Dr Matthew B. Avison, Senior Lecturer in Microbiology
School of Cellular & Molecular Medicine

AMR, a Microbiologist's Perspective.

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AMR Is Complicated

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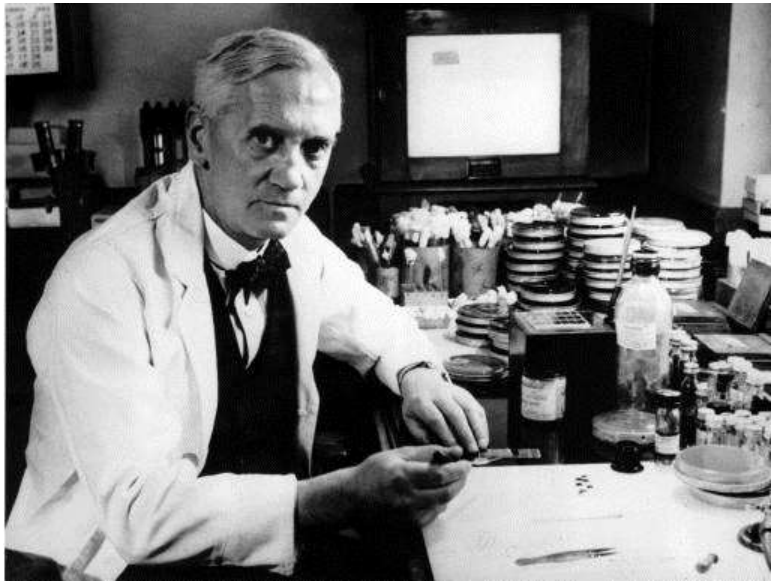
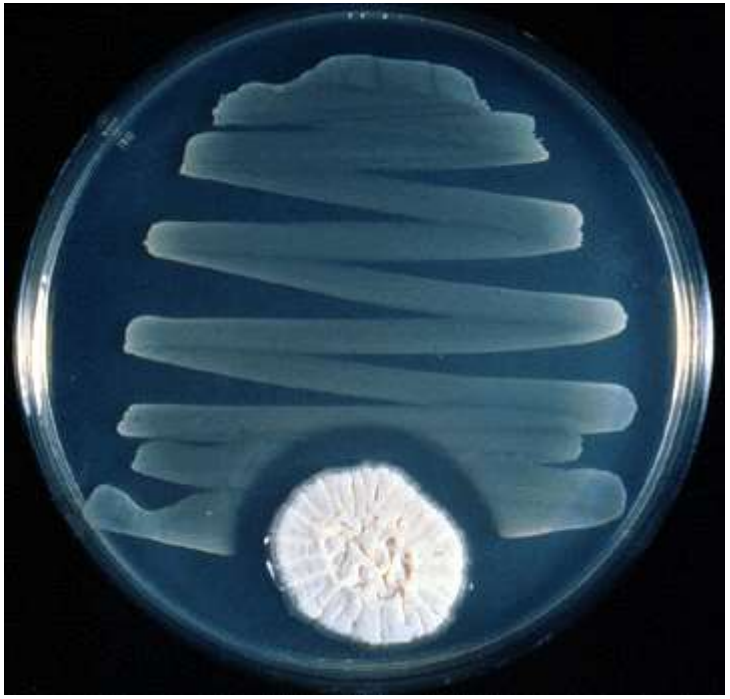
Penicillin: the β-lactam antibiotic class

