Reining in resistance: what role for organic farming methods?

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London, UK
Antibiotic Usage in Food Animals in EU, 2007

Figure 1. Amounts, in mg, of veterinary antibacterial agents sold in 2007 per kg biomass of pig meat, poultry meat and cattle meat produced plus estimated live weight of dairy cattle. *2005 data. **The abatements modelled vary from country to country.
Food-borne antimicrobial resistance: areas of current concern

- International spread of *Salmonella* organisms with SGI-1
- Increasing resistance to Critically Important Antimicrobials
  - Quinolones
  - 3 /4th generation cephalosporins
- Emergence & spread of new drug (multi)-resistant epidemic clones of *Salmonella* 1,4,[5],12:i:-
- *Campylobacter*: resistance to fluoroquinolones
- Epidemics of ESBLs / AmpC in humans and food animals
- Transmission of MRSA from pigs / calves/ horses to humans
SGI-1: arrangement of genes encoding pentaresistance (~ 13 kb)
SGI-1 complex integron variants

- S. Typhimurium
- S. Agona
- S. Albany
- S. Paratyphi B
- S. Meleagridis
- S. Newport
- S. Infantis
- S. Derby
- S. Cerro
- S. Kiambu
- S. Emek
- S. Dusseldorf
- S. Kentucky
- S. Tallahassee
- Proteus mirabilis

SGI1: ApCmFfSmSpSuTc
SGI1-A: ApCmFfSmSpSuTcTm
SGI1-B: ApSu
SGI1-C: SmSpSu
SGI1-D: SmSpTm
SGI1-E: ApSmSpSuTc
SGI1-F: ApCmFfSuTcTm
SGI1-G: ApSuTm
SGI1-H: ApCmFfGmScSmSpSuTc
SGI1-I: CmFfSmSpSuTcTm
SGI1-J: CmFfSuTcTm
SGI1-K: GmScSmSpSu
SGI1-L: ApCmFfSuTcTm
SGI1-M: ApCmFfGmKmSuTc
SGI1-N: CmFfSuTcTm
SGI1-O: SuTm

Kind permission of Axel Cloeckaert
Global spread of SGI-1 in non-Typhimurium serovars (kind permission of Axel Cloeckaert)
Quinolone-resistant *Salmonella Typhimurium* DT104 (UK)

November 93 – Enrofloxacin licensed for animal use

<table>
<thead>
<tr>
<th>Year</th>
<th>Chickens</th>
<th>Cattle</th>
<th>Pigs</th>
<th>Humans</th>
</tr>
</thead>
<tbody>
<tr>
<td>92</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>93</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>94</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>95</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>96</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>97</td>
<td>16%</td>
<td>4%</td>
<td>2%</td>
<td>8%</td>
</tr>
</tbody>
</table>
Quinolone resistance – *Salmonella* from humans and food, 10 MS, 2002-08

<table>
<thead>
<tr>
<th>Human</th>
<th></th>
<th>Food</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002:</td>
<td>&lt; 2%</td>
<td>[Serovars not specified]</td>
</tr>
<tr>
<td>2008:</td>
<td>&gt;14%</td>
<td>Pig meat: 2005 (5 MS) 0 – 17%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2006 (6 MS) 0 – 10%</td>
</tr>
</tbody>
</table>

**Serovars:**

<table>
<thead>
<tr>
<th>Typhimurium:</th>
<th></th>
<th>Broiler meat: 2006 (8 MS) 13 - 90%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002:</td>
<td>&lt;1%</td>
<td></td>
</tr>
<tr>
<td>2008:</td>
<td>2 – 6%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Enteritidis:</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2002:</td>
<td>6 - 10%</td>
<td></td>
</tr>
<tr>
<td>2008:</td>
<td>10 – 30%</td>
<td></td>
</tr>
</tbody>
</table>

[Highest incidence: *S. Virchow* : - 2006: > 50%]

Plasmid-mediated resistance to quinolones

1st identified: 1998 – *Klebsiella pneumoniae* – *qnrA* (nalidixic acid, low level to ciprofloxacin)

2005: *qnr B* – *K. pneumoniae* (USA, India)
2005: *qnrS* – *Shigella flexneri* (Japan)
2006: *qnrB* – *Salmonella* (UK)
2008: *qnrD* – *Salmonella* (China)

- *qnrA* - worldwide distribution, particularly Asian isolates
- *qnrB* – widespread – Senegal, USA, Korea
- *qnrS* – Germany, USA, Taiwan, Vietnam, France

Association with Extended Spectrum β-Lactamases (ESBLs). Therefore, many isolates resistant to β-lactam antibiotics

**Reported as:**
1,4,[5],12:i;-  
4, [5], 12:i: -  
4, 12: -  
4, [5], 12: -  
4, : -  
untypable

**Occurrence:**
Spain, Italy, Germany  
Luxembourg (outbreak), France, UK, Austria, Ireland, Hungary, Spain  
Denmark, Poland, The Netherlands

**Animal / food association:**
Pigs, pork  
[Also cattle, poultry]

**Resistance**
- ASSuT  
- ASSuT + C, G, Tm  
- *bla*TEM, *strA*, *sul*2, tet(B)  
- chromosomol island

also by phage type
(no antigenic structure)
Year on year trend of increasing ciprofloxacin resistance from 10% to 26%. An approximate 2.5 fold rise over a decade!

