# Curing AMR
# Is that a real thing?

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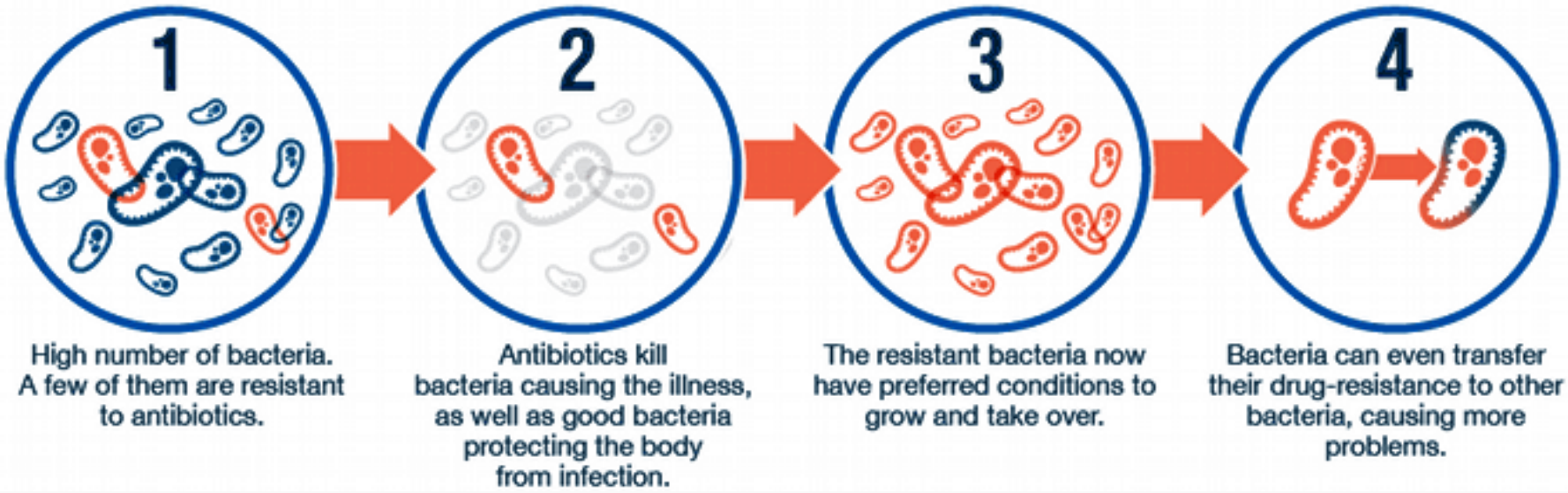
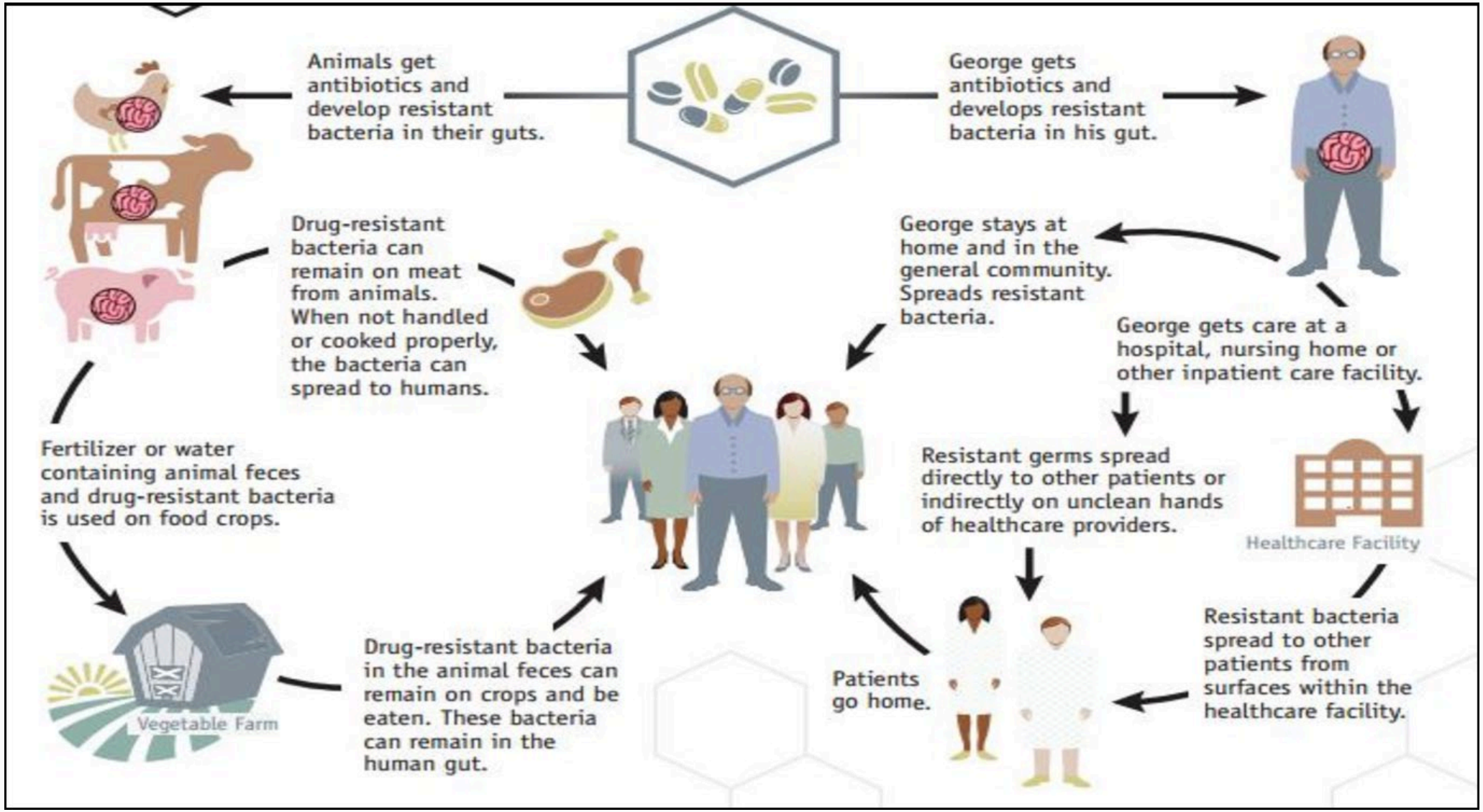
November 7th 2023

