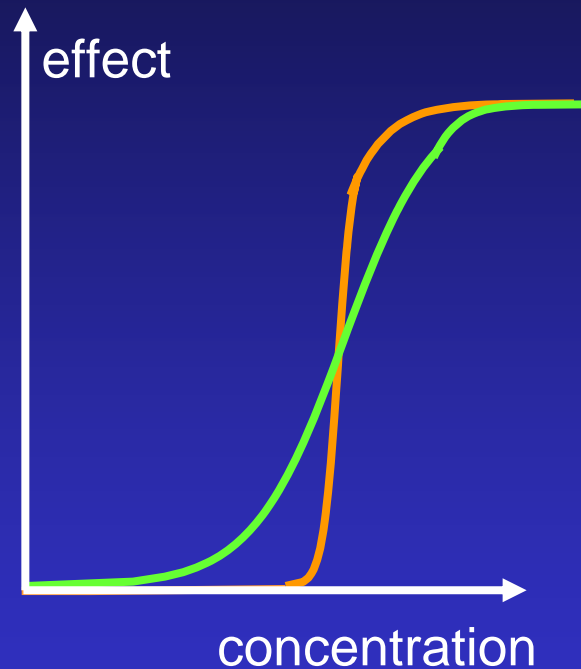


Pharmacodynamics: the concepts



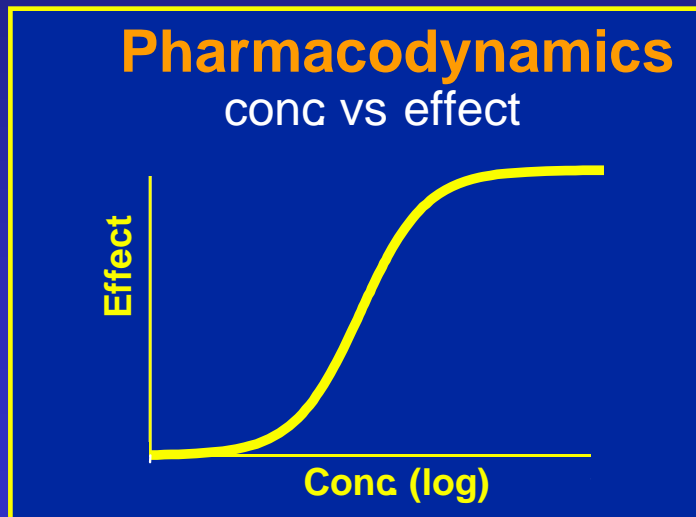
- What is pharmacodynamics ?
- dose-response models
 - the yes/no model
 - the linear model
 - The sigmoidal model
- influence of time

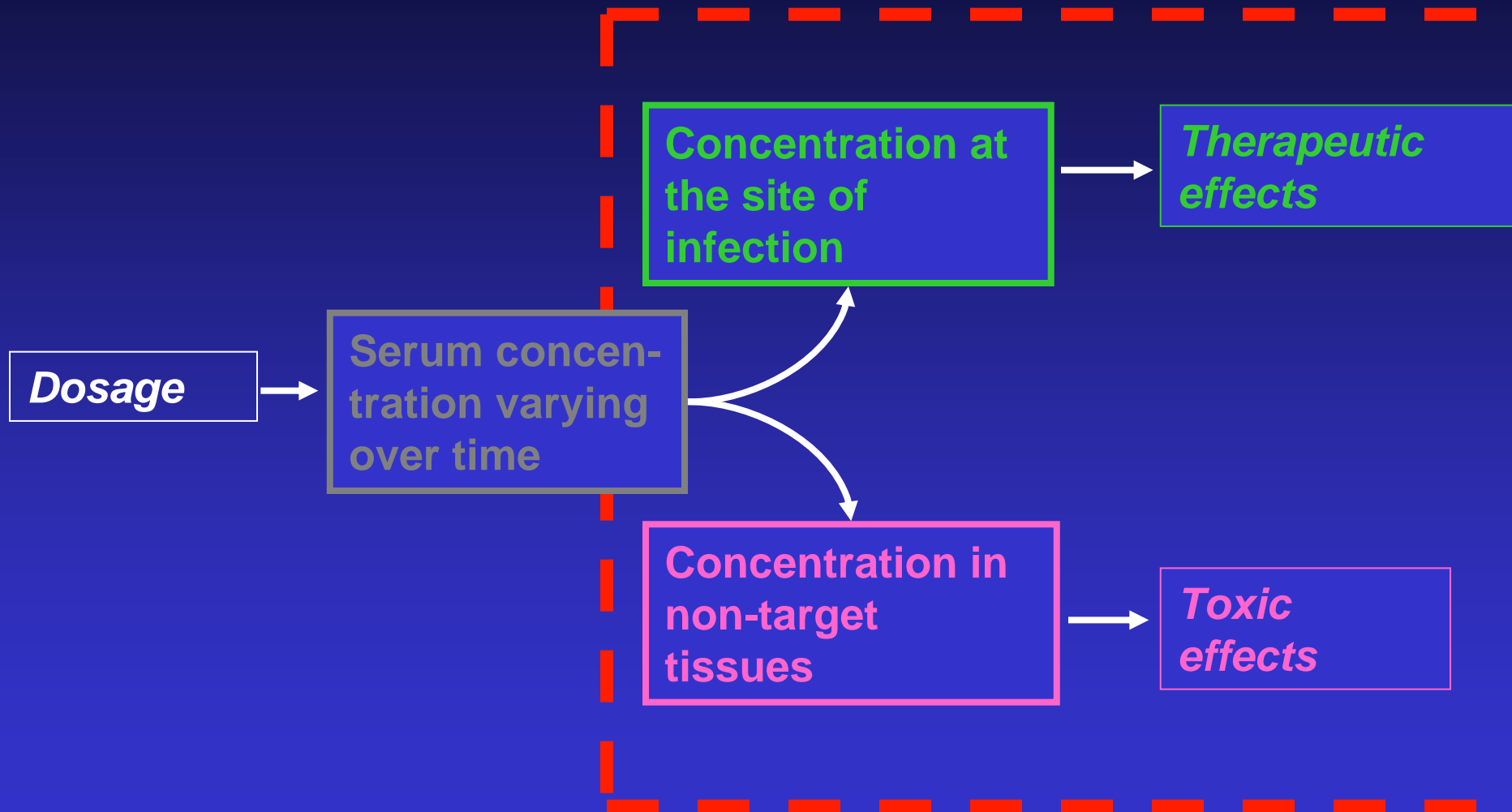
With the support of *Wallonie-Bruxelles-International*

