

Mechanisms of resistance: The many ways in which bacteria destroy antibiotics



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There are two types of resistance: Intrinsic or Inherent and Acquired

Intrinsic or Inherent:

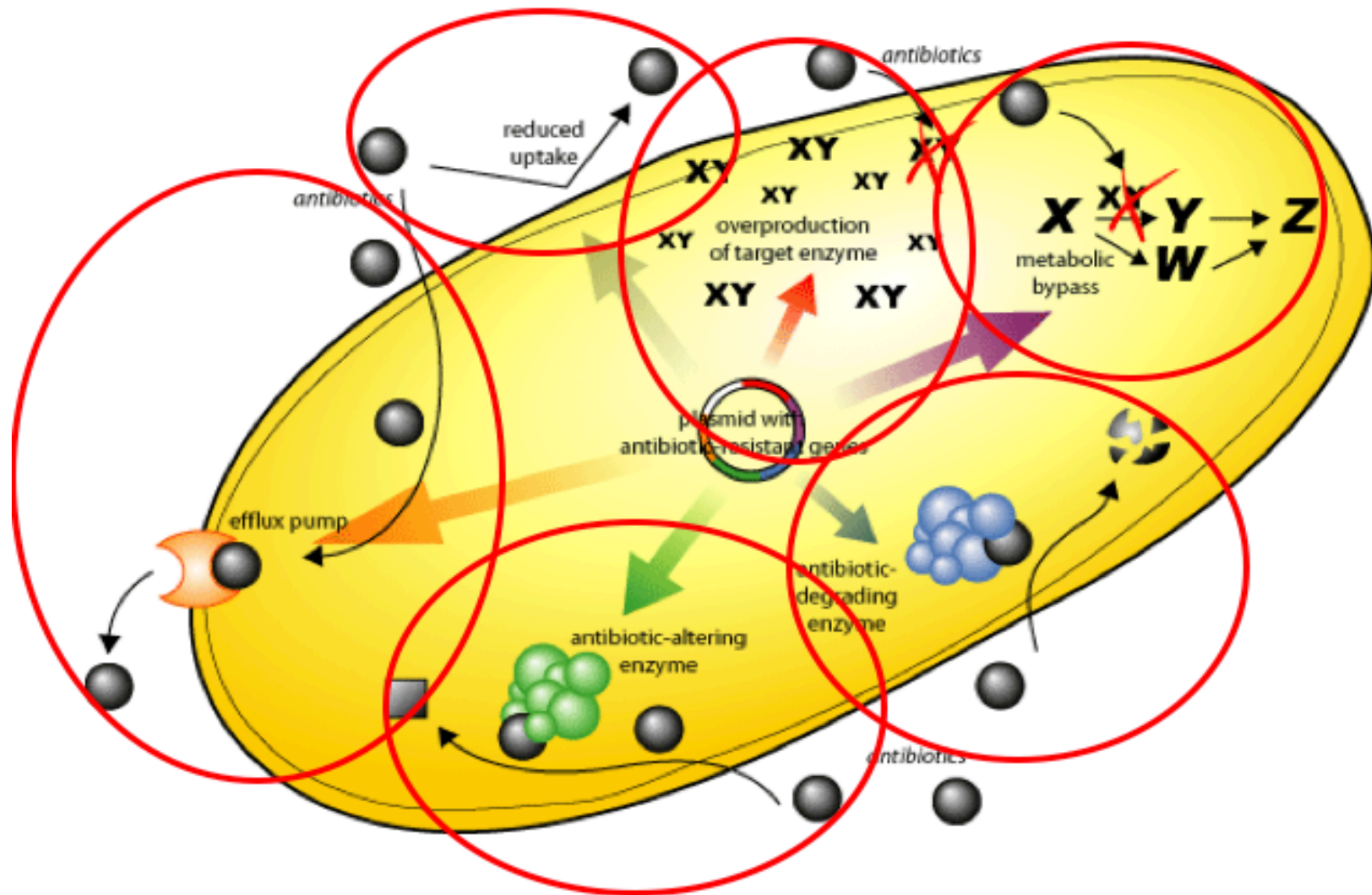
This is when resistance to a particular antibiotic, or group of antibiotics, is normal for a particular bacterial genus, species or entire bacterial group. It may be the result of the lack of a target for the particular antibiotic, or because that drug can't get to its target.