# The issue

- Antibiotic Resistance (AbR) is a major concern all over the world
- Gut bacteria cause > 50% of severe infections in hospitalised patients
- People who have a severe infection with antibiotic-resistant bacteria stay longer in hospitals and are twice as likely to die than those with severe infection due to antibiotic-sensitive bacteria

# How does antibiotic resistance occur?




Animals get antibiotics and develop resistant bacteria in their guts.
George gets antibiotics and develops resistant bacteria in his gut.
Drug-resistant bacteria can remain on meat from animals. When not handled or cooked properly, the bacteria can spread to humans.
George stays at home and in the general community. Spreads resistant bacteria.
George gets care at a hospital, nursing home or other inpatient care facility.
Fertilizer or water containing animal feces and drug-resistant bacteria is used on food crops.
Resistant germs spread directly to other patients or indirectly on unclean hands of healthcare providers.
Healthcare Facility
Vegetable Farm
Drug-resistant bacteria in the animal feces can remain on crops and be eaten. These bacteria can remain in the human gut.
Patients go home.
Resistant bacteria spread to other patients from surfaces within the healthcare facility.

# The issue

- The steady rise of AbR in Enterobacteriaceae, is particularly so in two pathogens seen in common urinary tract infection and lethal sepsis: Escherichia coli and Klebsiella pneumoniae.
- The most important vectors of this transmissible AbR are self-transmissible (conjugative) plasmids (extrachromosomal circular genetic element), the ‘vessels of the communal gene pool’.
- Plasmid-borne AbR is acquired very quickly and, once acquired, becomes fixed in the bacterial accessory genome by ‘addiction systems’ that poison cells from which the AbR plasmid is lost.
- As a result of these plasmid addictions, persistence of antibiotic resistance genes and their vectors is to be expected in the absence of antibiotic selective pressure, and reversibility (of AbR) proceeds slowly that it is unlikely to be of practical importance

