Antimicrobial resistance in equine practice: an evidence-based approach

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SVA FROM ABOVE
Swedish Veterinary Antimicrobial Resistance Monitoring

SVARM since 2000

www.sva.se
Different multiresistant bugs!
Attack of the acronyms!

AmpC  MRSA  VRE
ESBL  MRSP  NDM-1
KPC  PNP  VIM
XDR
Different multiresistant bugs!

- AmpC
- ESBL
- MRSP
- MRSA
- KPC
- NDM-1
- VRE
- VIM
- XDR
- PNP
ESBL - Extended-spectrum betalactamases

- Resistance to 3rd and 4th gen cephalosporins like ceftiofur and cefquinome
- >200 different betalactamase enzymes
- Gram-negative bacteria commonly belonging to Enterobacteriaceae like E. coli, klebsiella, salmonella
- AmpC
  - Chromosomal or plasmid (pAmpC)
ESBL+pAmpC

• Mobile genetic elements

• Genes or bacteria spreading rapidly around the world

• In humans: simple urinary tract infections to severe sepsis

• Often treated with carbapenems
ESBL+multidrug resistant *E. coli* 2012

Prevalence in UK and risk-factors (Maddox et al.)
- 65 equine practices selected; 475 premises, 627 horses
- faecal swabs & questionnaire

- 6.3% ESBL-producing
- Hospitalization – gentamicin resistance and ESBL
- Antimicrobial treatment <10 days –TMS resistance
- Penicillin not a risk factor
- Veterinary treatment – GI, respiratory and wounds
- Housed on a racing yard
- Stabled on the same yard as an ESBL-positive horse
ESBL+multidrug resistant *E. coli*

Risk-factors in UK (Ahmed *et al.* 2012)
- 264 faecal samples from 138 horses,
- hospitalized and non-hospitalized (livery stable & riding school) during 6 months

- Hospitalization and antimicrobial treatment

Faecal shedding after broad-spectrum antimicrobial prophylaxis (Damborg *et al.* 2012)
- 10 horses enrolled arriving to hospital
- Sampled before, during and after abx treatment

-CTX-producing coliforms zero before and increased ESBL in equine clinic & horse riding centre (Dolejska M *et al.* 2011)

- 32% and 9% horses positive + environment
During antimicrobial treatment...


... resistant bacteria are favoured

... not only the target organism is affected
Hospitalization - a risk factor for resistance

- Many susceptible individuals
- Many indirect or even direct "contacts"
- Crowding
- Stress
- High antimicrobial pressure
- Deficiencies in infection control
ESBL-producing *Enterobacteriaceae*

**Clinical isolates in NL (Dierikx *et al.*)**
- Oct 2007 – Aug 2009, 12 isolates mainly *E. coli*
  - Enzyme families: CTX
  - Wounds & uterus

**Clinical isolates in SE (SVARM 2011)**
- 9 *E. coli* and 5 *Enterobacter* spp.
  - Wounds & female genital tract
  - Enzyme families: CTX
<table>
<thead>
<tr>
<th></th>
<th><em>K. pneumoniae</em></th>
<th><em>E. coli</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>&gt;64</td>
<td>&gt;64</td>
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<tr>
<td>Cefotaxim</td>
<td>1</td>
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<tr>
<td>Ciprofloxacin</td>
<td>0,06 = <em>S</em></td>
<td>0,5</td>
</tr>
<tr>
<td>Florfenikol</td>
<td>8 = <em>S</em></td>
<td>8</td>
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<tr>
<td>Gentamicin</td>
<td>&gt;32</td>
<td>16</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>&gt;16</td>
<td>4 = <em>S</em></td>
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<tr>
<td>Tetracyklin</td>
<td>&gt;64</td>
<td>&gt;64</td>
</tr>
<tr>
<td>Trimetoprim</td>
<td>&gt;32</td>
<td>&gt;32</td>
</tr>
<tr>
<td>Sulfa</td>
<td>&gt;1024</td>
<td>&gt;1024</td>
</tr>
</tbody>
</table>
Carbapenemase producers

*Klebsiella pneumoniae* carbapenemase (KPC)
- Endemic in southern Europe

New Delhi Metallo-beta-lactamase-1 (NDM-1)
- *E. coli* or *Klebsiella pneumoniae*
- India

Susceptible to colistin, variably to fosfomycin and tigecycline
Different multiresistant bugs!

- MRSA
- MRSP
- ESBL
- AmpC
- KPC
- NDM-1
- VRE
- VIM
- PNP
- XDR
- SVA
Methicillin resistance

Staphylococci harbouring the gene *mecA*

Structural changes in the staphylococci

Antimicrobials cannot bind to staphylococci

Resistance to penicillin, aminopenicillins, amoxicillin+clavulanic acid, cephalosporins and carbapenems)

Often multiresistant!!

"Gene transfer seldom occur in staphylococci "
MRSA in horses

**Multiresistant** – susceptible to clindamycin, erythromycin, chloramphenicol and fusidic acid

- ST008
- ST398

Livestock associated MRSA or the ’pig clone’

Weese and van Duijkeren, 2010
MRSA during 2012

(Bergstom K et al.)

First nosocomial outbreak of MRSA in an equine hospital

- Summer of 2008, 6 horses with SSI
  - Infections cleared without antimicrobial treatment

Infection control intervention the outbreak

- interruption of indirect contact
- increased compliance with hygienic precautions
- outbreak strain in the environment
- no new cases occurred for over a year
MRSA during 2012

Carriage after cleared MRSA wound infections (Bergstom K et al.)

