Do you know your CRE from your CRAB?

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Disclosures

- I have research funding from the Guy’s and St. Thomas’ Charity
- I have given paid lectures for 3M, BD and Society for Applied Microbiology
THE END OF ANTIBIOTICS IS NIGH
What’s the problem?

“CRE are nightmare bacteria.”
Dr Tom Frieden, CDC Director

“If we don’t take action, then we may all be back in an almost 19th Century environment where infections kill us as a result of routine operations.”
Dame Sally Davies, Chief Medical Officer

“If we fail to act, we are looking at an almost unthinkable scenario where antibiotics no longer work and we are cast back into the dark ages of medicine where treatable infections and injuries will kill once again.”
David Cameron, Prime Minister, UK

“The rise of antibiotic-resistant bacteria, however, represents a serious threat to public health and the economy.”
Barack Obama, President USA
Rising threat from MDR-GNR

% of all HAI caused by GNRs. % of ICU HAI caused by GNRs.

Non-fermenters
- Acinetobacter baumannii
- Pseudomonas aeruginosa
- Stenotrophomonas maltophilia

Enterobacteriaceae
- Klebsiella pneumoniae
- Escherichia coli
- Enterobacter cloacae

DANGER
MINES
Acronym minefield

CPE
MDR-GNR
CPC
ESBL
MDR-GNB
CRO
CPE
CRE
CRC
KPC
CRAB

ESBL
KPC
What are CRE?

*Carbapenem-resistant Enterobacteriaceae (CRE)* – Enterobacteriaceae that are resistant to carbapenems by any mechanism.

*Carbapenemase-producing Enterobacteriaceae (CPE)* – Enterobacteriaceae that are resistant to carbapenems by means of an acquired carbapenemase.
Resistant Enterobacteriaceae v non-fermenters

<table>
<thead>
<tr>
<th>Microbiology</th>
<th>Enterobacteriaceae (<em>K. pneumoniae</em>)</th>
<th>Non-fermenters (<em>A. baumannii</em>)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At-risk population</td>
<td>Primarily acute pts</td>
<td>ICU, burns</td>
</tr>
<tr>
<td>Risk factors</td>
<td>Travel</td>
<td>Trauma, ICU stay</td>
</tr>
<tr>
<td>Epidemic potential</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Clinical manifestation</td>
<td>UTI</td>
<td>VAP</td>
</tr>
<tr>
<td>Attributable mortality</td>
<td>Stark increase (CPE)</td>
<td>Minimal increase</td>
</tr>
<tr>
<td>Prevalence</td>
<td>Emerging (rapidly)</td>
<td>Patchy but stable</td>
</tr>
<tr>
<td>Sites of colonisation</td>
<td>GI tract</td>
<td>Resp, GI, skin</td>
</tr>
<tr>
<td>Colonization duration</td>
<td>Months to &gt;1 year</td>
<td>Days to weeks</td>
</tr>
<tr>
<td>Transmission routes</td>
<td>Hands ++, Env +/-</td>
<td>Hands +, Env ++</td>
</tr>
<tr>
<td>Resistance</td>
<td>Mainly acquired</td>
<td>Intrinsic &amp; acquired</td>
</tr>
<tr>
<td>Common clones</td>
<td>KPC-producing ST258</td>
<td>Intl clones I-III</td>
</tr>
</tbody>
</table>
Acinetobacter baumannii

Klebsiella pneumoniae
# Risk factors & at-risk population

<table>
<thead>
<tr>
<th></th>
<th>Enterobacteriaceae</th>
<th>Non-fermenters</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk factors</strong></td>
<td>LOS  ICU stay  Catheters / devices  Ventilation  Prior antibiotics  <strong>Travel</strong></td>
<td>LOS  ICU stay  Catheters / devices  Ventilation  Prior antibiotics  <strong>Trauma (esp. burns)</strong></td>
</tr>
<tr>
<td><strong>At-risk population</strong></td>
<td>Patients in acute settings, particularly those with recent travel to areas of high prevalence. Potential for community spread.</td>
<td>High-risk patients in the ICU and burns units; rare cause of community-acquired infection.</td>
</tr>
</tbody>
</table>
Clinical manifestation

Zarb et al. ECDC PPS. *Euro Surveill* 2012;17.
# Attributable mortality

<table>
<thead>
<tr>
<th></th>
<th>Enterobacteriaceae</th>
<th>Non fermenters</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organism</strong></td>
<td>AmpC / ESBL</td>
<td>CPE</td>
</tr>
<tr>
<td><strong>Attributable mortality</strong></td>
<td>Moderate</td>
<td>Massive (&gt;50%)</td>
</tr>
</tbody>
</table>