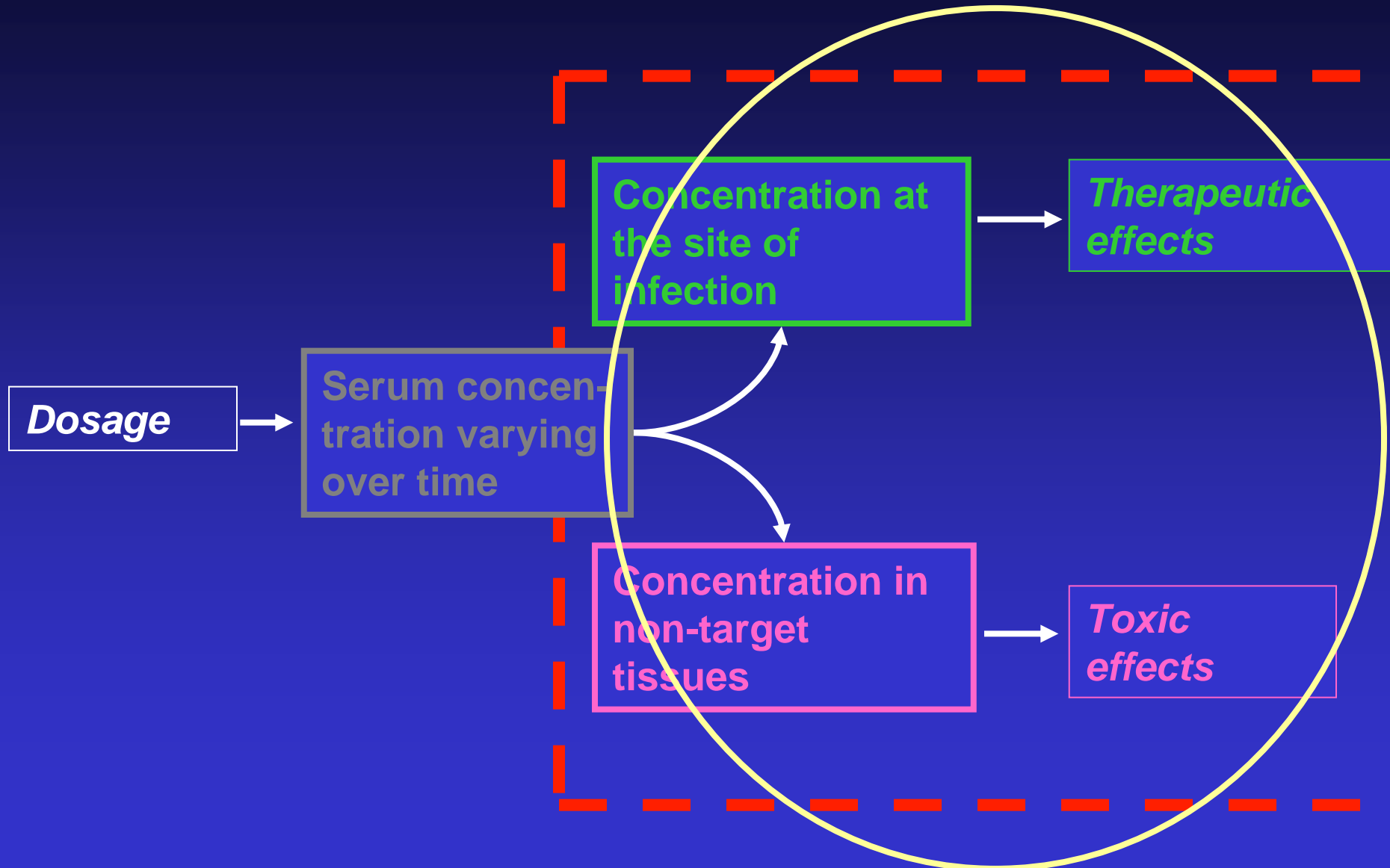


What is pharmacodynamics ?

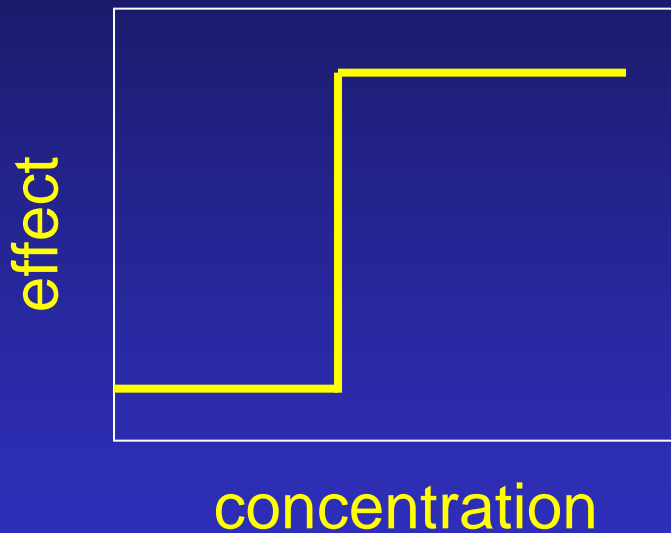
what the drug does to the body ...







Pharmacodynamics : the yes and no model



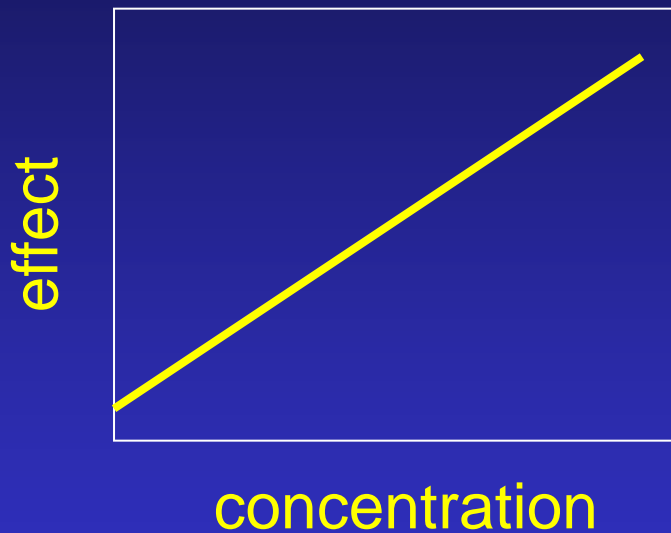
- sharp threshold
- maximal effect immediately observed

This is the model assumed by

- the breakpoints approach !!
(S - R)
- the cured / non-cured clinical endpoint !!

BUT can you be black or white ?

Pharmacodynamics : the linear model ...

