Real-time international surveillance of antimicrobial resistance by the Enter-net surveillance network

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The International network for the surveillance of Enteric Infections - Salmonella and VTEC O157

Funded by the European Commission, DG Health and Consumer Protection (SANCO)
(previously by DG 12 under Framework 4)
Objectives

For human isolates:

- Maintain timely international salmonella and VTEC O157 databases
- Rapidly recognise, investigate and report international outbreaks
- Monitor salmonella antimicrobial resistance
Methods

- Standardisation of accompanying data
- Rapid data collection and information exchange
- Harmonisation of National Reference Laboratory (NRL) methods and results
Microbiological achievements

- Harmonisation of salmonella phage-typing,
- Countries routinely reporting phage-type data increased from five to nine,
- Study to harmonise results of antimicrobial susceptibility testing,
Epidemiological achievements

• Creation of the international *E.coli* database.

• Application of new software to improve outbreak recognition,

• Development and maintenance of the international salmonella database,

• Expansion of the database to incorporate antimicrobial resistance testing results,
Salmonella database specification.

- Country
- Serotype
- Specimen
- Sex
- Date of report
- Region
- Phage type
- **Antibiogram**
- Age
- Travel associated
- Food Implicated
Antimicrobials surveilled

- Aminoglycosides
  - Streptomycin, gentamicin, kanamycin
- β-lactams
  - Ampicillin, cefotaxime
- Tetrahydrofolate inhibitors
  - Sulphonamides, trimethoprim
- Quinolones
  - Nalidixic acid, ciprofloxacin
- Other antimicrobials
  - Chloramphenicol, tetracyclines
Antimicrobial resistance standardisation

The questions?

Which standards to use?

NCCLS
BSAC
EUCAST

Which method?

MIC
Disk diffusion
Breakpoint
An alternative view

- Breakpoint
- Disk diffusion
- MIC
- Which method?

- EUCAST
- BSAC
- NCCLS

Which standards to use?

The questions?
Methods

Panel of 48 strains sent to 18 NRLs

30 different sero/phage-types
Ranging from fully sensitive to multi-resistant
Tested using own techniques

Results

Qualitative results (R, I, S)
Method used (DD, BP, MIC)
Transmitted electronically to Enter-net hub
Concordance of resistance results

Calculation of results

Resistence to antimicrobial “X”

\[
\begin{array}{l}
\text{N\textdegree\ of strains resistant} & 20 \\
\text{N\textdegree\ of labs testing} & 15/18 \\
\text{N\textdegree\ of tests for resistance} & 300 \\
\text{Results showing resistance} & \\
\quad \text{- actual} & 260 \\
\end{array}
\]

Percentage “concordance” 87% (260/300)
Results – I

Data returned

<table>
<thead>
<tr>
<th>Laboratories</th>
<th>Antimicrobials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eight laboratories</td>
<td>11 antimicrobials</td>
</tr>
<tr>
<td>Five laboratories</td>
<td>10 antimicrobials</td>
</tr>
<tr>
<td>Three laboratories</td>
<td>9 antimicrobials</td>
</tr>
<tr>
<td>One laboratory</td>
<td>8 antimicrobials</td>
</tr>
<tr>
<td>One laboratory</td>
<td>5 antimicrobials</td>
</tr>
</tbody>
</table>

Total number of tests 8,688 (9,504, 91.4%)
## Results – II (concordance)

<table>
<thead>
<tr>
<th>Resistant strains</th>
<th>%</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptomycin</td>
<td>99.8</td>
<td>Gentamicin</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>99.6</td>
<td>Ampicillin</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>100</td>
<td>Sulphonamides</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>99.1</td>
<td>Chloramphenicol</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>99.4</td>
<td>Nalidixic acid</td>
</tr>
<tr>
<td>Ciprofloxacin (BP 1.0)</td>
<td>100</td>
<td>Ciprofloxacin (BP 0.125)</td>
</tr>
</tbody>
</table>
For routine surveillance of resistant and sensitive strains

- mean difference for concordance of resistant strains
  - 99.7% (range 99.1-100)

- mean difference for non-concordance of sensitive strains
  - 0.7% (range 0.0-2.0)

∴ we can be confident that the results are comparable
Study conclusions – II

For routine surveillance of resistant and sensitive strains

• International data of harmonised antimicrobial resistance patterns are being exchanged

• Incorporated into the international surveillance database that had already been created.

