Improving Antimicrobial Use in Food Animal Production: Alternatives, Options and Incentives

APUA-sponsored National Stakeholder Meeting
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Alternative Strategies

10th presentation
H. Morgan Scott, DVM, PhD
Interventions to Prevent Resistance among Enteric Pathogens in Beef Cattle

Morgan thinks that systemic intervention is required both to achieve reduced reliance on antibiotics overall, and to avoid the unintended consequences that may occur through haphazard application of antibiotic policies across multiple classes and uses of these products. He presents an alternative systems-based approach that relies on consideration of both the microbial ecology and epidemiology of enteric (pathogenic and commensal) bacterial in food production systems to identify and optimize potential interventions. Using research on fecal flora he describes an approach that may be applied in beef cattle production with a focus on changes both to host gut and production environment.

Antibiotic interventions not directed to the gut. Effects on gut are unintended consequences. (treating for respiratory pathogens and others). Speaks about variety of perspectives – humans take precedence, precautionary principle, and decreasing order of defensible use. Producers’ perspective: antibiotic therapy should be viewed as a last resort. - Moral & political and monetary economics. Perspectives differ even within the veterinary profession.

Strategies to prevent resistance- intervene to reduce exposure in the environment. See Meta-populations of AMR: ecological patch model concept: interaction of cattle, feed, and water (transmitted via feces). Potential interventions target host bacteria (‘plasmid curing’, select for competing strains), environment (change of conditions to favor susceptible bacteria), feed (direct- fed microbials) and water. He cites Guy Loneragan’s work on changes in US beef cattle enteric populations due to influence of the feedlot environment.

11th presentation
Scott A. Brown, DVM, PhD, Dipl. ACVCP
Approaches to Reduce Risk of Infectious Diseases Losses in Livestock

{Scott referred to the book: “Thinking – Fast and Slow”} Fast response based on gut-level emotion
Not addressing post harvest approaches. Guidance #152 template for data gathering and enables a company to decide whether or not to pursue further development on a drug.

Scott related Pfizer’s perspective- a science-based regulatory approach, with priority to protecting human health. Human and animal health are interlinked. Veterinarian involvement is central in establishing broad herd heath programs that include proper housing, vaccines, therapeutics, and nutrition. Pfizer believes that prevention and management practices are the first course of action in animal health. Several non-bacterial approaches to consider to reduce disease are:

- Animal side diagnostic tests
- Pre- and at-harvest pathogen reduction programs (food safety vaccines, irradiation of carcasses)
• Improvements in NARMS to enable it as a prevalence tool (probabilistic modeling of ABR)
• Veterinarian involvement in about all decisions concerning antimicrobial use
• Improved transportation-related biosecurity, and reduction of commingling with subsequent dispersal of animals

Other alternatives to consider (which require additional data and clarification on regulatory requirements) include:
• Direct fed microbialis (see M. Scott)
• Amino acid and acidifiers
• Zinc and bacteriophages.

Best management practices (all in, all out, all clean in between together with on-farm husbandry education (Pfizer: Husbandry educator program in swine to reduce med. use and disease, and Join the Cause campaign for dairy producers) are essential to preventing infectious disease. **Graph: with the program in place, mortality reduced, medicine costs have gone down too! They also made money as they went along.** Ethical companies are investing in alternatives. Antibiotics (as well as new ones) will continue to be needed because animals (and people) will continue to get sick, despite management practices adopted.

**12th presentation**

Yvette J. Johnson-Walker, DVM, MS, PhD

*Infection Prevention and Control in the Poultry Industry: Current Trends and Future Directions*

The literature identifies the following benefits for using antimicrobials in livestock production: reduced production costs, enhanced food safety, improved animal welfare and environmental stewardship. Yvette defines four categories of antimicrobial use in poultry production: growth promotion, prophylaxis (herd or flock at risk for disease), metaphylaxis (mass medication @ therapeutics doses to clinically normal animals in response to clinical disease in other pen/herds/flock mates), and therapeutic. In commercial poultry production, prophylaxis and metaphylaxis are important health management strategies, because in many cases of infectious disease, the first clinical sign noted is acute death. Furthermore, therapeutic administration occurs via water- and is not individual treatment. Enteric and respiratory diseases principally affect poultry. Necrotic enteritis (*Clostridium perfringens*) is an enteric disease with few clinical signs prior to death; and, *E. coli* is a source of respiratory infections in poultry (*air sacculitis, rhinotracheitis, sinusitis, or pneumonia*). Treating infected birds reduces suffering, minimizes economic losses associated with illness and prevents birds from farms with sick birds from entering the food supply chain.