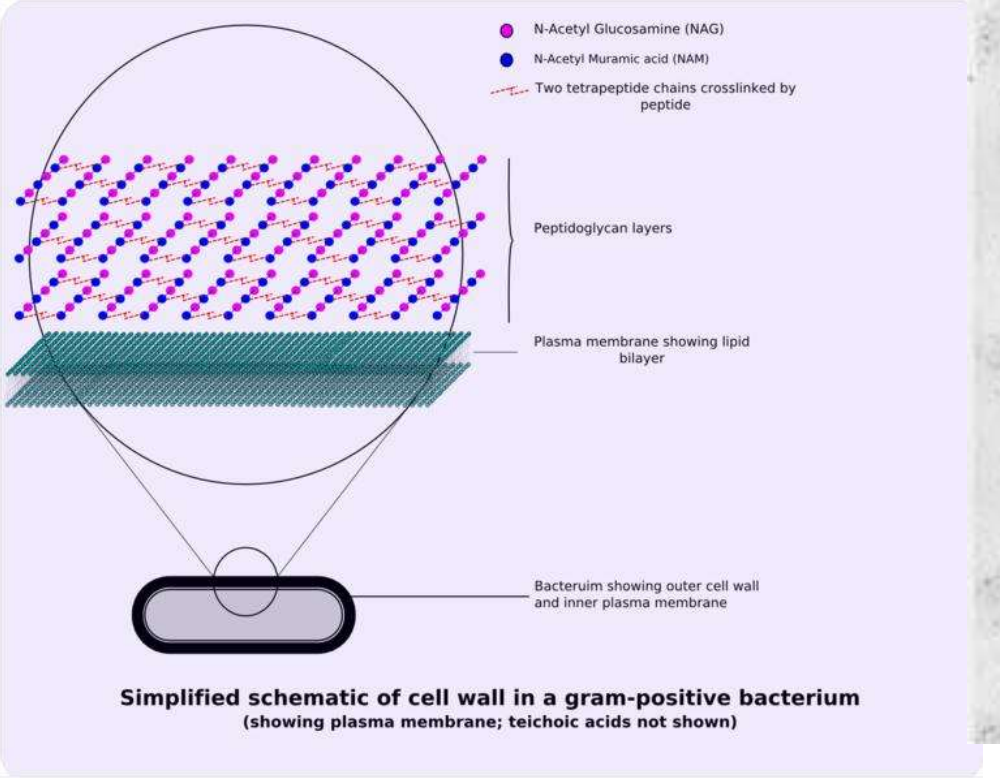


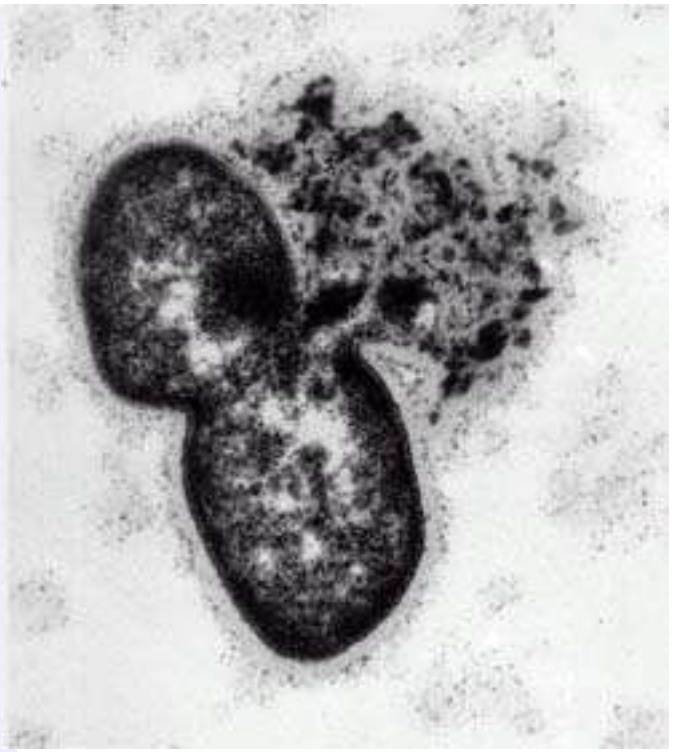
Alexander Fleming



The Mode of Action of β-Lactams

β-Lactams inhibit bacterial cell wall cross-linking by inhibiting Penicillin Binding Proteins (PBPs)





