Antibiotic Resistance:
A Veterinary Perspective

Pete Borriello
What are the issues
What actions are proposed
What about vet pathogen AMR surveillance
What influences prescribing practice
ESBLs and food: disinformation for mass consumption

New E.coli strain ‘more dangerous than MRSA’

Chickens linked to superbug rise

Alert over food superbug that kills 3,000 a year

Drug resistant bacteria in foreign chicken now kills more than MRSA

BY SUZY AUSTIN

BY Mark Reynolds

A RAPIDLY-SPREADING superbug that is ‘worse than MRSA’ has been linked to imported chickens. The strain of E.coli is resistant to antibiotics and is thought to cause urinary tract infections and blood poisoning, producing an enzyme.

Microbiology expert Pignon said: ‘It is worse than MRSA.’

MEGABUG

A SUPERBUG deadlier than MRSA and mad cow disease is killing 3,000 people a year – but most GPs have never heard of it.

But an investigation by ITV’s Tonight With Trevor McDonald programme found that 70 per cent of family doctors were totally unaware of it. Frighteningly, it is now spreading but is difficult to detect. Only one type of antibiotic can treat it reli-
New-Delhi metallo-carbapenemase hits the headlines
Hundreds killed by drug-resistant bugs in chicken

ABOUT 280 people are dying in Britain each year from antibiotic-resistance superbugs from chickens, spawned by the food Industry’s drive to maximise yields, according to a new study.

In the first study of its kind, scientists estimate that across Europe there are 1,500 deaths a year from the bugs from chickens treated with antibiotics to counter infections.
Government's top medical officer: 'Antibiotic resistance is as dangerous as terrorism'

'Ticking time-bomb': Professor Dame Sally Davies said that antibiotic resistance should be put on the Government's National Risk Register.

Top stories in News

- Haringey council blunders again in 'unlawful' investigation into blameless parents sparked by anonymous letter
- Video: Fat pets on 'deadly diets'
- At least 22 killed in Baghdad attacks
- Named: former Sunday Mirror staff arrested by phone hacking police
- Horse meat burgers a big favourite at Lond pubs
- Emma Bunton joins Ge Halliwell and takes a ti on the Tube
- Kate Moss: sheer decadence down the decades
- Before they were famo the dramatic makeover of stars

11 March 2013
Global Risks Landscape 2012

Fear of increasing antibiotic resistance in humans

It's the law of diminishing returns. The more they use them the more the risk they'll be ineffective for us.

Since I've had my two children, we've bought organic milk because we read an article that said about the antibiotics in cows.
There is a lot going on

- Commission 12pt. 5yr Action Plan
- Revision of VM Directive and AHL
- EFSA & ECDC – zoonotics
- National programmes
  - UK 5yr strategy
The Working Hypothesis

Antibiotic use → Selection for resistance

Commensal → R genes → Pathogen → Complicates treatment

Human
What are the issues

What actions are proposed

What about vet pathogen AMR surveillance

What influences prescribing practice
EU Activity: Commission Action Plan

Fundamental document: ‘One Health’ approach

Resistance is a natural phenomenon - accelerated and spread by a number of factors:

- Inappropriate use of therapeutic antimicrobials
- Use of antimicrobials for non therapeutic purposes
- Pollution of environment by antimicrobials
- Increasing global trade and travel
- Prolong life of what we have
- Reduce need for use
- Improve AMR surveillance
- Develop new/alternatives
EU Legislation – What’s changing?

- New Animal Health Law
- Veterinary Medicinal Products Directive (2001/82/EC)
- Medicated Feeds Directive (90/167/EEC)
- Official Controls Legislation (OFFC 82/2004)
EU Activity: Commission Action Plan

12 actions - 5 are Veterinary Specific
No. 2 Prudent Use of Antimicrobials in Vet medicine

- Strengthen regulatory framework-vet medicines and medicated feed
- Ensure appropriate warnings and guidance on SPC
- Consider restriction on use of certain CIAs for humans
- Consider amending rules for advertising
- Revisit authorisation requirements (risk:benefit)

No. 3 Introduce recommendations for Prudent Use in Veterinary Medicine
EU Legislation - What proposals are being put forward?

- Veterinary Medicinal Products Directive (2001/82/EC)
  - Controls on Critically Important Antibiotics (fluoroquinolones, 3/4\(^\text{th}\) generation Ceph's, Macrolides)?
  - Separation of right to prescribe from right to sell antimicrobials?
  - De-authorisation of older antibiotics?
  - Prevention of cascade use of antibiotics?
EU Legislation - What proposals are being put forward?