There are concerns that new regulatory policies will act as a disincentive for new drug development, reduce production efficiency, increase incidence of infectious disease and limit the ability of veterinarians and farmers to treat and prevent disease. Currently there is a thrust toward alternative housing for poultry which will substantially increase the cost of production as well as expose birds to environmental pathogens/stressors. Some alternatives to antimicrobial growth promoters discussed are: organic acids, probiotics, prebiotics, enzymes and herbal products.

Dr. Johnson puts forth an approach to move forward via building consensus, focusing on common goals to protect public health, preserve antibiotic effectiveness, and assure food safety and affordability. The development of evidence-based, sustainable policies that have wide reaching ramifications (on production animals, animal husbandry workers, consumers, and the surrounding ecosystem) requires input from multiple stakeholders, with ongoing evaluation and revision as new information becomes available.

**13th presentation**

Masoud Hashemi, PhD

*Livestock Operation Systems and Ruminants’ Health*
Perspective – Dr. Hashemi began his work in Massachusetts as a nutrient management specialist advising dairy farmers – one-on-one. Then he started teaching sustainable crop and pasture management. Pasture works well in small or medium sized farms and this discussion does not pertain to large farms. Livestock are naturally grazing animals with digestive systems that function well on a grass diet. Allowed to graze, these animals enjoy a much healthier life than those animals confined to feedlots. Animals raised in confinement facilities are routinely treated with antibiotics to prevent disease outbreaks. Furthermore, grain-fed ruminants frequently suffer from acidosis, mastitis, and respiratory disease due to compromised immune systems. Traditional livestock producers often supplement animal feed with unhealthy sources of protein – chicken manure, restaurant food wastes, animal blood, whereas grazing animals derive all the necessary nutrients from plants. The nutrient value of pastures may be enhanced with the introduction of specific plant species- and the introduction of medicinal plants -such as fennel or milk thistle- may eliminate or reduce the need for antibiotics. He spoke of the value of a pasture-based system on sustainability- with a reduction of negative impact on the environment – air, water, soil.

14th presentation
Kumar Venkitanarayanan, DVM, PhD
Potentiating the Efficacy of Antibiotics against Multi-Drug Resistant Bacteria Using Plant Molecules

Salmonella Typhimurium DT 104 (DT) has become a major public health problem due to multi-drug resistance (ampicillin, chloramphenicol, streptomycin, sulfonamides and tetracyclines). Since cattle, pigs and poultry are a reservoir for DT, people may become exposed to DT through the food supply. Hence there is a need to develop interventions to control DT in food animals. Dr. V. described a study to investigate the efficacy of plant-derived antimicrobials (PDA) such as resorcylic acid, carvacrol, thymol and eugenol or their combination for increasing the sensitivity of DT to five antibiotics. In addition, the authors also wished to delineate the potential mechanisms for enhancement of antibiotic sensitivity. Results indicate that these natural molecules both individually and synergistically increased the sensitivity of DT towards the antibiotics and may have a potential use for DT control in food animals.

15th presentation
Steven M. Kappes, Ph.D.
An Overview of USDA's Activities Related to Antibiotic Resistance; Criteria to Consider in Evaluating Alternatives to Antibiotics in Food Animal Production

Antibiotic resistance is a complex problem that requires multiple solutions. The USDA plan to address AMR includes:

- Surveillance – on animal health (NAHMS), antimicrobial use (APHIS), and resistance prevalence and distribution: NARMS, APHIS, ERS (Economics of antimicrobial use),
- Management & technology
- Education & training veterinarians and producers on judicious use
- Prevention & Control: One Health Initiative; identification of factors to reduce transmission of resistant pathogens in veterinary, agriculture, and aquaculture; and formulation of best practices

A large potential to reduce the need of antibiotics exists and could be exploited by more research and development in the areas of food safety (processing technologies) and on antibiotic resistance and alternatives to antibiotics in animal health, specifically:

- the ecology of antimicrobial resistance in farm animals and the environment
- the host’s immune system – to develop effective vaccines and biotherapeutics and/or enhance vaccine efficacy
• genome sequencing of major food animals to identify animals with reduced susceptibility to specific diseases
• Molecules of the innate immune system
• Prebiotics and probiotics
• Natural products- vit. D for mastitis
• Bacteriophage, bacteriophage lysins.

The adoption of management practices may also aid in disease prevention by reducing stress and enhancing biosecurity. All of the above together with diagnosis, vaccination and interventions to reduce pathogenic load on food via antimicrobial treatments and lysins are alternatives to consider in lieu of antibiotics in food animal production.