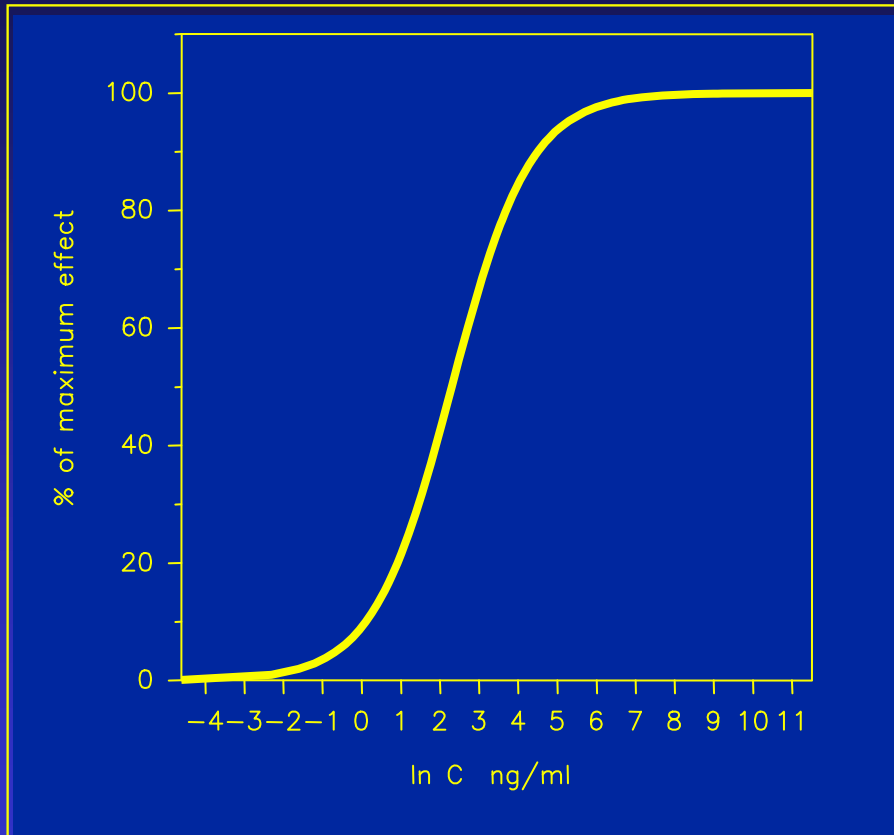


- continuously increasing effect
- effect matches dosing

This is the model assumed by the "high dosing in severe infections" approach ...

→ *the more you give, the more it must be active... No ?*

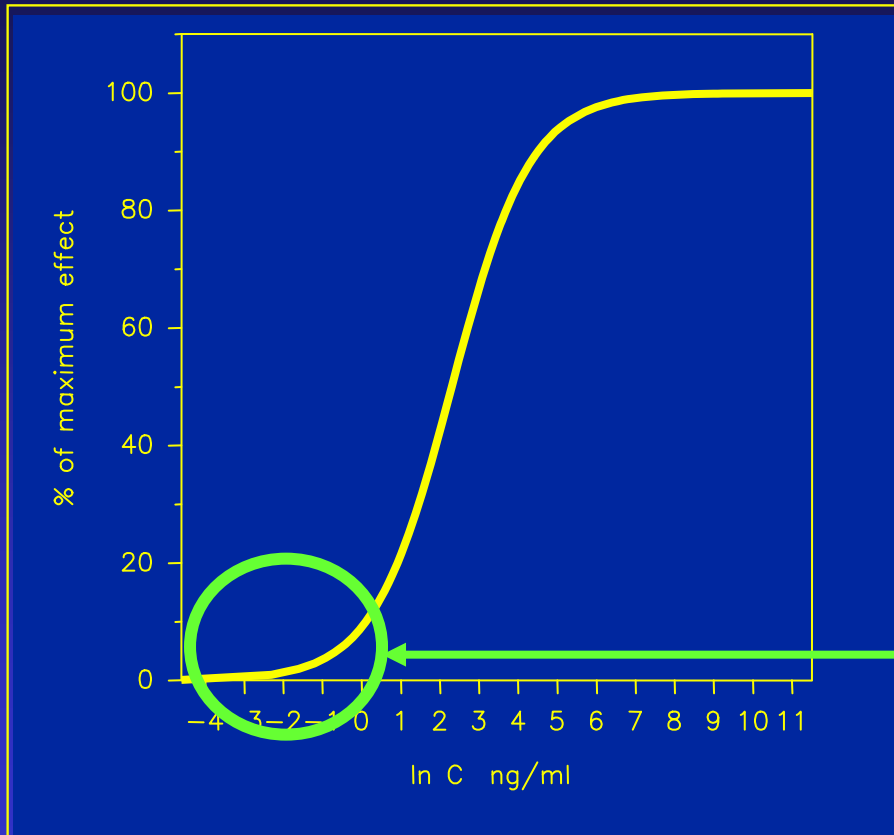
Pharmacodynamics : the sigmoidal dose-response model



- starting treshold
- dose-response in a given zone
- maximum reached

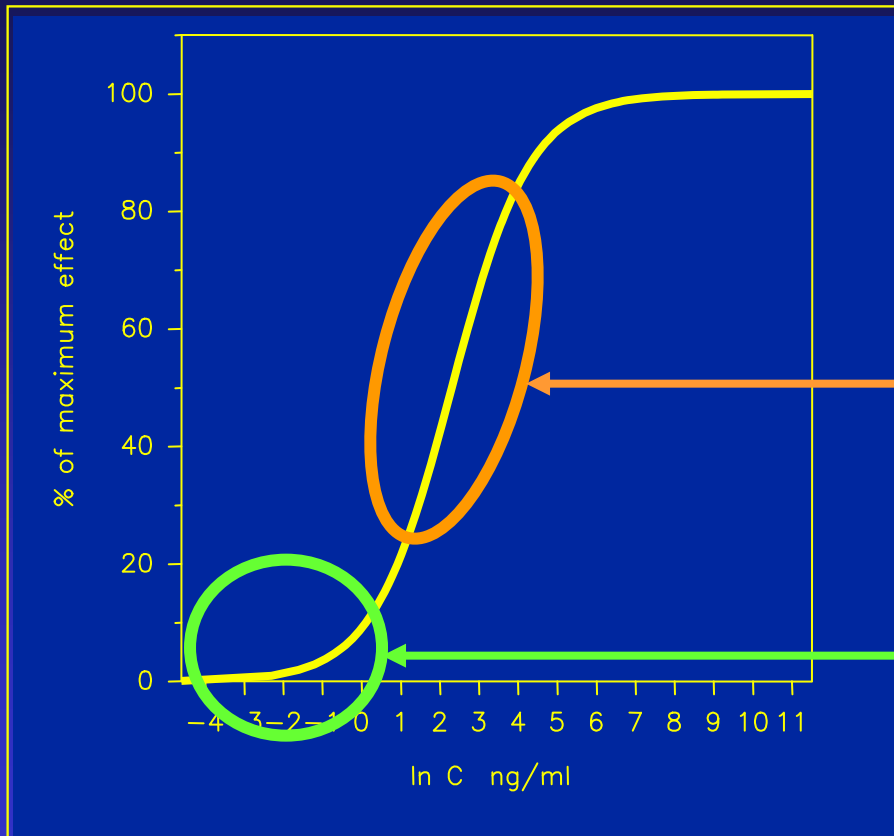
This is the classical pharmacological model and corresponds to reality