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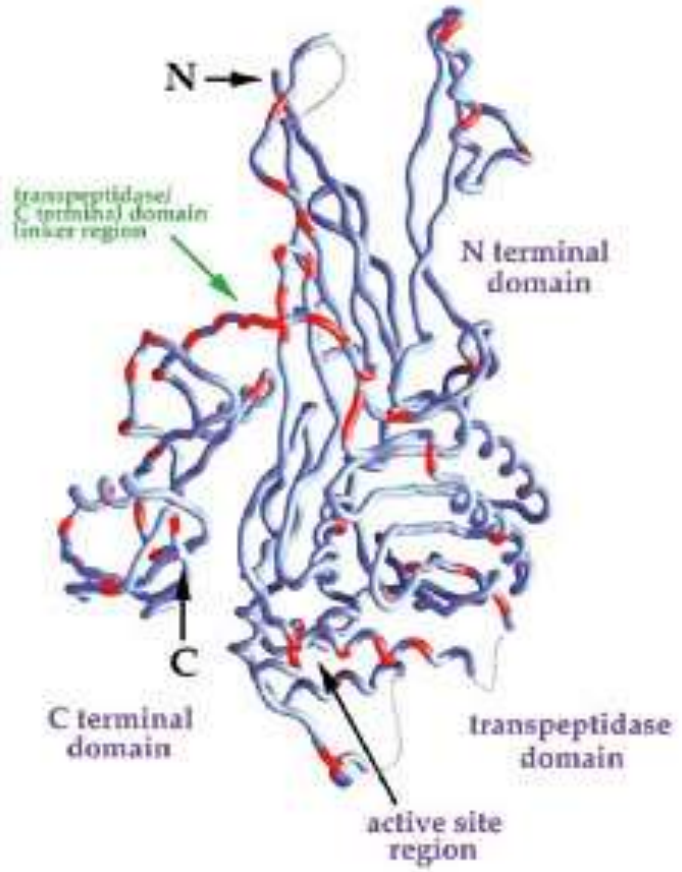
Penicillin Resistance due to Target Site Mutations

The target of penicillin is the penicillin binding protein



Mutations in this target can slightly increase the MIC of penicillin.

Multiple mutations gradually increase the MIC. Around 80 mutations are needed to make the bacterium clinically resistant.

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10. The diagram below best illustrates

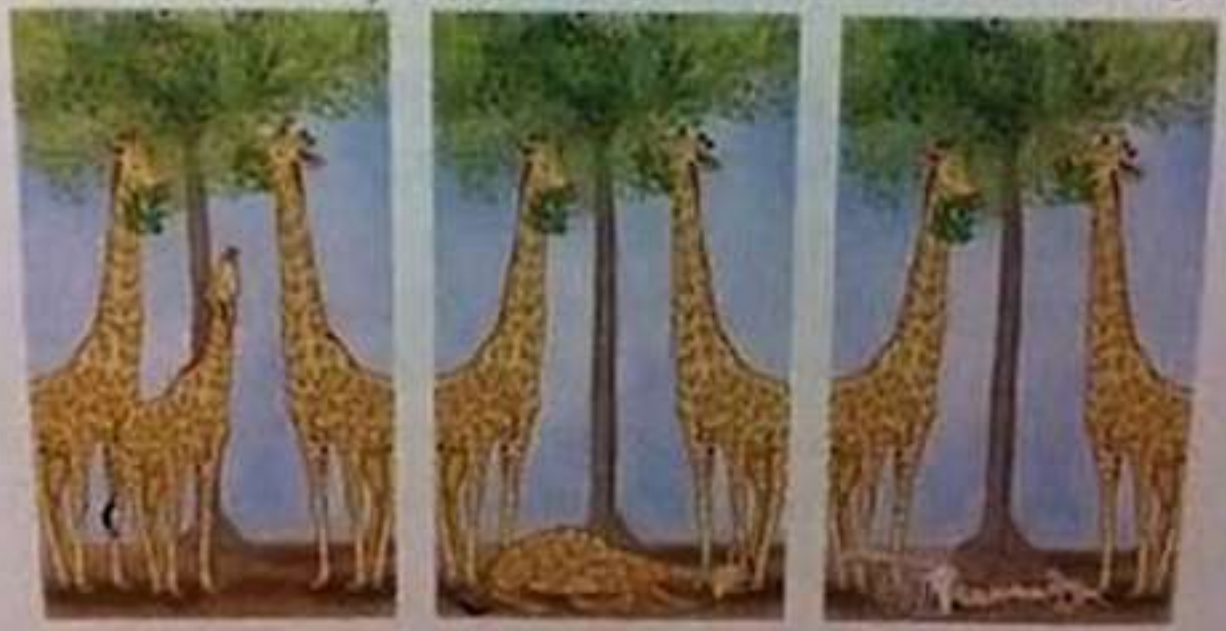
a. Lamarck's theory of evolution.

b. Darwin's theory of evolution.

