

## Optimising antimicrobial therapy – the MPC as a strategy to minimise antibiotic resistance



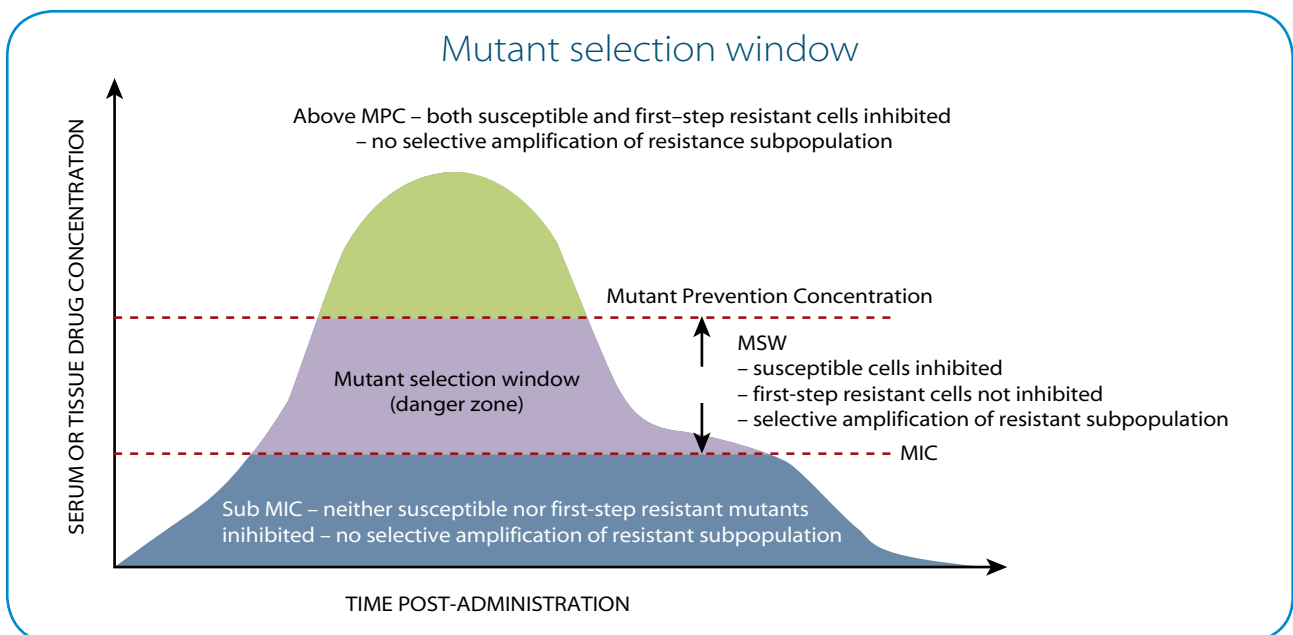
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Dr. Blondeau has published in excess of 125 peer reviewed publications in many different journals, and has over 175 abstracts of his research findings at various international meetings. He has given in excess of 470 invited presentations worldwide.

### Mutant Prevention Concentration\* (MPC)

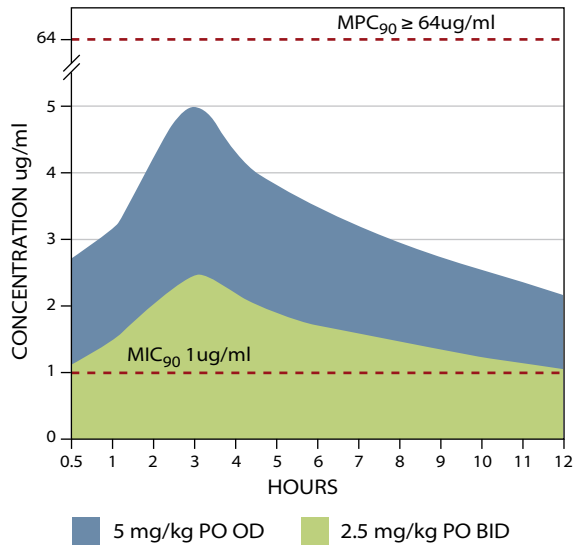
The MPC is the antimicrobial drug concentration that blocks the selection of bacterial sub-populations (from a high density bacterial inoculum) which require an amount of drug in excess of the susceptibility breakpoint to inhibit growth. The MPC is:

