The International Collaborative Conference in Clinical Microbiology & Infectious Diseases

PLUS: Antimicrobial stewardship in hospitals: Improving outcomes through better education and implementation of effective interventions

24 - 26 February 2015
Gulf Hotel, Kingdom of Bahrain

SPEAKER:
Dr. Agnes Sonnevend
Associate professor of microbiology at the College of Medicine, UAE University and consultant clinical microbiologist at Tawam Hospital, Al Ain
Antibiotic resistance in the hospital – the ticking bomb: where we stand?

Dr. Ágnes Sonnevend

ICMID Bahrain
February 2015
Federal Funding for the Study of Antimicrobial Resistance in Nosocomial Pathogens: No ESKAPE

- **Enterococcus faecium**
- **Staphylococcus aureus**
- **Klebsiella pneumoniae**
- **Acinetobacter baumannii**
- **Pseudomonas aeruginosa**
- **Enterobacter sp.**

CID 2009:49 (15 September)

**Bad Bugs, No Drugs: No ESCAPE Revisited**

Lance R. Peterson

Departments of Medicine and Laboratory Medicine and Pathology, University of Chicago, Chicago,
Spread of antibiotic resistance means:

2012, Director General of WHO
The three most urgent threats are:

- *Clostridium difficile*
- *Carbapenem Resistant Enterobacteriaceae*
- *Drug-resistant Neisseria gonorrhoeae*
“...any given day 1 out of 25 patients has a hospital infection, and of those people, as many as 1 out of 9 go on to die”

Michael Bell (CDC)
“...hip replacement. Currently, prophylaxis is standard practice, and infection rates are about 0.5-2%, so most patients recover without infection, and those who get an infection have it successfully treated. We estimate that without antimicrobials, the rate of postoperative infection is 40-50% and about 30% of those with an infection will die.”
THE FUTURE

Deaths attributable to AMR every year compared to other major causes of death

Tetanus: 60,000
Road traffic accidents: 1.2 million
Measles: 130,000
Diarrhoeal disease: 1.4 million
Cancer: 8.2 million
Cholera: 100,000 to 120,000
Diabetes: 1.5 million

AMR in 2050: 10 million

So, where do WE stand?

Resistance in nosocomial pathogens in the GCC countries
Difficulties regarding AMR in the Eastern Mediterranean Region of WHO incl. the GCC countries

- Limited availability of reliable data
- Although studies from some countries in the region show the geographically extensive emergence of AMR
- Lack of robust functioning national AMR surveillance systems
- Lack of collaboration with the animal health sector
- The absence of legislation or the lack of enforcement of laws
Available National Data* on Resistance for Nine Selected Bacteria/Antibacterial Drug Combinations, 2013

*National data means data obtained from official sources, but not that data necessarily are representative for the population or country as a whole.
Staphylococcus aureus resistance to methicillin
HA- or CA-MRSA
<table>
<thead>
<tr>
<th>Country</th>
<th>Study year</th>
<th>HA-MRSA</th>
<th>CA-MRSA</th>
<th>CA-MRSA spread within hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bahrain (1)</td>
<td>Jan-July 2005</td>
<td>86.7%</td>
<td>13.3%</td>
<td>No data</td>
</tr>
<tr>
<td>KSA (2)</td>
<td>2001</td>
<td>80%</td>
<td>20%</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>2008</td>
<td>41%</td>
<td>59%</td>
<td>No data</td>
</tr>
<tr>
<td>Kuwait (3)</td>
<td>2001</td>
<td>92.3%</td>
<td>1.7%</td>
<td>2012- Maternity Hospital, Kuwait (4)</td>
</tr>
<tr>
<td></td>
<td>2005</td>
<td>83%</td>
<td>17%</td>
<td>2012- Maternity Hospital, Kuwait (4)</td>
</tr>
<tr>
<td>Oman (5)</td>
<td>March-Dec 2011</td>
<td>8.8%</td>
<td>91.2%</td>
<td>No data</td>
</tr>
<tr>
<td>Qatar (6)</td>
<td>2009/2010</td>
<td>5%</td>
<td>95%</td>
<td>No data</td>
</tr>
<tr>
<td>UAE (7)</td>
<td>2003</td>
<td>62%</td>
<td>38%</td>
<td>No data</td>
</tr>
<tr>
<td></td>
<td>2008</td>
<td>26.9%</td>
<td>73.1%</td>
<td>68% of CA-MRSA type was HAI</td>
</tr>
</tbody>
</table>

Clostridium difficile in the GCC countries – not reportable
CDI in Kuwait

- 2003-2005: 697 diarrhea pts tested,
- 10.5% CDI
- Of which 76.7% was hospital acquired (8% CDI among hospitalized pts with diarrhea)
- Risk factors: age >71 years, nasogastric feeding and immunosuppressive therapy
- No ribotype O27