• Integrity is maintained by an annual QA scheme
Antibiotic-resistant Salmonella infections are a problem of increasing significance in the United States.

In the last 3 years, public health surveillance activities at the Centers for Disease Control and Prevention and in the U.S. have detected the emergence of a multidrug-resistant strain of Salmonella serotype Newport, the third most common Salmonella serotype in the United States. This multidrug-resistant strain is commonly resistant to ampicillin, amoxicillin/clavulanic acid, cephalothin, cefoxitin, ceftiotur, ceftriaxone, chloramphenicol, tetracycline, streptomycin, and sulfamethoxazole. Several isolates are also resistant to kanamycin. Clusters of human infection have recently been recognized in the United States and dairy cows have been identified as a major reservoir for this multidrug-resistant pathogen.
**Results**

<table>
<thead>
<tr>
<th></th>
<th>2000</th>
<th>2001*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nº of strains of S. Newport</td>
<td>659</td>
<td>748</td>
</tr>
<tr>
<td>Nº including antibiogram</td>
<td>242</td>
<td>214</td>
</tr>
<tr>
<td>Nº sensitive</td>
<td>197 (81.4%)</td>
<td>177 (82.7%)</td>
</tr>
<tr>
<td>Nº resistant to &lt;5 antimicrobials</td>
<td>30 (12.4%)</td>
<td>24 (11.2%)</td>
</tr>
<tr>
<td>Nº resistant to ≥ 5 antimicrobials</td>
<td>15 (6.2%)</td>
<td>13 (6.1%)</td>
</tr>
</tbody>
</table>

* Provisional
### Results – 2000

<table>
<thead>
<tr>
<th>R-type</th>
<th>Nº</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACSuTTm (K, Nx)</td>
<td>4</td>
<td>1.7</td>
</tr>
<tr>
<td>ACSSuT (Tm, K, Tm/G/K/Nx)</td>
<td>3</td>
<td>1.2</td>
</tr>
<tr>
<td>ASSuTK</td>
<td>3</td>
<td>1.2</td>
</tr>
<tr>
<td>ASSuTTm</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>SSuTTmG</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>SuTmKNxCp</td>
<td>1</td>
<td>0.4</td>
</tr>
</tbody>
</table>
## Results – 2001

<table>
<thead>
<tr>
<th>R-type</th>
<th>Nº</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACSSuTTm (K, 3 x G/K/Nx)</td>
<td>5</td>
<td>2.4</td>
</tr>
<tr>
<td>ACSSuTTmKNxCp</td>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>ACSuTTm (Cp/G)</td>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>ACSSuT</td>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>ACSuTTmKNx</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>ASSuTTmG</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>SuTTmGK</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>CSSuTTmK</td>
<td>1</td>
<td>0.5</td>
</tr>
</tbody>
</table>
Conclusions

- Isolates of multiple resistant S. Newport have been recognised by the Enter-net surveillance network,

- The incidence is very low at the moment,

- Vigilance is required to monitor any emergence of this virulent strain,

- A mechanism exists to rapidly identify any international distribution of this strain.
Acknowledgements

- The 18 NRLs that performed this study
- All Enter-net participants for supporting the network
- The European Commission (DG SANCO) for funding the network.
- John Threlfall, for his invaluable analysis of the results
References

• Fisher IST (on behalf of the Enter-net participants) The Enter-net international surveillance network – how it works. Eurosurv 1999 4: 52-55.

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