Introduction to MDRO's

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Disclosures

- Work funded by CDC grant
- Conflicts of interest

Learning Objectives

- What is an MDRO
- Review antibiotics and bacterial resistance
- Identify sources of MDRO's
- Review bacterial resistance mechanisms
- Identify Current CDC MDRO threat levels
- COVID-19 impact on U.S. MDRO's

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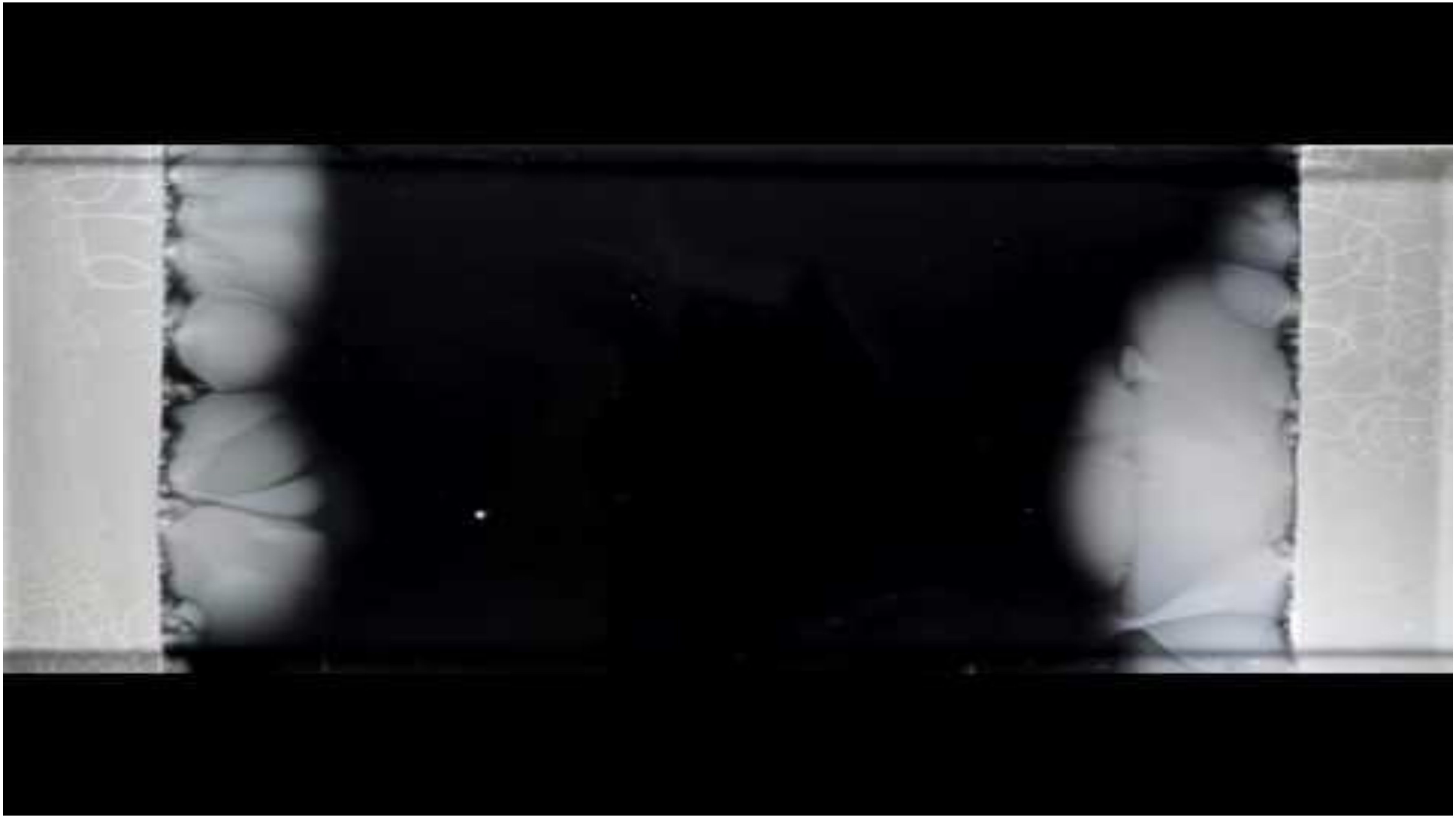
Setting the Table



https://www.youtube.com/watch?v=pIVk4NVIUh8

What is a MDRO

MDRO Definition:

- For epidemiologic purposes, MDROs are defined as microorganisms, predominantly bacteria, that are resistant to one or more classes of antimicrobial agents.
- Multi-Drug-Resistant-Organism

Common Examples

- Methicillin-Resistant *Staphylococcus aureus* (MRSA)
- Vancomycin-Resistant *Enterococcus* (VRE)
- Extended Spectrum Beta-Lactamases (ESBL)
- Carbapenem-Resistant Enterobacterales (CRE)

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Antibiotics and Resistance

- Penicillin was discovered in 1928 by Alexander Fleming
  - First resistance identified in 1940 in *Staphylococcus*
- Penicillin became commercially available in 1943
- After the discovery of each new antibiotic, there is acknowledgement of resistance alongside the discovery
- Bacteria know how to fight back, and they do so very quickly and efficiently

Bacterial Resistance Timeline

Antibiotic Approved or Released	Year Released	Resistant Germ Identified	Year Identified
Penicillin	1941	Penicillin-resistant *Staphylococcus aureus*[20, 21]	1942
		Penicillin-resistant *Streptococcus pneumoniae*[9,10]	1967
		Penicillinase-producing *Neisseria gonorrhoeae*[11]	1976
Vancomycin	1958	Plasmid-mediated vancomycin-resistant *Enterococcus faecium*[12,13]	1988
		Vancomycin-resistant *Staphylococcus aureus*[14]	2002
Amphotericin B	1959	Amphotericin B-resistant *Candida auris*[15]	2016
Methicillin	1960	Methicillin-resistant *Staphylococcus aureus*[16]	1960
Extended-spectrum cephalosporins	1980 (Cefotaxime)	Extended-spectrum beta-lactamase- producing *Escherichia coli*[17]	1983
Azithromycin	1980	Azithromycin-resistant *Neisseria gonorrhoeae*[18]	2011
Imipenem	1985	*Klebsiella pneumoniae* carbapenemase (KPC)-producing *Klebsiella pneumoniae*[19]	1996
Ciprofloxacin	1987	Ciprofloxacin-resistant *Neisseria gonorrhoeae*[20]	2007
Fluconazole	1990 (FDA approved)	Fluconazole-resistant *Candida*[21]	1988
Caspofungin	2001	Caspofungin-resistant *Candida*[22]	2004
Daptomycin	2003	Daptomycin-resistant methicillin-resistant *Staphylococcus aureus*[23]	2004
Ceftazidime-avibactam	2015	Ceftazidime-avibactam-resistant KPC-producing *Klebsiella pneumoniae*[24]	2015