Pharmacodynamics : the sigmoidal dose-response model



lowest limit of action

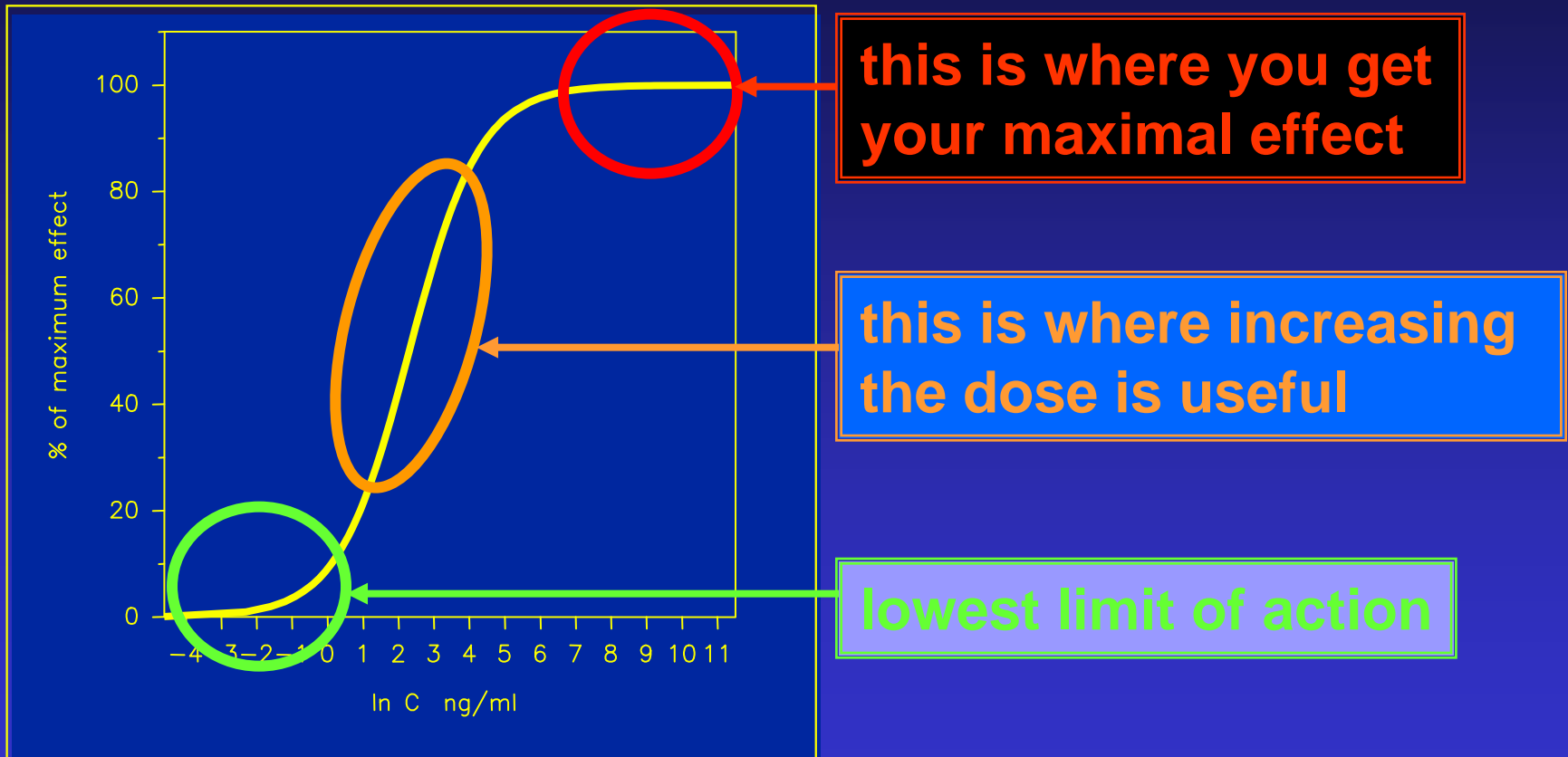
Pharmacodynamics : the sigmoidal dose-response model



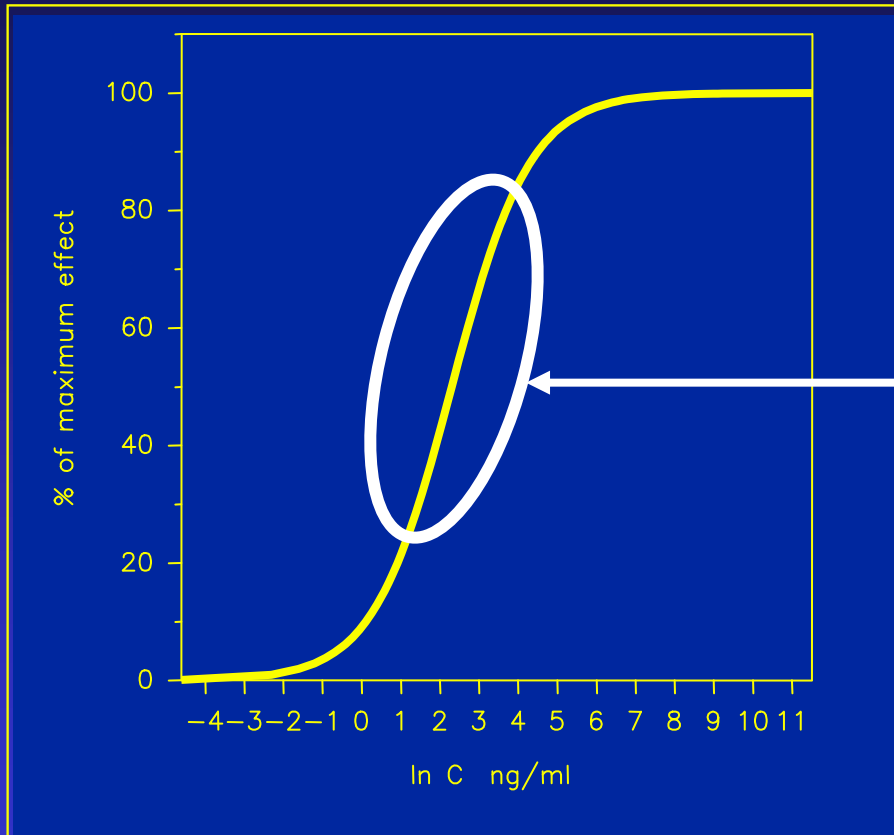
this is where increasing the dose is useful

lowest limit of action

Pharmacodynamics : the sigmoidal dose-response model

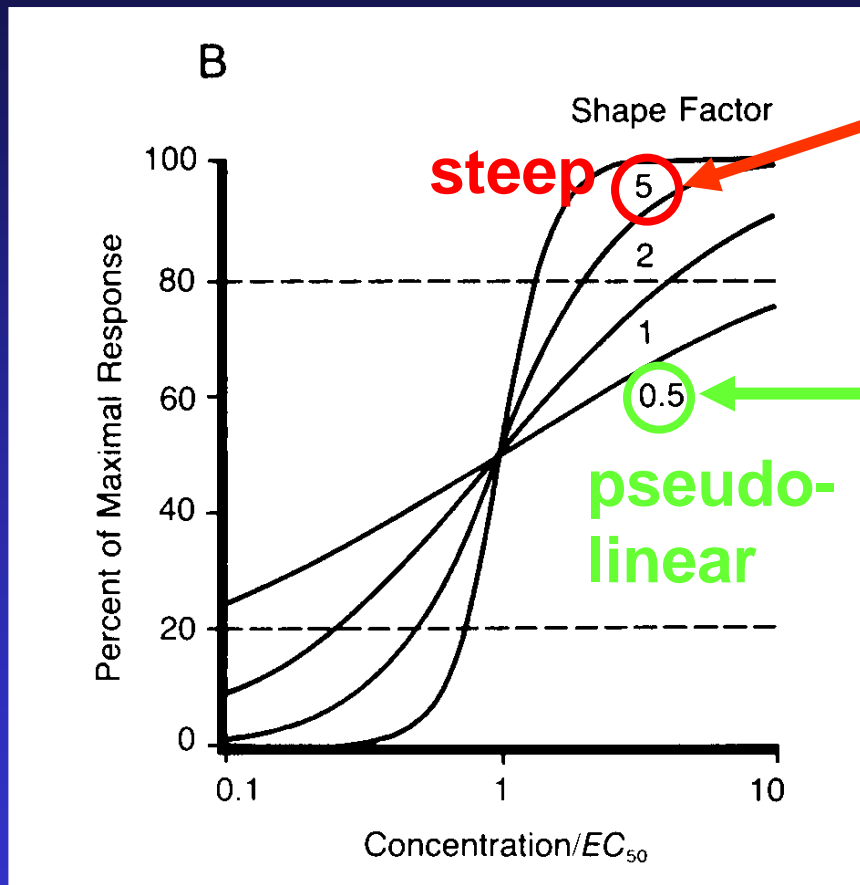


Sigmoidal response: the importance of the shape of the curve



The "shape factor" describes the steepness of the response ...

