# Enhancing Practitioner Knowledge about Antibiotic Resistance: Connecting Human and Animal Health

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### **SUMMARY**

The development of antibiotic-resistant bacteria is associated with increases in mortality, morbidity, length of hospitalization, and health-care costs (6). While the medical community and the general public are becoming increasingly aware of this association, widespread strategies are needed to prevent the spread of antimicrobial-resistant organisms. This article discusses the proceedings from a roundtable convened in Washington, D.C. to develop a collaborative dialogue among human and animal health communities on antibiotic resistance. A summary of the proceedings includes key recommendations for stakeholders to institute strategies for preventing the spread of antimicrobial-resistant organisms.

# **OVERVIEW**

Public health stakeholders need to work together to effectively manage the global public health threat of antibiotic resistance. The International Food Information Council (IFIC) Foundation convened a roundtable in Washington, D.C. to develop a collaborative dialogue among human and animal health communities. This unique roundtable consisted of representatives from medicine, veterinary science, public health, government agencies, and food safety. The group discussed ways to improve public understanding, knowledge gaps, strategies for science-based outreach, and mechanisms for reaching consumers and the media. The following is a summary of the proceedings, which includes key recommendations for stakeholders to institute strategies for preventing the spread of antimicrobial-resistant organisms.

# BACKGROUND

Penicillin was first used in the treatment of infections in the early 1940s. Within a year, the first penicillin-resistant *Staphylococcus aureus* was identified. Today, 2 million people in United States are infected each year with an antibioticresistant pathogen, and approximately 23,000 die as a result of antibiotic-resistant infections (3). Another 250,000 suffer from *Clostridium difficile* infections, an adverse event primarily due to antibiotic use (3). The primary contributor to antibiotic resistance is the use and misuse of antibiotics in humans and in food-producing animals and crops. Data show that in human health, 50 percent of antibiotic prescriptions are inappropriate, placing unnecessary pressure on bacteria to become resistant (2). Worldwide data on *Streptococcus pneumoniae* infections reveal that the countries with the highest use of penicillin have the highest penicillin resistance rates (1). An increase in bacterial resistance is associated with an increase in morbidity and mortality (1).

The public health community is also monitoring the risk of antimicrobial resistance caused by use in food-producing animals. Some speculation has perpetuated the notion that 80 percent of antibiotics sold in the United States are used in the agriculture industry for growth promotion and infection prophylaxis. However, this is simply not true (11). Regardless of the amount, food-producing animals that receive antibiotics must undergo a specified withdrawal time for the drug to be eliminated from the animal prior to it entering the food supply. Enhanced monitoring efforts currently under way will provide a more accurate indication of the amounts being administered in agriculture.

In addition to food-producing animals, imported food poses another threat. The United States imports approximately 20 percent of its food each year, including approximately 96 percent of fish, 10 percent of beef, 26 percent of fresh fruits,

\*Author Correspondence: Phone: +1 202.296.6540; Fax: +1 202.296.6547 E-mail: flood@ific.org 20 percent of fresh vegetables, and 41 percent of tree nuts (7). The National Academy of Sciences finds that over 110 countries do not yet have relevant legislation concerning the appropriate conditions for the importation, manufacture, distribution, and use of veterinary products, including antimicrobials (21).

This global issue will require worldwide commitment to mitigation strategies. Without a collaborative effort, the future U.S. food supply, with its international sources, will likely be an increased source for disseminating antibiotic-resistant foodborne pathogens. No one can completely avoid the risk of antimicrobial resistance, and without identifying strategies for judicious antibiotic use, the problem stands to become increasingly severe. Developing effective strategies to minimize resistance, accounting for all antibiotic uses, is critical.

# DISCUSSION

The roundtable participants discussed myriad strategies for addressing antibiotic resistance. These strategies are discussed and followed by proposed recommendations.

### Antibiotics as a precious resource

Antibiotics should be considered "global public goods" critical to human health. Part of the fear concerning antibiotic resistance is the possibility of returning to a preantibiotic era, especially because the new drug development pipeline has largely dried up. Antimicrobial stewardship efforts need to focus on strategies to minimize the risk of resistance in order to protect antibiotics, ultimately benefitting public health.

