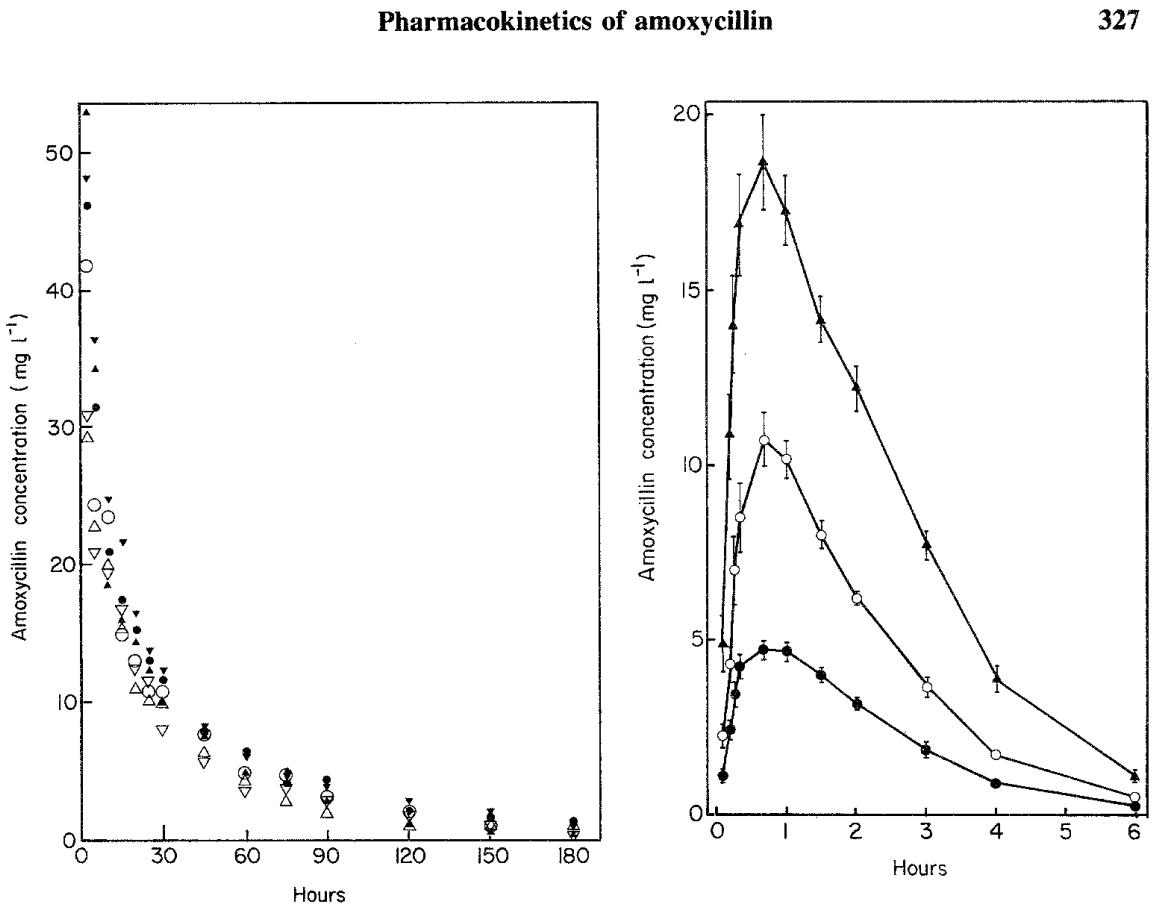
How Physiology-based Pharmacokinetic (PBPK) modelling can aid optimisation of antimicrobials

Christopher Darlow

NIHR Academic Clinical Lecturer (Infectious Diseases & Medical Microbiology)