Some antibiotics are steep, others are less steep...



β -lactams, vancomycin, ...

- narrow dose-response zone
- tendency to yes/no

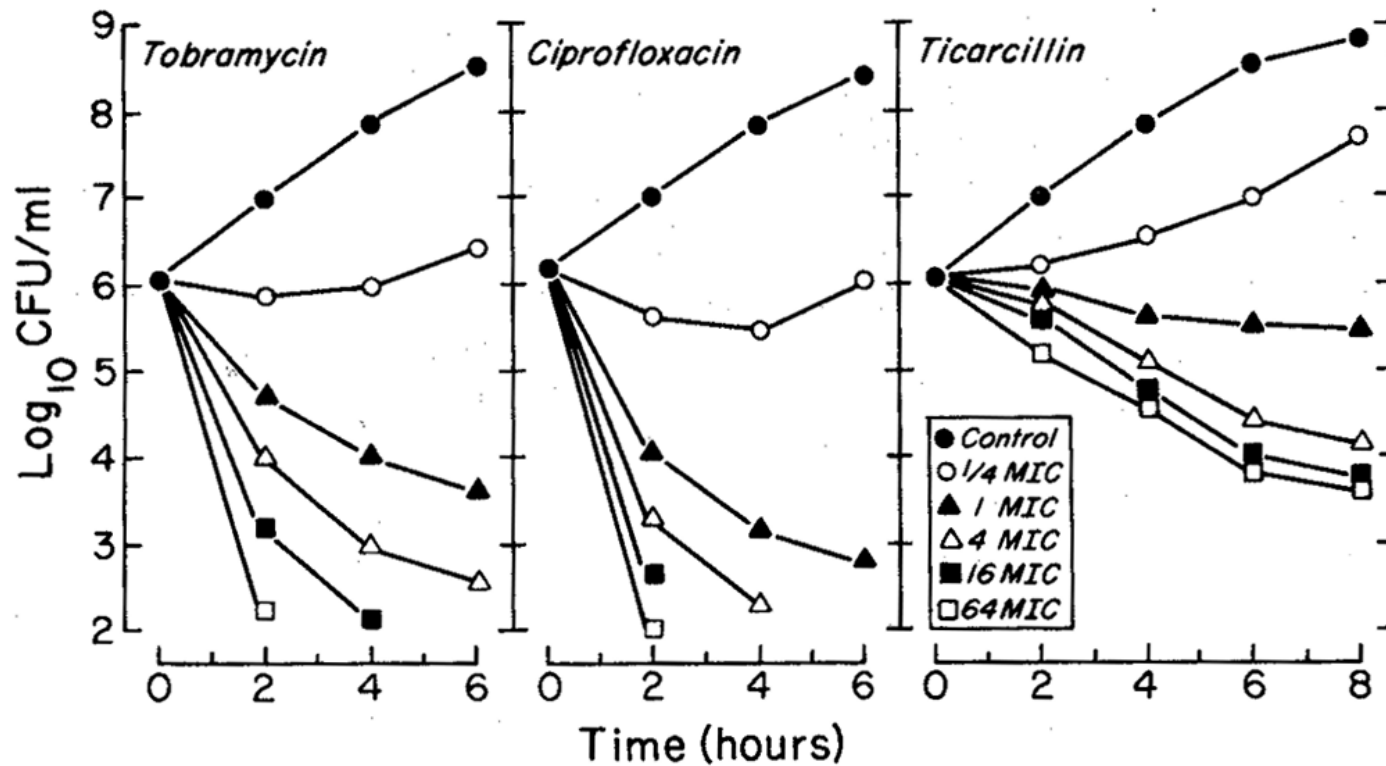
aminoglycosides,
fluoroquinolones

- wide dose-response zone
- increasing the concentration causes more effect

Pharmacodynamics : influence of time ...

all antibiotics are dependent on time...

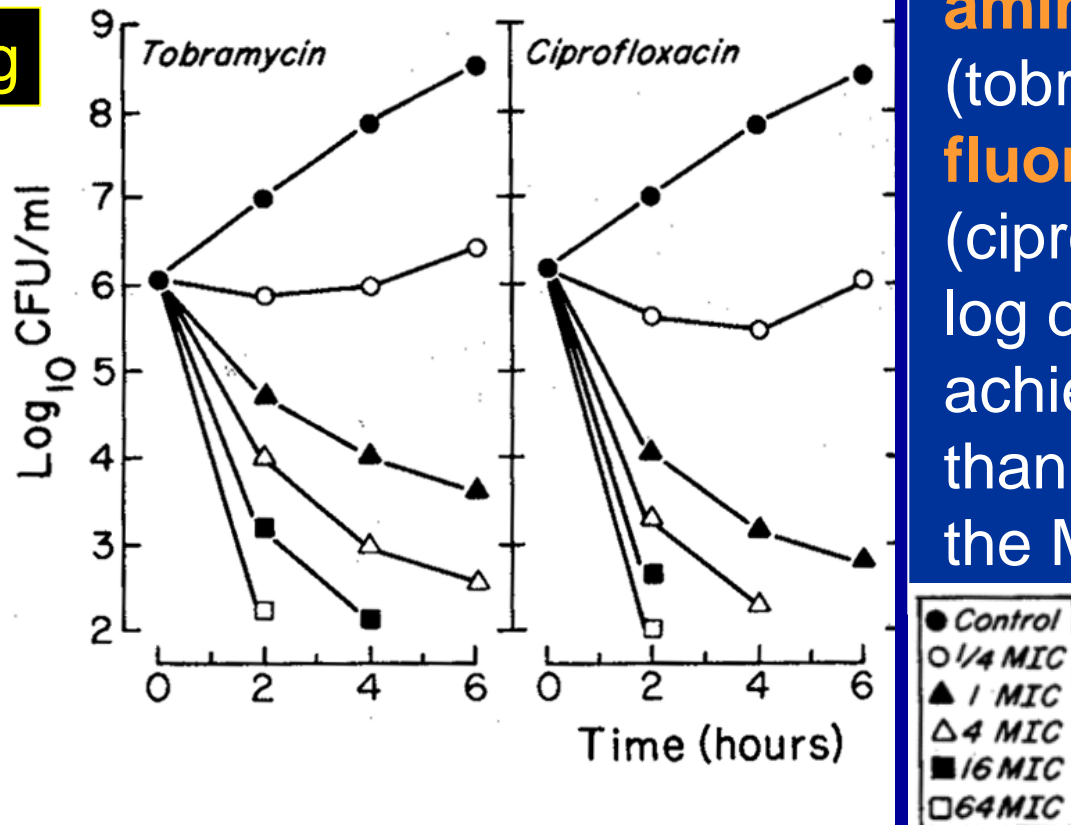
killing



Pharmacodynamics : influence of time ...