16th presentation
Steven L. Solomon, MD
Prevention, Control and Treatment of Infectious Disease in Animals: The Role of Surveillance

Public health surveillance is the systematic collection, analysis and dissemination of health data to inform program planning, implementation and evaluation. The measure of success is in the outcome -- how well surveillance can be used to prevent and control disease. For the prevention and control of antimicrobial resistance, the goals of surveillance are:

• Describe scope and magnitude of problem
• Identify early the emergence of new resistance
• Monitor (ongoing) spread of antimicrobial resistance
• Evaluate effectiveness of prevention and control measures
• Monitor antimicrobial use
• Enable predictive modeling of emergence and spread

Surveillance of antimicrobial resistance is difficult to conduct and data difficult to analyze due to the complex interactions among different ecosystems –bacterial, animal, human and inanimate environments and the continual changes wrought upon these ecosystems by the use of antimicrobials. Monitoring the use of antimicrobial agents is a critical to combating antimicrobial resistance and is considerably more difficult to implement on both a practical and a methodological basis. Nevertheless, surveillance can provide valuable data-- snapshots of current state and evidence of trends. Electronic records have the potential to improve surveillance capacity.

In the U.S., animal data sources are less developed than human data sources. (see chart of data types for human & animal health, p.3 slides). The Federal government operates several surveillance systems (see presentation of Dr. Kappes): incidence in humans, prevalence of antimicrobial resistant bacteria in food animals and retail meat, as well as antimicrobial use in select settings.

17th presentation
Martin Wierup, PhD, Dipl. ECVPH, Dipl. ECPHM
Strategies and policies in Scandinavia and EU for withdrawal of antimicrobials for growth promotion (AGP) and to further reduce their need for disease control

The withdrawal of AGPs (1995-99) in food animal production resulted in a significant reduction in the amount of antimicrobials used in animals in Sweden (65%), Denmark 45%), Norway (42%), and Finland (27%). In Denmark, there was a dramatic reduction in the animal reservoir of enterococci resistant to AGPs. WHO's assessment in 2002, together with other studies, revealed the following findings in Denmark:

• Decrease in feed efficiency in broiler production largely offset by cost savings in AGP
Temporary enteric diseases and decrease in growth rate with little to no negative effect noted in finisher production; 2010 studies indicate no long-term negative impact on swine production. (Aaerstrup et al. Am. J.Vet. Res. 2010 July 71(7):726-733)

Total cost from birth to slaughter per pig was approx. one US dollar.

Antimicrobial usage per kg of pig produced decreased by 50% (1992-2008); AGP ban 1995-1999

In addition, a decrease in antimicrobial therapeutic use was seen in Norway and Sweden in 2003, while in Denmark usage was the same as the year prior to termination. In 2012, only 28% of broiler producers used any antimicrobials. A continuous focus on biosecurity and disease prevention can reduce usage further. The Netherlands has the goal of reducing usage in farm animals by 50%

The withdrawal of growth promoters was accompanied by disease prevention efforts together with a focus on judicious use of antimicrobials. The following prevention strategies were utilized in Europe:

- Disease surveillance
- Monitoring: use of antimicrobials and resistance
- Education: farmers, employers and veterinarians
- Guidelines
- Batch production – “all in all out”; batch farrowing & raising of pigs – simple, large positive effect
- Biosecurity: cleaning & disinfection between batches (Sweden/EU); in US, once/year at most!
  - Sweden organized control of Salmonella in broiler production since 1970 with antimicrobials (apart from coccidiostats) used in 6 of 3185 broiler flocks, each flock consisting of 20-30, 000 birds (2011);
  - Reported human cases of salmonellosis were halved in Europe from 2006 to 2010 (197,000 to 99,000).
  - Low prevalence of Salmonella in both broiler and swine production in Scandinavia
- No economic incentive for prescribing antimicrobials

In Sweden, risk assessments are used to identify major hazards and guide actions regarding food and feed safety. Baseline studies, harmonized testing and results are reported to all Member States. EFSA (European Food Safety) is the Central agency in Europe, which provides scientific advice on existing and emerging risks.

Antimicrobial resistance is monitored and more needs to be done in monitoring antimicrobial use in animals. Thus far, 10 Member States provide this data, the analysis of which reveals a wide variation in usage between countries (8 – 188 mg/kg animal body weight), with Norway (lowest), Sweden, Denmark and Finland at the low end, and the Netherlands (highest), France and the U.S. at the high end (Grave et al. 2010).

Economic significance of disease prevention in swine production: the time from birth to slaughter is reduced by 30 days without AGP – 150 days, 180 days in conventional production, using SPF (Specific Pathogen Free)* and well-implemented batch production.