This issue is plagued by misinformation and one-sided arguments. Every use ultimately contributes to resistance, whether it is in humans, animals, or crops (20). The World Health Organization (WHO) declared antibiotic resistance to be a worldwide problem. It would be most effective if all stakeholders would own their share of the problem of mitigating growing resistance. In order to succeed at tackling this complex problem, all stakeholders should display credibility, balance, trust, and transparency.

# Crafting a message

Key stakeholders need to communicate information about antibiotic resistance that is simple, credible, balanced, and tailored to help consumers make informed decisions. Messages should be accessible to lay audiences. Real-world examples (e.g., eliminating antibiotic prescriptions for ear infections) can also demonstrate relevance to broad audiences.

With any contentious issue, there will always be a small number of extremists committed to their point of view, but most people reside somewhere in the middle, eager for knowledge and anxious to do what is best for themselves, their children, and their communities. Messages should target individuals who fall in the middle of the belief spectrum. Roundtable participants suggest that information about antibiotics should highlight four main themes:

- 1. Antibiotics are critical and precious and need protection. Antibiotics contribute greatly to our increased lifespan and quality of life.
- 2. Antibiotics are an important tool for the treatment and prevention of disease in both humans and animals. Healthy animals lead to a healthful food supply. There will likely always be some appropriate antibiotic use in the food supply. As in human health, animal antibiotics will be used at certain times in agriculture.
- **3. Antibiotic use leads to antibiotic resistance.** All uses, whether in the context of human medicine, veterinary medicine, or agriculture, exert selection pressure.
- 4. With antibiotics, less is better. Antibiotics must be used cautiously. Each usage increases the long-term risk borne by future generations. The balance of risk vs. benefit must be an ongoing dialogue among all stakeholders.

### Credible and trustworthy messengers

Messengers must be neutral and trustworthy to gain the public's trust. Organizations such as the American Medical Association (AMA), American Public Health Association (APHA), and the American Veterinary Medical Association (AVMA) are all appropriate bodies to disseminate information to human and animal medical communities. The roundtable participants agreed to build stronger messages to connect such entities to interested food organizations already working on these issues, such as Cargill and McDonald's. Drug companies that manufacture antibiotics also would be important stakeholders to engage. Trusted government agencies, such as the U.S. Centers for Disease Control and Prevention (CDC), have already identified medical use concerns (3).

Additional stakeholders could include the Pediatric Infectious Disease Society (PIDS), the Infectious Disease Society of America (IDSA), and the Society for Healthcare Epidemiology of America (SHEA). The Pew Research Center and the Natural Resources Defense Council (NRDC) may also represent potential partners. State and county public health leadership, people in community/grassroots efforts, and faith-based organizations can exert local influence. Supermoms Against Superbugs, a group that has advocated against agricultural use of antibiotics, is another potential collaborator.

# The role of social media

At present, Facebook is the most-used online social network for adults. In 2015, 62% of the entire adult population of the U.S. used Facebook (16). Twitter and blogs are other important platforms for discussion of two sides of an issue. Accordingly, conversations should discuss antibiotic resistance on and offline. Dr. Natasha Burgert, Dr. Kevin Pho, and others regularly contribute to online discussion groups like "KevinMD.com" where stories and insights are shared with and among members of the human health and medical community. The site features well-read blogs to discuss medical issues with lay audiences. Forming partnerships with such writers and encouraging new groups to establish their own platforms to dialogue with lay audiences offer other avenues for spreading messages.

# The food industry

Companies must manage animal production health in ways that minimize antibiotic use. However, although animal health (including immunization and good hygiene/ sanitation) is crucial, it isn't the total picture. Judicious use of antibiotics early in an animal's life can reduce the need for heavy antibiotic use later on. The food industry might consider a certification for products from companies that use antibiotics responsibly. Some large corporations are already setting the standards, and they may drive a certification process. The agricultural industry should continue to make educational videos. For example, in February 2011, Cargill aired a video on The Oprah Show detailing the processing of cattle in the beef industry, and viewer response was overwhelmingly positive (18).

