Surveillance data in Community Acquired Respiratory tract Infections

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OBJECTIVES

• Overview of *S. pneumoniae* importance as surveillance pathogen

• Surveillance data-SOAR

• Factors to consider in optimal management *using-Application of local susceptibility data*
“Arguably the greatest risk... to human health comes in the form of antibiotic resistant bacteria. We live in a bacterial world where we will never be able to stay ahead of the mutation curve.

A test of our resilience is how far behind the curve we allow ourselves to fall.”

Global Risk 2013, 8th Ed; An Initiative of the Risk Response Network, World Economic Forum 2013
WHO Global Report on surveillance (2014) and recommended priority pathogens

- Escherichia coli
- Acinetobacter baumannii
- Klebsiella pneumoniae
- Staphylococcus aureus
- Streptococcus pneumoniae
- Salmonella spp
- Shigella spp
- Neisseira gonorrhoeae

<table>
<thead>
<tr>
<th>Name of bacterium/resistance</th>
<th>Examples of typical diseases</th>
<th>No. out of 194 Member States providing data</th>
<th>No. of WHO regions with national reports of 50% resistance or more</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Escherichia coli</strong>/</td>
<td>Urinary tract infections, blood stream infections</td>
<td>86</td>
<td>5/6</td>
</tr>
<tr>
<td>- vs. 3rd gen. cephalosporins</td>
<td></td>
<td>92</td>
<td>5/6</td>
</tr>
<tr>
<td>- vs. fluoroquinolones</td>
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<td></td>
</tr>
<tr>
<td><strong>Klebsiella pneumoniae</strong>/</td>
<td>Pneumonia, blood stream infections, urinary tract infections</td>
<td>87</td>
<td>6/6</td>
</tr>
<tr>
<td>- vs. 3rd gen. cephalosporins</td>
<td></td>
<td>71</td>
<td>2/6</td>
</tr>
<tr>
<td>- vs. 3rd carbapenems</td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Staphylococcus aureus</strong>/</td>
<td>Wound infections, blood stream infections</td>
<td>85</td>
<td>5/6</td>
</tr>
<tr>
<td>- vs. methicillin “MRSA”</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Streptococcus pneumoniae</strong>/</td>
<td>Pneumonia, meningitis, otitis</td>
<td>67</td>
<td>6/6</td>
</tr>
<tr>
<td>- non-susceptible or resistant to penicillin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Nontyphoidal Salmonella</strong>/</td>
<td>Foodborne diarrhoea, blood stream infections</td>
<td>68</td>
<td>3/6</td>
</tr>
<tr>
<td>- vs. fluoroquinolones</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sheila species</strong>/</td>
<td>Diarrhoea (“bacillary dysenteria”)</td>
<td>35</td>
<td>2/6</td>
</tr>
<tr>
<td>- vs. fluoroquinolones</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Neisseria gonorrhoea</strong>/</td>
<td>Gonorrhoea</td>
<td>42</td>
<td>3/6</td>
</tr>
<tr>
<td>- vs. 3rd gen. cephalosporins</td>
<td></td>
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</tr>
</tbody>
</table>

• Represents the conc. of an antimicrobial that separates populations of micro-organisms into S/ I/ R\textsuperscript{1}

• Used to define S/ I/ R\textsuperscript{4}

USA

• CLSI (Formerly NCCLS) Clinical and Laboratory Standards Institute

Europe: 6 active European National Breakpoint Committees: Britain, France, Netherlands, Sweden & Norway

EUCAST (European Committee on Antimicrobial Susceptibility Testing)

Mechanisms of Resistance Among S pneumoniae.

- Resistance to beta-lactams - *stepwise alteration in PBPs*, ↓ binding affinity

- PBPs in *S pneumoniae*—1a, 1b, 2b, 2x, 2z, 3

- 1a, 2b, and 2x alteration most often associated to penicillin resistance  [MICs] range 0.25 mg/L - 8 mg/L vs. 0.06 mg/L for susceptible strains)

- MICs - S - 0.06-0.12 mg/ml, I - 0.12- 1mg/ml , R >2 mg/ml
Global surveillance programmes

Some examples

- **SENTRY**:
  - Antimicrobial Surveillance Program Asia-Pacific region and South Africa

- **MYSTIC**:
  - Meropenem Yearly Susceptibility Test Information Collection

- **ANSORP**:
  - Asian Network for Surveillance of Resistant Pathogens

GSK Surveillance Programs

- **Alexander Project: 1992-2002**
  - The first multicentre, international longitudinal study CA-RTI pathogens
  - More than 90 journal publications and abstracts presented based on these data

- **SOAR- Survey Of Antimicrobial Resistance: 2002 onwards**
  - Generates local susceptibility data for key CA-RTI pathogens such as *S.pneumoniae* and *H.influenzae*

References:
Survey of Antibiotic Resistance (SOAR)

- *S. pneumoniae* and *H. influenzae* -
- at least 100 *Streptococcus pneumoniae* + 100 *Haemophilus influenzae*

- Multinational and longitudinal – Africa, Middle East, Latin America, Asia-Pacific (since 2002)

