The public health impact of antibiotic use in Food Producing animals in The Netherlands and current Dutch control options

Dik Mevius
Antibiotic usage in humans and animals in Europe
Antibiotic sales for animals in NL (Source FIDIN)

90% oral administration by group/flock medication

Increase up to 2007 was the basis for mandatory reduction policy of the gouvernement of 20/50%
Sales data versus ADDD

Sales
- In KG product sold
- Not specified by animal species
- Not related to exposure of animals
- Rough estimate

Animal Defined Daily Dosages
- Register all antibiotics supplied (farm)
- Table with defined daily dosages for each licenced antibiotic
- Calculate the kg’s of animals that can be treated
- Relate that to the number of animals >> ADDD
- Precise estimate to compare farms/vets/countries
Trends in average ADDD/Y in NL (LEI)

Quantitative differences between animal species
Large variation: > 5% populations include farms with > 3 x average add/y
Trends have to be interpreted with care

www.maran.wur.nl
Resistance in 2009
(E. coli as commensal in the GI-tract ) (MARAN-2009)
Expressed as multi-drug resistance
What does this mean

- Dutch food-producing animals are an ideal environment for multidrug resistant organisms

- Risk??
  - Animal health?
    - Yes, if they cause infections
  - Public health?
    - Yes if:
      - Food-borne pathogens
      - Zoonotic organisms
      - Transferable genes
Relation between resistance in animals and humans?

- In spite of long term differences in usage, the resistance levels in Dutch Health care are low!
- So does a relation with resistance in animals exist?
  - Unfortunately, yes
    - MRSA!
    - ESBLs!
EARSS-net 2010 report (ECDC)
Livestock associated MRSA (ST398)

Methicillin-resistant Staphylococcus aureus in Pig Farming

Andreas Voss,*† Frans Loeffen,* Judith Bakker,* Corne Klaassen,† and Mireille Wulf*
Live Stock associated MRSA (ST398)

- Many pigs and veal calves carry LA-MRSA in their noses (poultry, horses, companion animals…)

- Increased risk for carriernship of farmers and vets

- Global problem

- In NL, measurable effects in human health care
  - Infections
  - Increased costs
Cefotaxime resistance in E. coli (ESBL/AmpCs)

Ban of ceftiofur use at hatcheries

ESBL prevalence
- Broilers/meat 100%
- Veal calves 66%
- Pigs > 50%
- Turkeys 50%
- Dogs 50%
- Wild birds 22%
- Etc.
**Association with humans**

**ORIGINAL ARTICLE**

**EPIDEMIOLOGY**

**Dutch patients, retail chicken meat and poultry share the same ESBL genes, plasmids and strains**

M. A. Leverstein-van Hall¹,², C. M. Dierikx³, J. Cohen Stuart¹, G. M. Voets¹, M. P. van den Munkhof⁴, A. van Essen-Zandbergen⁵, T. Platteeu⁶, A. C. Fluit¹, N. van de Sande-Bruinenma², J. Scharinga¹, M. J. M. Bonten¹,⁵ and D. J. Mevius³,⁴; on behalf of the national ESBL surveillance group*¹

¹) Department of Medical Microbiology, University Medical Centre Utrecht, Utrecht, 2) Centre for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven, 3) Department of Bacteriology and TSEs, Central Veterinary Institute of Wageningen UR, Lelystad, 4) SALTO, Primary Health Care Laboratory, Utrecht, 5) Julius Centre for Health Sciences and Primary Care, University Medical Centre, Utrecht and 6) Department of Infectious Diseases & Immunology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, the Netherlands

<table>
<thead>
<tr>
<th>Level of genetic typing</th>
<th>% of human isolates with poultry associated genetic element¹</th>
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<tbody>
<tr>
<td>ESBL genes (bla_{CTX-M-1}, bla_{TEM-52}, bla_{SHV-12}, bla_{SHV-2} and bla_{CTX-M-2})</td>
<td>35% (see Table 1)</td>
</tr>
<tr>
<td>bla_{CTX-M-1} and bla_{TEM-52} genes</td>
<td>30% (23.7% bla_{CTX-M-1}; 6.2% bla_{TEM-52})</td>
</tr>
<tr>
<td>bla_{CTX-M-1} and bla_{TEM-52} genes on IncI plasmid</td>
<td>20% (14.2% bla_{CTX-M-1}; 6.2% bla_{TEM-52})</td>
</tr>
<tr>
<td>bla_{CTX-M-1} and bla_{TEM-52} genes on IncI plasmid belonging to complex CC7 or CC3 and CC5 resp.</td>
<td>19% (12.6% bla_{CTX-M-1}; 6.2% bla_{TEM-52})</td>
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<td>bla_{CTX-M-1} and bla_{TEM-52} genes on IncI plasmid belonging to complex CC7 or CC3 and CC5 resp. in a poultry-associated MLST strain (ST10, ST58 or ST117)</td>
<td>11% (9.5% bla_{CTX-M-1}; 2.0% bla_{TEM-52})</td>
</tr>
</tbody>
</table>
Association with humans

Extended-Spectrum β-Lactamase Genes of *Escherichia coli* in Chicken Meat and Humans, the Netherlands

Ilse Overdevest, Ina Willemsen, Martine Rijnsburger, Andrew Eustace, Li Xu, Peter Hawkey, Max Heck, Paul Savelkoul, Christina Vandenbroucke-Grauls, Kim van der Zwaluw, Xander Huijsdens, and Jan Kluytmans

Figure 1. Distribution of extended-spectrum β-lactamase genes in chicken meat (A), human rectal swabs (B), and human blood cultures (C), the Netherlands. Values in parentheses are no. positive.
Measures implemented