But some kill so fast that time becomes unimportant.

killing

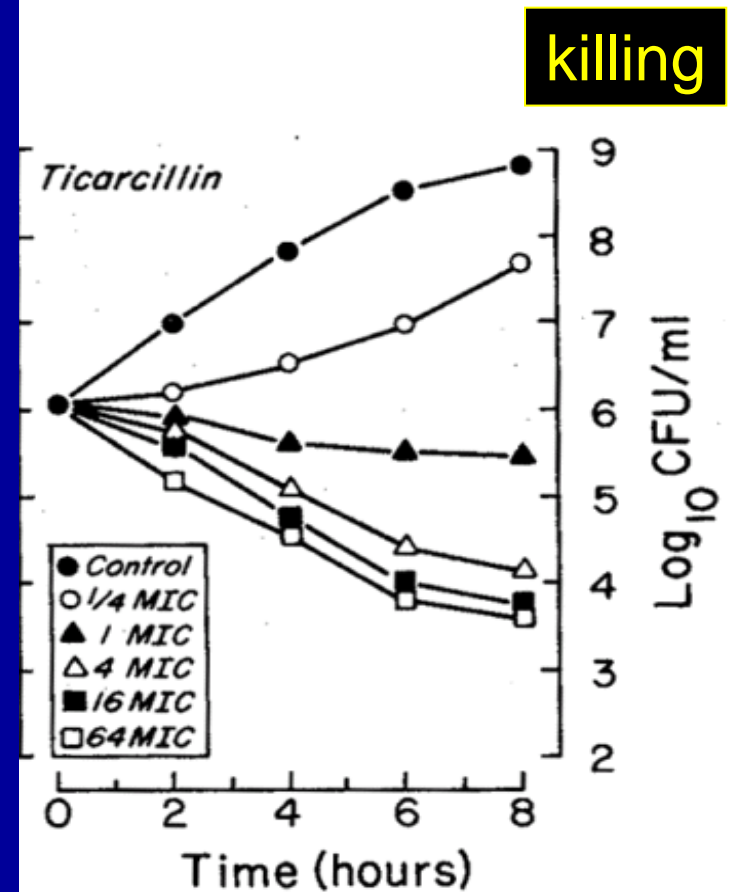


With an **aminoglycoside** (tobramycin), or a **fluoroquinolone** (ciprofloxacin) a 4 log decrease is achieved in less than 4-6 h at 4 X the MIC

Pharmacodynamics : influence of time ...

But some kill so fast that time becomes unimportant.

But with a **β -lactam**, you achieve only a 2 log decrease in 6 h,
... and it does not go much faster if you increase the concentration above 4 X the MIC