- Examples would be vancomycin or linezolid resistance in gram-negatives. They're resistant to vancomycin because the molecule can't get through the gram-negative outer membrane. Linezolid is inactive because it's pumped out of gram-negative cells.

Acquired:

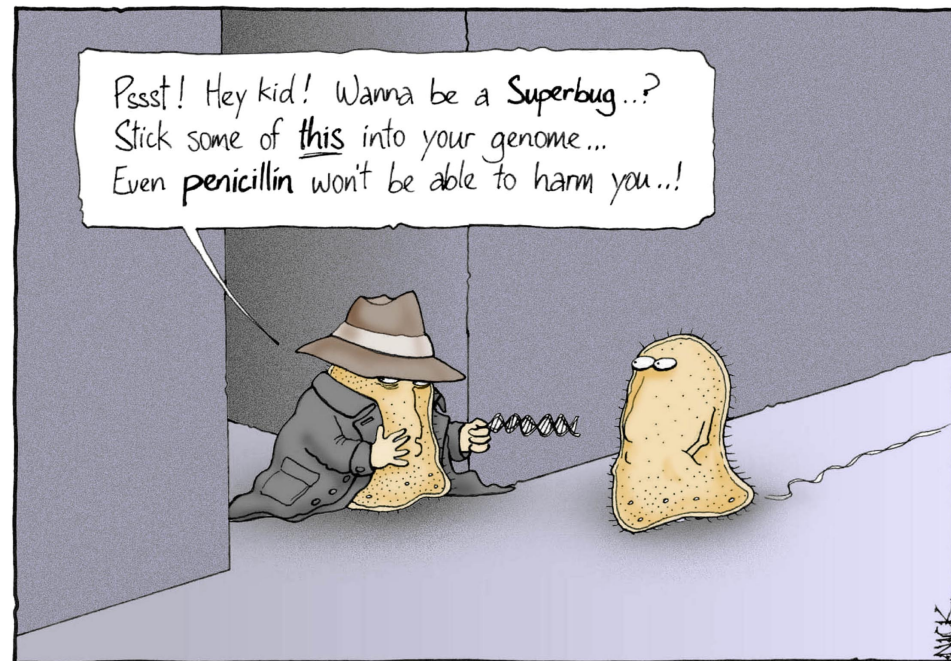
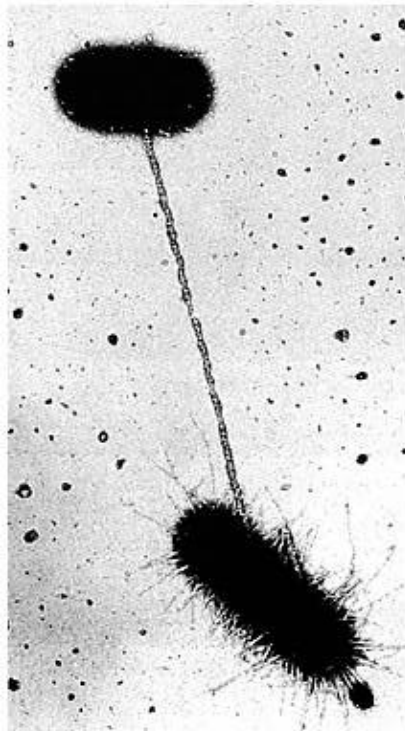
This is the type of resistance where most isolates of a bacterial species, genus, or group, would be fully susceptible to the particular antibiotic, but where resistance may arise in a few, or in some cases in many isolates. It may arise through mutation of a chromosomal gene.