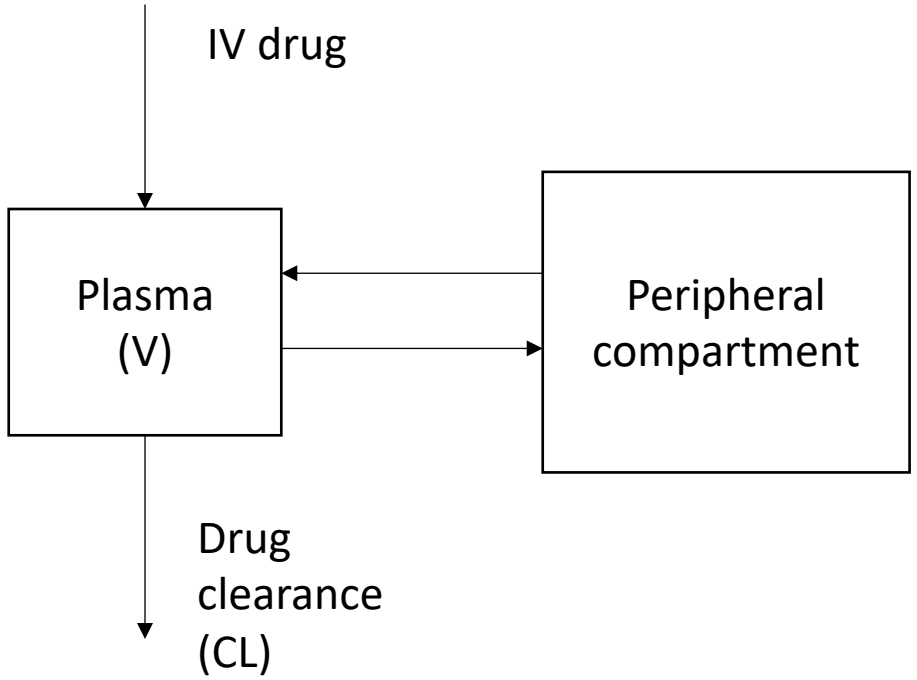
University of Liverpool

Tradition antimicrobial pharmacokinetics



Hill et al, Journal of Infection 1980 ***2****, 320-332*

Population Pharmacokinetics

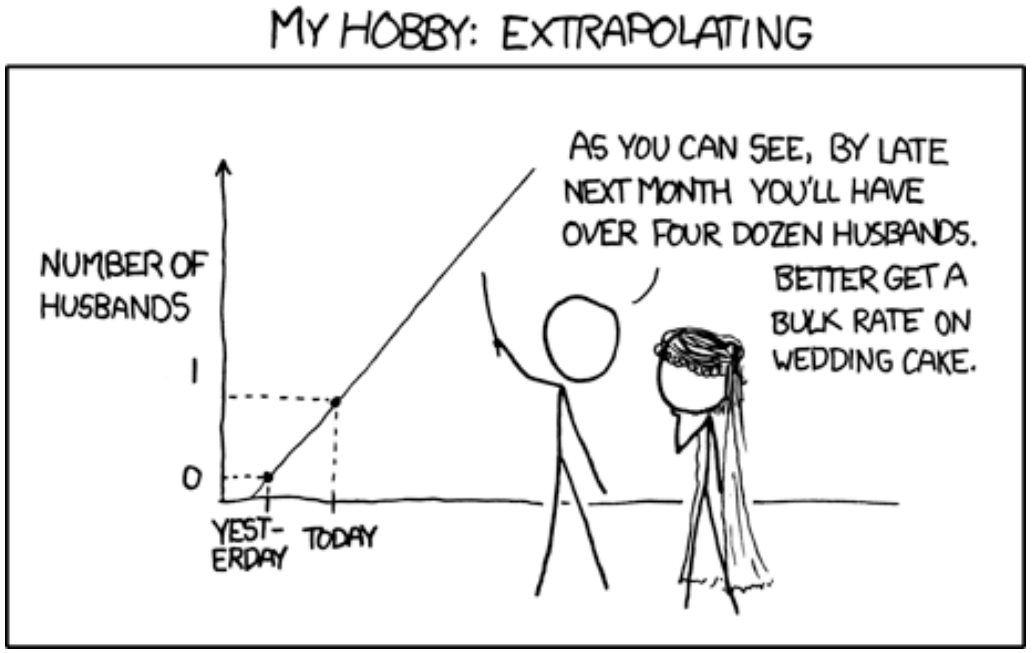


$V = x * (y*\text{body weight}) * (z*\text{age})$

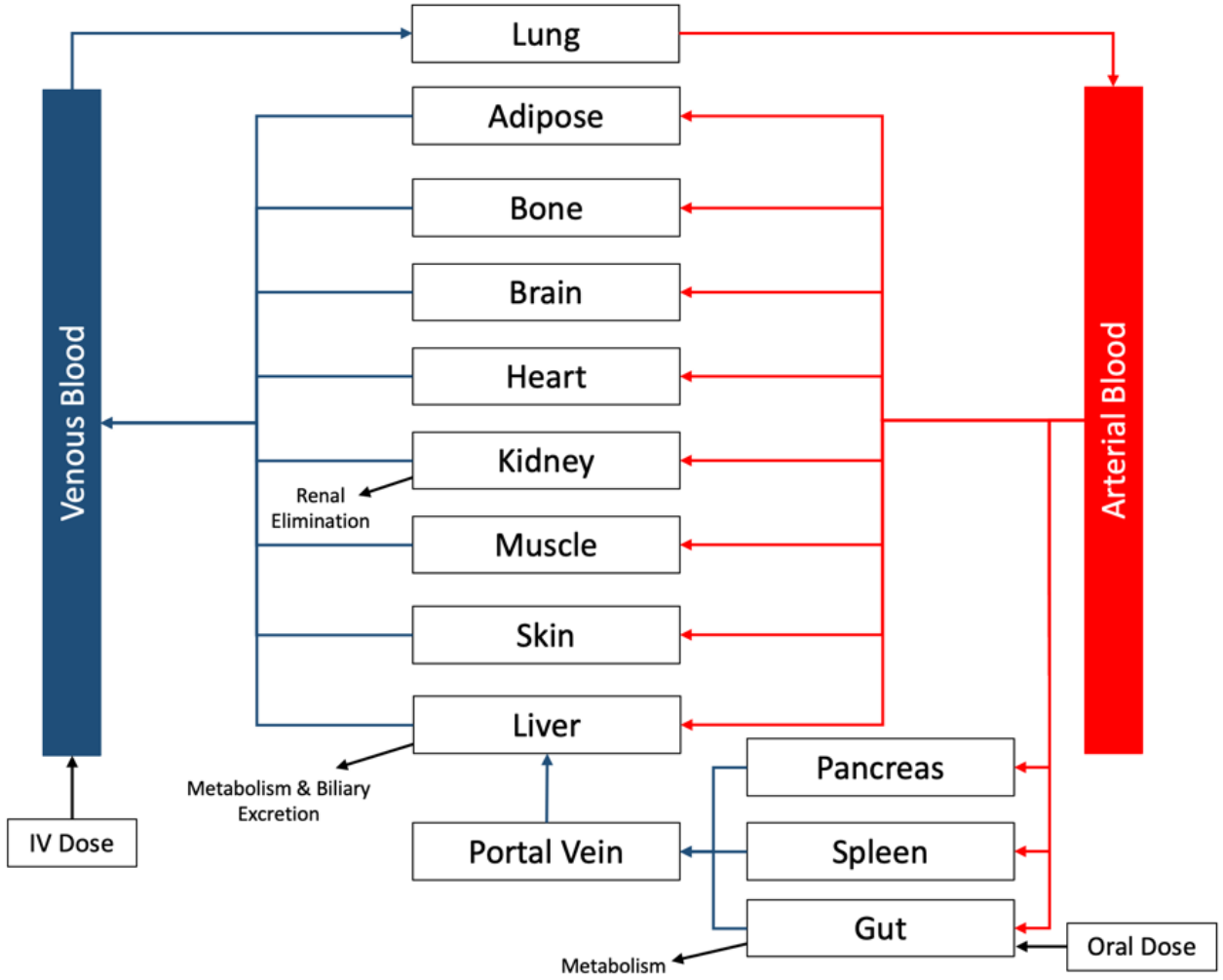
$CL = x * (y*\text{renal function}) * (z*\text{liver function})$

Issues with this approach

- Data often only from healthy volunteers and from a narrow demographic range
- Consequently, use limited to confines of the data
- Use in special populations and demographics extrapolates beyond the data.



PBPK modelling



Role of PBPK modelling in CAMO-Net

1. Prediction of antimicrobial PK in varying physiologies
   a. Different demographics (e.g. ethnicities)
   b. Different age groups (e.g. children, neonates, elderly)
   c. Different physiological circumstances (e.g. obesity, renal failure, pregnancy)

2. Prediction of tissue concentrations where sampling impractical

3. Prediction of the effect of drug-drug interactions

Specific plans

1. Build PBPK models for amoxicillin, clavulanic acid and flucloxacillin

2. Use these models to explore systemic and tissue drug exposures in special populations (neonates, obesity etc) and differing demographics (e.g. non-Caucasian ethnicities)

3. Long term look to integrating with a systems pharmacology pharmacodynamic model

Thank you