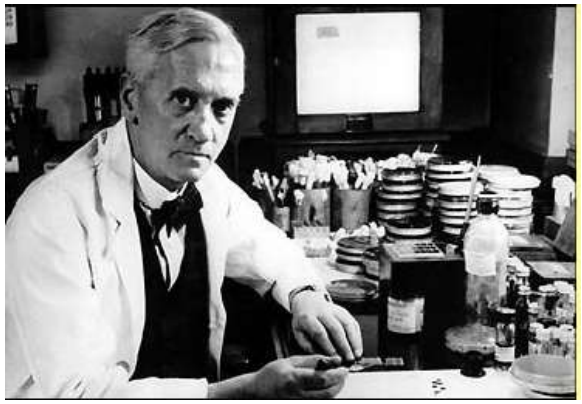
c. Malthus's principles.

d. Lyell's theory about past changes.

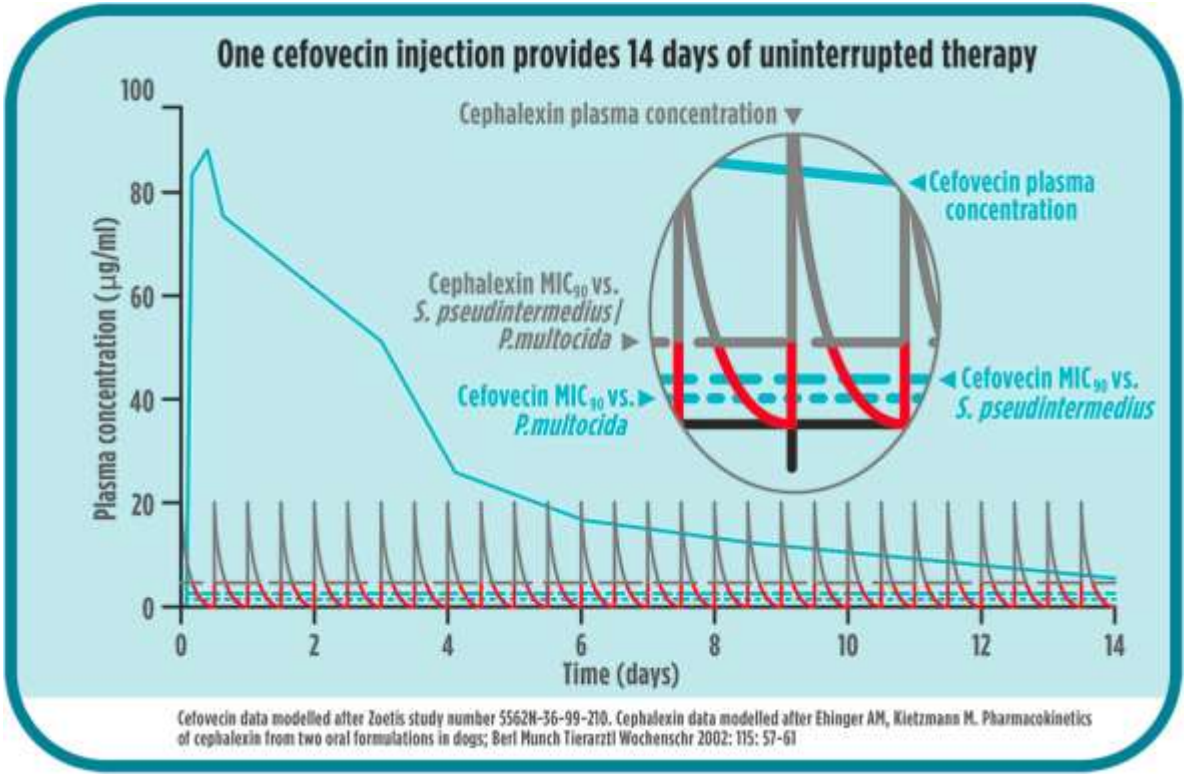
e. Giraffes are heartless creatures.