Jamal et al, Anaerob 2010;16:560
CDI in Qatar

Between 2011-12

• 1532 suspected CDI tested: 7.9% positive
• Of which ribotype O27 was 1.3%
• Age ≥65 years and use of proton pump inhibitors were associated with CDI

Al Thani et al BMC Infectious Diseases 2014;14:502
CDI in the KSA

- Study between 2007-08 in Saudi ARAMCO MSO
- 913 suspected CDI tested: 4.6% positive, 61.9% of positives were HAI
- Prevalence 2.4 (2007) and 1.7 (2008) per 10000 patient days

  Al Tawfiq and Abed. Travel Med Infect Dis 2010;8:373

- Emergence of a highly resistant *Clostridium difficile* strain (NAP/BI/027) in a tertiary care center in Saudi Arabia

EUCLID study

- 20 European countries with a mean of 7.0 case/10000 patient days reported
- 23% of diagnosis were missed when testing was indicated by clinical suspicion, only

*Lancet ID 2014;14:1208*

**ARE WE TESTING PROPERLY HERE?**
Gram negative non-fermenters

- Not included in the WHO Global report on AMR 2014

- Study reports
  - mainly on *Acinetobacter baumannii*
  - few on *Pseudomonas aeruginosa*
## Carbapenem resistance in non-fermenters

<table>
<thead>
<tr>
<th>Country</th>
<th>Study year</th>
<th>Acinetobacter baumannii</th>
<th>Pseudomonas aeruginosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bahrain (1)</td>
<td>2007-08</td>
<td>58%</td>
<td>No data</td>
</tr>
<tr>
<td>KSA (2,3)</td>
<td>1990-2013</td>
<td>3-90%</td>
<td>5-34%</td>
</tr>
<tr>
<td>Kuwait (4,5)</td>
<td>1996-97</td>
<td>-</td>
<td>5-10%</td>
</tr>
<tr>
<td></td>
<td>2007</td>
<td>39-50%</td>
<td>-</td>
</tr>
<tr>
<td>Oman (6)</td>
<td>2007</td>
<td>0%</td>
<td>15%</td>
</tr>
<tr>
<td>Qatar (7)</td>
<td>2007-08</td>
<td>50%</td>
<td>33%</td>
</tr>
<tr>
<td>UAE (8,9)</td>
<td>2008</td>
<td>67.5%</td>
<td>19.6%</td>
</tr>
<tr>
<td></td>
<td>2012</td>
<td>52-60%</td>
<td>25.6%</td>
</tr>
<tr>
<td>Europe (10)</td>
<td>2011</td>
<td>56.6-58.7%</td>
<td>26.6-33.6%</td>
</tr>
</tbody>
</table>

1. Mugnier et al. JAC 2009;63:1071  
5. Al-SweihJIPH 2011;5:102  
8. Al-Kaabi et al. EMJH 2009;17:479  
Inter hospital transmission of *Acinetobacter baumannii* in the UAE

All subtypes of the three epidemic clones carried the \(\text{blaOXA-23} \) gene

Sonnevend et al. 2013 JMM 62:582
Carbapenem resistant Acinetobacter baumannii

- Majority of the isolates are carbapenemase producers
- The carbapenemase genes (OXA-23, OXA-58, OXA-72, GES-14) are plasmid located, and aminoglycosid resistance genes are often co-located on the same plasmid
- The isolates with epidemic potential are usually multidrug resistant

Mugnier et al., 2009;63:1071
Bonnin AAC 2013;57:183
Sonnevend et al. 2013 JMM 62:582,
Zowawi et al JCM, 2015
Resistance in *Escherichia coli*

- **Fluoroquinolone**
- **3rd generation cephalosporin**

<table>
<thead>
<tr>
<th>Country</th>
<th>Fluoroquinolone</th>
<th>3rd generation cephalosporin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bahrain</td>
<td>60</td>
<td>50</td>
</tr>
<tr>
<td>Kuwait</td>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td>Oman</td>
<td>40</td>
<td>30</td>
</tr>
<tr>
<td>Qatar</td>
<td>30</td>
<td>20</td>
</tr>
<tr>
<td>KSA</td>
<td>30</td>
<td>20</td>
</tr>
<tr>
<td>UAE</td>
<td>30</td>
<td>20</td>
</tr>
</tbody>
</table>
Resistance in *Klebsiella pneumoniae*

![Bar chart showing resistance levels of 3rd generation cephalosporin and carbapenem in different countries.](chart.png)