- Enterobacteriaceae often develop resistance by acquiring new DNA. This is an example of so-called horizontal gene transfer, horizontal spread. The typical vehicle responsible for this would be a ring of DNA known as a plasmid.



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 FutureLearn course - Antimicrobial Stewardship: Managing antibiotic resistance.

Bacteria don't keep resistance to themselves



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

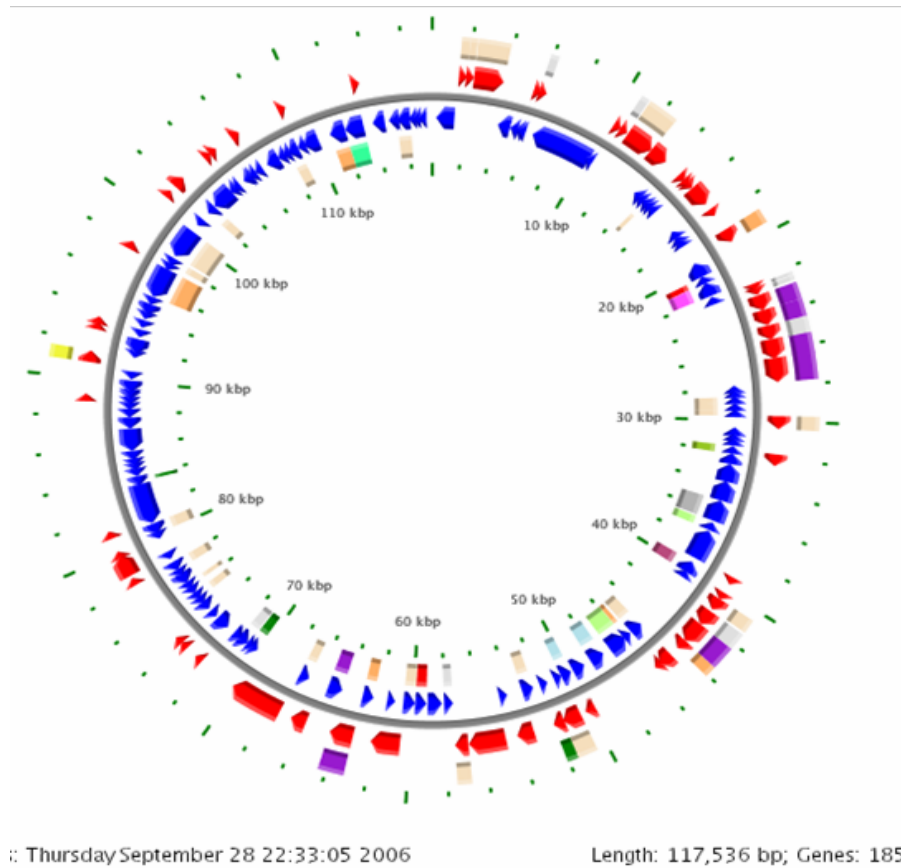
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Neat packages of multi-resistance

Antibiotic classes	Genes	Mechanism
Aminoglycosides	<i>aac6'-Ib-cr</i> <i>aadA5</i>	Modify drug
β -lactams	<i>bla</i> _{CTX-M-15} <i>bla</i> _{OXA-1} <i>bla</i> _{TEM-1}	Destroy drug
Chloramphenicol	<i>catB4</i>	Modify drug
Macrolides	<i>mph(A)</i>	Efflux
Fluoroquinolones	<i>aac6'-Ib-cr</i>	Modify drug
Sulfonamides	<i>sulI</i>	By-pass
Trimethoprim	<i>dhfr</i> _{XVII}	By-pass
Tetracycline	<i>tet(A)</i>	Efflux

Neat packages of multi-resistance



Woodford *et al. Antimicrob Agents Chemother* 2009; 53: 4472-82

The Forensics of AMR

- Resistance involves
 - emergence of mutations
 - spread of resistance genes
 - spread of resistant strains
- Tracking and characterizing
 - the resistant strains
 - their resistance genes