Antibiotic underdosing is bad because it selects resistant mutants….



"…..there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant".



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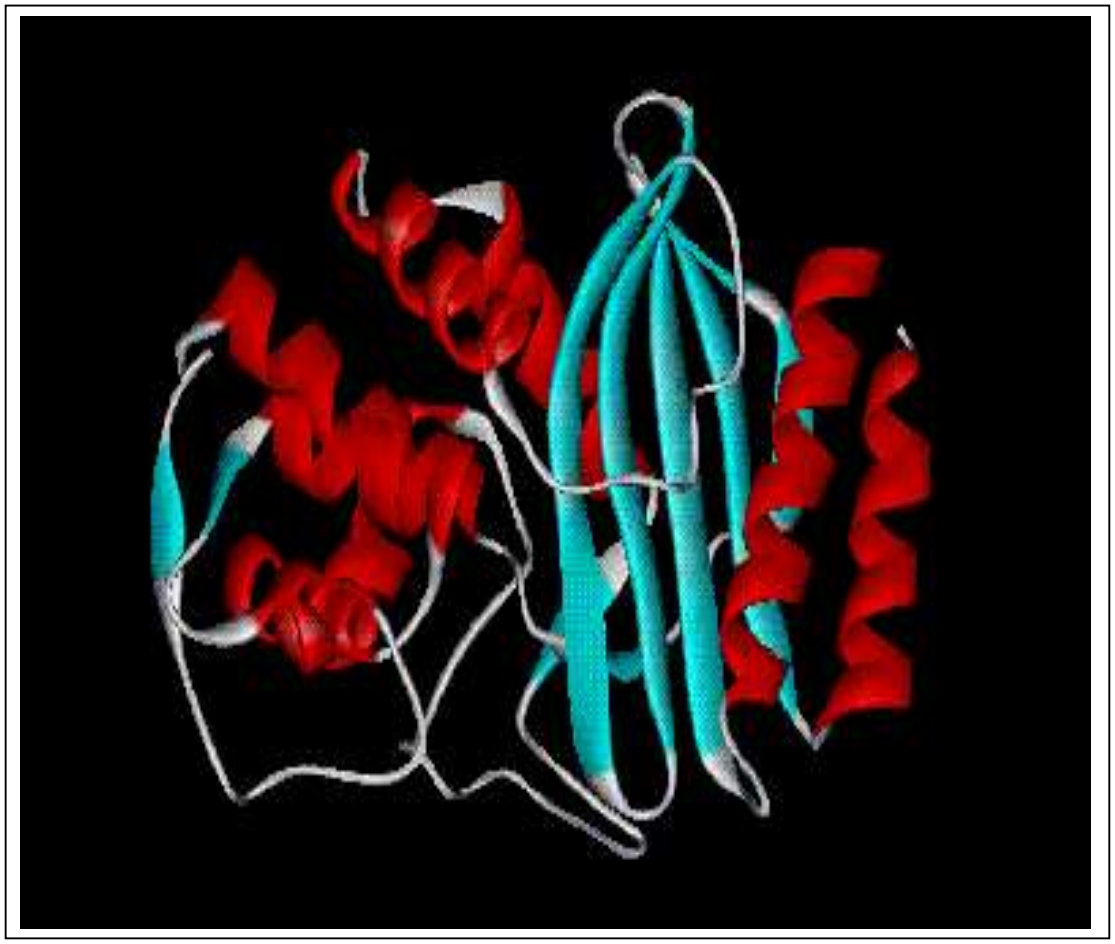
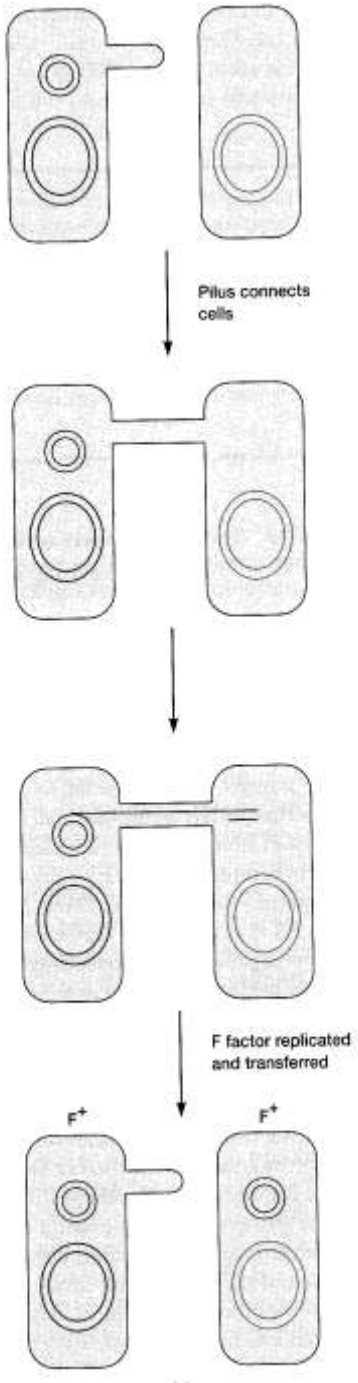
Superbugs are not Giraffes