https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

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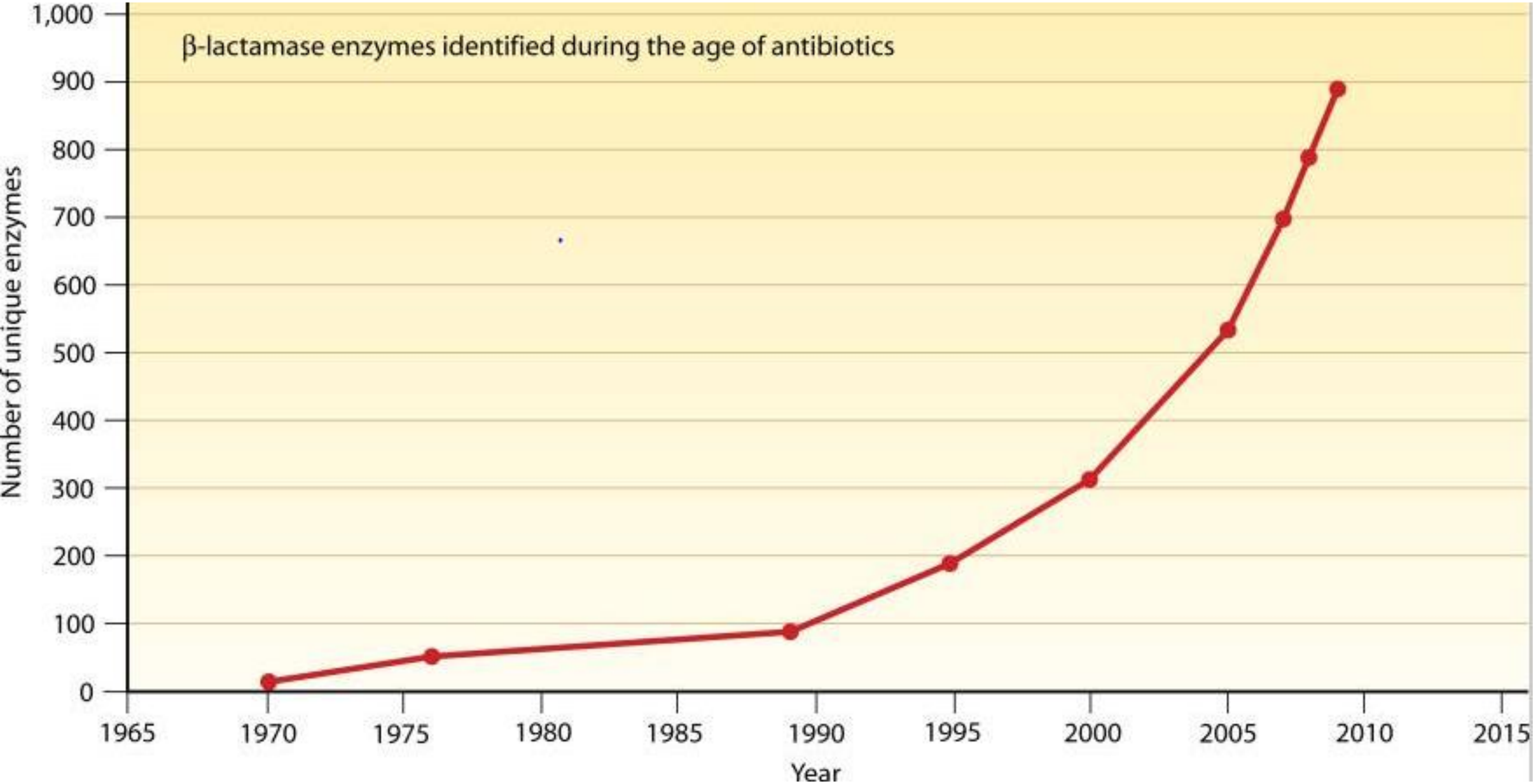
Beta lactamase enzymes identified



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2937522/

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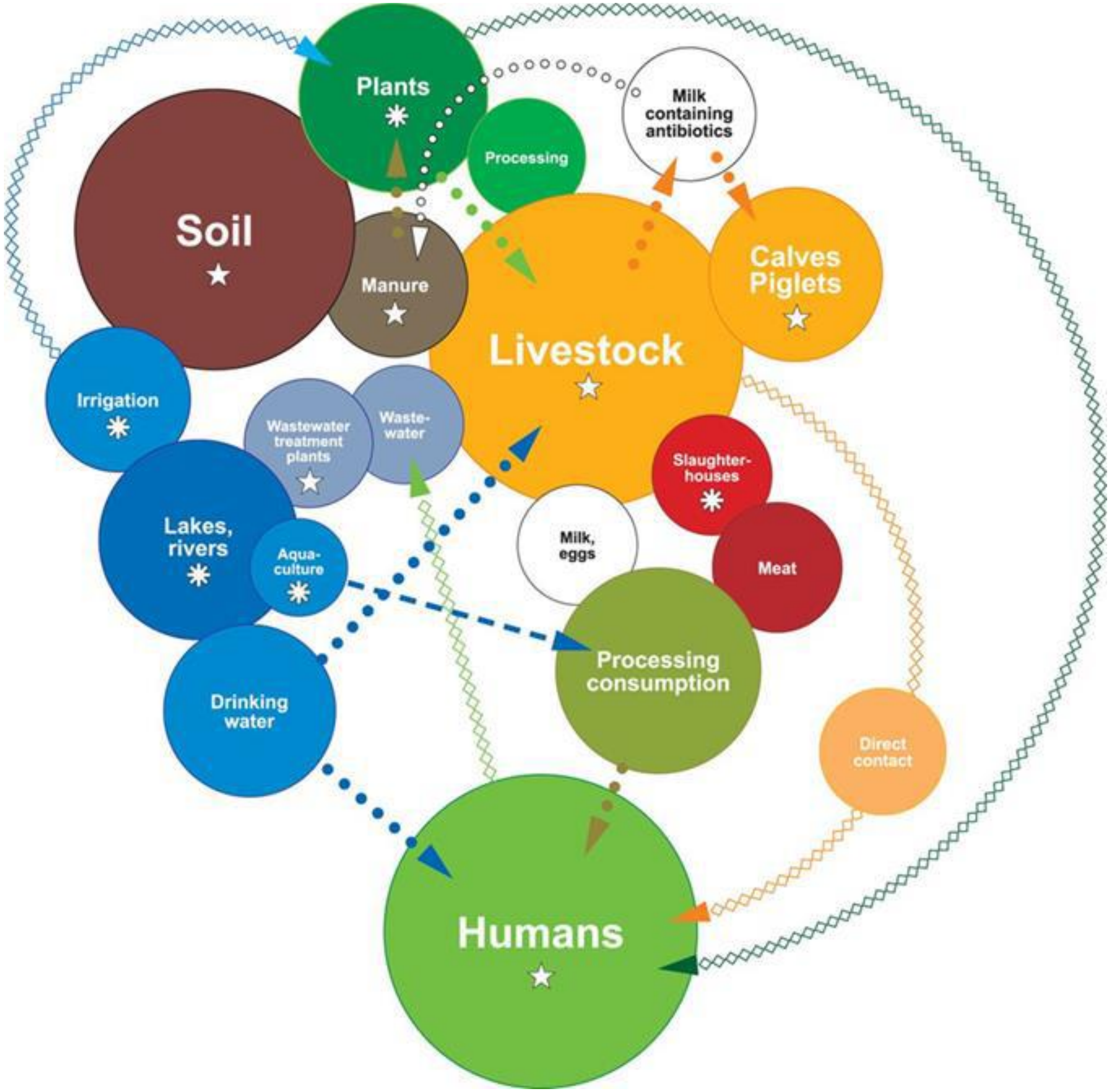
Where do MDRO's Come From? (page 1)

