BSAC antimicrobial susceptibility testing - from Stokes to European harmonization to world?

Derek Brown

23 March 2011
BSAC antimicrobial susceptibility testing pre-Working Party

- BSAC meetings from the first on 29 September 1972 included methodology for susceptibility testing
- Laboratory Methods in Antimicrobial Chemotherapy 1978
  - MIC methods, no breakpoints
  - Disc diffusion, different methods described and Stokes approach recommended
Stokes method

- Coping with variation in reagents
  - Variable quality discs
  - Inconsistent media
- A reference for susceptibility
  - Compare with “normal” susceptible isolate
BSAC antimicrobial susceptibility testing working party

- Antibiotic sensitivity testing working party 1985

  - MIC breakpoints
  - Stokes disc diffusion method
Stokes method - Time for a change?

- Improved quality of discs and media
- Limitations of control
- Standard criteria for interpretation do not fit new agents
- No reference to MIC breakpoints
BSAC antimicrobial susceptibility testing

• BSAC Working Party Report 2001
  – MIC breakpoints
  – Standardized disc diffusion method with zone diameter breakpoints correlated with MIC breakpoints
# Breakpoint committees 2001

<table>
<thead>
<tr>
<th>Committee</th>
<th>Country</th>
<th>Disc diffusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSAC</td>
<td>United Kingdom</td>
<td>Yes</td>
</tr>
<tr>
<td>CA-SFM</td>
<td>France</td>
<td>Yes</td>
</tr>
<tr>
<td>CRG</td>
<td>The Netherlands</td>
<td>No</td>
</tr>
<tr>
<td>DIN</td>
<td>Germany</td>
<td>Yes</td>
</tr>
<tr>
<td>NWGA</td>
<td>Norway</td>
<td>No</td>
</tr>
<tr>
<td>SRGA</td>
<td>Sweden</td>
<td>Yes</td>
</tr>
<tr>
<td>NCCLS (CLSI)</td>
<td>USA</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Implications of differences between breakpoints in different countries

- Different guidance on appropriate therapy
- Resistance rates may be different in different surveillance studies despite no difference in MIC distribution
National Breakpoint Committees
France, Germany, Netherlands
Norway, Sweden, UK

EUCAST
European Committee on Antimicrobial Susceptibility Testing
European Society of Clinical Microbiology and Infectious Diseases

EUCAST Steering Committee
Chairman, Scientific Secretary, Clinical Data Co-ordinator
BSAC, CA-SFM, CRG, DIN, NWGA, SRGA
2 representatives from the General Committee

EUCAST General Committee
All European Countries, ISC, FESCI

Subcommittees
Antifungals, Anaerobes, Expert Rules

Consultation with expert groups and industry
The European Committee on Antimicrobial Susceptibility Testing - EUCAST

EUCAST is a standing committee jointly organized by ESCMID, ECDC, and European national breakpoint committees. EUCAST deals with breakpoints and technical aspects of phenotypic in vitro antimicrobial susceptibility testing and functions as the breakpoint committee of EMEA and ECDC.

EUCAST does not deal with antibiotic policies, surveillance or containment of resistance or infection control.

The Steering Committee is the decision making body. It is supported by a General Committee with representatives from European countries, EESC and ISO. The Steering Committee also consults experts within the fields of Infectious Diseases and Microbiology, pharmaceutical companies and susceptibility testing device manufacturers on EUCAST proposals.

EUCAST has subcommittees on antifungal susceptibility testing, expert rules for antimicrobial susceptibility testing, and antimicrobial susceptibility testing of antibiotics.

Most antimicrobial MIC breakpoints in Europe have been harmonised by EUCAST. However, breakpoints for new agents are set as part of the licensing process for new agents through EMEA. EUCAST breakpoints will be available in devices for automated susceptibility testing during 2009 and 2010. A disk diffusion test calibrated to EUCAST MIC breakpoints was launched at the end of 2009.
Setting breakpoints in EUCAST

• Harmonization of European breakpoints
• Setting breakpoints for new agents (with EMA)
• Review of established breakpoints
EUCAST procedure for harmonizing breakpoints

- Collect and evaluate data in Steering Committee
- Consult on proposed breakpoints
- Decision and publication with rationale

Breakpoints for all more widely used agents have been reviewed and harmonized breakpoints agreed
Setting breakpoints for new agents

- Pharmaceutical company submits new agent to European Medicines Agency (EMA) for marketing approval
- Relevant data are shared with the EUCAST Steering Committee (confidential process)

- EMA approves (or not) clinical indications, dosages, administration forms and target organisms
- In consultation with national breakpoint committees EUCAST sets breakpoints for organisms approved by EMA

- Breakpoints set for daptomycin, tigecycline, doripenem and retapamulin (epidemiological cut-off value)
- Currently three agents in process
- Ceftobiprole, garenoxacin, iclaprim, oritavancin withdrawn
Review of breakpoints by EUCAST

- New resistance mechanisms
- New agent in class
- New clinical data
- Extended indications
- Change in dosing or administration
- Change in target organisms

Breakpoints reviewed

Glycopeptides, carbapenems, colistin, cephalosporins, monobactams
Adoption of EUCAST breakpoints in Europe, March 2011
Breakpoints 2011

<table>
<thead>
<tr>
<th>Committee</th>
<th>Country</th>
<th>Disk diffusion test</th>
</tr>
</thead>
<tbody>
<tr>
<td>EUCAST</td>
<td>Europe</td>
<td>Yes</td>
</tr>
<tr>
<td>CLSI</td>
<td>USA</td>
<td>Yes</td>
</tr>
</tbody>
</table>

- EUCAST and CLSI differ in funding, organisation, relationship to regulatory authorities
- Documents and breakpoints are free from EUCAST, for sale from CLSI
## EUCAST and CLSI breakpoints

<table>
<thead>
<tr>
<th>Microorganisms</th>
<th>Number of Breakpoints</th>
<th>S and R</th>
<th>S</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacteriaceae</td>
<td>33</td>
<td>3</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td><em>Pseudomonas</em></td>
<td>16</td>
<td>1</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td><em>Acinetobacter</em></td>
<td>10</td>
<td>1</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td><em>Staphylococcus</em></td>
<td>27</td>
<td>4</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td><em>Enterococcus</em></td>
<td>6</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Streptococci</td>
<td>13</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
<td>24</td>
<td>3</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td><em>H. influenzae</em></td>
<td>25</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>
BSAC antimicrobial susceptibility testing

- Stokes
- European harmonization – EUCAST
- The world....?