- 9 horses enrolled
- 5 anatomical sites were sampled on 7 occasions: a month a part and 6 months after

- Nostrils yielded most MRSA
- With 2 consecutive negative samples as definition of being MRSA negative, median carriage time of 143 ranging from 55 to 711 days

Sampling sites for MRSA screening (Van den Eede et al.)

- 40 horses
- Nasal chambers + skin
MRSP
(methicillin resistant *Staphylococcus pseudintermedius*)

*S. pseudintermedius* is a common pathogen in dogs

MRSP in at University hospital (*Stull J et al.*)

- 2 horses, isolated sinus and urine

- Same type as found in dogs
- Multiresistant - only susceptible to fusidic acid of the veterinary drugs

SVARM
Different multiresistant bugs!

- AmpC
- ESBL
- MRSA
- MRSP
- NDM-1
- KPC
- VRE
- Enterococci
- VIM
- PNP
- Pseudomonas
- MRCoNS
- XDR
Methicillin resistant coagulase negative staphylococci

MRCoNS in horses and staff (Aslantas Ö. et al.)

- 209 horses sampled on admittance to hospital
- 13 clinic staff was sampled
- 14 environmental samples

- 48%, 92% and 71% positive respectively
- *S. lentus*, 22% multiresistant
- Same MRSCoNS clone indicate intra-hospital spread
Laboratory report

<table>
<thead>
<tr>
<th>Antibiotic Susceptibility Pattern</th>
<th>Staphylococcus haemolyticus</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMIKACIN</td>
<td>R RESISTANT( 16.0000 )</td>
</tr>
<tr>
<td>AMPICILLIN</td>
<td>R RESISTANT( 16.0000 )</td>
</tr>
<tr>
<td>AZITHROMYCIN</td>
<td>R RESISTANT( &gt;4.0000 )</td>
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<tr>
<td>CEFAZOLIN</td>
<td>R RESISTANT( &gt;16.0000 )</td>
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<tr>
<td>CEFTAZIDIME</td>
<td>R RESISTANT( 64.0000 )</td>
</tr>
<tr>
<td>CEFTIOFUR</td>
<td>R RESISTANT( &gt;4.0000 )</td>
</tr>
<tr>
<td>CHLORAMPHENICOL</td>
<td>R RESISTANT( &gt;32.0000 )</td>
</tr>
<tr>
<td>CLARITHROMYCIN</td>
<td>R RESISTANT( 8.0000 )</td>
</tr>
<tr>
<td>DOXYCYCLINE</td>
<td>I INTERMEDIATE( 8.0000 )</td>
</tr>
<tr>
<td>ENROFLOXACIN</td>
<td>R RESISTANT( 2.0000 )</td>
</tr>
<tr>
<td>ERYTHROMYCIN</td>
<td>R RESISTANT( &gt;8.0000 )</td>
</tr>
<tr>
<td>GENTAMICIN</td>
<td>R RESISTANT( &gt;8.0000 )</td>
</tr>
<tr>
<td>IMIPENEM</td>
<td>R RESISTANT( &lt;=1.0000 )</td>
</tr>
<tr>
<td>OXACILLIN + 2% NAACL</td>
<td>R RESISTANT( &gt;4.0000 )</td>
</tr>
<tr>
<td>PENICILLIN</td>
<td>R RESISTANT( &gt;8.0000 )</td>
</tr>
<tr>
<td>RIFAMPIN</td>
<td>R RESISTANT( 4.0000 )</td>
</tr>
<tr>
<td>TETRACYCLINE</td>
<td>R RESISTANT( &gt;8.0000 )</td>
</tr>
<tr>
<td>Ticarcillin</td>
<td>R RESISTANT( &gt;64.0000 )</td>
</tr>
<tr>
<td>TIMENIN</td>
<td>R RESISTANT( &gt;64.0000 )</td>
</tr>
<tr>
<td>TRIM/SULFA</td>
<td>R RESISTANT( &gt;4.0000 )</td>
</tr>
</tbody>
</table>

Notes on antimicrobial susceptibilities:

Pure growth *Staphylococcus hemolyticus*

from catheter used for flushing the tendon sheet in horse
A case report

Enterococcal infections (Herdan CL et al.)

- 3 horses with synovitis on hospital in NZ
- Wound debridement, lavage, local, topical and systemic antimicrobial treatment
- All euthanized due to unsuccessful treatment

- Early identification of causative agent – fast diagnostics needed
- Challenge of multidrug resistant bacteria
- Initial empirical treatment fails
Take home messages

- Increased reports on *E. coli* producing extended spectrum betalactamases (ESBL) horses
- Risk factors for resistance: hospitalization and antimicrobial treatment (except penicillin)
- Infections with multiresistant bacteria can be a severe treatment challenge
- Zoontic potential
Sure glad the hole isn't at our end.
Thanks to Christina Greko!
Multidrug resistant bacteria

Some infectious diseases will not be treatable

Obstruct advanced medicine, like

– transplants
– prosthesis
– cancer treatment
– intensive care
– neonatal care
What to do?
What to do?

Sir Alexander Fleming 1928
"The more we use them the more we lose them"
What to do?

To minimize the spread of resistant bacteria:

• Prudent (or decreased) use of antimicrobials
  – When is treatment really indicated?
  – Culture and susceptibility testing
What to do?

To minimize the spread of resistant bacteria:

- Prudent (or decreased) use of antimicrobials
  - When is treatment really indicated?
  - Culture and susceptibility testing

- Improved infection control in equine hospital, clinics and stud farms
  - Hand hygiene
Despite our monumental achievements in philosophy, technology and the arts, to bacteria, humans are no more than an organic mass to be utilised for growth and reproduction.