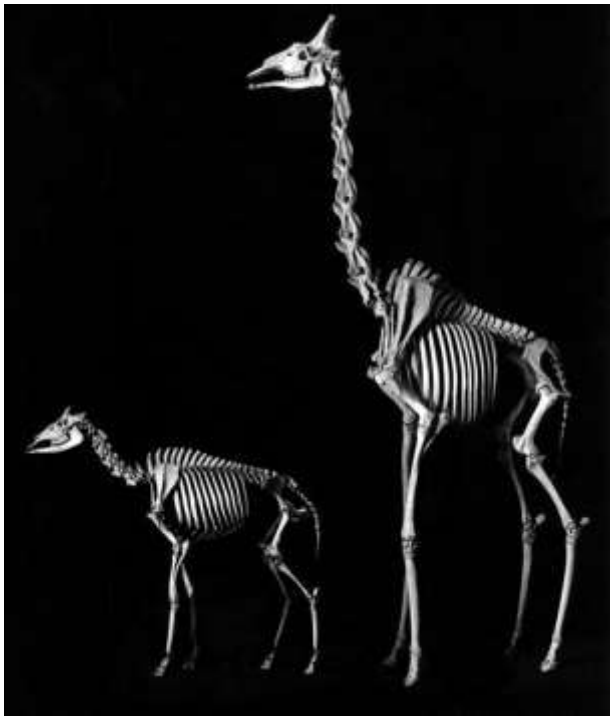


The TEM β-lactamase

The Evolution and Spread of TEM



- Penicillin is a natural compound.
- Evolution of TEM enzyme occurred slowly in environmental bacteria.
- Plasmids move into clinical bacteria – spread TEM very quickly.



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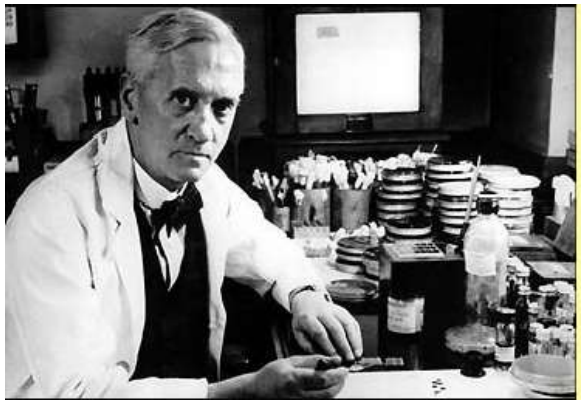
Long acting dosing is bad because it selects acquisition of resistant bacteria….