Invasive CR *K. pneumoniae* trends

- Greece
- Italy
- UK

CR *K. pneumoniae* invasive isolates

2005 2006 2007 2008 2009 2010 2011 2012
Invasive CR non-fermenters trends

- **Greece - CRPA**
- **UK - CRPA**
- **Italy - CRPA**
- **UK - CRAB**

**CR P. aeruginosa invasive isolates (EARS-Net)**

**CR A. baumannii bacteraemias (PHE)**

*P. aeruginosa*: ECDC EARS-Net
Emergence of CPE in the UK

PHE AMRHI, 24/01/14
Courtesy of Dr Neil Woodford
Prevalence at Guy’s and St. Thomas’, London

- A. baumannii
- P. aeruginosa
- K. pneumoniae
- All Enterobacteriaceae

% meropenem resistance in A. baumannii and P. aeruginosa

% meropenem resistance in K. pneumoniae and all Enterobacteriaceae

CRE in the USA

- K. pneumoniae / oxytoca
- All Enterobacteriaceae

NHSN / NNIS data; *MMWR* 2013;62:165-170.
CRE and CRNF in the USA

Central line-associated bloodstream infection (CLABSI) resistant to carbapenems in the national NHSN network.¹

![Bar chart showing the percentage of carbapenem resistance among K. pneumoniae, P. aeruginosa, and A. baumannii.]

Sites of colonisation – 103 CRAB patients

- 69% sternal skin
- 80% tracheal aspirate
- 25% urine
- 69% rectal

Duration of colonisation - CRKP

Rectal or stool specimens from 103 CRKP patients over 24 months.¹

Range of colonisation duration 6-42 days for *A. baumannii*.²

Surface survival

- Log (10) cfu / disc vs. Time / weeks
- C. difficile
- Acinetobacter
- K. pneumoniae

CPE in the UK: mainly KPC, OXA-48 and NDM

PHE AMR HAI, 24/01/14
Courtesy of Dr Neil Woodford
Non-fermenters in the UK: mainly VIM

PHE AMRhai, 24/01/14
Permission of Dr Neil Woodford
Common clones – CC258 KPC
*K. pneumoniae*

Common clones – *A. baumannii* clones I, II, III

Diancourt *et al.* PLoS ONE 2010;5:e10034.
## Infection prevention and control challenges

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>CRE$^1$</th>
<th>CRAB$^2$</th>
<th>MRSA</th>
<th>VRE</th>
<th>C. difficile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistance</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Resistance genes</td>
<td>Multiple</td>
<td>Multiple</td>
<td>Single</td>
<td>Single</td>
<td>n/a</td>
</tr>
<tr>
<td>Species</td>
<td>Multiple</td>
<td>Single</td>
<td>Single</td>
<td>Single</td>
<td>Single</td>
</tr>
<tr>
<td>HA vs CA</td>
<td>HA &amp; CA</td>
<td>HA (ICU)</td>
<td>HA</td>
<td>HA</td>
<td>HA</td>
</tr>
<tr>
<td>At-risk pts</td>
<td>All</td>
<td>ICU</td>
<td>Unwell</td>
<td>Unwell</td>
<td>Old</td>
</tr>
<tr>
<td>Virulence</td>
<td>+++</td>
<td>+/-</td>
<td>++</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Environment</td>
<td>+/-</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>+++</td>
</tr>
</tbody>
</table>

1. Carbapenem-resistant Enterobacteriaceae.
2. Carbapenem-resistant *Acinetobacter baumannii*. 
CRE prevention & control

- Hand hygiene
- Cleaning / disinfection
- Antibiotic stewardship
- Active screening
- Contact precautions
- Education?

SDD?
Topical CHX?
<table>
<thead>
<tr>
<th>Share</th>
<th>Differ</th>
</tr>
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<tbody>
<tr>
<td>Gram stain reaction</td>
<td>Risk factors &amp; at-risk population</td>
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<tr>
<td>Concerning AMR</td>
<td>Potential for epidemic spread</td>
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<td></td>
<td>Infection profile &amp; mortality</td>
</tr>
<tr>
<td></td>
<td>Prevalence</td>
</tr>
<tr>
<td></td>
<td>Colonisation site &amp; duration</td>
</tr>
<tr>
<td></td>
<td>Transmission routes</td>
</tr>
<tr>
<td></td>
<td>Resistance profile &amp; mechanisms</td>
</tr>
</tbody>
</table>
Summary

1. Resistant Gram-negative rods represent a more serious threat than the ‘usual suspects’, mainly due to the threat of pan-drug resistance.

2. Enterobacteriaceae (mainly *K. pneumoniae*) and non-fermenters (mainly *A. baumannii*) have fundamental differences in their epidemiology.

3. CRE and CRNF are both emerging problems, but they are not the same problem.

4. The prevention and control strategy will look different for Enterobacteriaceae vs. non-fermenters.