Incentives for using prevention strategies are:

- Improve production economy and sustainability
- Avoid further ban on antimicrobial use in animals
- Gain consumer trust and demand

18th presentation

* As related in an e-mail from Martin Wierup: SPF is a system introduced in Sweden 15-20 years ago, irrespective of the AGP ban, in which the “first generations of animals are born by caesarian section and then brought up normally in farms but with high biosecurity. They are free from most common respiratory and enteric infections, and therefore can grow much faster. Batch production, introduced at the time of the AGP ban, can, when well-implemented, give the same magnitude of weight gain.”
Steve Gilman
The Organic Farming Alternative to Antimicrobial Use in the Management of Livestock

NOFA- Northeast Organic Farming Association, established in 1971, is one of the oldest grassroots, organic farming organizations in the U.S. with seven independent state chapters totaling 5,000 members (diverse). NOFA has media outreach to 20,000 food system-aware citizens in the Northeast.

Organic practices and standards prohibit the use of antibiotics in livestock management. USDA’s National Organic Program has developed strict standards that allow the use of antibiotics only to treat sick animals. If an antibiotic is required, that animal cannot be represented or sold as organic. Further use of sub-therapeutic doses of antibiotics or other drugs for growth promotion/production purposes are prohibited.

Organic production and standards focus on disease prevention and underlying causes and include:
- Beneficial management practices
- Proper nutrition and effective sanitation (use of manure in feed formulations is prohibited)
- Prohibit overcrowding
- Allow animals access to the outdoors: pasture and direct sunlight
- Choice of genetically diverse breeding stock (naturally less susceptible to disease)
- Quarantine incoming stock
- Maintain appropriate environment for specific animal species
- Certified organically grown- without synthetic fertilizers, GMOs, herbicides, pesticides
- Meat processed in certified facilities
- Organic farms are certified annually by USDA and 3rd party agents

Steve Gilman cites public health study indicating that withdrawing antibiotic use from large-scale poultry farms can result in immediate and significant reductions in antibiotic resistance for some bacteria (Enterococcus faecalis, Enterococcus faecium) (Aug. 10, 2011).

19th presentation
Diane H. Kull
Food Animal Production without the Use of Sub-Therapeutic Antibiotics

Applegate, founded in 1987 by Stephen McConnell, is a company dedicated to the prudent use of antibiotics to maintain efficacy for human medicine. Their standards include:
- No antibiotics,
- High quality feed ingredients without animal by-products (100% veg. diet)
- Natural probiotics to boost digestive health
- Adequate space to raise animals
- Environmental enhancements to reduce stress and boredom
- Science-based improved production practices
- Mandatory annual farm audits.

Applegate sources from 1000 farm suppliers who produce pork, poultry and beef from livestock raised without antibiotics. Diane cited January 2009 USDA report that the economic and production benefits of antibiotics in animal feed can be largely achieved by improved cleanliness of animal houses and improved testing for diseases. Although prevention/management practices employed by Applegate can cost more than conventional farming (see above practices), consumers are becoming increasingly aware and willing to pay more for antibiotic-free products from livestock raised humanely. Double digit growth continues over 25
years, despite the economic downturn in the US. Diane maintained that 75% of Americans want the government to restrict the use of antibiotics on farms.

Perceived barriers to growth are:
- Supply of “no antibiotics used” protein
- Lack of education on antibiotic-free farming: agricultural colleges, conventional farming families
- Myth that raising antibiotic-free meat is not scalable.

20ᵗʰ presentation
Sean B. Cash
Incentives for Antimicrobial Reduction: The Role and Limits of Consumer Information

The use of sub therapeutic doses of antimicrobials in food animal production poses economic issues characterized by high external costs of antimicrobial resistance and asymmetric information between producers and consumers. External costs to society are often underestimated. Use of antimicrobials – economic benefits accrue to the producers One way to overcome the asymmetry and promote voluntary consumer reductions in purchases of meats produced with antimicrobials is through certification and labeling schemes, e.g., “USDA organic” and “no antibiotics” labeling. Costs of verification and certification are typically paid by the consumer, covered through price premia. More labeling can put more pressure on industry if non-use becomes a new social norm, and can increase consumer awareness (and set new norms) of existing production processes, especially regarding organic standards. Despite the evidence that consumers are willing to pay more for antibiotic-free meat – this action is insufficient protection against the threat of antimicrobial resistance and is not a substitute for tighter, mandatory industry standards. Consumers undervalue risk of non-linear processes of antimicrobial resistance.