

# ANTIBIOTIC RESISTANCE – ARE WE DOING TOO LITTLE, TOO LATE?

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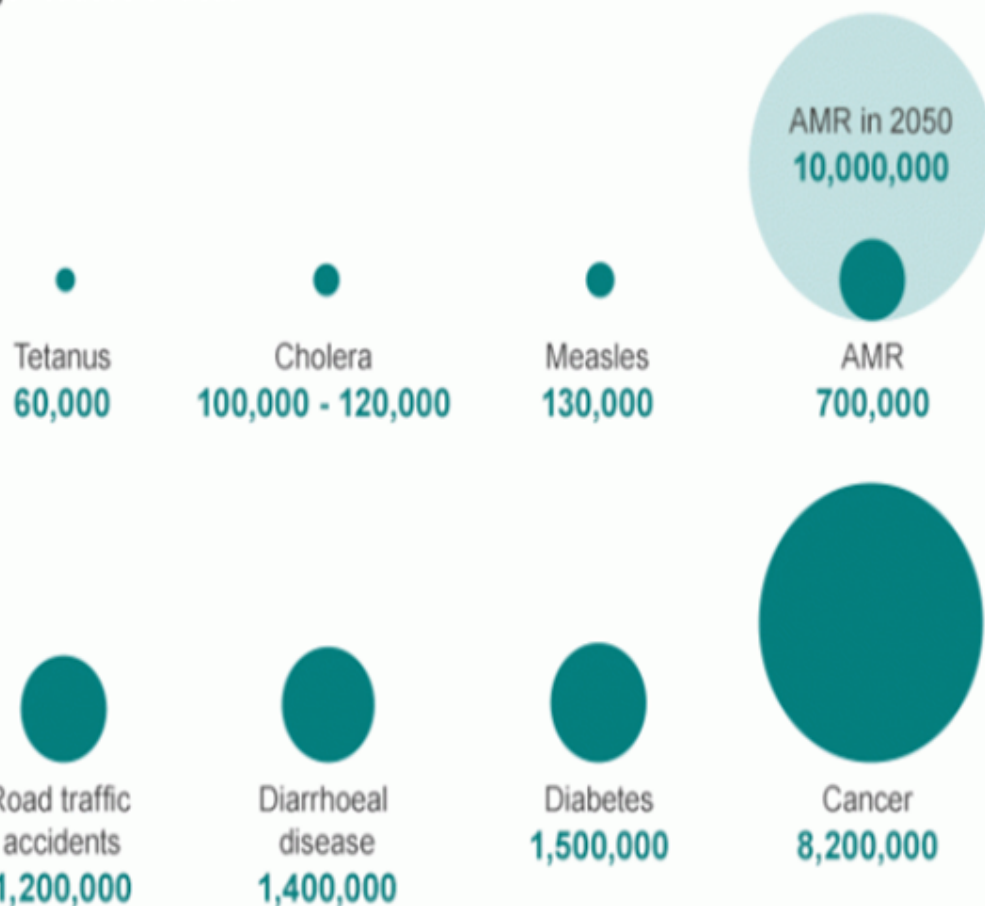




Surgery  
Invasive devices  
Intubation and Ventilation  
Chemotherapy  
Immune-suppression  
Antibiotics  
Hospital – acquired infections

# How bad is the problem of resistance?

Deaths attributable to antimicrobial resistance every year compared to other major causes of death



Source: Review on Antimicrobial Resistance 2014

Antimicro  
can affect an  
in any

#Antimicro



g-resistant  
ions are a  
challenge on  
the scale of  
climate change

Jeremy Farrar  
Director Wellcome Trust



**We have caused this problem**



## Total Number of New Antibacterial Agents

0 2 4 6 8 10 12 14 16



**ANTIBIOTIC  
DEVELOPMENT  
IS DWINDLING**

Source: *The Epidemic of Antibiotic-Resistant Infections*, CID 2008;46 (15 January)  
Clin Infect Dis. (2011) May 52 (suppl 5): S397-S428. doi: 10.1093/cid/cir153