Pharmacodynamics : concentration x time

antibiotic

dose
response

influence
of time

clinical
consequence

- β -lactams (all)
- glycopeptides
- macrolides
- tetracyclines

narrow

critical

- exposure must be prolonged
- high concentrations are unimportant

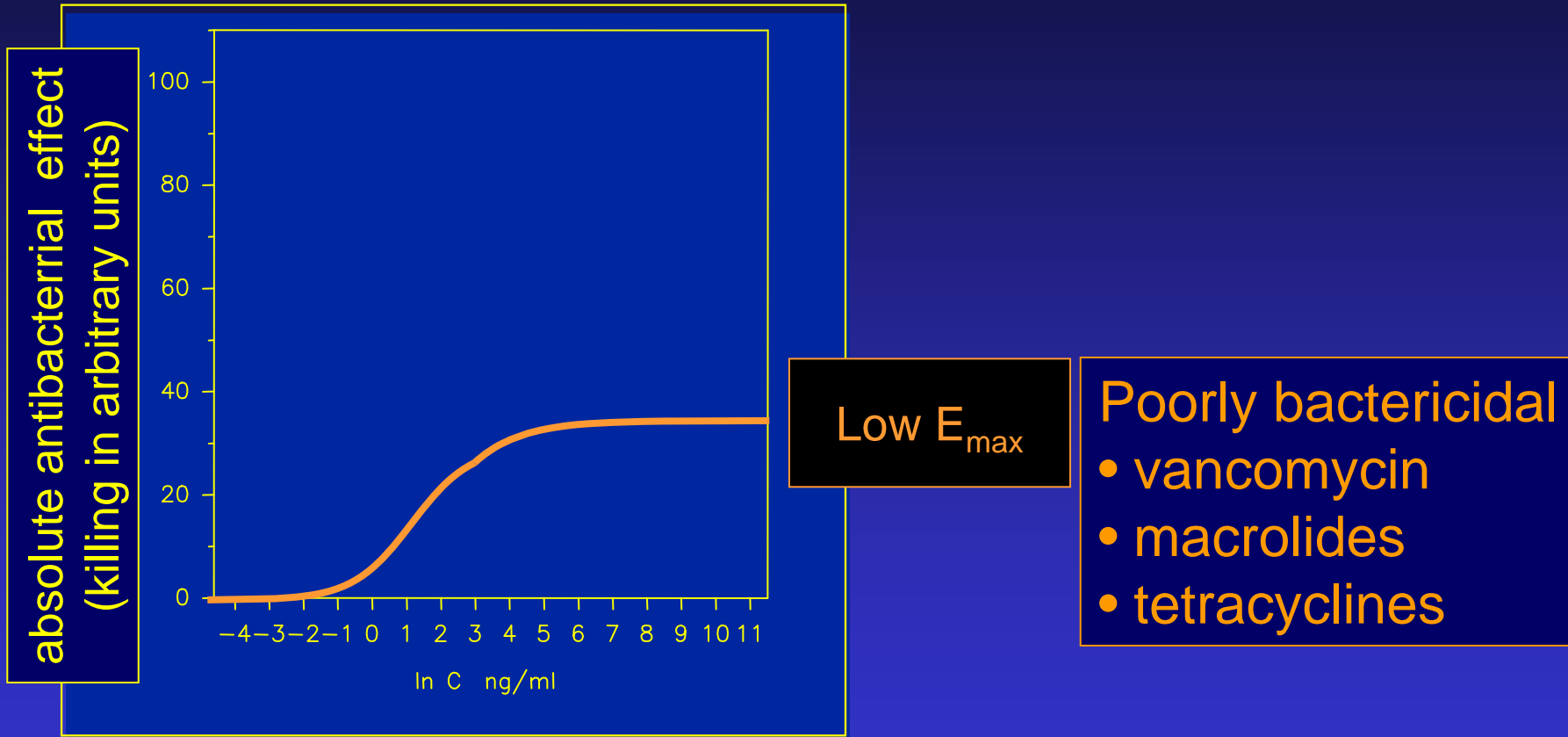
- aminoglycosides
- fluoroquinolones

large

limited

- concentrations are important
- time is not critical

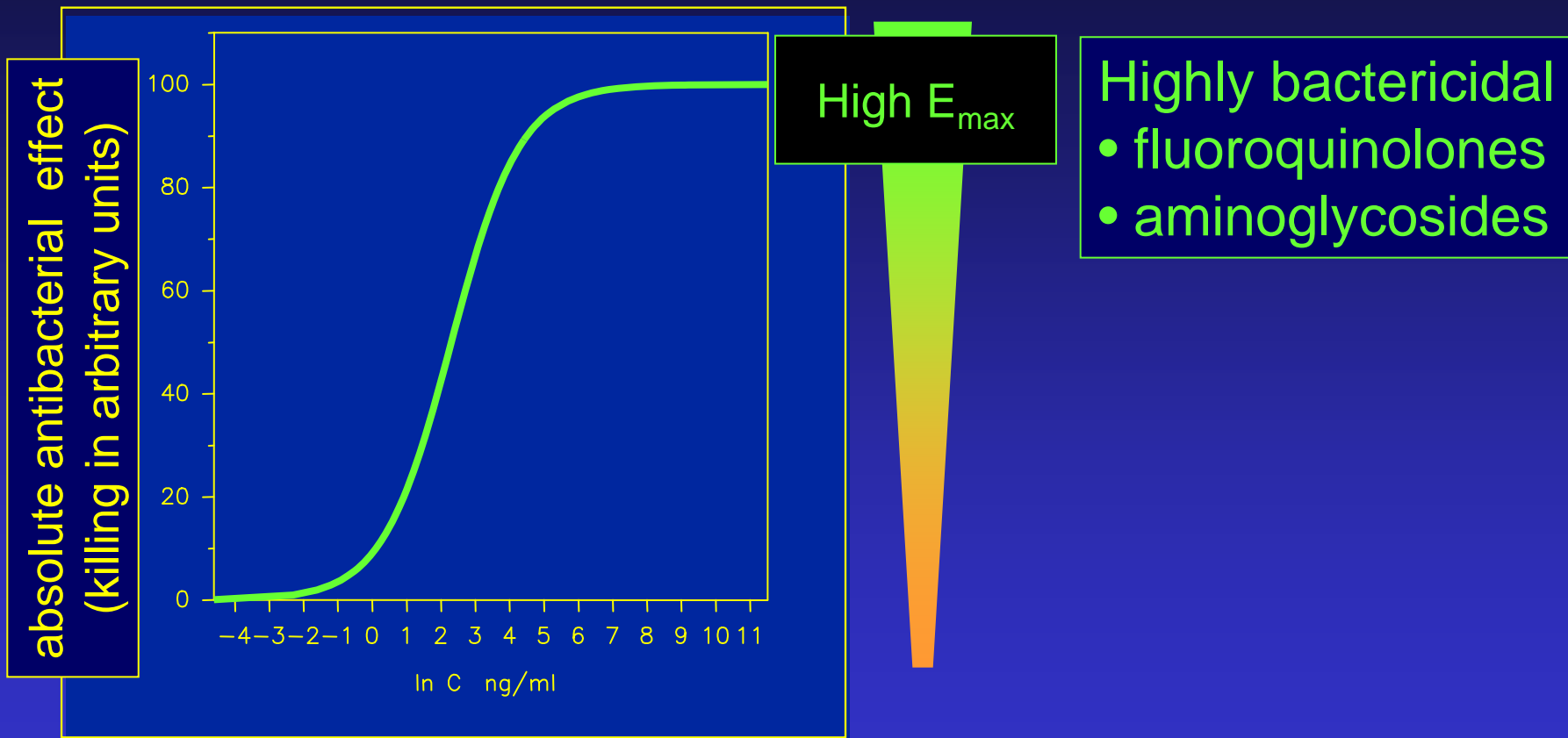
Some antibiotics are less powerful than others: look for E_{\max}



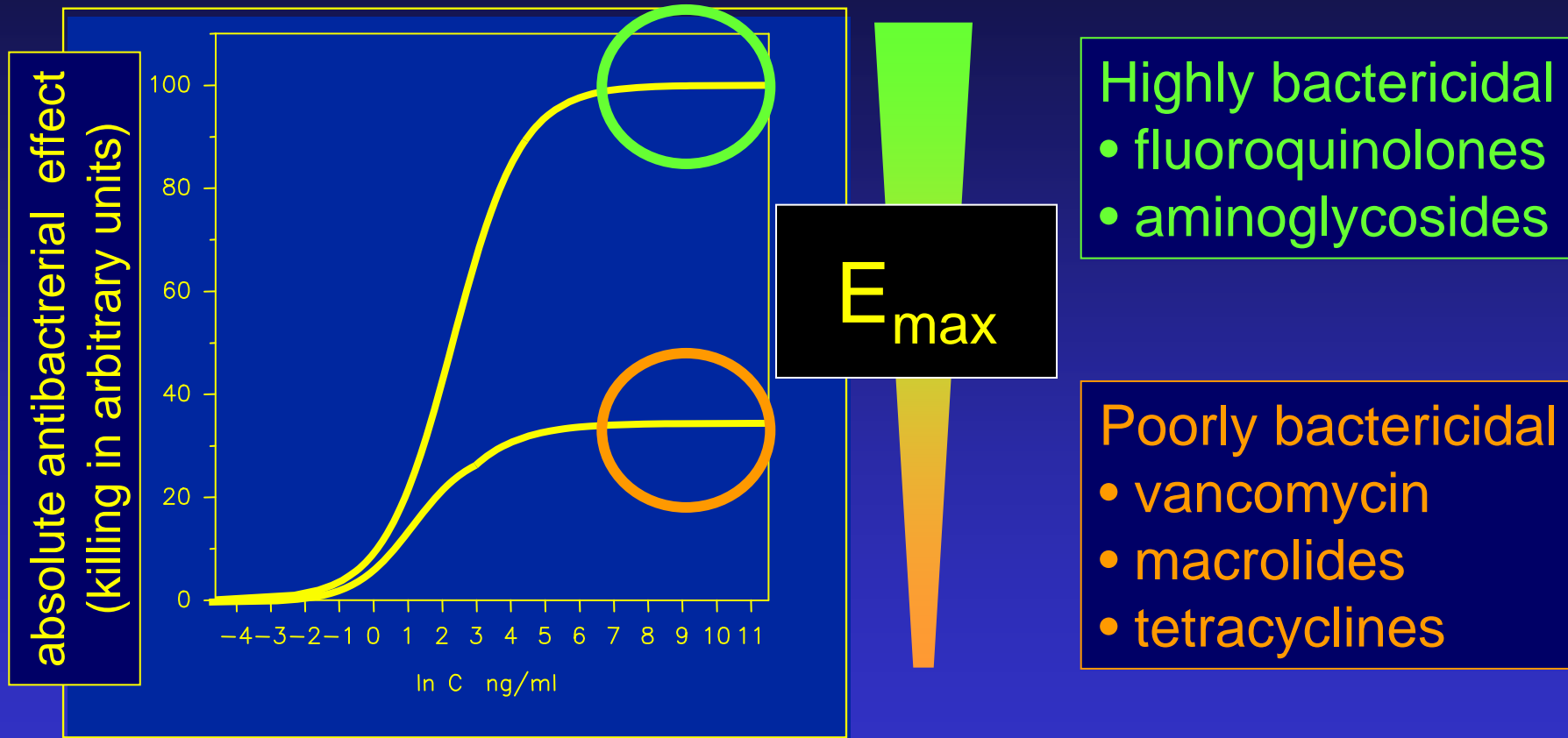
But some antibiotics are more powerful than others