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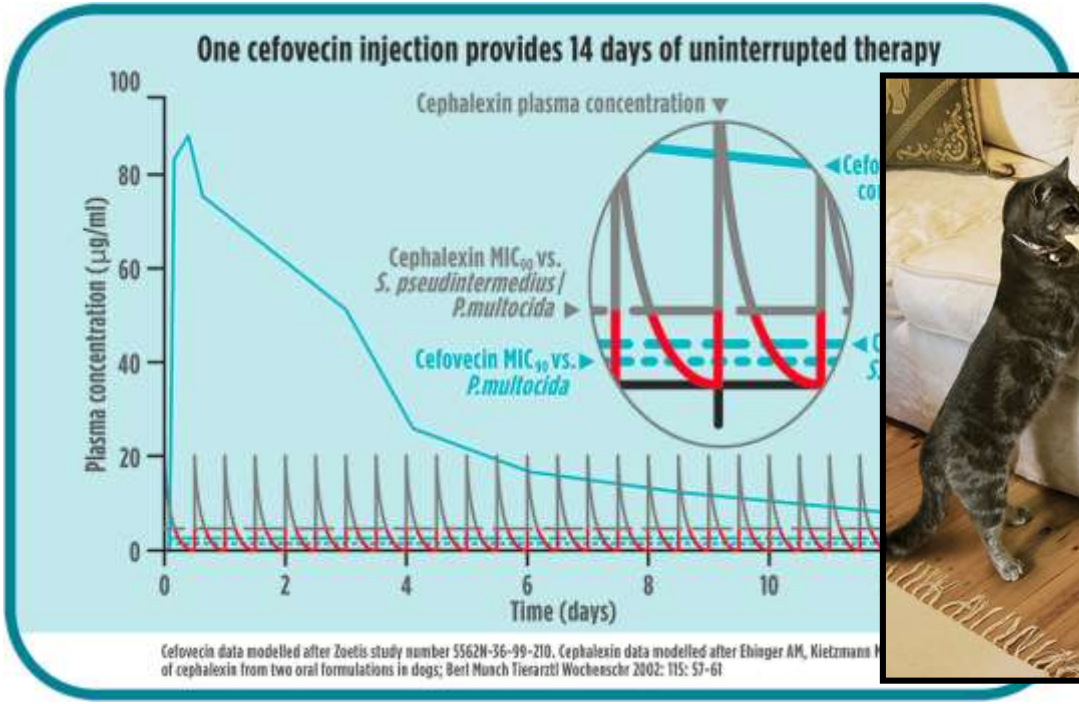

What Can We Do About AMR?

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Key Technological Challenges.

- Infection resisting materials
- Targeting of antimicrobials to the site of infection
- Novel (specific) antimicrobials
- **Primary driver for inappropriate antibiotic use in the UK is lack of rapid/sensitive diagnostics**

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BristolBridge

- Aim is to “Bridge the Gaps” between Engineering/Physical Sciences and Antibiotic Resistance Researchers.
- Delivering Innovative Technological Solutions to the Problem of AMR

