Antibiotic Resistance Mitigation: a Complicated Issue Begging for Targeted Investigation

Taking on antibiotic resistance calls for an integrated strategy that involves properly assessing risks and coordinating research and mitigation efforts

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The rapid emergence of antibiotic-resistant pathogens has major public health and social impact. In the past decades, the extensive research on the correlation between the use of antibiotics in human and veterinary medicine, food animal production, as well as other agriculture applications and the development of resistance in human and foodborne pathogens has already led to several government policy changes in both European Union and the United States. However, significant scientific gaps remain in antibiotic resistance (AR) and hinder the development of effective mitigation. Antibiotic-resistant bacteria were found prevalent not only in various food products, environment samples, but also in hosts without the history of direct exposure to antibiotics [H. H. Wang, 267–281, *in* L. Jaykus, H. H. Wang, and L. Schlesinger (ed.), Foodborne Microbes: Shaping the Host Ecosystems, ASM Press, 2009]. The potential impact of commensal bacteria across the food, host and environmental ecosystems on AR origination, dissemination, and persistence has just become recognized by the scientific community. It is particularly important to realize that once resistance derived in pathogens, it can be much more difficult to get rid of. On the other hand, the emergence of AR in commensal bacteria may serve as an early and more accurate indication for the resistance status and the potential trend in microbial population, which is critical for proper risk assessment and targeted mitigation (H. H.Wang, Alliance for the Prudent Use of Antibiotics, http://www.tufts.edu/med/apua/news/press_release_9–13-10.shtml, 2009).

Following the ASM press release "Antibiotics in Our Food Chain" (http://www.eurekalert.org/pub_releases/2007–05/asfm-rgi051707.php, 2007), and ASM general meeting symposia "Impact of Food Chain on Antibiotic Resistance in Humans" (2007) and "Foodborne Microbes: Shaping the Host Ecosystems(2008), USDA-CSREES and The Ohio State University cosponsored the conference on "Food Safety and Public Health Frontier: Minimizing Antibiotic Resistance Transmission through the Food Chain" in April 2009, which brought together experts from academia, industry, and federal agencies to provide a balanced and scientific review on AR. More than 20 invited senior experts shared their most up-to-date discoveries

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and visions on AR management through oral presentations. Close to 80 expert attendees participated in the conference discussion. It is the consensus view of the conference organization committee that systematic studies for a comprehensive understanding, both at macroscopic and microscopic levels, of AR connected to the food chain, is central to design targeted and integrated intervention strategies for effective mitigation.

The following approaches are recommended that proceed incrementally throughout the food chain, so that multiple targeted interventions along each link of the chain can be combined, yielding the net result that will minimize and contain antibiotic-resistant bacteria and resultant human illness. It is also recognized that because of the interactions among microbial ecosystems, a collaborative effort from the government, academia, and industry, involving not only professionals in medicine, veterinary preventive medicine, food science and agriculture, and public health, but also the pharmaceutical, agriculture, and aquaculture industries, as well as the general public, is essential for targeted mitigation.

Fundamental studies at the ecosystem level are needed to (i) develop novel experimental and systematic approaches and systematically investigate the AR ecology such as main resistance gene reservoirs and key microbial players within the ecosystems, at and between various links in the food chain from farm to table, including pre- and post-harvest environment (agriculture and aquaculture farms, surrounding soil, air and water, processing, transportation, storage, retail chain, etc.), raw and processed foods, as well as animal and human hosts; (ii) reveal the impact of natural and implemented factors (such as the application of antibiotics, compost, processing treatment, etc.) including dosage effect on the evolution and mitigation of AR in the corresponding ecosystems.

Fundamental studies at the individual microorganism (both pathogen and commensal) level are needed to (iii) reveal molecular mechanisms involved in AR origination, dissemination, persistence and environmental fitness as related to the food system, and (iv) investigate the impact of natural and implemented factors on the evolution and persistence of AR in such organisms as well as ecologically relevant bacterial species.

Developing effective mitigation strategies and outcome measurements by pursuing the following directions: (i) identify critical control points for AR based on sophisticated and ecological measures and risk assessment outcomes, and develop and implement agriculture, aquaculture and industrial practices to minimize and contain the spread and persistence of AR in the pre- and post-harvest food environment, products and host ecosystems; (ii) conduct studies with a focus on disease prevention and biosecurity, such as developing vaccines or alternatives for subtherapeutic uses of antibiotics in animal production; (iii) develop and implement integrated research, education, and outreach programs engaging academic, government agencies, industry and consumers including the lay public for effective mitigation; (iv) design and implement studies to measure the impact or effect of potential interventions on existing AR at the macro or micro level.

Information from the recommendation has since been incorporated into 2010 USDA-NIFSI document and USDA-ARS food safety strategic plan. Because of the inseparable relationship of microbes circulating among the environment, food and hosts, a broad involvement of professionals with expertise in food, environmental, and medical microbiology, veterinary preventive medicine and public health, along with proper multiagency support to the lead groups are greatly needed to address the issue.