# 7 Deadly Antibiotic Resistant Bacteria

1. CRE - carbapenem-resistant Enterobacteriaceae
2. MRSA - methicillin-resistant *Staphylococcus aureus*
3. Penicillin resistant *Streptococcus pneumoniae*
4. ESBL - producing Gram negatives
5. VRE – vancomycin resistant Enterococci
6. MDR – *Pseudomonas aeruginosa*
7. MDR – Acinetobacter spp

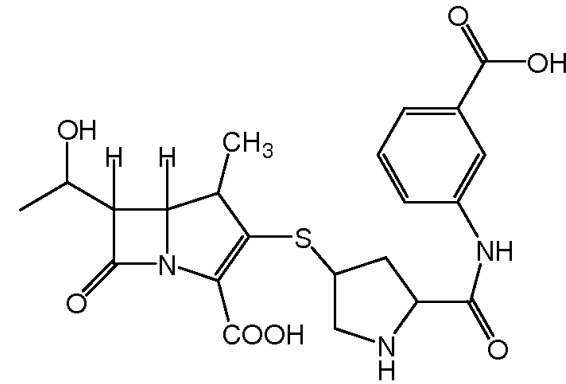


# What are CREs?

- Carbapenem Resistant Enterobacteriaceae
- They are highly antibiotic resistant Gram negatives to all classes of antibiotics except Colistin/Tigecycline
- They normally live in the gut
- Klebsiella, E coli, Enterobacter, Serratia, Citrobacter

# What are carbapenems?

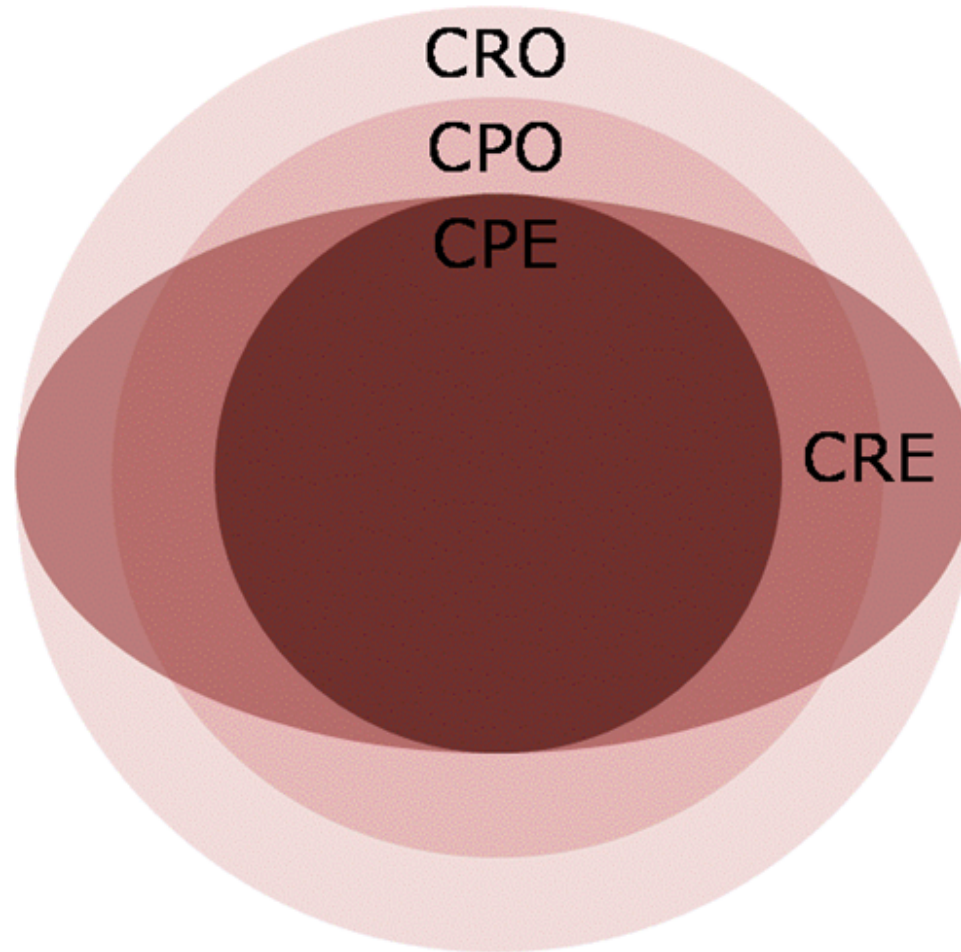
- Meropenem
- Ertapenem
- Imipenem
- Doripenem



