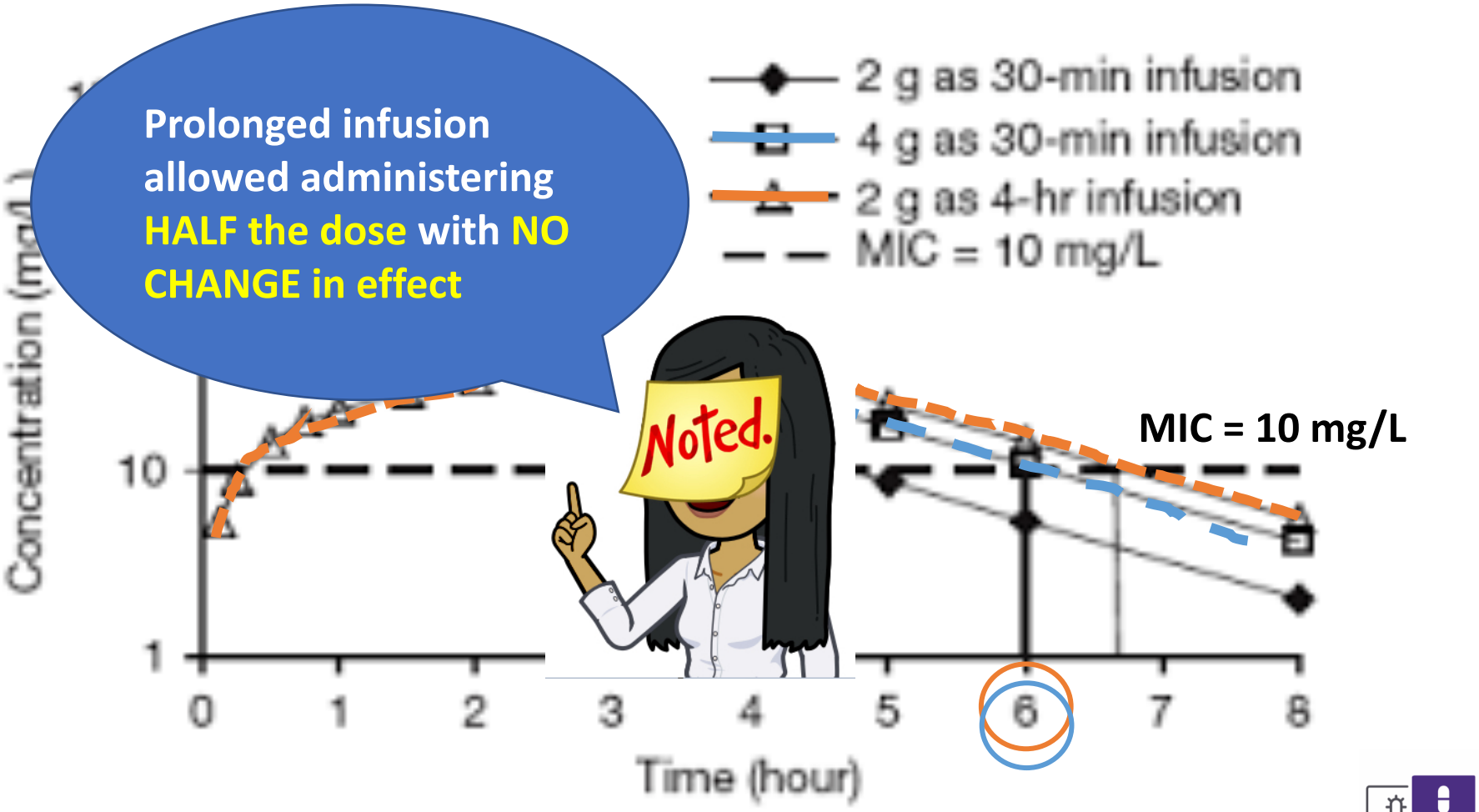

Lodise TP. Pharmacotherapy 2006;26:1320

Summary

PK/PD Dosing Principles

To optimize antibiotic activity (i.e. pick a dose) consider
-How the body acts on the drug (PK)
-How the drug acts on the body/bacteria (PD).

Application: Obesity

Drug concentration does not always increase linearly with weight.
Hydrophilic vs hydrophobic drugs will accumulate differently

Application: Prolonged Infusion

For Pip/Tazo, giving less drug over a prolonged infusion allows reduction in total dosage used without compromising efficacy