2008 memoranda of understanding signed

- Mandatory reduction of antibiotic usage of 20% in 2012 and 50% in 2013 (compared to 2009)
  - New target = 70%
  - All antibiotic use on farms registered (VetCis)
    - Mandatory since 2012 (since 2013 legal obligation)
- Preventive use not legal
- Independent control institute
  - Veterinary Drug Authority (SDa, www.autoriteitdiergeneesmiddelen.nl)
    - Tasks
      » Report usage data publically,
      » Define target for usage
      » Identify frequent users
      » Control measures to improve usage
**ACTION LEVEL**
Direct measures necessary to reduce antibiotic usage

**SIGNALING LEVEL**
Please be aware

**TARGET LEVEL**
No direct measures necessary to reduce antibiotic usage
Broilers usage data 2011 (N = 737) treatment days

Median -20%

P75
Pig-production farms (top), veal calves (bottom)

Figuur 3A. Frequentieverdeling van DDD/J zoals berekend voor zeugenbedrijven in 2011. De doorgestreepte lijn is de berekende afgevlakte verspreiding op basis van het histogram, gebaseerd op de bedrijven met een DDD/J van 0 tot 150.

Figuur 2A. Frequentieverdeling van DDD/J zoals berekend voor blankvleesbedrijven in 2011. De doorgestreepte lijn is de berekende afgevlakte verspreiding op basis van het histogram, gebaseerd op de bedrijven met een DDD/J van 0 tot 150.
Antibiotica in de veeteelt en resistente bacteriën bij mensen

Om het probleem van de toenemende resistentie van bacteriën tegen antibioticum te keren, moeten bepaalde soorten antibioticum gereserveerd worden voor menselijk gebruik. Deze middelen zouden uitgesloten moeten worden van gebruik in de veeteelt, om overdracht van resistente bacteriën van dier naar mens tegen te gaan. Dit schrijft de Gezondheidsraad in zijn advies Antibiotica in de veeteelt en resistente bacteriën bij mensen dat de raad vandaag aanbiedt aan de minister van VWS en de staatssecretaris van EL&I.
**ESBLs considered the most important PH threat**

<table>
<thead>
<tr>
<th>Never allow usage of new classes:</th>
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<tbody>
<tr>
<td>Carbapenems, tigecycline, daptomycine, oxazolidones, mupirocine etc.</td>
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<tr>
<th>3rd/4th generation Cephalosporines</th>
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<tr>
<td>Not for group treatment</td>
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<tr>
<td>Not for mastitis prevention in dry cow treatment</td>
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<tr>
<td>Solely allowed for individual treatment based on appropriate diagnostics and ABG</td>
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<table>
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<tr>
<th>Colistin, beta-lactams, fluoroquinolones, aminoglycosides</th>
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<tr>
<td>Usage needs to be reduced in time</td>
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<td>FQ solely based on ABG</td>
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## 1st, 2nd and 3rd choice drugs defined based on Health Council advice

<table>
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<tr>
<th>Choice</th>
<th>Description</th>
<th>Examples</th>
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<tr>
<td>1st</td>
<td>Allowed for empiric therapy with no direct effect on ESBLs</td>
<td>Pen, OTC, TmpS, Tylo</td>
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<tr>
<td>2nd</td>
<td>No unless, appropriate argumentation provided</td>
<td>Ampi/Amox, Aminog, Col</td>
</tr>
<tr>
<td>3rd</td>
<td>No unless, no alternatives based on ABG</td>
<td>3/4gen Cephs, FQs</td>
</tr>
<tr>
<td>Banned</td>
<td>Not allowed for FP-animals</td>
<td></td>
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http://wvab.knmvd.nl/wvab

In Drug Regulation by 01-01-2013
“Formularia” adjusted based on this guideline

• Formularia are now essential parts of quality chain management systems for animal production sectors
  – Basis for controllable prescription behaviour
  – Basis for treatment plans on each farm
    • Only first choice drug allowed

“Stichting Geborgde dierenarts”
Foundation for Certified Vets
Certified Veterinarians

- Contractual 1-in-1 relation between vet and farmer
  - Vets need to follow training

- Mandatory on each farm
  - Treatment plans based on formularies
    - Only 1st choice drugs allowed on farms (max 1 treatment)
      - 2nd choice AB: no unless argumentation by vet
      - 3rd choice AB (cefs and FQs): no unless there is no alternative, based on antibiogram (in new Drug Law by January 2013)
  - Health plan

- 2012: Dairy cows, pigs (October)
- 2013: Poultry, veal calves
Voluntary measures by animal production sectors

- Limitations on usage of fluoroquinolones and cephalosporins
- Implemented antibiotic registration systems (databases and portals) developed for cattle, pigs, poultry (also layers)
  - ADDD/Y supplied to SDa for > 40000 farms in February 2013
- Stop of in feed medication by mid 2011 (NEVEDI)
Trends in Antibiotic Usage in Animals in NL

**Figure 3.1** Therapeutic antibiotic sales, 1999-2012 a)

Sales for 2012 are estimates, based on preliminary data of the first half year.
Source: FIDIN (2012).

(FIDIN/LEI 2012)
www.maran.wur.nl
Sales of antibiotics for (mg) per kg biomass produced (PCU) in Europe

2007

2010

Antibiotic use in mg/PCU in 19 EU Member States
Success versus conflicts

**Success factors**
- Private system with support of authorities
  - Organized bottom-up
- Full transparency which enables
  - Benchmarking
  - Control
- Independent Drug Authority
- Sanctioning
  - Private organisations
  - Food Safety Authority

**Conflicts**
- More disease problems?
  - Health control in animal production chains
  - Vets afraid to use antibiotics.
- Effect on resistance???
  - Global problem
  - More determinants than antibiotic usage
  - May need structural changes in animal husbandry practices
Thanks to Manon