Erythromycin rates typically low (< 3%) over same period
Resistance to antimicrobials in *Campylobacter* spp. EU countries, 2009

<table>
<thead>
<tr>
<th>Country</th>
<th>n</th>
<th>% R to Cp</th>
<th>% R to Ery</th>
<th>% R to Tet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>1516</td>
<td>56</td>
<td>1</td>
<td>28</td>
</tr>
<tr>
<td>Italy</td>
<td>330</td>
<td>59</td>
<td>10</td>
<td>58</td>
</tr>
<tr>
<td>Slovenia</td>
<td>950</td>
<td>58</td>
<td></td>
<td>21</td>
</tr>
<tr>
<td>Spain</td>
<td>109</td>
<td>76</td>
<td>6</td>
<td>70</td>
</tr>
<tr>
<td>UK</td>
<td>19431</td>
<td>37</td>
<td>3</td>
<td>36</td>
</tr>
</tbody>
</table>

Source: TESSy data
Cephalosporin-resistant *E. coli* from bacteraemias

- Explosive increase recorded since start of 21st century
- In the UK,
  - c. 25,000 cases *E. coli* bacteraemia p.a. (voluntary)
  - c. 10% CTX and/or CAZ resistance = c. 2500 cases p.a.

http://www.earss.nivm.nl.
Cefotaxime resistance in *E. coli* from food animals: Netherlands data

Cefotaxime R% in *E. coli*

- Dairy cattle
- Veal calves
- Pigs
- Broiler chickens


R%

0 5 10 15 20 25

Courtesy of Dik Mevius
Prevalence of ESBL-producing *E. coli* on Dutch broiler farms [Dierikx et al 2010]

- 100% of the farms: ESBL *E. coli* positive
- On 85% (22/26) within-farm prevalence ≥ 80%

Prevalence UK: 3.6%

Courtesy of Dik Mevius
MRSA in food animals

2004: Netherlands: MRSA (CC398) in pigs and pig farmers

2010: 16/24 MS. Canada, USA, Asia: Pig farms, veal farms, poultry, horses

[Netherlands: 925% increase, July 2002 – December 2008 (Wulf et al, 2011)]
## Resistance: Organic vs. conventional (Poultry) [1]

<table>
<thead>
<tr>
<th>Country</th>
<th>Organism</th>
<th>Antibiotic</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td><em>Campylobacter</em></td>
<td>6 agents</td>
<td>Con &gt; Organic</td>
<td>Avrain et al 2003</td>
</tr>
<tr>
<td>Spain</td>
<td><em>Enterococcus</em></td>
<td>8 agents</td>
<td>Con &gt; Organic</td>
<td>Miranda et al 2007</td>
</tr>
<tr>
<td>NZ</td>
<td><em>E. coli</em></td>
<td>Ampicillin</td>
<td>No difference</td>
<td>Pleydell et al 2007</td>
</tr>
<tr>
<td>Germany</td>
<td><em>Salmonella</em></td>
<td>9 agents</td>
<td>No difference</td>
<td>Schwaiger et al 2008</td>
</tr>
<tr>
<td></td>
<td><em>E. coli</em></td>
<td></td>
<td>Con &gt; Organic</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Campylobacter</em></td>
<td></td>
<td>Con &gt; Organic</td>
<td></td>
</tr>
</tbody>
</table>
## Resistance: Organic -v- conventional (Poultry) [2]

<table>
<thead>
<tr>
<th>Country</th>
<th>Organism</th>
<th>Antibiotic</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td><em>Salmonella</em></td>
<td>Sulphonamides</td>
<td>Resistant (no difference)</td>
<td>Melendez et al 2010</td>
</tr>
<tr>
<td>USA</td>
<td><em>Salmonella</em></td>
<td>6 agents</td>
<td>Streptomycin: Con &gt; Organic MDR: Con only Also <em>Salmonella</em> Con &gt; organic</td>
<td>Alali et al 2010</td>
</tr>
</tbody>
</table>
## Resistance: Organic -v- conventional (Pigs)