- Bahrain: High resistance to 3rd generation cephalosporin and moderate resistance to carbapenem.
- Kuwait: Moderate resistance to 3rd generation cephalosporin and low resistance to carbapenem.
- Oman: Low resistance to both 3rd generation cephalosporin and carbapenem.
- Qatar: Very low resistance to both 3rd generation cephalosporin and carbapenem.
- KSA: Low resistance to both 3rd generation cephalosporin and carbapenem.
- UAE: Low resistance to both 3rd generation cephalosporin and carbapenem.
# Carbapenem resistance in Enterobacteriaceae

<table>
<thead>
<tr>
<th>Country</th>
<th>Study year</th>
<th>Prevalence of CRE</th>
<th>Carbapenemase produced</th>
<th>Nosocomial transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bahrain (1)</td>
<td>2011-13</td>
<td>No data</td>
<td>none</td>
<td>No data</td>
</tr>
<tr>
<td>KSA (1,2,3)</td>
<td>2009-13</td>
<td>&lt;9%</td>
<td>NDM-1, OXA-48-type, VIM-4</td>
<td>Yes</td>
</tr>
<tr>
<td>Kuwait (4)</td>
<td>2009-11</td>
<td>No data</td>
<td>NDM-1, VIM-4</td>
<td>No</td>
</tr>
<tr>
<td>Oman (5,6)</td>
<td>2010-11</td>
<td>No data</td>
<td>NDM-1, OXA-48 and OXA-181</td>
<td>No data</td>
</tr>
<tr>
<td>Qatar (1)</td>
<td>2011-13</td>
<td>No data</td>
<td>NDM-1, OXA-48-type</td>
<td>No data</td>
</tr>
<tr>
<td>UAE (7,8,9)</td>
<td>2009-12</td>
<td>0-7%</td>
<td>NDM-1, OXA-48-type, VIM-4</td>
<td>Yes</td>
</tr>
<tr>
<td>Europe (10)</td>
<td>2011</td>
<td>0-9%</td>
<td>IMP, NDM, VIM, OXA-48-type, KPC</td>
<td>Yes</td>
</tr>
</tbody>
</table>

1. Zowawi et al. AAC 2014; 58:3085  
CRE in Abu Dhabi Emirate in the past 5 years

*Data only until early October*

\[ E. \text{coli, average } \% \text{ non-susceptible (R+I) to Carbapenems (IMP+MEM), 2010-2014 trend, Abu Dhabi Emirate} \]

\[ K. \text{pneumoniae, average } \% \text{ non-susceptible (R+I) to Carbapenems (IMP+MEM), 2010-2014 trend, Abu Dhabi Emirate} \]

J. Thomsen – AD ARS – in preparation
The UAE on the scale of nation-wide expansion of healthcare-associated carbapenem-non-susceptible *Enterobacteriaceae*

<table>
<thead>
<tr>
<th>Epidemiological scale</th>
<th>Description</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cases reported</td>
<td>No cases reported</td>
<td>0</td>
</tr>
<tr>
<td>Sporadic occurrence</td>
<td>Single cases, epidemiologically unrelated</td>
<td>1</td>
</tr>
<tr>
<td>Single hospital outbreak</td>
<td>Outbreak defined as two or more epidemiologically related cases in a hospital</td>
<td>2a</td>
</tr>
<tr>
<td>Sporadic hospital outbreaks</td>
<td>Unrelated hospital outbreaks with independent, i.e. epidemiologically different strains, no autochthonous inter-institutional transmission</td>
<td>2b</td>
</tr>
<tr>
<td>Regional spread</td>
<td>More than one epidemiologically related outbreak confined to hospitals that are part of a regional referral network, suggestive of regional autochthonous inter-institutional transmission</td>
<td>3</td>
</tr>
<tr>
<td>Inter-regional spread</td>
<td>Multiple epidemiologically related outbreaks occurring in different health districts, suggesting inter-regional autochthonous inter-institutional transmission</td>
<td>4</td>
</tr>
<tr>
<td>Endemic situation</td>
<td>Most hospitals in a country are repeatedly seeing cases admitted from different sources</td>
<td>5</td>
</tr>
</tbody>
</table>
Actions to be taken to tackle AMR - in the USA

Executive order to address the problem, with a $1.1 billion price tag

Two especially important response to practitioners

- A comprehensive surveillance system that is combined with whole-genome sequencing and global connections.

- Requirement for an antibiotic stewardship program
What is needed in the GCC countries?

Effective antibiotic stewardship programs

AND

In order to estimate the true burden and the effect of the interventions:

• Robust national AMR surveillance
• Yearly data reporting
• Collaboration between member states
• ...and all this should be supported by national reference laboratories to perform prevalence surveys, test for molecular traits, confirm clinical laboratories’ results etc.
Thank you!