Reservoirs

- Food sources
- Agricultural animals and plants
- Companion animals
- Water / Soil
- Plumbing – drains (biofilms)



Thanner et al. mBIO 2016.

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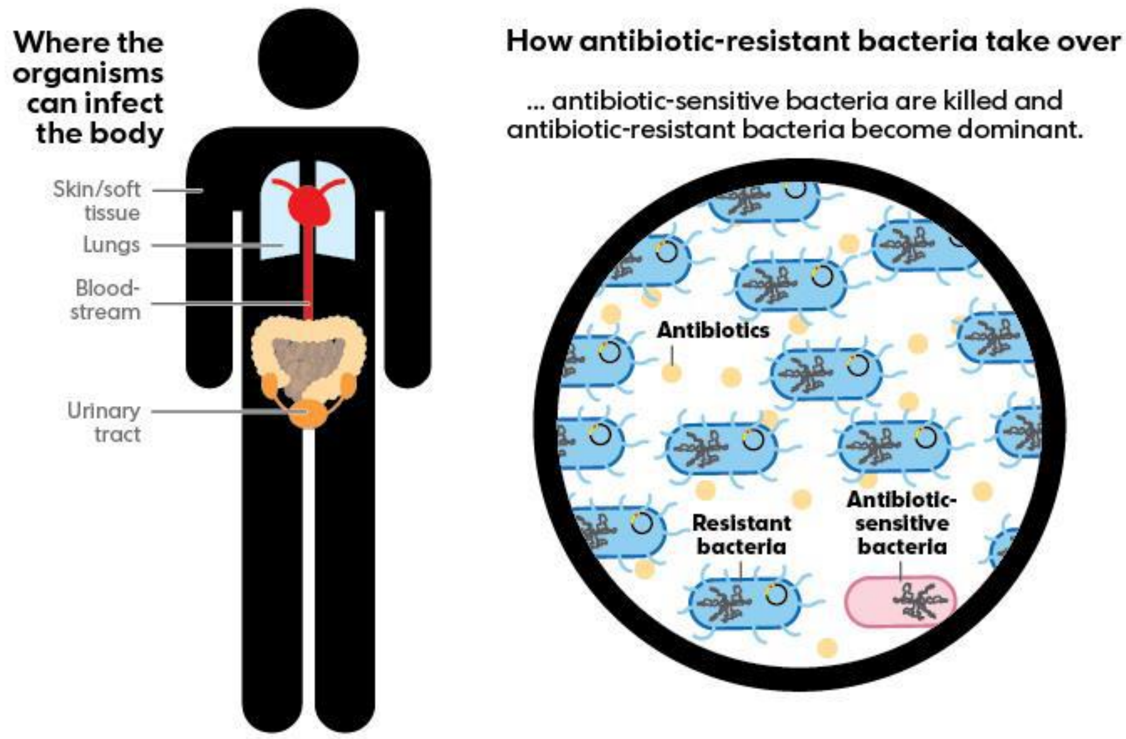
Where do MDRO's Come From? (page 2)