# Causes of septic shock

**Table 4.2:** Summary of antimicrobial resistance for high-priority organisms

| Organism | Main types of infection | Most common setting | Important antimicrobials for treatment | % resistant | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | 2015 | 2016 | 2017 | 2018 | 2019 |
| *Acinetobacter baumannii* complex | Ventilator-associated pneumonia, severe burn infections | Intensive care units, burn units | Ciprofloxacin/norfloxacin | 5.0 | 6.5 | 4.8 | 4.2 | 5.4 |
| | | | Gentamicin | 2.1 | 4.9 | 3.8 | 3.1 | 3.6 |
| | | | Meropenem | 2.6 | 4.9 | 3.6 | 2.4 | 3.1 |
| | | | Trimethoprim–sulfamethoxazole | 5.2 | 8.5 | 6.1 | 7.5 | 5.8 |
| *Enterobacter cloacae* complex | Urinary tract infections, biliary tract infections, other intra-abdominal infections, septicaemia | Hospitals | Cefepime | 3.6 | 1.6 | 7.1 | 5.8 | 2.3 |
| | | | Ceftriaxone/cefotaxime | 30.4–39.7 | 33.2–38.7 | 35.0–41.5 | 34.7–42.6 | 32.2–43.2 |
| | | | Ciprofloxacin/norfloxacin | 3.7–6.1 | 1.9–6.1 | 4.5–7.2 | 5.9–6.9 | 5.7–8.0 |
| | | | Gentamicin | 7.2–8.4 | 4.5–6.7 | 5.7–6.8 | 6.1–6.8 | 5.3–7.9 |
| | | | Meropenem | 1.6–1.7 | 1.1–1.2 | 1.0–1.1 | 1.4–1.5 | 1.4–2.0 |
| | | | Piperacillin–tazobactam | 23.4–27.8 | 28.2–28.2 | 28.2–33.8 | 30.1–30.5 | 28.9–30.5 |
| | | | Trimethoprim (urine) | 20.2 | 19.4 | 18.7 | 18.1 | 18.2 |
| | | | Trimethoprim–sulfamethoxazole (non-urine) | 14.7 | 13.5 | 16.1 | 14.8 | 15.6 |
| | | | Multidrug-resistant (blood)* | 9.6 | 7.1 | 11.1 | 8.2 | 7.3 |
| *Enterococcus faecalis* | Urinary tract infections, biliary tract infections, other intra-abdominal infections, septicaemia, endocarditis | Community, hospitals | Ampicillin/amoxicillin | 0.2–0.8 | 0.4–1.0 | 0.4–0.8 | 0.2–0.7 | 0.0–0.4 |
| | | | Ciprofloxacin/norfloxacin (urine) | 16.2 | 20.3 | 30.7 | 30.3 | 9.3 |
| | | | Linezolid | 0.5–1.7 | 0.4–1.1 | 0.5–0.8 | 0.4–0.5 | 0.1–0.5 |
| | | | Nitrofurantoin (urine) | 0.4 | 0.3 | 0.3 | 0.6 | 0.7 |
| | | | Teicoplanin | 0.0–<0.1 | 0.0–0.1 | 0.0–0.4 | 0.0–0.1 | 0.0–0.3 |
| | | | Vancomycin | 0.3–0.4 | 0.2–0.6 | 0.3–0.5 | 0.2–0.4 | 0.1–0.3 |

# Causes of septic shock

**Table 4.2:** *continued*

| Organism | Main types of infection | Most common setting | Important antimicrobials for treatment | % resistant | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | 2015 | 2016 | 2017 | 2018 | 2019 |
| *Enterococcus faecium* | Urinary tract infections, biliary tract infections, other intra-abdominal infections, septicaemia | Hospitals | Ampicillin/amoxicillin | 85.1–96.0 | 86.1–95.9 | 88.1–96.6 | 85.8–96.5 | 87.8–96.9 |
| | | | Linezolid | 0.4–0.7 | 0.2–0.6 | 0.4–1.0 | 0.1–0.4 | 0.2–0.4 |
| | | | Teicoplanin | 9.5–15.4 | 10.8–18.2 | 10.0–19.8 | 7.4–20.4 | 1.1–17.7 |
| | | | Vancomycin | 45.7–55.5 | 44.6–47.2 | 39.3–44.5 | 36.4–41.6 | 33.1–38.0 |
| *Escherichia coli* | Urinary tract infections, biliary tract infections, other intra-abdominal infections, septicaemia | Community, hospitals | Amoxicillin–clavulanic acid | 10.3–16.4 | 10.7–15.3 | 13.5–16.4 | 10.6–16.0 | 10.9–17.6 |
| | | | Ampicillin/amoxicillin | 44.1–52.3 | 44.4–52.6 | 45.3–53.2 | 45.1–54.0 | 44.9–54.0 |
| | | | Cefalexin (urine) | 6.5 | 7.2 | 7.6 | 8.3 | 8.7 |
| | | | Cefazolin | 16.2–21.4 | 16.7–21.8 | 17.3–23.3 | 19.9–26.3 | 20.0–27.3 |
| | | | Ceftriaxone/cefotaxime | 6.6–9.6 | 7.1–9.7 | 7.8–10.4 | 7.9–12.0 | 8.0–11.9 |
| | | | Ciprofloxacin/norfloxacin | 7.1–10.7 | 8.4–10.3 | 10.0–12.4 | 10.8–12.8 | 11.4–13.7 |
| | | | Gentamicin | 4.6–7.4 | 4.9–7.1 | 5.2–8.1 | 5.5–8.1 | 6.0–8.4 |
| | | | Meropenem | 0.00–0.02 | 0.01–0.05 | 0.01–0.03 | 0.02–0.04 | 0.01–0.05 |
| | | | Nitrofurantoin (urine) | 1.3 | 1.2 | 1.0 | 1.1 | 1.1 |
| | | | Piperacillin–tazobactam | 4.9–5.8 | 5.2–5.9 | 5.3–6.2 | 5.5–5.9 | 5.4–6.1 |
| | | | Trimethoprim (urine) | 22.1 | 22.8 | 24.2 | 23.9 | 24.0 |
| | | | Trimethoprim–sulfamethoxazole (non-urine) | 28.6 | 28.0 | 29.4 | 28.6 | 28.4 |
| | | | Multidrug-resistant (blood)* | 24.2 | 25.2 | 25.1 | 26.9 | 26.0 |

