Antimicrobial Resistance: Research and Priorities

Mary E. Torrence  DVM, Ph.D., DACVPM
National Program Leader, Food Safety
USDA, ARS
“Paralyze Resistance with Persistence”

Woody Hayes
(American Football coach, 1913–1987)

en.wikipedia.org
Current Influences

- Congressional, public health, regulation and scientific reports
- GAO report on Antibiotic Use in Animals
- US Public Health Action Plan (Interagency task force)
Collect detailed antibiotic use in food animals, work with industry, and seek resources and evaluate effectiveness

Modify NARMS, especially animal and retail

Assess previous research efforts on alternatives, identify research gaps, and specify steps in the Action Plan to address them
US Public Health Action Plan

- Public meeting, November 15th, Washington DC
- Chaired by Interagency Task Force on AR, specifically by FDA, NIH, and CDC
- Updated annually and released on the web
- This year, specifies goals, action items, projects, and implementation steps
Action Plan

- Surveillance
- Prevention and Control
- Research
- Product Development
Goals within Key Areas

- **Surveillance**
  - Determine, monitor and characterize drug resistance in humans and animals
  - Define, characterize, and measure importance of antimicrobial use in humans and animals
USDA research and activities

- Surveillance
  - Updating of database, web interface, quicker reports, and IT (NARMS)
  - Re-evaluate and modify the animal arms sampling (NARMS)
  - Continued collaborations with NAHMS
  - Collaborations with universities
  - Other databases (NCBI), VetNet
Prevention and Control

- Develop, implement, and evaluate strategies to prevent emergence, transmission, and persistence
- Develop, implement, and improve appropriate use of antibiotics
USDA research - Prevention and Control

- Evaluate critical control points for resistance in food animals
- Promote research, development of processing technologies
  - Clay Center - research on sprays, sanitizers, and physical interventions (like wash cabinets) to reduce pathogen contamination in feedlot cattle
  - Russell - research on alternatives to current antibiotic rinses and sanitizers in poultry and as interventions in egg production
Preharvest

- Risk factors for transmission and persistence (e.g. darkling beetles as risk factors, and also as models for plasmid transfer)

- Evaluation of risk factors for development, persistence and fluctuations, and transmission of resistance in food animals (e.g. milk liners in dairy, biocides and metals in swine)

- Understanding the ecology of the production “environment” and the ecology of the intestinal microflora
Research

- Basic, clinical, translational
- Epidemiology - for drivers of emergence and spread of a.r.
- Advanced research and development contracts to facilitate progress in antimicrobial drug and vaccine candidates through the pipeline
General research topics

- Prevalence of resistance through food production chain
- Identification and characterization of genotypic and phenotypes
- Identifying risk factors for development, transmission, and resistance
- Understanding transfer of resistance (integrons, plasmids)
- Ecology and epidemiology of resistance
- Changes in intestinal microbiota following different treatments
- Antibiotic use, organic versus conventional
Research on commensals and microbiome

- Does the gut microbiome change in composition over time?
- Does a growth promoting antibiotic or infectious bacteria alter the growth and composition of the microbiome?

(NIFA, Isaacson; ARS, Stanton)
Conclusions

- The majority of microbes in pigs are Firmicutes and Bacteroidetes
  - As pigs get older, there is an increase in Firmicutes and decrease in Bacteroidetes
  - There is a clear shift in components that are not dominant members of the microbiome
  - Closely housed pigs have similar but not identical microbiomes

- Growth promoting antibiotics do perturb the pig gut microbiome
  - Causes an increase maturation of the microbiome
  - Cause a shift in resistant genes and in E.coli populations

- There are interactions between pathogens and members of the entire microbiome (Lawsonia intracellularis and Salmonella enterica)
  - One pathogen can predispose to another
  - Infections alter the composition of the gut microbiome
Product Development

- Rapid diagnostics
- Harmonization of susceptibility testing
- New Product development
Alternatives to antibiotics

- Natural ingredients (e.g. citrus oil, metals)
- Interventions (e.g. competitive exclusion, bacteriophages)
- Management (e.g. vaccine and immune modulator, genetics)
USDA – NIFA Special Research Grant

- OSU- OARDC - “Reducing by the Transmission of AMR Organisms by Wildlife within the Food Supply- a Research, Control, and Outreach Strategy”
- Extent to which wildlife contribute to antimicrobial resistance in livestock and how it spreads to humans
RFA for 2012-2013 for Special emphasis grant entitled, “Effective mitigation strategies for antimicrobial resistance” (800k). Due December 5 (identify critical control points for mitigation based on ecology, risk assessments, develop, implement, and evaluate mitigation strategies

Safety of Fresh and Fresh-cut Produce- Ecology, processing, and safe handling but includes antimicrobial resistance.
Lessons learned?

Now what?
Now what?

- A new model for funding research?
- Assess what we’ve already done, and do something different (systematic review)
- Strengthening collaborative efforts and integrating basic and applied research with population-based studies (field)
- Epidemiology- sampling, population-based studies, design of outcome measurements
- Infrastructure and design in place before the event, e.g. growth promoter ban
Yesterday and Today
The significant problems we face cannot be solved at the same level of thinking we were at when we created them - Einstein