Reservoirs

- Asymptomatic carriers – transmission or environmental contamination
- Selected during treatment: not just the infection, but entire microbiome
- Topical antibiotics & colistin resistance



Thanner et al. mBIO 2016.

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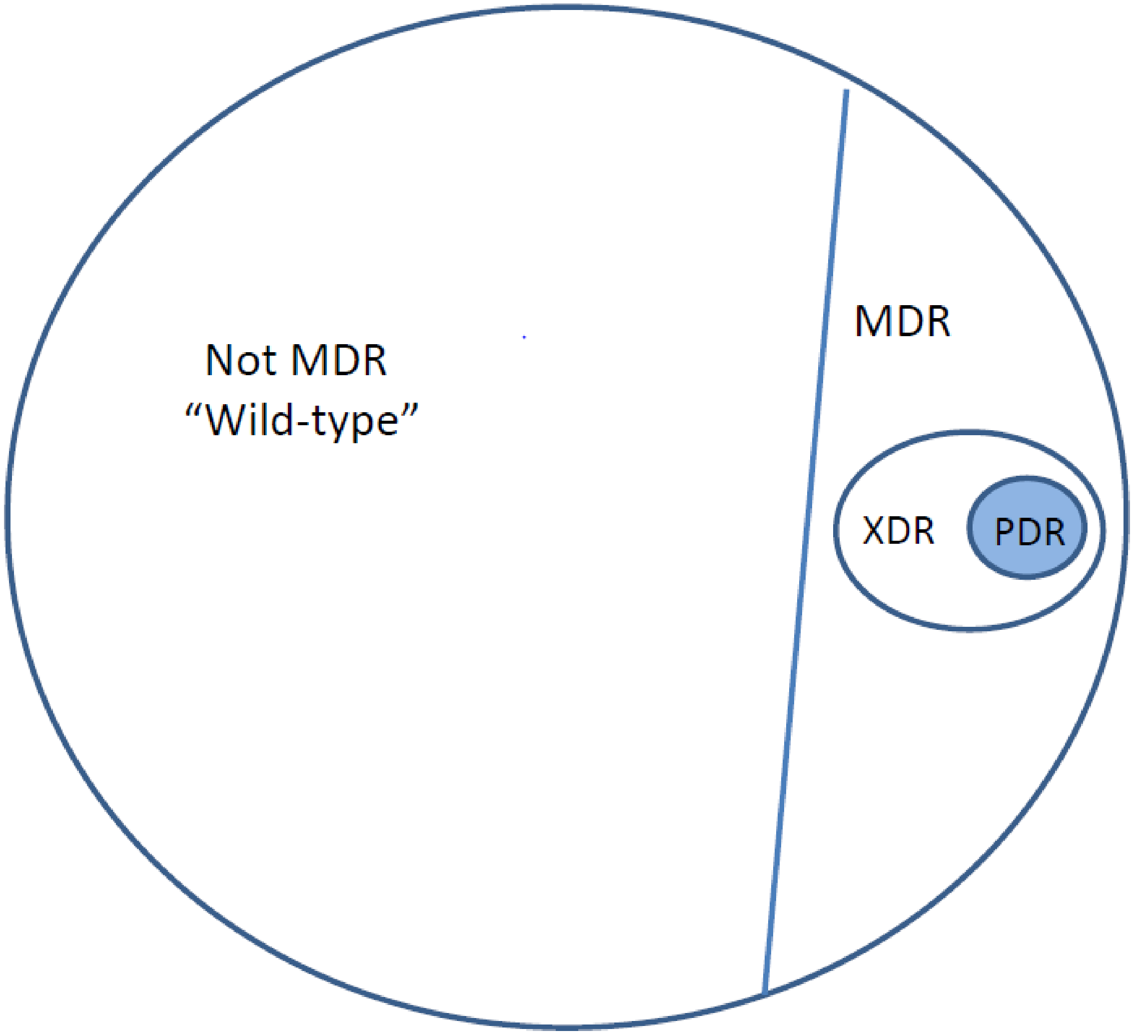
Gram Negative MDRO Distribution



https://www.sciencedirect.com/science/article/pii/S1198743X14616323?via%3Dihub

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Bacterial Resistance to Antimicrobials