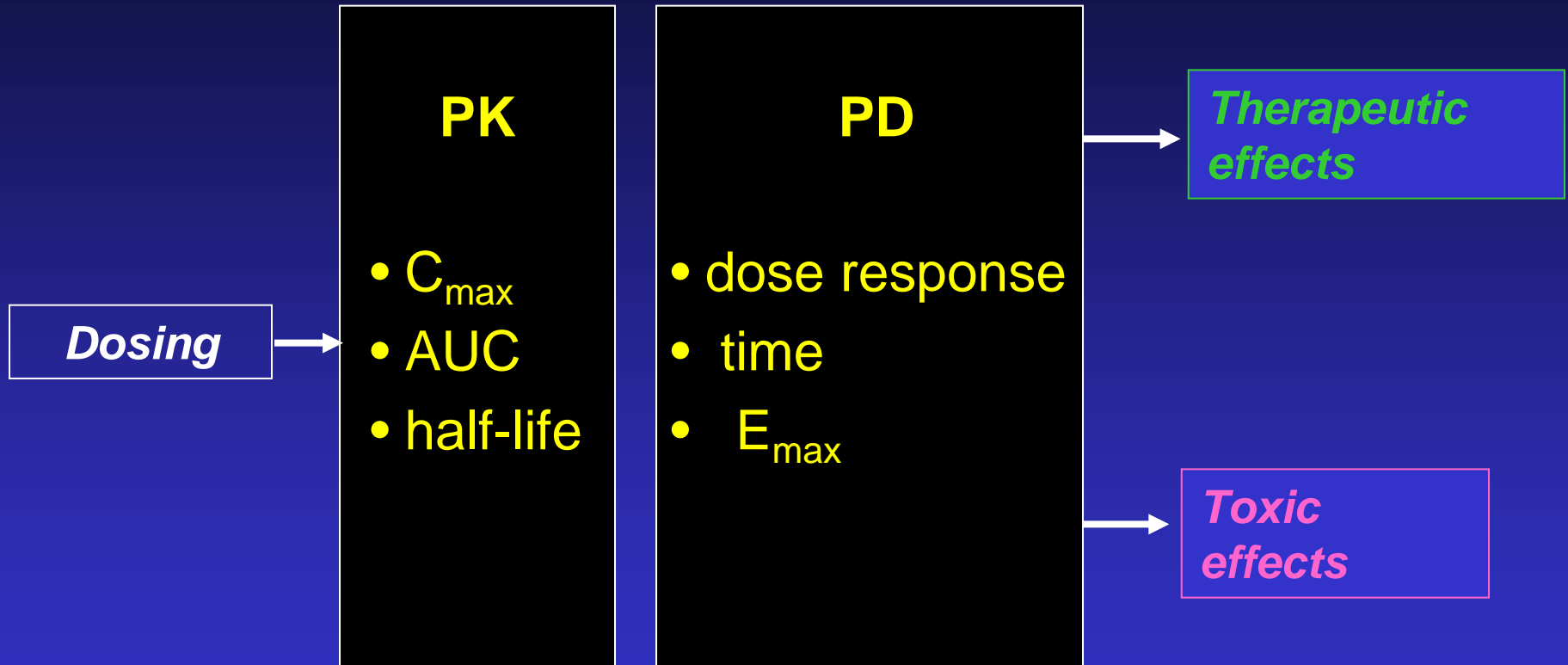
Some antibiotics are more powerful than others: look for E_{\max}




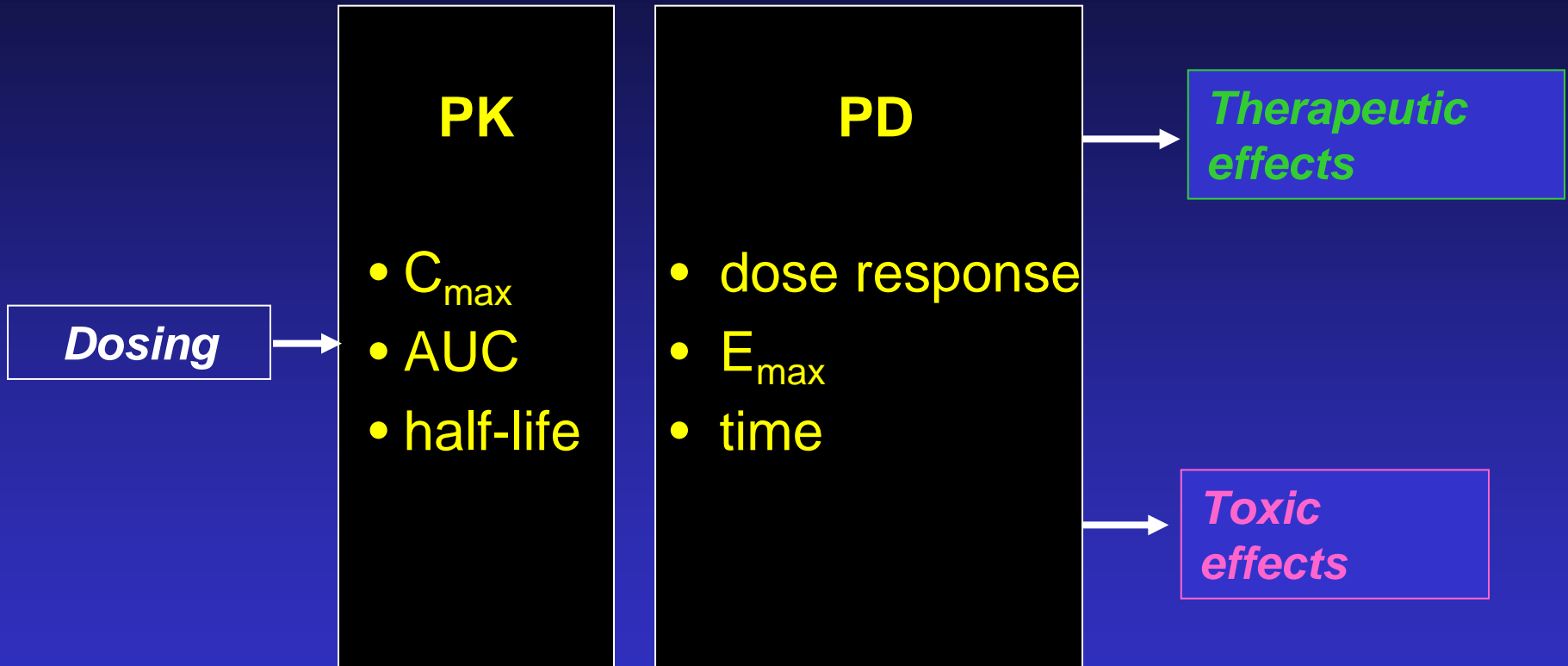
E max tells you how active you are ...



This is where we are now ...



This where we are now ... 



We will now see the methods used ...

 **Section 3 b**