Antimicrobial Resistance: Research and Priorities

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“ Paralyze Resistance with Persistence”

en.wikipedia.org

Woody Hayes
(American Football coach, 1913–1987)

Current Influences

- Congressional, public health, regulation and scientific reports
- GAO report on Antibiotic Use in Animals
- US Public Health Action Plan (Interagency task force)

GAO Report

- 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

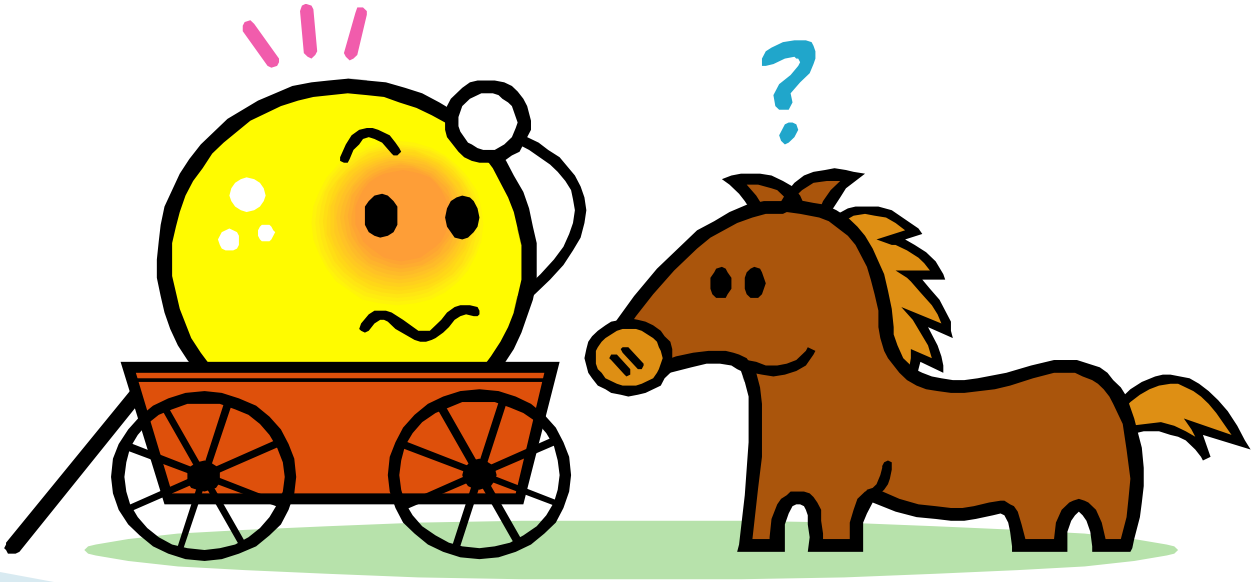
- **Surveillance**
  - Determine, monitor and characterize drug resistance in humans and animals
  - Define, characterize, and measure importance of antimicrobial use in humans and animals

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
- Multi-disciplinary and multi-institutional (Colleges of Vet. Medicine and Public Health, Univ. of Guelph, Univ. of British Columbia, EPA, Public Health Agency of Canada, National Wildlife Research Center in Fort Collins, USDA)

USDA Research at NIFA

- 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?

- **ASM (2002) Research colloquium on Role of Antibiotics in Agriculture.** *Recommendations:* Antibiotic usage data, pharmacoeconomics, commensals, impact of interventions/prevention, gene reservoirs, selective pressures and factors, quantitative risk assessments, surveillance, growth promoters reevaluated, alternatives, collaborative rather than blaming environment.

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*