*continues*

# Causes of septic shock

**Table 4.2:** *continued*

| Organism | Main types of infection | Most common setting | Important antimicrobials for treatment | % resistant | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | 2015 | 2016 | 2017 | 2018 | 2019 |
| *Klebsiella pneumoniae* complex | Urinary tract infections, biliary tract infections, other intra-abdominal infections, septicaemia | Community | Amoxicillin–clavulanic acid | 4.9–6.2 | 4.3–5.5 | 6.3–6.8 | 4.5–6.4 | 4.6–7.3 |
| | | | Cefazolin | 7.3–8.2 | 7.0–9.5 | 7.6–11.5 | 7.9–12.1 | 8.0–14.9 |
| | | | Ceftriaxone/cefotaxime | 5.3–5.5 | 4.4–5.5 | 5.4–7.3 | 5.3–7.3 | 5.7–6.1 |
| | | | Ciprofloxacin/norfloxacin | 4.1–4.6 | 3.5–4.7 | 6.0–6.7 | 6.1–7.3 | 6.3–7.2 |
| | | | Gentamicin | 3.3–3.8 | 2.6–3.7 | 3.0–4.1 | 2.8–3.4 | 2.7–3.8 |
| | | | Piperacillin–tazobactam | 5.5–7.6 | 6.6–7.8 | 7.6–8.1 | 7.7–7.9 | 7.7–7.9 |
| | | | Meropenem | 0.2–0.3 | 0.1–0.2 | 0.3–0.5 | 0.1–0.5 | 0.3–0.6 |
| | | | Trimethoprim (urine) | 12.6 | 11.7 | 12.8 | 12.6 | 12.4 |
| | | | Trimethoprim–sulfamethoxazole (non-urine) | 11.0 | 12.3 | 12.4 | 13.8 | 12.8 |
| | | | Multidrug-resistant (blood)* | 9.7 | 10.9 | 10.9 | 12.1 | 11.8 |
| *Mycobacterium tuberculosis* | Pulmonary tuberculosis, extrapulmonary tuberculosis | Community | Ethambutol | 0.9 | 1.5 | 0.7 | 1.3 | 1.8 |
| | | | Isoniazid | 10.7 | 9.4 | 8.9 | 9.2 | 10.8 |
| | | | Pyrazinamide | 2.7 | 2.1 | 1.5 | 1.8 | 2.2 |
| | | | Rifampicin | 3.8 | 2.8 | 2.2 | 2.8 | 2.7 |
| | | | Multidrug-resistant† | 2.9 | 2.4 | 2.1 | 2.5 | 2.3 |
| *Neisseria gonorrhoeae* | Gonorrhoea | Community | Azithromycin | 2.6 | 5.0 | 9.3 | 6.2 | 4.6 |
| | | | Benzylpenicillin | 22.5 | 32.5 | 26.1 | 21.1 | 22.1 |
| | | | Ceftriaxone (decreased susceptibility) | 1.8 | 1.7 | 1.1 | 1.7 | 1.3 |
| | | | Ciprofloxacin | 27.2 | 30.0 | 27.5 | 25.6 | 28.4 |

# Causes of septic shock

**Table 4.2:** *continued*

| Organism | Main types of infection | Most common setting | Important antimicrobials for treatment | % resistant | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | 2015 | 2016 | 2017 | 2018 | 2019 |
| *Neisseria meningitidis* | Septicaemia, meningitis | Community | Benzylpenicillin (decreased susceptibility) | 25.6 | 44.4 | 44.9 | 35.4 | 21.0 |
| | | | Ceftriaxone | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| | | | Ciprofloxacin | 0.0 | 0.0 | 0.7 | 0.5 | 0.0 |
| | | | Rifampicin | 0.9 | 0.0 | 0.4 | 0.0 | 0.6 |
| *Pseudomonas aeruginosa* | Urinary tract infections, septicaemia, burn infections, cystic fibrosis exacerbations | Community, hospitals | Ceftazidime | 4.3 | 4.7 | 4.8 | 4.6 | 4.4 |
| | | | Ciprofloxacin | 5.7 | 5.3 | 5.9 | 6.3 | 6.6 |
| | | | Gentamicin | 4.0 | 4.7 | 5.0 | 4.6 | 4.2 |
| | | | Meropenem | 3.5 | 3.2 | 3.4 | 3.2 | 3.1 |
| | | | Piperacillin–tazobactam | 6.2 | 5.6 | 5.8 | 5.9 | 5.8 |
| *Salmonella* species (non-typhoidal) | Gastroenteritis, septicaemia | Community | Ampicillin/amoxicillin | 2.8–7.2 | 5.6–7.7 | 6.1–8.0 | 5.7–8.6 | 4.9–6.8 |
| | | | Ceftriaxone/cefotaxime | 0.5–1.3 | 0.4–0.9 | 0.8–0.8 | 0.0–2.2 | 0.9–2.1 |
| | | | Ciprofloxacin | 1.6–2.3 | 2.2–2.9 | 0.6–2.7 | 2.1–4.8 | 1.9–5.1 |
| | | | Trimethoprim–sulfamethoxazole | 0.7–4.3 | 1.9–5.4 | 2.1–4.4 | 1.7–4.5 | 0.8–1.8 |
| *Salmonella* Typhi/ Paratyphi | Typhoid fever (septicaemia) | Community | Ampicillin/amoxicillin | 5.9 | 7.2 | 12.1 | 6.1 | 8.3 |
| | | | Ceftriaxone/cefotaxime | 1.2 | 0.0 | 0.0 | 1.8 | 3.4 |
| | | | Ciprofloxacin | 36.3 | 34.2 | 42.4 | 65.2 | 78.3 |
| | | | Trimethoprim–sulfamethoxazole | 4.1 | 3.8 | 11.5 | 5.8 | 7.2 |

