Antimicrobial Resistance – Food Animal Antibiotic Use

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Former Deputy Undersecretary for Food Safety USDA
Today’s objectives

• Discuss the human health risk of on-farm antibiotic use
• Mention current events
• Answer SOME of your questions
The issues

• Antibiotic resistance in human infections is rising
  – CDC list of bacteria
• Some folks think modern agriculture is wrong
  – Use antibiotics as one of the “sticks”
• MOST people don’t understand
Residue vs Resistance

- **Residue**: A residue indicates that traces of a substance are present in meat. Residue does not mean that the substance is harmful, and it can be one of many classes of compounds. For antibiotics in particular, if a residue is present, it is likely due to the producer not waiting long enough after the animal was given antibiotics to send it to market (not following proper withdrawal guidelines).

- **Resistance**: If resistance is detected, this means that there are bacteria on the meat that have tested resistant to one or more antibiotics. Resistance is measured and reported through the National Antimicrobial Resistance Monitoring System ([NARMS](http://hurdhealth.com/2013/08/14/its-all-antibiotic-free-baby/)).

- If resistance is detected, that does not mean there are residues; likewise, if a residue is found, that does not mean that there are resistant bacteria to that antibiotic.
Antibiotic resistance risk due to on-farm antibiotic use

SUMMARY

1. Risk to humans is negligible
2. Failure to prevent or treat animal illness causes unnecessary suffering and death
3. Animals with residual effects of illness are more likely to cause human foodborne disease
Evidence that risk is negligible?

• “Long way from farm to harm”
  – Many events must occur
  – Many interventions exist to prevent those events
  – Peer-reviewed risk assessments show low risk

• Resistant human illnesses of concern are unrelated to animal agriculture

• Antibiotics used on farm are dissimilar from those used in human medicine
IT'S A LONG WAY FROM THE FARM TO HARM

Antibiotic Resistant Bacteria

Non-resistant Bacteria

HACCP

Cooking

Health & Immunity

Risk
Most important Resistant Bacteria of Concern
NONE related to animal agriculture

• **Staphylococcus infections (MRSA)** –
  - hospital nosocomial infections,
  - occasionally associated with schools and athletic facilities.
  - CDC said “not a foodborne infection and cannot be acquired by eating meat. “

• **Acinetobacter baumannii** is an opportunistic pathogen associated with a high rate of infections in soldiers wounded in Iraq.

• **Vancomycin Resistant Enterococcus (VRE)**
  - hospital nosocomial infection due to extensive use of vancomycin in U.S. hospitals.
  - Vancomycin or drugs in its class have never been approved for or used in U.S. food producing animals.

• **Pseudomonas aeruginosa**
  - opportunistic pathogen found in intensive care units,
  - occurs rarely in dairy mastitis

• **Streptococcus pneumoniae** - strictly human pathogen causes respiratory disease

• **Neisseria gonorrhea** sexually transmitted human pathogen

• **Drug resistant tuberculosis (M tuberculosis)**: no known connection to food producing animals.

Human vs Animal Antibiotic Sales are Relatively Different in U.S.

Tetracyclines: 41.06% vs 3.9%

Penicillins: 6.4% vs. 43.9%

Human data (2010): [Link to Human Data]
Animal data (2011): [Link to Animal Data]
Antimicrobial resistant bacteria are a **Hazard**

- We are concerned
- But concern does not mean there is a great risk

- Risk $\sim$ exposure and dose
- Risk $\sim$ probability and consequence

- Manage the risk by multiple methods
Hazard Does Not Mean Risk

\[
\text{Hazard} \times \text{Dose (Exposure)} = \text{Risk}
\]

= Drowning
Example Hazardous Material

• Human Health Effects
  – cramps
  – nausea
  – dizziness
  – respiratory difficulties
  – convulsions capable of leading to death
Example Hazardous Material = Oxygen

- Human Health Effects
  - cramps
  - nausea
  - dizziness
  - respiratory difficulties
  - convulsions capable of leading to death
Conversion of hazard to risk requires a causal pathway

Pathway provided by FDA guidance doc 152
What does risk science say?

• No peer-reviewed scientific quantitative risk assessment has demonstrated any detectable risk of treatment failure in humans caused by current on-farm antibiotic uses in animals.
Quantitative risk assessments report negligible risk

<table>
<thead>
<tr>
<th>Risk (High to Low)</th>
<th>Yearly Probability</th>
<th>Outcome Comments</th>
</tr>
</thead>
</table>
| Enrofloxicin use in poultry to treat disease           | 1 in 30,000 (low)         | Compromised treatment - *By FDA, overestimated attributable fraction*  
| All macrolide uses (cattle, swine, poultry)            | 1 in 10 million           | Compromised treatment                                                                                                  |
| Streptogramin/Virginiamycin use                         | ~ 100 in 100 million      | Impaired treatment: *By FDA, still a draft*  
| Penicillin growth promoter                              | ~4 in 1 billion           |                                                                                                                        |
| Fluoroquinolone use in dairy heifers                   | ~1 in 61 billion          | Compromised treatment                                                                                                  |
|                                                        |                           | H. Scott Hurd, Michael B. Vaughn, Derald Holtkamp, James Dickson, and Lorin Warnick.  
2. Failure to prevent or treatment illness causes unnecessary animal suffering and death