The food industry must consider all uses of antibiotics, including in grain crops and in the fermentation process of producing ethanol, where antibiotics are used to control overgrowth. Byproducts of fermentation are used in cattle feed. An estimated 30–50 percent of the diet of cattle may have low levels of antibiotics in it as a result of antibiotic use in fermentation processes (14). In addition, stakeholders must consider the liquid waste produced by these processes that wind up in streams.

# Medical professionals

While hospitals generally recognize the need for antimicrobial stewardship programs, there are many pressures working against such programs. For example, health care providers are sometimes compelled to prescribe antibiotics to increase patient satisfaction (8). Other factors could include lack of clinician knowledge or time, or their attitudes and beliefs (8). As professionals in the field, the roundtable participants stressed the need to improve surveillance of prescribing habits in order to identify and remedy overuse and to track prescribing practices of all health care professionals and provide individual feedback.

#### Researchers

Studies should develop biomarkers to identify when to stop antibiotic treatment in patients, thereby using the minimum amount needed. Roundtable participants also suggested that new rapid diagnostic tests are needed to quickly identify the pathogen responsible for the disease we need to treat. These tests would lead to targeted (rather than broad-spectrum) antibiotic treatment.

The CDC's National Antimicrobial Resistance Monitoring System, Enteric Bacteria (NARMS) is a public health surveillance system that tracks antimicrobial resistance in foodborne and other enteric bacteria (4). NARMS helps monitor changes in antibiotic resistance. It would also be useful for hospitals to have more NARMS-type tests. In addition, while resistance rates in local own medical centers are known, resistance typically cannot be monitored by region. CDC provides some state profiles, but data on resistance by smaller regions could impact prescriber behavior.

Next, waste management remains a largely unexplored question. Both animals and humans may be contributing to antibiotic resistance by way of excreted metabolites of antibiotics. It is important for researchers to help us understand the extent of this underappreciated source of resistance.

The National Institute of Health's (NIH) National Institute of Allergy and Infectious Diseases (NIAID) is an important stakeholder in the research endeavor. Many clinical trials are funded by industry, and there is a pervasive attitude that such research findings may be tainted (17). The roundtable recognizes that this attitude is counterproductive, while also recognizing that NIH and its various institutions such as NIAID need to play key roles.

# Policymakers

Developing strategies that address the National Action Plan for Combatting Antibiotic Resistant Bacteria is paramount for policymakers, given the national and global (WHO) strategies that are in place or being developed. Developing safeguards is a key aspect of our strategy to protect antibiotics. The FDA has maintained a central role in the elimination of use of antibiotics for growth promotion in food animals. In a 2010 congressional testimony, FDA Director Dr. Janet Woodcock for the Center for Drug Evaluation and Research reported, "Preserving the effectiveness of current antimicrobials and encouraging the continued development of new ones is vital to protecting human and animal health against infectious microbes" (9). The report led to U.S. FDA Guidance #209, which established two voluntary principles (10):

- Use of medically important antimicrobial drugs in foodproducing animals should be limited to uses considered necessary for animal health.
- Use of medically important antimicrobial drugs in food-producing animals should include veterinary oversight/consultation.

This guidance led to FDA Guidance #213, establishing procedures for voluntarily phasing out growth promotion indications for medically important antibiotics in alignment with Guidance #209, and proposing changes to the Veterinary Feed Directive (VFD) regulation (12). As a result, the use of antibiotics in animal feed for growth promotion has been eliminated. The FDA could play a role in helping consumers identify food companies using antibiotics responsibly. Worldwide, policy makers can work to demand regulatory oversight of food production.

# Consumers

Many consumers in the United States today are not touched by infectious disease directly and do not think of infectious diseases as a problem anymore. Consumers should be aware that part of the concern about antibiotic resistance is the possibility of returning to a pre-antibiotic era, where many infectious diseases were untreatable. In order to personally reduce their contribution to that possibility, consumers can use medically prescribed antibiotics responsibly. That means not demanding antibiotics from their health care provider when these drugs are not indicated. It means taking antibiotics, if prescribed, as prescribed, and not sharing them.

### Handle food safely

Consumers should do everything reasonably possible to reduce microbial contamination when handling food in the home. Safe food handling includes washing hands and utensils, separating cooked from raw foods, cooking to a safe internal temperature (using a food thermometer to assure it has reached the proper temperature), and storing food quickly and properly. These strategies will help reduce the risk of foodborne illness. Reducing foodborne illness means fewer humans will need to be treated with antibiotics, further reducing use.