# The solution

- First-in-human clinical trial
  - Evaluate safety and efficacy of a genetically modified (GM) plasmid given to patients with antibiotic-resistant infections
  - Uses a GM bacteria (*E. coli*) to deliver a genetically modified plasmid to gut bacteria and restore sensitivity to antibiotics
    - Displaces AbR plasmids from enteric bacterial populations in vivo without killing the populations in which they were present
  - Process has already achieved success in mice (Kamruzzam et al., 2017)

# The solution

- First-in-human clinical trial
  - Performed in the Prof Iredell Lab at Westmead Institude of Medical Research (WIMR)
  - Funding via the National Health and Medical Research Council of Australia
  - Approved under a licence (DIR-183) to use genetically modified organisms (GMO) given by the Office of the Gene Technology Regulator (OGTR).
    - Thorough risk assessment → negligible risk to the health and safety of patients, staff and wider population
  - Approved by Western Sydney LHD, Human Research Ethics Committee (HREC)

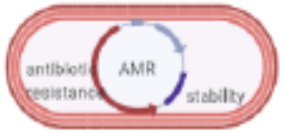
# How does Plasmid therapy work?

- Antimicrobial resistance (AMR) in most sepsis pathogens is carried in and between bacteria on gene… …plasmids'
- Plasmid resistance c… …l can persist for months
- Genetically engine… …MR plasmids without harming normal bac…
- Following treatment, the g… …be free of the AMR and susceptible to 'first-line' antibiotics such as penicillin.
- Curing plasmids may have been altered to reduce their ability to persist in bacteria.

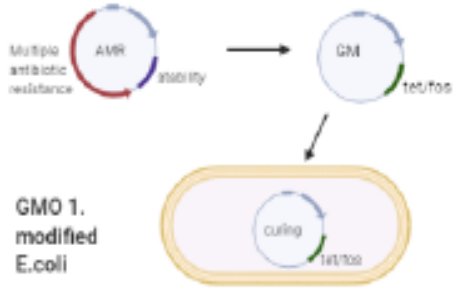
In mice, the plasmids were undetectable 10 days after the removal of the antibiotic selection (Kamruzzaman et al., 2017)

# How does Plasmid therapy work?

1. Some bacteria have become resistant to the antimicrobials commonly used to treat them. This resistance (AMR) is often carried on bacterial plasmids.

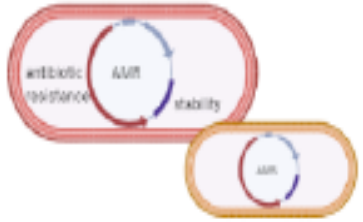



2. Genetic modification was used to create "curing plasmids".




GMO 1. modified E.coli

3. Participant with target AMR plasmid is identified

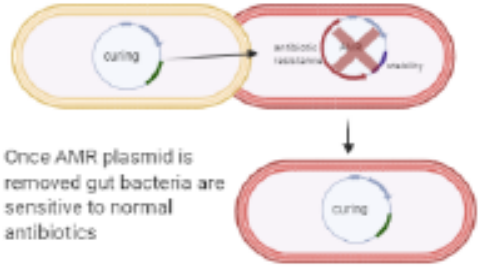



4. GMO *E. coli* carrying curing plasmid and selective antibiotic is administered to participant


5. Inside participant's gut GM plasmid spreads to many gut bacteria through conjugation.

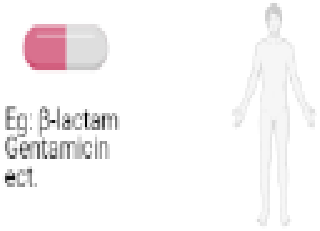
GMO 2. Human gut bacteria that contain the GM plasmid

6. AMR plasmid is swapped for curing plasmid because bacteria can't hold two overly similar plasmids and there is now a selective advantage for Tet resistance




Once AMR plasmid is removed gut bacteria are sensitive to normal antibiotics

7. Participant can now be treated with a common antibiotic



Eg: β-lactam
Gentamicin
ect.