ertapenem





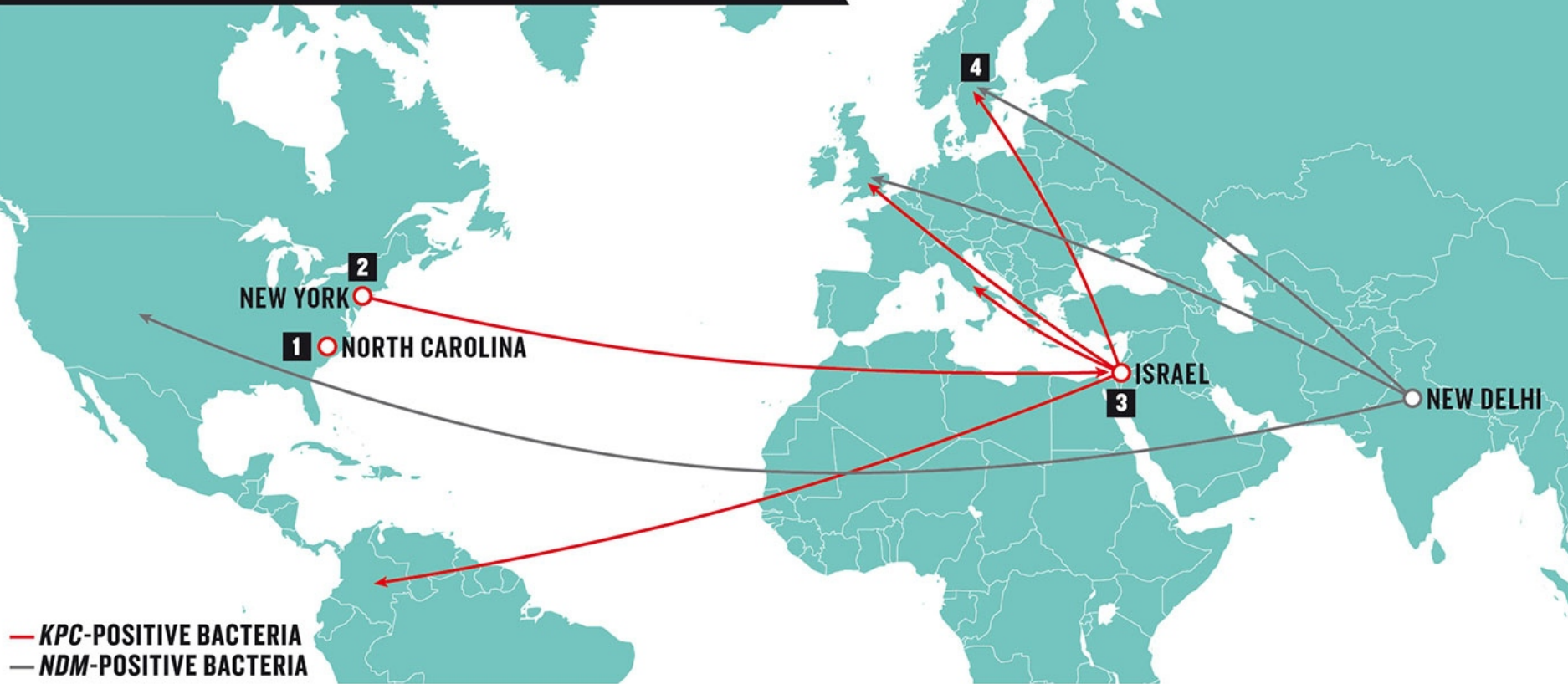


# Names of CROs

- CRO – carbapenem - resistant organism
  - CRE – carbapenem - resistant Enterobacteriaceae
  - CPO – carbapenamase - producing organism
  - CPE – carbapenamase - producing Enterobacteriaceae
- 
- NDM- New Delhi metallo-beta-lactamase
  - KPC – *Klebsiella* producing carbapenamase

# THE RESISTANCE MOVEMENT

Carbapenem-resistant Enterobacteriaceae have been on the move since at least 1996.



**1** **2000:** Analysis of a 1996 sample from a North Carolinian hospital finds infectious *Klebsiella pneumoniae* carrying a gene called *KPC* that confers resistance to carbapenems.

**2** **2003:** *KPC*-positive bacteria are found spreading rapidly through hospitals across New York City. By 2007, 21% of *Klebsiella* in the city carry the resistance gene.