### Become informed about antibiotic-free meat

According to the 2015 IFIC Foundation Food & Health Survey, approximately one-quarter, or 25 percent, of Americans regularly purchase foods labeled as "raised without antibiotics" (13). However, most people agree that it is appropriate to use antibiotics to treat a sick cow or chicken, and when companies produce antibiotic-free meat, it means they use no antibiotics. There is even more controversy in using antibiotics for disease prevention, both in food animals and humans. However, if one administers a small dose of antibiotics to chicks in the first week of life, one can avoid larger doses of antibiotics to treat infected chickens later on. The roundtable concluded that a complete elimination of antibiotic use in animals intended for food is likely too extreme to serve the ultimate purpose of reducing the risk of antibiotic resistance. Some antibiotic use to treat and prevent disease in agricultural animals is appropriate. However, current food labeling practices make it almost impossible for consumers to identify companies attempting to use antibiotics responsibly.

# Place pressure on industry

Companies are addressing the issue of antibiotic use in meats because consumers are demanding it (5, 13). When consumers demand meat from animals raised without antibiotics, companies will meet the demand.

#### Buy foods produced in the United States

Whenever possible, consumers should opt to purchase foods produced domestically. Domestic food continues to

be safe, abundant, and high in quality. Some, although not all, imported food products are less likely than domestic products to be produced in ways that will reduce or minimize the global threat of antibiotic resistance (19).

### RECOMMENDATIONS

Given today's environment and efforts currently under way to address antibiotic resistance, such as the President's Task Force on Antibiotic Resistance, our roundtable proceedings reflect a necessary and critical first step toward raising awareness and effecting change. Our goal is that readers will go to their respective professional organizations and affiliates and spread the word, helping to identify strategies within a community to combat antibiotic resistance.

Leading organizations such as IFIC Foundation could form an interdisciplinary task force to engender more discussion among stakeholders. It will be important to enlist the aid of influential food producers already proactive on food safety issues. We suggest including an animal health company that takes a stand against antibiotics for growth promotion in food animals but encourages their use to treat sick animals. Medical organizations in addition to the veterinary and public health communities should also be included. The goal of this task force would be to identify ways to drive change. The hope is that the representatives from multiple interested communities can galvanize around a strategy and carry that message to their communities. These stakeholder organizations, along with IFIC, could also facilitate engagement with the One Health initiative.

The One Health Initiative is a worldwide strategy for expanding interdisciplinary collaborations in all aspects of health care for humans, animals, and the environment (15). The goal of this platform is to develop equal, all-inclusive collaborations between physicians, osteopaths, veterinarians, dentists, nurses, and other scientific-health and environmentally related disciplines. One Health is a venue that can foster conversations about antibiotic protection among the many users and stakeholders involved.

Another possibility is for IFIC to develop an action plan on the basis of which others might act. IFIC might convene more small roundtables. This dynamic area of science can benefit from ongoing dialogue of all kinds. It is important for IFIC to support long-term collaboration with the CDC's NARMS program, as we must carefully track trends in resistance. It is urgent for stakeholders to begin by taking whatever small steps they can. The medical and agricultural communities are robust and will adapt to the changes we need to combat antibiotic resistance.

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# REFERENCES

- Albrich, W. C., D. L. Monnet, and S. Harbarth. 2004. Antibiotic selection pressure and resistance in *Streptococcus* pneumoniae and *Streptococcus pyogenes*. *Emerg. Infect. Dis.* 10:514–517.
- Bartlett, J. G., D. N. Gilbert, and B. Spellberg. 2013. Seven ways to preserve the miracle of antibiotics. *Clin. Infect. Dis.* 56:1445–1450.
- Centers for Disease Control and Prevention (CDC). 2013. Antibiotic resistance threats in the United States, 2013. Available at: http:// www.cdc.gov/drugresistance/threat-report-2013/. Accessed 3 June 2016.
- CDC. 2015. National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS). Available at: http://www.cdc. gov/narms/. Accessed 3 June 2016.
- Consumer Reports. 2012. Meat on drugs. Available at: https://www.consumerreports. org/content/dam/cro/news\_articles/ health/CR%20Meat%20On%20Drugs%20 Report%2006-12.pdf. Accessed 1 June 2016.
- Cosgrove, S. E. 2006. The relationship between antimicrobial resistance and patient outcomes: Mortality, length of hospital stay, and health care costs. *Clin. Infect. Dis.* 42:S82–89.
- Department of Agriculture (USDA). 2015. U.S. food imports. Available at: http://www. ers.usda.gov/data-products/us-food-imports. aspx. Accessed 30 May 2016.
- Ebert, S. C. 2007. Factors contributing to excessive antimicrobial prescribing. *Pharmacotherapy* 27(10P2):126S–130S.
- Food and Drug Administration (FDA). 2010. Promoting the development of antibiotics and ensuring judicious use in humans. Avail-

