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

Dr Carmel Curtis
Consultant Microbiologist
UCLH Hospitals
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:

- Tetanus: 60,000
- Cholera: 100,000 - 120,000
- Measles: 130,000
- AMR: 700,000
- AMR in 2050: 10,000,000
- Road traffic accidents: 1,200,000
- Diarrhoeal disease: 1,400,000
- Diabetes: 1,500,000
- Cancer: 8,200,000

Source: Review on Antimicrobial Resistance 2014
We have caused this problem
ANTIBIOTIC DEVELOPMENT IS DWINDLING

7 Deadly Antibiotic Resistant Bacteria

1. CRE - carbapenem-resistant Enterobacteriaceae
2. MRSA - meticillin-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
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.


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...
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.
Is the patient currently in isolation?  □ NO  □ YES
Type of Isolation (check all that apply)  □ Contact  □ Droplet  □ Airborne  □ Other:

<table>
<thead>
<tr>
<th>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?</th>
<th>Colonization or history</th>
<th>Active infection on Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methicillin-resistant Staphylococcus aureus (MRSA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vancomycin-resistant Enterococcus (VRE)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acinetobacter, multidrug-resistant*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. coli, Klebsiella, Proteus etc. w/Extended Spectrum B-Lactamase (ESBL)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbapenemase resistant Enterobacteriaceae (CRE)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

- □ Cough or requires suctioning
- □ Diarrhea
- □ Vomiting
- □ Incontinent of urine or stool
- □ Open wounds or wounds requiring dressing change
- □ Drainage (source)__________________________
- □ Central line/PICC (Approx. date inserted ___/___/____)
- □ Hemodialysis catheter
- □ Urinary catheter (Approx. date inserted ___/___/____)
- □ Suprapubic catheter
- □ Percutaneous gastrostomy tube
- □ Tracheostomy
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

WHO 2015
Central Asian and Eastern European Surveillance of Antimicrobial Resistance
<table>
<thead>
<tr>
<th>Country or area</th>
<th>National AMR focal point appointed</th>
<th>Intersectoral coordinating mechanism to contain AMR set up</th>
<th>National AMR action plan developed</th>
<th>National AMR reference laboratory in place</th>
<th>National AMR surveillance in place</th>
<th>AMR data reported to CAESAR</th>
<th>Subset of laboratories participate in CAESAR EQA</th>
<th>National AMR workshop held</th>
</tr>
</thead>
<tbody>
<tr>
<td>Georgia</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✗</td>
<td>✗</td>
<td>✔</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td>✔</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Montenegro</td>
<td>✔</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Republic of Moldova</td>
<td>✔</td>
<td>✔</td>
<td>❌</td>
<td>✗</td>
<td>✔</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>✔</td>
<td>✔</td>
<td>❌</td>
<td>✗</td>
<td>✔</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Serbia</td>
<td>✔</td>
<td>✔</td>
<td>❌</td>
<td>✗</td>
<td>✔</td>
<td>✗</td>
<td>✗</td>
<td>✔</td>
</tr>
<tr>
<td>Switzerland</td>
<td>✔</td>
<td>✔</td>
<td>❌</td>
<td>✗</td>
<td>✔</td>
<td>✗</td>
<td>✗</td>
<td>✔</td>
</tr>
<tr>
<td>Tajikistan</td>
<td>✔</td>
<td>✔</td>
<td>❌</td>
<td>✗</td>
<td>✔</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>The former Yugoslav Republic of Macedonia</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Turkey</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Turkmenistan</td>
<td>✔</td>
<td>✔</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Ukraine</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
</tbody>
</table>
Table 6. Resistance levels for *E. coli* and *K. pneumoniae* among blood and CSF isolates in Belarus

<table>
<thead>
<tr>
<th>Antibiotic class</th>
<th>E. coli</th>
<th></th>
<th>K. pneumoniae</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Resistance (%)</td>
<td>N</td>
<td>Resistance (%)</td>
</tr>
<tr>
<td>Aminopenicillins (R)*</td>
<td>33</td>
<td>94</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>3rd-generation cephalosporins (R)*</td>
<td>30</td>
<td>87</td>
<td>76</td>
<td>92</td>
</tr>
<tr>
<td>3rd-generation cephalosporins (I+R)*</td>
<td>30</td>
<td>87</td>
<td>76</td>
<td>92</td>
</tr>
<tr>
<td>Aminoglycosides (R)*</td>
<td>33</td>
<td>58</td>
<td>74</td>
<td>89</td>
</tr>
<tr>
<td>Fluoroquinolones (R)*</td>
<td>32</td>
<td>75</td>
<td>77</td>
<td>84</td>
</tr>
<tr>
<td>Fluoroquinolones (I+R)*</td>
<td>32</td>
<td>75</td>
<td>77</td>
<td>87</td>
</tr>
<tr>
<td>Carbapenems (R)*</td>
<td>25*</td>
<td>0*</td>
<td>65</td>
<td>3*</td>
</tr>
<tr>
<td>Carbapenems (I+R)*</td>
<td>25*</td>
<td>0*</td>
<td>65</td>
<td>3*</td>
</tr>
</tbody>
</table>

NA: not applicable.

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

* The aminopenicillins group consists of amoxicillin and ampicillin.

* The third-generation cephalosporin group consists of cefotaxime, ceftiraxone and ceftazidime.

* The aminoglycoside group consists of amikacin, gentamicin and tobramycin.

* 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

<table>
<thead>
<tr>
<th>Antibiotic class</th>
<th><em>E. coli</em></th>
<th></th>
<th></th>
<th><em>K. pneumoniae</em></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>N</strong></td>
<td><strong>Resistance (%)</strong></td>
<td></td>
<td><strong>N</strong></td>
<td><strong>Resistance (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Aminopenicillins (R)*</td>
<td>3,687</td>
<td>49</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>3rd-generation cephalosporins (R)*</td>
<td>3,983</td>
<td>7</td>
<td>707</td>
<td>7</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>3rd-generation cephalosporins (I+R)*</td>
<td>3,983</td>
<td>8</td>
<td>707</td>
<td>8</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Aminoglycosides (R)*</td>
<td>3,991</td>
<td>8</td>
<td>705</td>
<td>5</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Fluoroquinolones (R)*</td>
<td>3,992</td>
<td>16</td>
<td>706</td>
<td>6</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Fluoroquinolones (I+R)*</td>
<td>3,992</td>
<td>17</td>
<td>706</td>
<td>7</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Carbapenems (R)*</td>
<td>3,990</td>
<td>0</td>
<td>706</td>
<td>1</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Carbapenems (I+R)*</td>
<td>3,990</td>
<td>0</td>
<td>706</td>
<td>1</td>
<td></td>
<td>NA</td>
</tr>
</tbody>
</table>

NA: not applicable.

* The aminopenicillins group consists of amoxicillin and ampicillin.
* The third-generation cephalosporin group consists of cefotaxime, ceftriaxone and ceftazidime.
* The aminoglycoside group consists of amikacin, gentamicin and tobramycin.
* The fluoroquinolone group consists of ciprofloxacin, ofloxacin and levofloxacin.
* 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
HANDLE ANTIBIOTICS WITH CARE
SUCCESS

Because you too can own this face of pure accomplishment