- Veterinary Medicinal Products Directive (2001/82/EC) - continued
  - Revision of authorised indications – particularly on older antibiotics?
  - Revised warnings on labelling?
  - Collection of prescription level data from vets?
What is Responsible Use

- Little as possible
- Reduce risk of disease challenge
  - Farm management.
  - Biosecurity
  - Farm health planning
  - Vaccination programmes
- Animal genetics
What is Responsible Use

- **As much as necessary**
  - For antibiotics, diagnosis and prescription by vet
  - All medicines
    - Purchased from authorised supplier
    - Follow label and vet instructions
    - Correct dose
    - Full course
    - Withdrawal Period
What are the issues

What actions are proposed

What about vet pathogen AMR surveillance

What influences prescribing practice
For behavioural change you need to understand what influences behaviour
Survey

- Joint HMA/FVE web based survey
- Ran for one month (March 2012)
- 5 languages
- 3004 responses from
- 25 European countries
How often do you consult the SPC before treatment?
Reasons for ignoring responsible use warnings – Top 3

- Owner request (easy to administer broad spectrum with short withdrawal period)
- Easier to administer
- Critically ill animals – start with broad spectrum
Importance of factors influencing prescribing behaviour

Asked about 17 different factors

For example:
- Experience
- Sensitivity
- Price/profit
- Availability
Sensitivity Testing - Why

Reasons to perform sensitivity testing

- Poor response to initial therapy
- Owner request
- No knowledge of animal/farm
- Prior experience of poor response

Legend:
- Total
- Companion animals
- Food Producing animals
Sensitivity Testing - Obstacles

Factors to increase sensitivity testing

- Cheaper testing
- Easy access to labs
- Rapid results
- Support interpretation results
- SPC recommending susceptibility testing
- Advise in guidelines/formulary
Country Differences

- Yes, in most cases
- Yes, always
- Regularly (disease status herd/flock)
- Seldom (poor response or complicated case)
- Seldom (at random)
- No

Country 1 vs Country 2
Preliminary Conclusions

- Education and Training – Key levers to influence prescribing
- Need for wider promotion and access to SPCs
- Large variation between countries in extent of sensitivity testing
- Wider use if sensitivity testing cheaper and gave rapid results
- Prolong life of what we have
- Reduce need for use
- Improve AMR Surveillance
- Develop new/alternatives
EU Activity:
Commission Action Plan

No.5 Introduce new Animal Health Law – focus on disease prevention and reducing use of antibiotics
No 5. New Animal Health Law

- New Regulation laying down general principles of animal health, animal health requirements for movements of animals and their products, and principle and measures for disease control

- Specific disease prevention and control rules on ‘listed’ diseases
- Prolong life of what we have
- Reduce need for use
- Improve AMR Surveillance
- Develop new/alternatives
No.10 Strengthen surveillance systems on AMR and antimicrobial consumption in vet medicine

- Legal basis for monitoring AMR in animal pathogen in new AHL
- Extension of ESVAC to obtain data on use by species and production categories and by indication
- Review monitoring AMR in zoonotic and commensal bacteria
EU Legislation - What proposals are being put forward?

  - Draft commission Implementing Decision on harmonised monitoring of AMR in zoonotic and commensal bacteria
<table>
<thead>
<tr>
<th>Bacterial Type</th>
<th>As of 2014</th>
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<tbody>
<tr>
<td>Enterococci</td>
<td>- No change</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td>- V → M</td>
</tr>
<tr>
<td><em>C. coli</em></td>
<td>- M → V</td>
</tr>
<tr>
<td><em>C. jejuni</em></td>
<td>- No change</td>
</tr>
<tr>
<td>Salmonella &amp; <em>E. coli</em></td>
<td>- expanded</td>
</tr>
</tbody>
</table>
1. Commensal *E. coli*
   - ESBLs
   - AMP-C
   - Carbapenemases

2. Resistant salmonella
   - ESBLs

3. Colistin
Target Pathogen Monitoring Programme

- Pathfinder group of France, Germany, Spain and UK
- Identify key issues
- Engage others
- Implement
Issues

Which animal disease – pathogen combination

Which pathogens – antibiotics combinations

Where from and when
- pre/post treatment
- only failures
- individual/flock/herd
- How many
- Sampling, transport & storage (specimen/isolate)
- What information to collect
- Method of susceptibility testing
- Definition of resistance
MARAN: Salmonella Cip^R

2004  0.3%

2005  10.1%
MARAN: Salmonella Cip$$^R$$

2004  0.3%  CBp > 2µg/ml

2005  10.1%  ECV  0.06µg/ml
## UK Salmonella 2011

<table>
<thead>
<tr>
<th></th>
<th>All (2862)</th>
<th>S. Typhimurium (427)</th>
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</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>0.5%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Ceftazidime &amp;</td>
<td>0.2%</td>
<td>None</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
- Prolong life of what we have
- Reduce need for use
- Improve AMR Surveillance
- Develop new/alternatives
No. 7 Promote efforts to analyse the need for new antibiotics into veterinary medicine

- Request for scientific advice on whether new antibiotics would reduce AMR

- Evaluate need for incentives to trigger development of veterinary antibiotics within boundaries of new legislation
EU Activity: Commission Action Plan

Sets out 12 actions - 3 Joint Human/Veterinary

- No. 8 Develop/strengthen multilateral and bilateral commitments for prevention and control of AMR
- No. 11 Reinforce and co-ordinate research efforts
- No. 12 Survey and comparative effectiveness research
There is a lot going on

TATFAR     FAO

WHO        OIE

G8
Conclusions

- Need to separate fact from fiction
- Belief is not a substitute for evidence
- Need to speak the same language
- We need defined outcome measures of interventions
We need a revolution in anti-infectives research

We need investment stimulation

The response must be global and co-ordinated