**3** **2005:** *KPC*-positive bacteria make their way from New York to several other countries, including Israel. From Israel, the bacteria travel to Italy, Colombia, the United Kingdom and Sweden.

**4** **2008:** Doctors in Sweden find a new carbapenem-resistance gene, *NDM*. Traced back to India, *NDM*-positive bacteria have moved quickly.



# THINK YOU ARE TRAVELLING LIGHTLY?

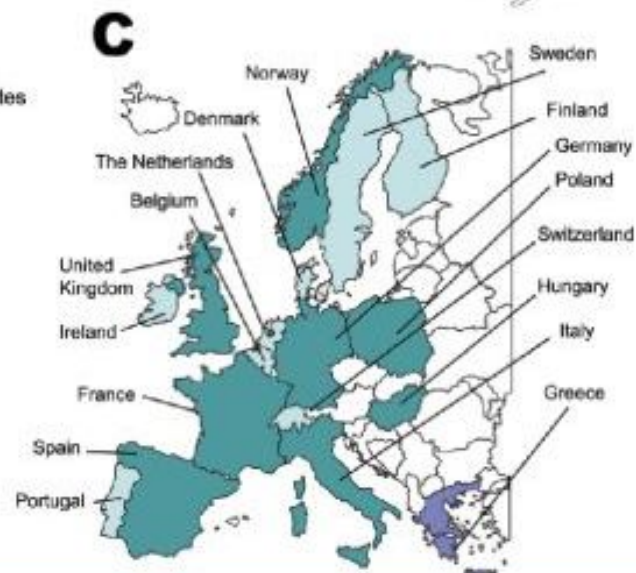
As we travel around the world, bacteria travel with us...







- Single KPC-producing isolates
- Several outbreaks of KPC-producing isolates
- Endemicity of KPC-producing isolates



# What did Israel learn about CROs?

- The organism spread through the healthcare system really QUICKLY
- Long term care facilities e.g. rehab units were 'reservoirs' of the infection
- Control was achieved through really well co-ordinated infection control and public health measures