- Internationally recognised standardised methodology (CLSI/EUCAST/PK/PD-breakpoints)
- Not a clinical study- *in vitro* antibiotic surveillance study
Specimen collection & patient characteristics

- Sputum -36.8%
- Middle ear effusion- 18.2%
- Blood-26.8%
- Bronchoalveolar lavage- 10.8%
- Pleural aspirate- 7.4%

Kenyan sites:
- Aga Khan University hospital
- Kenyatta National hospital.
- Outpatients
- Paediatric isolates 30%
Methodology E-test

- Cost is expensive
- Gives quantitative value i.e. ug/ml=the MIC value
- This enables the MIC50, MIC90, MIC mode to be calculated for resistance profile
- Data obtained would be useful to be applied in the PK/PD concept

→ Numerical figure e.g. 2 mcg/mL
→ ‘the lower the MIC the more sensitive that specific bacteria is to that specific antibiotic’

SOAR 2009 – *S. pneumoniae* Susceptibility

<table>
<thead>
<tr>
<th></th>
<th>Africa&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Middle East&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Asia Pacific&lt;sup&gt;2,3,4&lt;/sup&gt;</th>
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</thead>
<tbody>
<tr>
<td>%</td>
<td>Cote d’Ivo. (n=100)</td>
<td>Kenya (n=123)</td>
<td>Seneg. (n=89)</td>
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<tr>
<td>Penicillin</td>
<td>89.0</td>
<td>33.3</td>
<td>66.0</td>
</tr>
<tr>
<td></td>
<td>82.0</td>
<td>54.9</td>
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<tr>
<td></td>
<td>63.3</td>
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<tr>
<td></td>
<td>20.0</td>
<td>11.5*</td>
<td>60.0</td>
</tr>
<tr>
<td></td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Amox/Clav</td>
<td>100</td>
<td>100</td>
<td>97.8</td>
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<tr>
<td></td>
<td>100</td>
<td>100</td>
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<tr>
<td></td>
<td>99</td>
<td>96.7</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>92.0</td>
<td>98.7*</td>
<td>98.5</td>
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<td></td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>Erythrom</td>
<td>89.0</td>
<td>85.4</td>
<td>92.2</td>
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<td>87.6</td>
<td>48.1</td>
<td>68.6</td>
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<td>76.2</td>
<td>70.0</td>
<td>70.3</td>
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<td>28.0</td>
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<td>44.9</td>
<td>91.2</td>
<td>28.6</td>
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<td>93.1</td>
<td>89.3</td>
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<td></td>
<td>99</td>
<td>97.5</td>
<td>-</td>
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</table>

2. Van et al. Presented at the 13<sup>th</sup> International Congress on Infectious Diseases (2008), Kuala Lumpur, Malaysia.
### Kenya Susceptibility trends for S. Pneumoniae

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>2003 N=92</th>
<th>2007/2008 n=89</th>
<th>2013/2014 * (n= 84 )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Penicillin</strong></td>
<td>52.5</td>
<td>33.3</td>
<td>19%</td>
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<tr>
<td>Cefuroxime</td>
<td>95.0</td>
<td>87.8</td>
<td>66.7%</td>
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<tr>
<td>Erythromycin</td>
<td>NT</td>
<td>85.4</td>
<td>64.1%</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>90.1</td>
<td>NT</td>
<td>65.2%</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>NT</td>
<td>NT</td>
<td>96.4%</td>
</tr>
</tbody>
</table>

Question time

What threshold of % R indicates “This antibiotic should be used with caution”?

a) 50%
b) 15-20%
c) 90%
d) 5%
e) Have no idea
SOLUTIONS?
Time dependent killing -

Optimal $T>MIC$ is 35-40%:
- Increase dose frequency
- High dose
- Improved pharmacodynamic profile
- Increased duration of infusion

Minimum Inhibitory Concentration (MIC) vs. Time (hours):

$T above MIC (T>MIC)$
Staying ahead of the game!

• Penicillin resistance verses amoxicillin guideline in CAP
• Benzyl Penicillin in current guidelines for severe pneumonia- dosages optimum/use of cephalosporins?
• Macrolide role in immunomodulation and/or coverage of atypical organisms in immunosuppresion
• Surveillance –facility based, National systems, GARPEC
• Multidisciplinary approach in management of critically ill children
Results from the Survey of Antibiotic Resistance (SOAR) 2011–14 in the Democratic Republic of Congo, Ivory Coast, Republic of Senegal and Kenya

A. Kacou-Ndouba¹, G. Revathi², P. Mwathi³, A. Seck⁴, A. Diop⁵, M. J. Kebdi-Bajani⁶, W. Mwiti⁷, M. J. Anguibi-Pokou⁸, I. Morrissey⁹ and D. Torumkuney¹⁰*

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2000 B.C. – Here, eat this root

1000 A.D. – That root is heathen. Here, say this prayer.

1850 A.D. – That prayer is superstition. Here, drink this potion.

1920 A.D. – That potion is snake oil. Here, swallow this pill.

1945 A.D. – That pill is ineffective. Here, take this penicillin.

1955 A.D. – Oops….bugs mutated. Here, take this tetracycline.

1960-1999 – 39 more "oops"...Here, take this more powerful antibiotic.

Presently- Here take this root??????

Anonymous
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