- Resistance is not new or unexpected, it's a natural phenomenon associated with DNA replication/transcription errors
- Three fundamental mechanisms of antimicrobial resistance. All DNA based.
  1. Enzymatic degradation of antibacterial drugs
  2. Alteration of bacterial proteins that are antimicrobial targets
  3. Changes in membrane permeability to antibiotics

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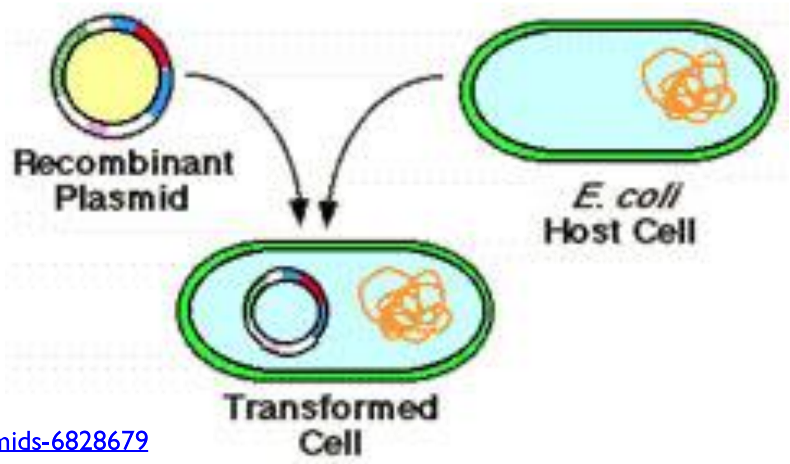
Plasmid Mediated Resistance

- Plasmids harbor genes coding for antibiotic resistance and virulence factors.
- This allow bacteria to survive a hostile environment, and resist treatment.
- Examples:
  - *Pseudomonas aeruginosa* can become more mucoid
  - *K. pneumonia* with a KPC enzyme can resist most antibiotics
- Most CRE's are resistant due to having a plasmid



https://www.slideshare.net/doctorrao/plasmids-6828679

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CDC Concerning Threats

Concerning Threats

These germs are public health threats that require careful monitoring and prevention action:

ERYTHROMYCIN-RESISTANT
GROUP A *STREPTOCOCCUS*

CLINDAMYCIN-RESISTANT
GROUP B *STREPTOCOCCUS*

https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf

CDC Serious Threats

Serious Threats

These germs are public health threats that require prompt and sustained action:

DRUG-RESISTANT ***CAMPYLOBACTER***

DRUG-RESISTANT ***CANDIDA***

ESBL-PRODUCING **ENTEROBACTERIACEAE**

VANCOMYCIN-RESISTANT ***ENTEROCOCCI***

MULTIDRUG-RESISTANT ***PSEUDOMONAS AERUGINOSA***

DRUG-RESISTANT **NONTYPHOIDAL *SALMONELLA***

DRUG-RESISTANT ***SALMONELLA* SEROTYPE TYPHI**

DRUG-RESISTANT ***SHIGELLA***

METHICILLIN-RESISTANT ***STAPHYLOCOCCUS AUREUS***

DRUG-RESISTANT ***STREPTOCOCCUS PNEUMONIAE***

DRUG-RESISTANT **TUBERCULOSIS**

https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf

CDC Urgent Threats

https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf

COVID-19 U.S. Impact on Antimicrobial Resistance

Concerning Threats Impact

- Prior to pandemic, both Erythromycin-resistant group A *Streptococcus* and Clindamycin-resistant group B *Streptococcus* were on the rise

BUT

Updated data for 2020, 2021, 2022, and data collection delayed due to the COVID-19 Pandemic

https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf

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COVID-19 U.S. Impact on Antimicrobial Resistance

