Animal Agriculture & Antibiotic Resistance
What should (& should not) be on the table

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Key Resistance Issues at the Human–Animal Interface

Develop Specific Stewardship Guidelines

Antimicrobial – Bacteria Combinations
Understand the Risk – Benefit of Antimicrobial Use
Antimicrobial Resistance is ...

- A Phenomenon that is:
  - Real
  - Complex
  - Incompletely Understood

- A Bacterial Response Propagated by both Agricultural and Human Uses of Antimicrobials
Antimicrobial Use is ...

- A Risk – Reward Proposition

Clinical Outcome & Resistance Development Treatment Costs

IDSA – Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship
Resistance Issues to Leave “off the table”

- Growth Promotion / Feed Efficiency
- Environmental / Indirect Spread of Resistance
- International Spread of Resistance
What is the Human Perspective?

What are the Bacterial Diseases of Concern and Antimicrobials of Importance?

- CDC “Antibiotic Resistance Threats in the United States, 2013”
- WHO “Critically Important Antimicrobials for Human Medicine, 3rd Rev.” 2011
Population approach
  ◦ Estimated annual number of illnesses / deaths
    • Laboratory–based surveillance with extrapolation to entire US population
    • Underestimate of true disease prevalence
  ◦ Multiplied by average prevalence of resistance for that bacterial organism
    • NARMS
CDC
Antibiotic Resistance Threats in the United States

Based on:
- Clinical impact
- Economic impact
- Incidence
- 10-year projected incidence
- Transmissibility
- Availability of effective antibiotics
- Barriers to prevention

Threats classified as:
- Urgent
- Serious
- Concerning
CDC
Antibiotic Resistance Threats in the United States

- **Urgent Threats**
  - *Clostridium difficile*
  - Carbapenem–resistant Enterobacteriaceae
  - Drug–resistant *Neisseria gonorrhea*

- **Serious Threats**
  - Multidrug–resistant *Acinetobacter*
  - Drug–resistant *Campylobacter*
  - Fluconazole–resistant *Candida*
  - Extended spectrum β–lactamase producing Enterobacteriaceae (ESBL)
  - Vancomycin–resistant *Enterococcus*
  - Multidrug–resistant *Pseudomonas aeruginosa*
  - Drug–resistant non–typhoidal *Salmonella*
  - Drug–resistant *Salmonella typhi*
  - Drug–resistant *Shigella*
  - Methicillin–resistant *Staphylococcus aureus*
  - Drug–resistant *Streptococcus pneumoniae*
  - Drug–resistant tuberculosis

- **Concerning Threats**
  - Vancomycin–resistant *Staphylococcus aureus*
  - Erythromycin–resistant Group A *Streptococcus*
  - Clindamycin–resistant Group B *Streptococcus*
CDC
Antibiotic Resistance Threats in the United States

- Antimicrobial Use in Agriculture Specifically Discussed as a Risk Factor
  - Drug-resistant *Campylobacter*
    - Azithromycin
    - Ciprofloxacin
  - Drug-resistant non-typhoidal *Salmonella*
    - Ceftriaxone
    - Ciprofloxacin
    - Multidrug resistance
WHO
Critically Important Antimicrobials for Human Medicine

Prioritization within *Critically Important* Antibiotics

- Number of people affected by diseases to which the antimicrobial is the sole or one of limited therapies
- Frequency of use in human medicine for any indication
- Degree of confidence that there are non-human sources of resistant bacteria or their resistance genes
WHO
Critically Important Antimicrobials for Human Medicine

- Glycopeptides
  - Enterococci
- 3rd / 4th generation Cephalosporins
  - Enterobacteriaceae (*E. coli* and *Salmonella*)
- Fluoroquinolones
  - *Campylobacter* and Enterobacteriaceae (*E. coli* and *Salmonella*)
- Macrolides / Ketolides
  - *Campylobacter*
Human Perspective

Bacteria of Concern

- Campylobacter
- Enterobacteriaceae
  - *Salmonella*

Antimicrobials of Importance

- Macrolides
- Fluoroquinolones
- Cephalosporins
  - 3rd/4th gen
- Fluoroquinolones
What are the Bacterial Diseases of Concern and Antimicrobials of Importance?

- OIE “List of Antimicrobials of Veterinary Importance” 2007
- Animal Drugs @ FDA
- USDA – Industry Death loss summaries
OIE

Critically Important Veterinary Antimicrobials

- OIE Working Group on Antimicrobial Resistance and input from Member Countries

  A. Classification by majority (>50%) of respondents
  B. Agents essential against specific infections and lack of sufficient therapeutic alternatives

- Classification of Antimicrobials
  - Critically Important (both A & B)
  - Highly Important (A or B)
  - Important (neither A or B)
OIE
Critically Important Veterinary Antimicrobials

- Aminoglycosides
- Penicillins
- Phenicols
- Sulfonamides
- Tetracyclines
- Cephalosporins
  - Treatment of serious infections
  - Limited alternatives due to spectrum or resistance
- Macrolides
  - Few alternatives for swine / poultry *Mycoplasma* infections and liver abscesses in cattle
  - Treatment of respiratory infections in cattle
- Quinolones
  - Therapy of serious infections in poultry, cattle, swine, fish and other species
What are the Diseases of Concern in the US?