8. Faecal/rectal samples to monitor GMO 1, GMO2 and AMR

# How does Plasmid therapy work?

- Chose two locally endemic plasmids:
  - IncL/M-type plasmid pE11573, endemic in Sydney hospitals and carries *bla*$_{\text{IMP-4}}$ carbapenamase gene → confers resistance to most B-lactams including third-gen cephalosporins and genes encoding resistance to gentamicin and a single type II addiction system (*pemIK*).
  - IncI1 plasmid pJIE512b (type I) addiction system (*pndAC*) and carries *bla*$_{\text{CMY-2}}$ AmpC gene, which is implicated in the spread of broad-spectrum high-level β-lactam resistance, including CTX$^{R}$
- HREC approval for the other plasmids (CTX **C**/**I1**/**M**/A/X3/L, NDM X3, OXA, F2)

# How does Plasmid therapy work?

- Constructed low-copy conjugative probiotic plasmid pJIMK46 by replacing the entire 28.5 kb AbR region (including *bla*IMP-4) of pEl1573 (IncL/M *rep* as in pEl1573) with *tetA* (tetracycline resistance, TET-R) and the *pemK* toxin gene with *fosA3* (fosfomycin resistance, FOS-R) and pJIMK56 was constructed by replacing the *bla*CMY-2 gene and flanking IS of pJIE512b with *fosA3* and *pndA* with *tetA*.
- Both of these probiotic plasmids were then tested in curing their respected target plasmids in vitro and in mice gut, and in both cases, a complete cure of AbR plasmids was obtained without any adverse effects in mice.
- Now we need to test this in humans….

# What are the risks?

- OGTR conducted a thorough risk review and concluded that the risk to the health and safety of staff and carers is negligible based on the following:
  - The E. coli Nissle strain used is not pathogenic and is commonly used as a probiotic so there is no risk in ingesting small amounts.
  - Acquired antibiotic resistance by persons inadvertently exposed to small amounts of the curing plasmid is unlikely, but even if it did occur would be short-lived and would be susceptible to antibiotic treatment if needed.
  - In the absence of antibiotic selection, wild-type strains would outcompete the GM bacteria.
  - All bacteria that might carry the GMO are susceptible to the decontamination procedures designed for other biohazards such as human biological waste.
  - Standard clinical practices and good hygiene are sufficient to protect against possible exposure during administration or to any GMO subsequently shed in faeces.
  - The GMO will be administered in the hospital and the patient will remain under the care of qualified and trained clinical staff for at least 4 days following the last administration of the GM bacteria, or earlier if two consecutive samples are found to be clear of the GMO.

# Patient selection

- Patients need to be carrying of the two targeted antimicrobial resistance plasmids following pre-clinical or pre-treatment screening
- Category A:

  Medicines/biologicals: **Category A** *patient* means a person who is seriously ill with a condition from which death is reasonably likely to occur within a matter of months, or from which premature death is reasonably likely to occur in the absence of early treatment.

  - Admitted with life-threatening conductions caused by Enterobacteriaceae to Intensive care unit or a screened critical care unit such as Haematology or Transplant
  - Scheduled for organ or bone-marrow transplantation, or treatment for leukaemia or lymphoma
- Category B:

  **The SAS Category B application form should be completed if guidance for use of an unapproved good will be met and the SAS Category A or SAS Category C pathways are not applicable.**
- Category C: ‘unapproved’ therapeutic goods deemed by the TGA to have an established history of use

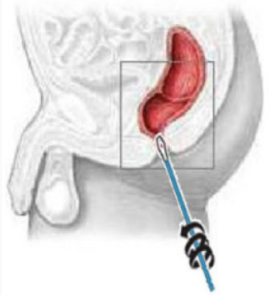
# Where are we doing this?

- Here!
- Soon…Children's Hospital Westmead, Royal North Shore, Concord, St George

# Administration

- The patient will consume two doses of $10^8$ cfu E. coli Nissle strain/day, containing a curing plasmid in normal saline for three consecutive days. Either consumed by patient or administered via feeding tube.
- An antibiotic (Tetracycline or Fosfomycin) will be co-administered with the GM bacteria from day 2. Tetracycline would be administered for 3 days and the dosage would be the standard dose (Doxycycline 50mg bd for 2 days). Fosfomycin will be given as a single dose of 3g.
- To reduce the stomach acids, Esomeprazole or Lansoprazole (30 mg single dose) will be provided to the participants before starting the probiotic plasmid administration.
- Participants will stay at the hospital for at least 4 days following the last administration of GMO.
  - Faecal and/or rectal swabs will be taken at regular intervals and analysed to monitor the success of the treatment.
  - Samples will be taken to the certified PC2 laboratory for analysis.
  - Analysis will include culturing the gut bacteria on media containing various antibiotics and PCR-based analysis for the detection, quantification and characterisation of bacteria and the target and GM-curing plasmids.
- Once discharged, participants will be provided with sample collection containers and instructions for collecting samples at home.  Will occur at 2 weeks post-probiotic, 28 days and 90 days.