Serious Threats Impact

- Drug-resistant *Campylobacter*, 10% decrease in drug resistance
- Antifungal-resistant *Candida*, overall 12% increase, and 26% increase of Hospital-onset cases
- ESBL's, overall 10% increase in cases and 32% increase in Hospital –onset cases
- VRE, overall 16% increase, and 14% increase of Hospital-onset cases
- *Pseudomonas aeruginosa* counts stable, but saw a 32% increase in Hospital-onset cases
- Drug-resistant *Salmonella*, and *Shigella* had delayed data, but saw increase in drug resistant vs non drug resistant cases.
- MRSA cases counts stable, but saw a 13% increase in Hospital-onset cases
- Drug-resistant *Streptococcus pneumoniae*, data delayed
- Drug-resistant *Tuberculosis* (TB), saw a decrease in cases

https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf

COVID-19 U.S. Impact on Antimicrobial Resistance

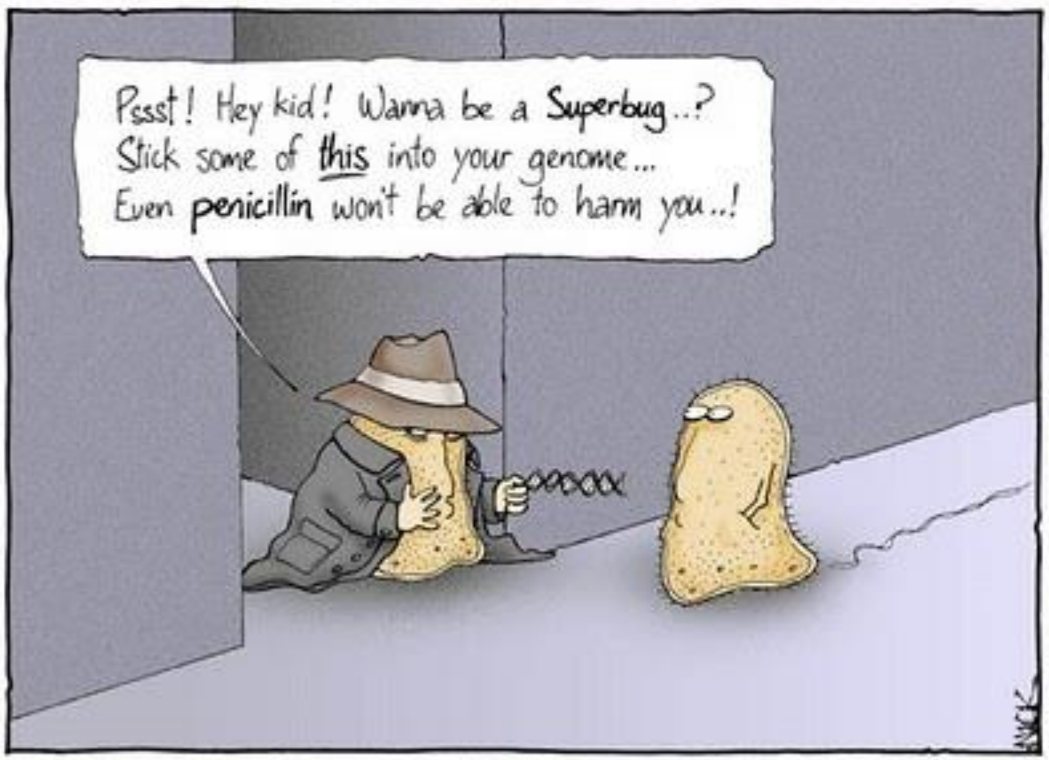
Urgent Threat Impact:

- Carbapenem-resistant *Acinetobacter*, overall 35% increase, and 78% in Hospital-onset cases
- *C. auris*, 60% increase in cases to 754 cases in 2022. Newest report is now 3,270 cases, as 200% increase
- *Clostridioides difficile*, data delayed.
- Carbapenem-resistant Enterobacterales, overall stable, but 35% increase in Hospital-onset cases
- Drug-resistant *Neisseria gonorrhoeae*, data unavailable due to pandemic

https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf
https://www.acpjournals.org/doi/10.7326/M22-3469

We have work to do!

Questions?



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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Resources

- CDC Antibiotic Resistance Threats in the U.S., 2019
- CDC COVID-19 U.S. Impact on Antimicrobial Resistance, Special Report 2022
- https://www.acpjournals.org/doi/10.7326/M22-3469

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