- the minimum inhibitory concentration (MIC) of the least susceptible organism in a population
- applies to organisms considered susceptible by routine testing
- independent of the mechanism of resistance
- determined in the laboratory using agar solution as for the MIC but by applying  $10^{10}$  cells rather than  $10^5$



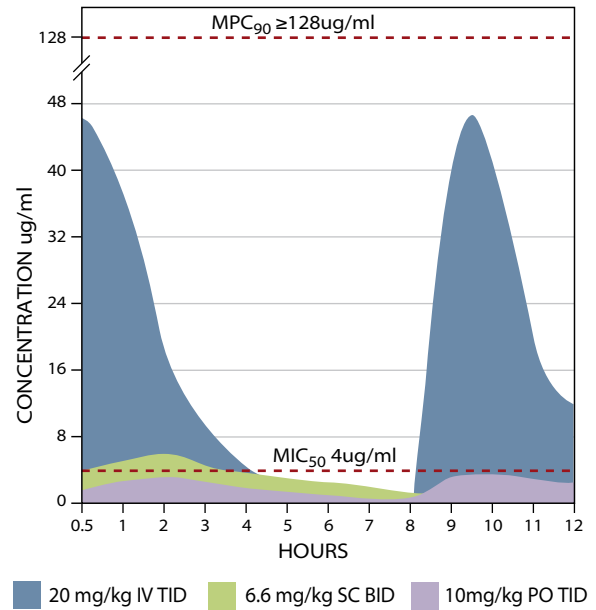
## Doxycycline - *E. coli*

TIME DEPENDENT



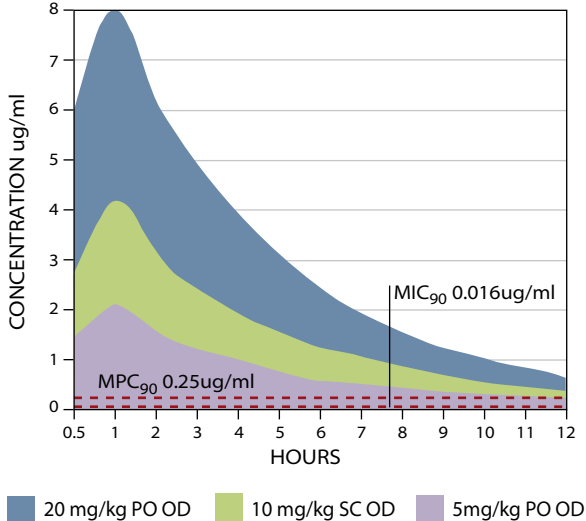
## Ampicillin - *E. coli*

TIME DEPENDENT



## Enrofloxacin - *E. coli*

DOSE DEPENDENT



How do we make antimicrobial resistance prevention a goal of therapy?

- Use drugs only when necessary
- Incorporate microbiological and pharmacological breakpoints/endpoints
- Dose based on MPC? Is this possible?
- Does 'save the best for last' work, and is it the best strategy?
- There is no such thing as a benign drug

## Conclusions

- Antimicrobial resistance is prevalent domestically and globally
- Antimicrobial resistance is clinically relevant
- MPC modeling demonstrates the necessity of having drug concentrations achieving, maintaining, and remaining in excess of MPC values
- Less active agents more readily select for resistance leading to cross resistance of other agents within the class
- Newer agents or agents that are dosed to achieve Pharmacokinetic/pharmacodynamic and microbiological breakpoints may be less likely to select for resistance, however, this needs to be resolved clinically