## How CRE Take Over

1. Lots of germs,  
1 or 2 are CRE



2. Antibiotics kill off  
good germs



3. CRE grow



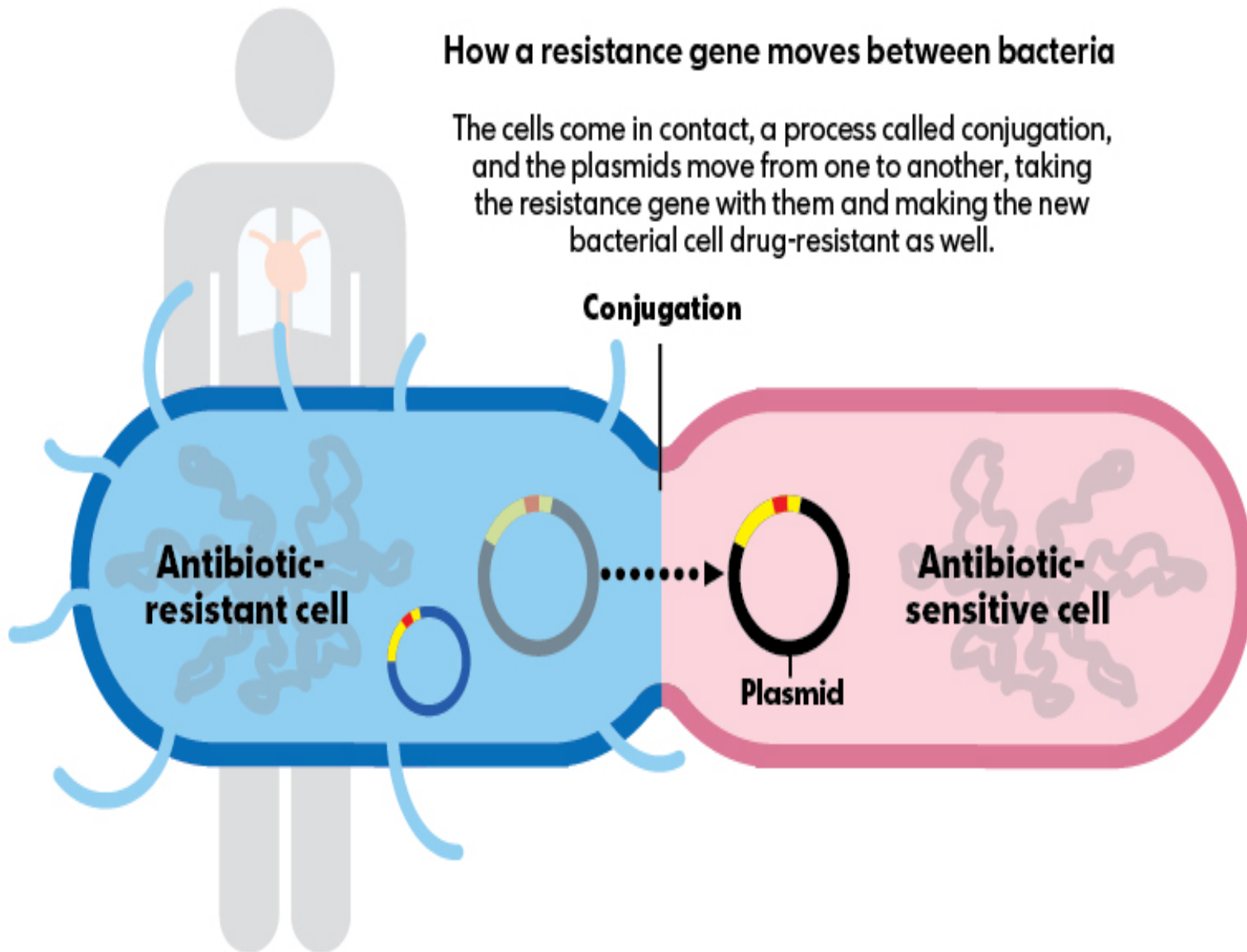
4. CRE share genetic defenses to  
make other bacteria resistant