- Farm is a day care and a maternity hospital
- Need medicine
- Moral and ethical issue
  - Will we deny treatment?
  - Wrong to withhold veterinary care
  - How long can you wait to treat?
Antibiotics are needed

• Only 13% is used for growth promotion  
  – This will decline further due to FDA 209
• Treatment of a group requires water or feed medication
• Organic/antibiotic free farms must treat and remove →, financial penalty.
Group prevention needed in human & animal medicine

• Infectious individual not evident until has spread
• Infection can move quickly through group
• Animals cannot “stay home” when ill
• Prevention stops spread reducing treatments and suffering
Why is group prevention needed?
(DRAFT animation)
Stop and Ponder

Why take additional risk??
3. Animals with residual effects of illness are more likely to cause human foodborne illness

- Meat Inspection Act 1906 requires healthy animals
- Antemortem inspection enforces

Largest meat recall in U.S. history due to slaughter of downer cows February, 2008
Adhesions increase chance of fecal contamination
Table 4. Regression coefficients (univariate and multivariate with antibiotic use group as a covariate) between percentage of representative health variables and percentage of carcasses positive for *Enterococcus* spp. or *Campylobacter* spp. in the bung or pleural cavities\textsuperscript{a,b}

<table>
<thead>
<tr>
<th>Health indicator</th>
<th>Bacterial contamination</th>
<th>Location on carcass</th>
<th>Regression coefficient (β)</th>
<th>95% CI</th>
<th>Regression coefficient (β)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>(univariate)</td>
<td></td>
<td>(multivariate)</td>
<td></td>
</tr>
<tr>
<td>Fatigued\textsuperscript{c}</td>
<td>Campylobacter</td>
<td>Bung</td>
<td>41.0</td>
<td>(219.0, 102.0)</td>
<td>10.0</td>
<td>(−50.0, 70.0)</td>
</tr>
<tr>
<td>Peel-outs\textsuperscript{d}</td>
<td>Campylobacter</td>
<td>Pleura</td>
<td>5.7</td>
<td>(20.3, 11.7)</td>
<td>5.1</td>
<td>(0.4, 9.9)</td>
</tr>
<tr>
<td>Peel-outs</td>
<td>Enterococcus</td>
<td>Bung</td>
<td>5.1</td>
<td>(21.3, 11.5)</td>
<td>4.4</td>
<td>(1.3, 7.4)</td>
</tr>
<tr>
<td>Abscessed heads\textsuperscript{a}</td>
<td>Campylobacter</td>
<td>Pleura</td>
<td>−12.7</td>
<td>(231.0, 5.0)</td>
<td>−6.2</td>
<td>(−33.0, 21.0)</td>
</tr>
<tr>
<td>Abscessed heads</td>
<td>Enterococcus</td>
<td>Bung</td>
<td>−13.3</td>
<td>(231.0, 0.5)</td>
<td>−2.5</td>
<td>(−24.0, 19.0)</td>
</tr>
</tbody>
</table>

\textsuperscript{a} All health and contamination relationships were tested. Only those with \(p<0.2\) in the univariate comparison are shown.

\textsuperscript{b} Conventionally raised animals received antibiotics for growth promotion and disease prevention and treatment; antibiotic-free animals never received antibiotics.

\textsuperscript{c} Anaerobic metabolism, respiratory distress, recurrent

\textsuperscript{d} Pleuritis and pleural adhesions

\textsuperscript{a} Heads condemned due to visible abscess(es)
Impact of pig health on foodborne Risk (*Salmonella*)

- Study of 358 healthy pigs: (passed FSIS antemortem inspection, not visibly ill)
- ~7% had internal adhesions from previous infection
- Compared to carcasses without lesions (case-control study)
Lesioned and non-lesioned swine carcass

90% more likely to be contaminated with Salmonella

Residual impacts of illness
Pathologist score ~ 6

Normal healthy
Pathologist score ~ 0 to 1
## Public Health Risk of Residual Animal Illness Effects

<table>
<thead>
<tr>
<th>Foodborne illness / animal condition studied</th>
<th>Quantitative results</th>
<th>Citation</th>
</tr>
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References available at [www.hurdhealth.com](http://www.hurdhealth.com)
Antibiotic resistance risk due to on-farm antibiotic use

*Layman’s Summary*

1. Long way from farm to harm
2. Animals, like children, need Medicine
3. Healthy Animals make Safe Food
QUESTIONS

References available at www.hurdhealth.com
4. Managing the risk in U.S.

- Case by case (bug-drug) risk assessments required by FDA (Guidance 152)
- Prudent use guidelines without broad legislation
- Voluntary removal of growth promotion claims (Guidance 209)
- Producer quality assurance programs
- Increasing veterinary oversight
A word about foodborne illness outbreaks and resistance

- Most foodborne illness are not supposed to be treated with antibiotics
  - Therefore resistance is irrelevant
  - Treat with fluoroquinolones (never in poultry) and 3rd generation cephalosporins (rarely in poultry for illness)

- Almost every species of bacteria is resistant to some antibiotics
  - Therefore on-farm use may not be the cause

- Current Salmonella Heidelberg isolates are resistant to ampicillin, chloramphenicol, gentamicin, kanamycin, streptomycin, sulfisoxazole, and tetracycline