- **Respiratory Disease**
  - #1 cause of death in beef operations
  - #2 cause of death in dairy operations
  - #7 cause of death in sheep operations
  - #1 cause of death in swine nursery & grower operations

- **Digestive Diseases**
  - #4 cause of death in beef operations
  - #5 cause of death in dairy operations
  - #3 cause of death in sheep operations
  - #3 cause of death in pre-weaned swine
  - #4 cause of death in nursery swine

- **Other Diseases (includes mastitis, foot rot)**
  - #1 cause of death in dairy operations
  - #6 cause of death in beef operations
  - #6 cause of death in sheep operations

- USDA “Cattle and Calves Death Loss in the US”, 2000
- USDA “Sheep and Lamb Nonpredator Death Loss in the US”, 2009
- USDA “Reference of Swine Health, Productivity, and General Management in the US”, 2006
Macrolides / Lincosamides

- Bovine Respiratory Disease
- Swine Respiratory Disease
- Ovine Respiratory Disease
- *Mycoplasma gallisepticum* (chickens)
- *Haemophilus gallinarum* (chickens)
- Mastitis (cattle)
- Porcine Proliferative Enteritis (swine)
- Calf Diphtheria (cattle)
- Metritis (cattle)
- Swine Arthritis (*Mycoplasma* spp.)
- Swine Erysipelas
- Swine Dysentery
- Necrotic Enteritis (chickens)
- *Paenibacillus larvae* (honeybees)
- Liver Abscesses (cattle)
- Interdigital Necrobacillosis “Footrot” (cattle)
Fluoroquinolones

- Bovine Respiratory Disease
- Swine Respiratory Disease

- Federal law currently prohibits the extra-label use of fluoroquinolones in food animals
Interdigital Necrobacillosis “Footrot” (cattle)
Swine Respiratory Disease
*E. coli* colibacillosis (chicks / turkey poults)
Bovine Respiratory Disease
Sheep Respiratory Disease
Caprine (Goat) Respiratory Disease
Acute Metritis (cattle)
Mastitis (dairy cattle)

- Federal law currently limits the extra-label use of cephalosporins in food animals
Agricultural Perspective

Diseases of Concern
- Respiratory Disease
- Digestive Diseases
- Other Diseases (mastitis, foot rot)

Antimicrobials of Importance
- Macrolides
- Fluoroquinolones
- Cephalosporins
  - 3rd generation
- Cephalosporins
- Macrolides
- Macrolides
- Cephalosporins
Understanding the Risks & Benefits of Antimicrobial Use in Agriculture
What are the Risks of Agricultural Use of Antimicrobials?

- Contribute to Bacterial Resistance in Human Medicine (annual estimates in US)
  - Drug Resistant *Campylobacter*
    - 310,000 illnesses / 28 deaths
  - Drug Resistant non-typhoidal *Salmonella*
    - 100,000 illnesses / 40 deaths
What are the Risks of Agricultural Use of Antimicrobials?

- Contribute to Bacterial Resistance in Veterinary Medicine
  - Since 2011, >60% of *Mannheimia haemolytica* isolates recovered at KSVDL have been MDR
What are the **Benefits** of Agricultural Use of Antimicrobials?

- Improved Animal Health
What are the Benefits of Agricultural Use of Antimicrobials?

- Improved Food Safety
  - *Campylobacter* counts were higher on processed chickens with air sacculitis infections
    • Russell (2003)
  - *Enterococcus* and *Campylobacter* contamination of processed swine carcasses was associated with presence of pleural adhesions
    • Hurd (2008)
What are the Benefits of Agricultural Use of Antimicrobials?

- Economic
  - Direct benefit to farmer through decreased animal loss
  - National economic benefit
    - Agriculture / agriculture-related industries contributed $775 billion to the 2012 US economy (~5% GDP)

What are the **Benefits** of Agricultural Use of Antimicrobials?

- **Economic**
  - Direct benefit to consumer through decreased food prices
    - 6.8% of US consumer expenditures was on food [2012]
    - World AVG – 23% (6.7%–57%) million households

[Graph showing prevalence of food insecurity from 2000 to 2013]

Note: Food-insecure households include those with low food security and very low food security.
The Path Forward

- [For this group] focus on the antimicrobials of critical importance to human and veterinary medicine
  - Dynamic situation

- Understand the risks / benefits of antimicrobial use

- Design Stewardship programs that are:
  - Specific
  - Practical
  - Measureable
Questions?