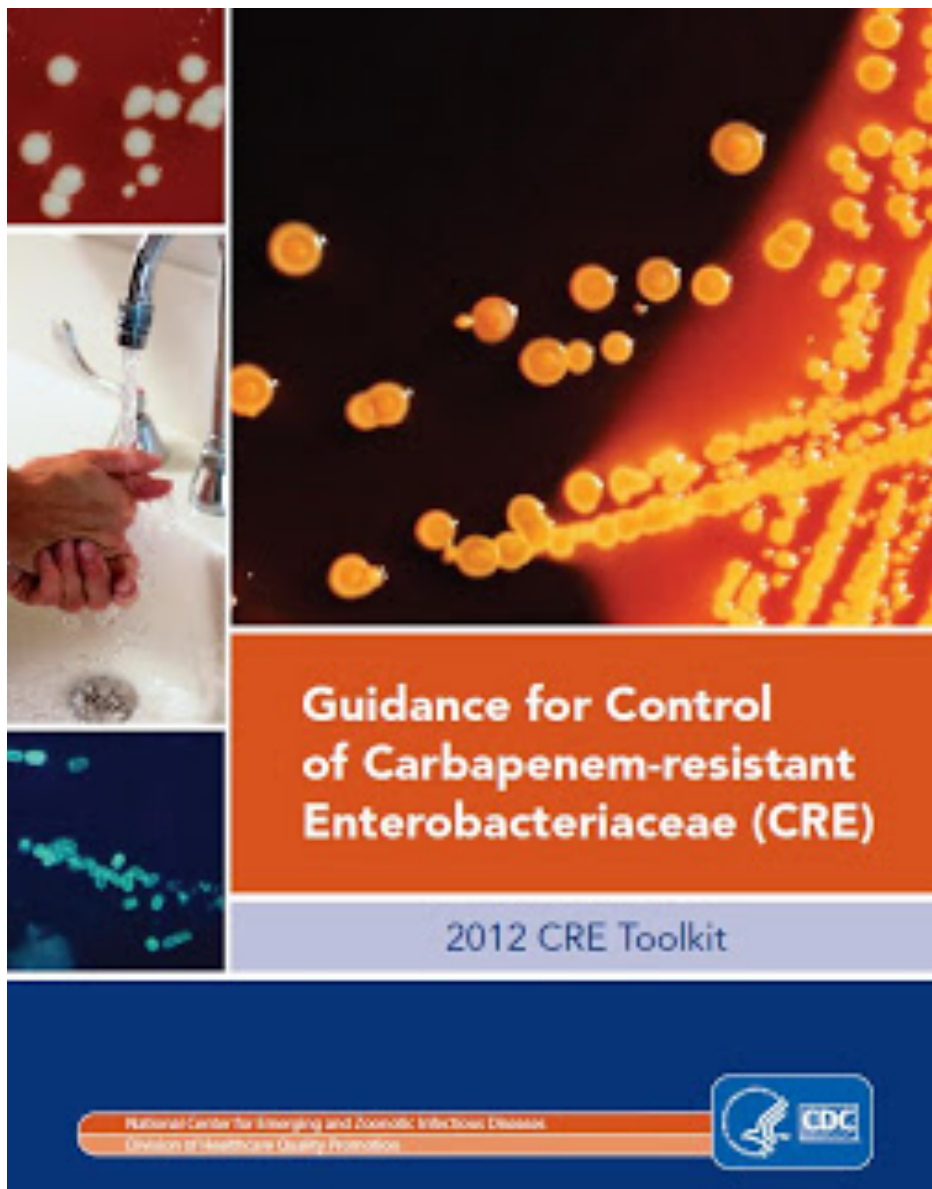




## How a resistance gene moves between bacteria

The cells come in contact, a process called conjugation, and the plasmids move from one to another, taking the resistance gene with them and making the new bacterial cell drug-resistant as well.





# Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE)

2012 CRE Toolkit

National Center for Emerging and Zoonotic Infectious Diseases  
Division of Healthcare Quality Promotion



Is the patient currently in isolation? ☐ NO ☐ YES

Type of Isolation (check all that apply) ☐ Contact ☐ Droplet ☐ Airborne ☐ Other:

Does patient currently have an infection, colonization OR a history of positive culture of a multidrug-resistant organism (MDRO) or other organism of epidemiological significance?	Colonization or history <i>Check if YES</i>	Active infection on Treatment <i>Check if YES</i>
Methicillin-resistant Staphylococcus aureus (MRSA)		
Vancomycin-resistant Enterococcus (VRE)		
Clostridium difficile		
Acinetobacter, multidrug-resistant*		
E coli, Klebsiella, Proteus etc. w/Extended Spectrum B-Lactamase (ESBL)*		
Carbapenemase resistant Enterobacteriaceae (CRE)*		
Other:		

Does the patient/resident currently have any of the following?

- |  |   |
|--|---|
| <input type="checkbox"/> Cough or requires suctioning                    | <input type="checkbox"/> Central line/PICC (Approx. date inserted __/__/__) |
| <input type="checkbox"/> Diarrhea  | <input type="checkbox"/> Hemodialysis catheter                              |
| <input type="checkbox"/> Vomiting  | <input type="checkbox"/> Urinary catheter (Approx. date inserted __/__/__)  |
| <input type="checkbox"/> Incontinent of urine or stool                   | <input type="checkbox"/> Suprapubic catheter                                |
| <input type="checkbox"/> Open wounds or wounds requiring dressing change | <input type="checkbox"/> Percutaneous gastrostomy tube                      |
| <input type="checkbox"/> Drainage (source) _____                         | <input type="checkbox"/> Tracheostomy                                       |



Public Health  
England

## **Acute trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae**

# Countries with high known incidence

- India, Bangladesh, Pakistan
- Israel and the Gulf states
- Greece, Cyprus, Turkey, the Balkans
- Malta and North Africa
- Hotspots in UK and Ireland
- USA and South America
- China and South Korea

# Who is at risk?

- Healthy patients do not usually get CRO infections
- Patients in hospitals, nursing homes and long term care facilities are most vulnerable
- Those with devices e.g. catheters, lines, on ventilators and those on long courses of antibiotics are at greatest risk

# How do we tackle CROs?

- Be on the lookout for possible cases
- Screening
- Hand hygiene
- Isolation and contact precautions
- Contact tracing of other related cases
- Effective cleaning of equipment and the environment
- Careful antibiotic prescribing

# Screening: How and Who?

## How?

- Rectal swab (or faeces)
- Label 'CRO screen'
- 3 samples 48 hours apart

## Who?

- Those patients who have been in a hospital abroad in the last 12 months
- From a UK hospital with a known CRO problem
- Previously known CRO positive







# THE CAESAR NETWORK

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WHO 2015



Country or area	National AMR focal point appointed	Intersectoral coordinating mechanism to centralise AMR set up	National AMR action plan developed	National AMR reference laboratory in place	National AMR surveillance in place	AMR data reported to CAESAR	Subset of laboratories participate in CAESAR EQA	National AMR workshop held
Georgia	✓	✓	✓	✓	✗	⚙️	✓	✓
Kazakhstan	✗	✗	✗	✗	✗	✗	✗	✗
Kyrgyzstan	✓	✗	✗	✗	✗	✗	✓	✗
Montenegro	✓	✓	✓	⚙️	✗	⚙️	✓	✗
Republic of Moldova	✓	✓	✗	✓	✓	⚙️	✓	✓
Russian Federation	✓	✓	✗	✓	✓	⚙️	✓	✗
Serbia	✓	⚙️	✗	✓	✓	✓	✓	✓
Switzerland	✓	✓	✗	✓	✓	✓	✗	✗
Tajikistan	✓	✗	✗	✗	✗	✗	✗	✗
The former Yugoslav Republic of Macedonia	✓	✓	✓	✓	✓	✓	✓	✓
Turkey	✓	✓	✓	✓	✓	✓	✓	✓
Turkmenistan	✓	✗	✗	✗	✗	⚙️	✗	✗
Ukraine	✓	✗	✗	✓	✗	✗	✗	✗