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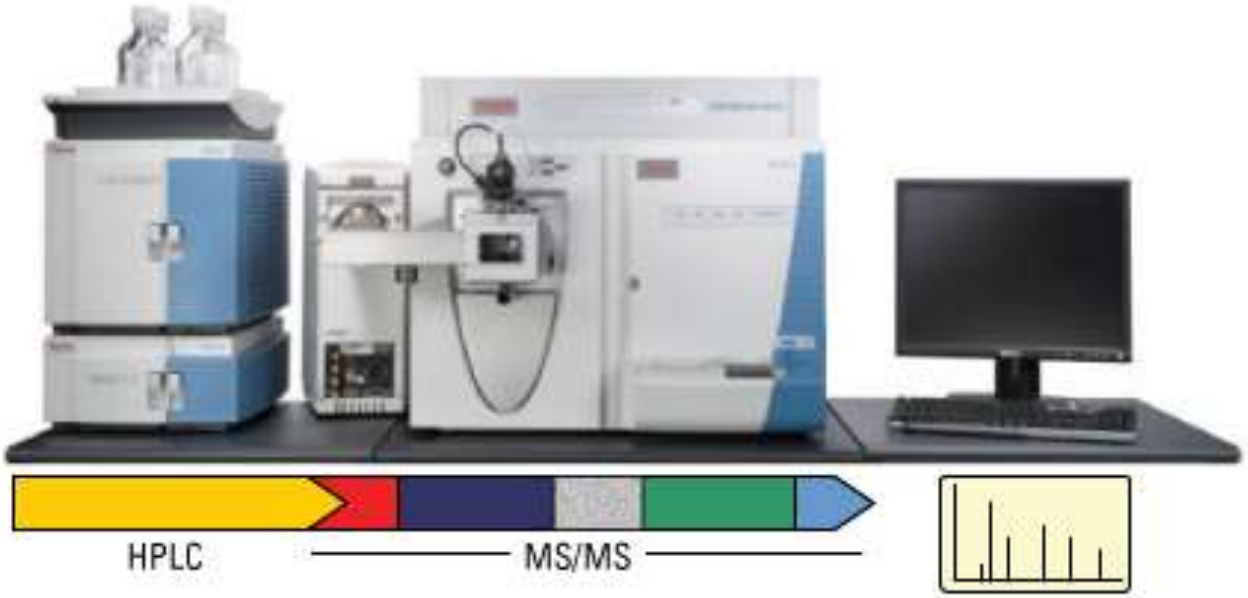
LC-MS/MS Proteomics to Identify AMR.



AMR
Tackling Antimicrobial Resistance

Theme 2

MRC Medical Research Council

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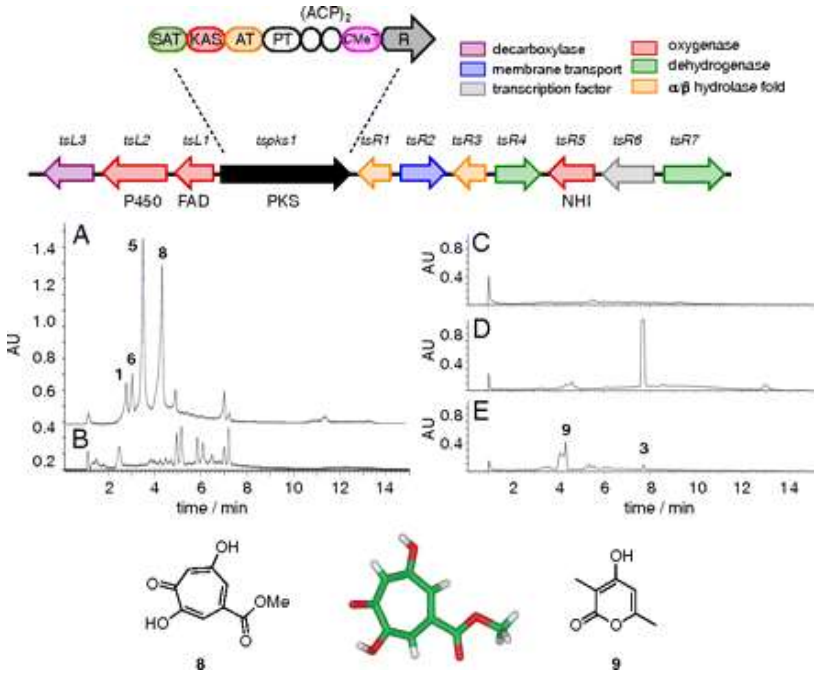
Finding New Antibiotic Lead Compounds



AMR
Tackling Antimicrobial Resistance

Theme 2

MRC Medical Research Council

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AMR transmission in the real world.

- Dairy Farming uses a lot of cephalosporins.
- Is there a link with AMR and can it be reversed?
- Do dogs pick up *E. coli* from the environment?
- Is there a link to UTIs caused by Cephalosporin Resistant *E. coli* in humans?
- And can this be reversed?

AMR
Tackling Antimicrobial Resistance

Theme 3

50
NERC SCIENCE OF THE ENVIRONMENT

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bioscience for the future

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