# Patient samples

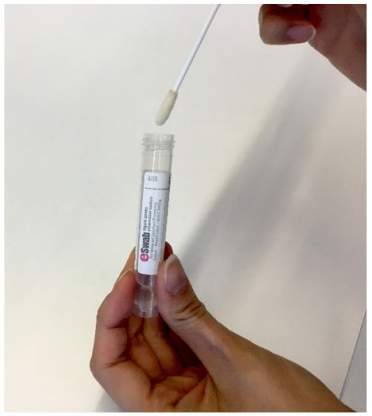
**How to collect specimens:**

**1. Perianal or rectal swab (with visible faecal material)**

**Step 1: Insert the swab through the rectal sphincter (2-3 cm) and gently rotate three times.**

**When finished, make sure there is some brown visible on the tip of the swab.**

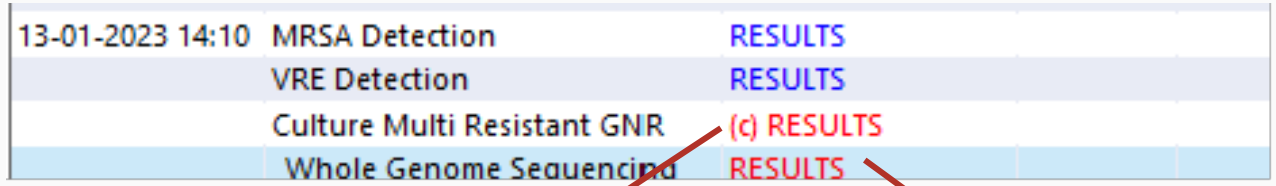
**Step 2: Place swab with visible brown into the eSwab liquid amies container.**



| Visit Day | Pre-Screen | Pre-therapy | 1[a] plasmid therapy | 2 | 3 | 4 | 5 | 6 | 7 | 2 weeks after discharge | 30 days after discharge | 90 days after discharge |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Check eligibility | x | x | | | | | | | | | | |
| Informed consent | x | x | | | | | | | | | | |
| Plasmid therapy (2 doses $10^8$ cfu E. coli Nissle strain/day) | | | x | x | x | | | | | | | |
| Antibiotic: Tetracycline (TET) (3 days) or Fosfomycin (FOF) (a single dose 3 grams) | | | | x (FOF single dose or TET) | x (TET) | x (TET) | | | | | | |
| Culture relevant pathogen: Routine Micro: CIDMLS ICPMR | x | x | | | | | | | | | | |
| Rectal specimens | x[b] | x[b] | x[b] | x[b] | x[b] | x[b] | x[b] | x[b] | x[b] | x | x | x |
| Stool as available | x[b] | x[b] | x[b] | x[b] | x[b] | x[b] | x[b] | x[b] | x[b] | x | x | x |
| Metagenomics | x | x | x | x | x | x | x | x | x | x | x | x |
| Adverse events | x | x | x | x | x | x | x | x | X | x | x | x |

# How YOU can help!

- Get Rectal swabs for your patients in ICU (twice weekly) and on Haematology/transplant/dialysis wards (weekly)