Table 6. Resistance levels for *E. coli* and *K. pneumoniae* among blood and CSF isolates in Belarus

Antibiotic class	<i>E. coli</i>		<i>K. pneumoniae</i>	
	N	Resistance (%)	N	Resistance (%)
Aminopenicillins (R) <sup>a</sup>	33	94	NA	NA
3rd-generation cephalosporins (R) <sup>b</sup>	30	87	76	92
3rd-generation cephalosporins (I+R) <sup>b</sup>	30	87	76	92
Aminoglycosides (R) <sup>c</sup>	33	58	74	89
Fluoroquinolones (R) <sup>d</sup>	32	75	77	84
Fluoroquinolones (I+R) <sup>d</sup>	32	75	77	87
Carbapenems (R) <sup>a</sup>	25 <sup>*</sup>	0 <sup>*</sup>	65	3
Carbapenems (I+R) <sup>a</sup>	25 <sup>*</sup>	0 <sup>*</sup>	65	3

NA: not applicable.

<sup>\*</sup> A low number of isolates were tested (N < 30), and the percentage resistance should be interpreted with caution.

<sup>a</sup> The aminopenicillins group consists of amoxicillin and ampicillin.

<sup>b</sup> The third-generation cephalosporin group consists of cefotaxime, ceftriaxone and ceftazidime.

<sup>c</sup> The aminoglycoside group consists of amikacin, gentamicin and tobramycin.

<sup>d</sup> The fluoroquinolone group consists of ciprofloxacin, ofloxacin and levofloxacin.

Table 17. Resistance levels for *E. coli* and *K. pneumoniae* among blood and CSF isolates in Switzerland

Antibiotic class	<i>E. coli</i>		<i>K. pneumoniae</i>	
	N	Resistance (%)	N	Resistance (%)
Aminopenicillins (R) <sup>a</sup>	3 687	49	NA	NA
3rd-generation cephalosporins (R) <sup>b</sup>	3 983	7	707	7
3rd-generation cephalosporins (I+R) <sup>b</sup>	3 983	8	707	8
Aminoglycosides (R) <sup>c</sup>	3 991	8	705	5
Fluoroquinolones (R) <sup>d</sup>	3 992	16	706	6
Fluoroquinolones (I+R) <sup>d</sup>	3 992	17	706	7
Carbapenems (R) <sup>e</sup>	3 990	0	706	1
Carbapenems (I+R) <sup>e</sup>	3 990	0	706	1

NA: not applicable.

<sup>a</sup> The aminopenicillins group consists of amoxicillin and ampicillin.<sup>b</sup> The third-generation cephalosporin group consists of cefotaxime, ceftriaxone and ceftazidime.<sup>c</sup> The aminoglycoside group consists of amikacin, gentamicin and tobramycin.<sup>d</sup> The fluoroquinolone group consists of ciprofloxacin, ofloxacin and levofloxacin.<sup>e</sup> The carbapenem group consists of imipenem and meropenem.

How do we protect patients in the era?





- Follow strict contact precautions when looking after patients with resistant bacteria (gloves and aprons)
- Ideally dedicated rooms and equipment for affected patients. (Some units also use dedicated staff)
- Take out temporary medical devices e.g urinary catheters, CVP lines as soon as possible
- Prescribe antibiotics only if patients are infected
- Write antibiotic guidelines for your unit if you don't have any







- **Roll up your shirt sleeves** (even better, wear scrubs!)
- **Guys: go necktie-free** (or tuck it into your shirt)
- **Don't wear a white coat** (or hang it here before seeing patients)
- **Wash your hands before & after every patient contact**
- **Wipe down your stethoscope after every patient exam**





# S U C C E S S

Because you too can own this face of pure accomplishment