<table>
<thead>
<tr>
<th>Country</th>
<th>Organism</th>
<th>Antibiotic</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td><em>Campylobacter</em></td>
<td>6 agents</td>
<td>MDR in both Con &gt; Organic</td>
<td>Thakur &amp; Gebreyes 2007</td>
</tr>
<tr>
<td>USA</td>
<td><em>E. coli</em></td>
<td>7 agents</td>
<td>MDR in both Con &gt; Organic</td>
<td>Bunner et al 2007</td>
</tr>
<tr>
<td>USA</td>
<td>Clostridia</td>
<td>MLS</td>
<td>High in both Con &gt; Organic</td>
<td>Zho et al 2009</td>
</tr>
<tr>
<td>USA</td>
<td><em>Campylobacter</em></td>
<td>3 agents</td>
<td>Con &gt; Organic</td>
<td>Rollo et al 2010</td>
</tr>
<tr>
<td>USA</td>
<td><em>Campylobacter</em></td>
<td>6 agents</td>
<td>Tet: common in both Con &gt; Organic</td>
<td>Tadesse et al 2011</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Ery: Con &gt; Organic</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cip: Con &gt; Organic</td>
<td></td>
</tr>
</tbody>
</table>
# Resistance: Organic -v- conventional (Cattle)

<table>
<thead>
<tr>
<th>Country</th>
<th>Organism</th>
<th>Antibiotic</th>
<th>Result</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td><em>Salmonella</em></td>
<td>10 agents</td>
<td>Little difference</td>
<td>Ray et al 2006</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>MDR: Con &gt; Organic</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td><em>Campylobacter</em></td>
<td>5 agents</td>
<td>Low levels</td>
<td>Halbert et al 2006</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tet: Con &gt; Organic</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td><em>E. coli</em></td>
<td>Amp, Tet</td>
<td>Con &gt; Organic</td>
<td>Walk et al 2007</td>
</tr>
<tr>
<td>USA</td>
<td><em>Staphylococcus</em></td>
<td>4 agents</td>
<td>Different patterns</td>
<td>Bombyk et al 2008</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Con &gt; Organic</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td><em>E. coli</em></td>
<td>8 agents</td>
<td>MDR in both</td>
<td>Berge et al 2010</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Con &gt; Organic</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td><em>Enterococcus</em></td>
<td>MLS</td>
<td>High in both</td>
<td>Zhang et al 2010</td>
</tr>
<tr>
<td>USA</td>
<td><em>E. coli</em></td>
<td>6 agents</td>
<td>No differences</td>
<td></td>
</tr>
</tbody>
</table>
ESBL contamination of organic vs conventional retail chicken meat: 84% of organic meat samples ESBL-positive versus 100% of conventional samples.

Qualitative culture results

Source: James Cohen Stuart, Medische Microbiologie, UMCU, The Netherlands
Conclusions from study

Majority of organic meat samples also harbour ESBLs

All conventional meat samples and 84% of organic meat samples harbored ESBL-producing Enterobacteriaceae.

Median load of ESBL-producing Enterobacteriaceae lower on organic samples.

Consistent with less antibiotic use in organic rearing process

Different ESBL genes in isolates from conventional versus organic samples.

ESBL strains from both rearing types found in humans

Source: James Cohen Stuart, UCMU, The Netherlands
IN GENERAL:
- AMR less in organic farms than in ‘conventional’ farms

BUT:
- MDR strains still present
- High prevalence of ESBLs
- No differences in some farms
- Spread of resistant organisms through contaminated feed

ALSO:
- Evidence of higher pathogen contamination in some organic farms
Other measures to control antibiotic resistance in food-borne micro-organisms

• Prudent use of antimicrobials

• Measures to reduce pathogen load
  Legislation – e.g, Zoonoses Directive
  Biosecurity
  Decontamination of carcasses

• Good hygiene at farm level
WHO 2007

Critically Important Antimicrobials for Human Medicine:

Categorization for the Development of Risk Management Strategies to contain Antimicrobial Resistance due to Non-Human Antimicrobial Use

Report of the Second WHO Expert Meeting
Copenhagen, 29–31 May 2007

UK CMO Report 2009

‘There should be a ban on the use of certain types of antibiotics (quinolones and cephalosporins) in animals, in order to protect their activity in humans’

CMO, 2009
Zoonoses Directive 2006

Rules for: monitoring of flocks for *Salmonella* infection.

monitoring of *Salmonella* at processing and slaughter

*Salmonella* contamination of feed.

- Measures to be taken if breeding flocks test positive
- Targets for the reduction of zoonoses
- Destruction of contaminated eggs
Concluding remarks

Reigning in resistance: what role for organic farming methods?

- Possibly effective in long term
- Best results if in conjunction with other methods
  - pathogen reduction
  - sterilisation of feed
- Cross-sectional challenges - linking resistance in humans and animals, and then prevention

Overall reduction in antibiotic usage still a critical factor for conventional farming and also organic farming because of spread of resistant organisms
AMR not just an animal problem!! - Antibiotic usage in humans in EU

doi:10.1093/jac/dkp333
Advance Access publication 21 April 2009

European Surveillance of Antimicrobial Consumption (ESAC):
outpatient parenteral antibiotic treatment in Europe

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