**Culture Multi Resistant GNR - Accession:** [redacted]
**Result Status - Modified**

**Micro Reports** | Susceptibilities | Specimen | Action List

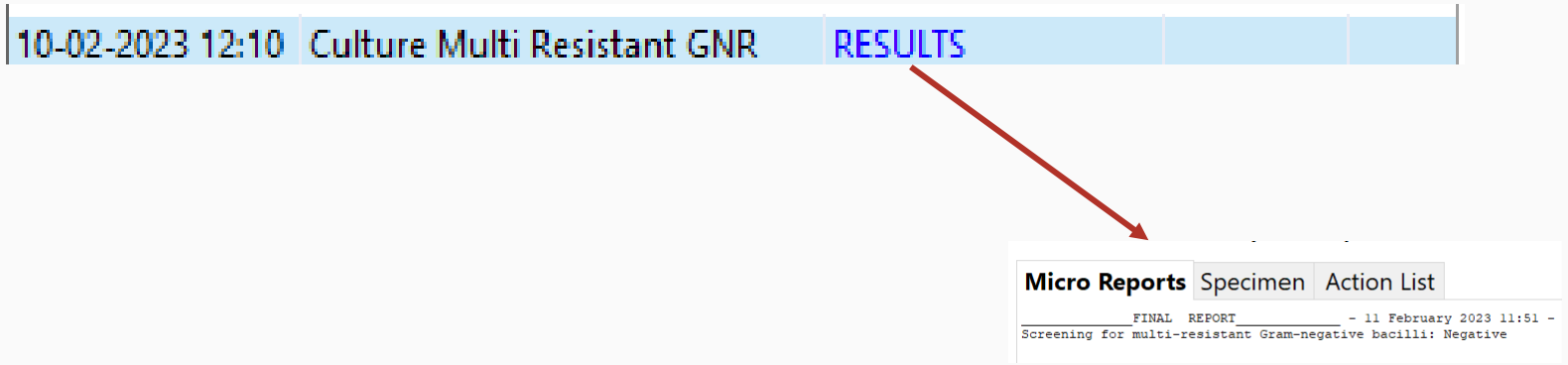
_____FINAL REPORT_____ - 16 January 2023 07:24 -
Escherichia coli was isolated
This organism produces a Carbapenemase
The Carbapenemase gene detected by PCR is blaIMP-like
Infection Control Alert . Further assessment required .
For therapeutic advice on patients colonised with multi-resistant organisms , please contact the Clinical Microbiologist

**Micro Reports** | Specimen | Action List

_____FINAL REPORT_____ - 01 March 2023 12:24 -
The submitted isolate has been identified by whole genome sequencing as
Escherichia coli , sequence type (ST) 80 .
Carbapenemase gene was blaIMP-4-like .
Extended Spectrum Beta Lactamase (ESBL) gene was not detected .
Plasmid-mediated ampC Beta-lactamase gene was not detected .
16S rRNA Methylase gene was not detected .
Mobile Colistin Resistance (MCR) gene was not detected .
Note - Presence of antimicrobial resistance genes does not necessarily infer phenotypic resistance and the absence of resistance genes do not imply susceptibility
These results have been electronically notified to the NSW Ministry of Health.
Please contact the Clinical Microbiologist for further information, if required

# But we haven't had much luck recently…

- Get Rectal swabs for your patients in ICU (twice weekly) and on Haematology/transplant/dialysis wards (weekly)



# However the search goes on…

- 67M HSCT for AML.

  Febrile neutropenia post HSCT

| | A | B |
|---|---|---|
| 1 | Escherichia coli | |
| 2 | | PInt |
| 3 | **EUCAST Int Legend*** | Comment |
| 4 | Amoxicillin/Clavulanic Acid | R |
| 5 | Ampicillin | R |
| 6 | Gentamicin* | S |
| 7 | Piperacillin/Tazobactam | R |

| | | |
|---|---|---|
| 13-10-2023 23:42 | Culture Blood | RESULTS |
| 13-10-2023 23:40 | Culture Blood | RESULTS |
| 13-10-2023 23:33 | Culture Blood | (c) RESULTS |
| | Min Inhib Conc Level | RESULTS |
| | _Whole Genome Sequencing | RESULTS |

| | A | B | C |
|---|---|---|---|
| 1 | Escherichia coli | | |
| 2 | | TREKMIC | TREKInt |
| 3 | Aztreonam | < 0.125 | S |
| 4 | Aztreonam/Avibactam | <0.125/4 | - |
| 5 | Meropenem | 1 | S |
| 6 | Meropenem/Vaborbactam | 1/8 | S |
| 7 | Imipenem | 2 | S |
| 8 | Imipenem/Relebactam | 2/4 | S |
| 9 | Eravacycline | 0.25 | S |
| 10 | Polymyxin B | 0.5 | - |
| 11 | **EUCAST Int Legend*** | | Comment |
| 12 | Colistin | 0.5 | S |

| | | |
|---|---|---|
| 30-10-2023 13:15 | Culture Multi Resistant GNR | RESULTS |

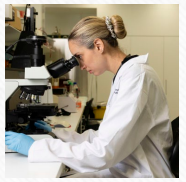
**Micro Reports** Specimen Action List

_____FINAL REPORT_____ - 31 October 2023 10:18 -
The submitted isolate has been identified by whole genome sequencing as
Escherichia coli , sequence type (ST) 224 .
Carbapenemase gene was blaOXA-48 .
Extended Spectrum Beta Lactamase (ESBL) gene was not detected .
Plasmid-mediated ampC Beta-lactamase gene was not detected .
16S rRNA Methylase gene was not detected .
Mobile Colistin Resistance (MCR) gene was not detected .
Note - Presence of antimicrobial resistance genes does not necessarily infer phenotypic resistance and the absence of resistance genes do not imply susceptibility
Please contact the Clinical Microbiologist for further information, if required
These results have been electronically notified to the NSW Ministry of Health.

# ACKNOWLEDGEMENTS


- Prof Jonathan Iredell – slides
- The Iredell team:



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