able at: http://www.fda.gov/NewsEvents/ Testimony/ucm214913.htm. Accessed 1 June 2016.

- Food and Drug Administration (FDA). 2012. The judicious use of medically important antimicrobial drugs in food-producing animals. Available at: http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ UCM216936.pdf. Accessed 30 May 2016.
- Food and Drug Administration (FDA). 2013. FDA cautions in interpretation of antimicrobial resistance data. Available at: http://www. fda.gov/AnimalVeterinary/NewsEvents/ CVMUpdates/ucm348794.htm. Accessed 30 May 2016.
- 12. Food and Drug Administration (FDA). 2013. Guidance for industry: New animal drugs and new animal drug combination products administered in or on medicated feed or drinking water of food-producing animals: Recommendations for drug sponsors for voluntarily aligning product use conditions with GFI #209. Available at: http://www. fda.gov/downloads/AnimalVeterinary/ GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf. Accessed 1 June 2016.
- International Food Information Council (IFIC). 2015. The 2015 food & health survey: Consumer attitudes toward food safety, nutrition, & health. Available at: http://www. foodinsight.org/2015-food-health-surveyconsumer-research. Accessed 3 June 2016.
- Lowrance, T. C., G. H. Loneragan, D. J. Kunze, T. M. Platt, S. E. Ives, H. M. Scott, B. Norby, A. Echeverry, and M. M. Brashears. 2007. Changes in antimicrobial suscep-

tibility in a population of *Escherichia coli* isolated from feedlot cattle administered ceftiofur crystalline-free acid. *Am. J. Vet. Res.* 68:501–517.

- One Health Commission. 2016. One Health Commission. Available at: https://www.onehealthcommission.org/. Accessed 3 June 2016.
- Pew Research Center. 2015. The demographics of social media users. Available at: http:// www.pewinternet.org/2015/08/19/the-demographics-of-social-media-users/. Accessed 3 June 2016.
- Rowe, S., N. Alexander, F. M. Clydesdale, R. S. Applebaum, S. Atkinson, et al. 2009. Funding food science and nutrition research: Financial conflicts and scientific integrity. *Am. J. Clin. Nutr.* 89:1285–1291.
- Vallery-Mills, C. 11 November 2011. Cargill accepts a date with Oprah Winfrey. Available at: http://beefmagazine.com/cowcalfweekly/1111-cargill-oprah-winfrey. Accessed 2 June 2016.
- Van Boeckel, T. P., C. Brower, M. Gilbert, B. T. Grenfell, and S. A. Levin, et al. 2014. Global trends in antimicrobial use in food animals. *Natl. Acad. Sci. Pro.* 112: 5649–5654.
- 20. World Health Organization (WHO). 2014. Antimicrobial resistance: Global report on surveillance. Available at: http://apps.who.int/iris/bitstre am/10665/112642/1/9789241564748\_ eng.pdf?ua=1. Accessed 3 June 2016.
- 21. Zuraw, L. 28 December 2015. 2015 in review: Animal antibiotics. Available at: http://www. foodsafetynews.com/2015/12/2015-in-review-animal-antibiotics/#.V1H7Vecx8gt. Accessed 3 June 2016.

# **In Memory** Gary P. Jansen Franklin, Tennessee

We extend our deepest sympathy to the family of Gary Jansen who recently passed away. Mr. Jansen was a member of the Association since 1997. IAFP will always have sincere gratitude for his contribution to the Association and the profession.