White Paper

A One Health Approach to Antimicrobial Use & Resistance: A Dialogue for a Common Purpose

Information synthesized from Nov. 13-15, 2012, symposium in Columbus, Ohio: "A One Health Approach to Antimicrobial Use & Resistance: A Dialogue for a Common Purpose"

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EXECUTIVE SUMMARY

Antibiotics improve human, animal and plant health, and increase life expectancy.[1] While a majority of individuals acknowledge the positive role antibiotics play in the health of humans, animals and plants, the topic of antimicrobial resistance—when antibiotics can no longer cure bacterial infections[2]—is frequently misunderstood, misappropriated and polarizing.

Antimicrobial resistance occurs via three mechanisms, each requiring only minor changes in biochemistry: 1) Bacteria may possess enzymes that degrade antibiotics; 2) Bacteria may replace or alter the method through which the antibiotic enters the cell; and 3) Bacteria may alter the cellular target site of the antibiotic.[3] A historical look at antimicrobial resistance shows it is not a new phenomenon but existed before widespread use in human and animal medicine.

Antimicrobial resistance is not a black-and-white issue. Antimicrobial resistance is complex and is more than science and evidence. It is about politics, behavior, economics and conflicting opinions. And it is not merely a consequence of use; it is a consequence of use and misuse, with each community—animal health, human health and environmental health—responsible for antibiotic stewardship.

A significant amount of finger pointing regarding antimicrobial use and misuse has been aimed at animal agriculture. Since 2010, bloggers and media use 80 percent as a *de facto* number for antibiotic usage in animals. While animal agriculture does use antibiotics in the care and treatment of food animals, the statement that 80 percent of antibiotics in the United States is used in healthy animals is not accurate as it was deduced from comparing two sets of data that are not comparable.[4] The 80 percent figure demonstrates a different way antibiotic use is counted, with the estimates for animal use collectively were derived by an entirely different methodology than the estimate presented for human use.[5] In addition, 35 percent of the use the calculation attributed to animals are compounds not used in human medicine, thus minimizing potential interference with effectiveness of antibiotics used to treat human disease.

Use of antibiotics in food animal production is highly regulated by the U.S. Food and Drug Administration Center for Veterinary Medicine (FDA CVM). In addition, regulatory oversight provides assurance in the development of safe products. Education and training (e.g. livestock species Quality Assurance Programs[6,7,8,9,10] encourages producers to have a strong relationship with their veterinarians and provides guidance on the responsible use of antibiotics. Government surveillance and testing ensures that no harmful residues, as established by the FDA, enter the food supply.

On the human side, the discovery of antibiotics in the 1930s has allowed physicians to shift their patient care approach from diagnoses without means to intervene to a treatment-focused approach that saves lives.[11] To date, physicians have significant freedom to use antibiotics, and antibiotics are being used off-label, which can lead to inappropriate usages.[12] Given the societal value of antimicrobials, the diminishing effectiveness due to antimicrobial resistance, and the fact that 200 million to 300 million antibiotics are prescribed annually, the Infectious Diseases Society of America (IDSA)—which represents physicians, scientists and other health care professionals who specialize in infectious diseases—is taking steps to address antibiotic misuse through an antimicrobial stewardship program. The Centers for Disease Control has implemented a "Get Smart for Healthcare" program that focuses on improving antibiotic use in inpatient healthcare facilities, starting with hospitals, then expanding to long-term care facilities.[13]

Human medicine's focus on stewardship and other important areas is an action taken to lessen antibiotic misuse as uncovered in these studies: 1) Studies indicate that nearly 50% of antimicrobial use in hospitals is unnecessary or inappropriate;[14] 2) In another study, antibiotics were prescribed in 68 percent of acute respiratory tract visits – and of those, 80 percent were unnecessary according to Centers for Disease Control guidelines;[15] 3) In other surveys, 80% of physicians in the United States admitted to writing outpatient prescriptions for antibiotics when they thought it unnecessary because their patients adamantly demanded antibiotics.[16]

Antimicrobial use is not limited to animal agriculture and human medicine. Antimicrobials are also used in plant agriculture. Streptomycin has been utilized in plant disease management since the early 1950s.[17]Other antibiotics used in plant agriculture include oxytetracycline and kasugamuycin. While estimates from a U.S. Geological Survey and from the National Agricultural Statistics Service show that plant use of antibiotics is less than 0.5 percent of 22.6 million kilograms of annual U.S. production of antibiotics, antibiotic use in plant agriculture contributes to the antimicrobial resistance equation.

The scale and complexity of animal and human medical challenges embedded in a changing environment demand that those within the animal, human and environmental health fields move beyond the confines of their own disciplines and explore new organizational models for team science.
The time has come for those in animal health, human health and environmental health to disentangle the facts vs. perceived facts regarding antimicrobial resistance, separate people from problems and focus on creating mutually satisfying outcomes and interests. Finding common ground and reaching agreement is essential.

With animal, human and environmental health inextricably linked, one logical answer is to take a One Health approach. This approach would call for all to think in a much larger dimension and work toward improving and defending the health and well-being of all species by enhancing cooperation and collaboration between physicians, veterinarians, other scientific health and environmental professionals, and by promoting strengths in leadership and management to achieve these goals.

For strides to be made, leaders in animal, human and environmental health must find common ground. This is not about compromise where everyone gives up something. It's about suspending reactions, emotions and distrust; putting positions aside and interests first; and reaching consensus on the issue of antibiotic use and resistance. Reaching agreement must begin with the end in mind: improving health.

Background

The symposium *A One Health Approach to Antimicrobial Use & Resistance: A Dialogue for a Common Purpose* was developed by the National Institute for Animal Agriculture and conducted November 13-15, 2012, in Columbus, Ohio. The symposium was a continuation of discussions and sharing of information that began a year prior at NIAA's *Antibiotic Use in Food Animals: A Dialogue for a Common Purpose* symposium conducted October 26-27, 2011, in Chicago, Illinois.

The National Institute for Animal Agriculture (NIAA) is a non-profit, membership-driven organization that unites and advances animal agriculture: the beef, dairy, equine, goat, poultry, sheep and swine industries. NIAA is dedicated to furthering programs working toward the eradication of diseases that pose risk to the health of animals, wildlife and humans; promote the efficient production of a safe and wholesome food supply for our nation and abroad; and promote best practices in environmental stewardship, animal health and well-being.

The symposium was funded in part by Alltech, American Association of Veterinary Medicine, American Dairy Association Mideast, American Farm Bureau Federation, Animals for Life Foundation, Bayer, BEEF magazine, the Beef Checkoff, Bovine Veterinarian, DairyBusiness, Dairy Herd Management, Drovers, Merck Animal Health, Ohio Farm Bureau Federation, Ohio Soybean Association, Ohio Soybean Council, PBS+ Animal Health, Pfizer Animal Health, the Pork Checkoff, PORK magazine, The Ohio State University College of Veterinary Medicine, United Soybean Board, USDA/Veterinary Services and Validus.

Purpose and Design of the Symposium

An October 2012 Hart Research Associates and Public Opinion Strategies study, conducted on behalf of The Pew Health Group, found just one in four Americans (25 percent) have heard a great deal about antibiotic resistance, with another 33 percent have heard a fair amount. Additional findings showed that 81 percent view antibiotic resistance as being at least somewhat of a problem, and fewer than half indicated that antibiotic resistance is a "big problem." The same study also showed that those who have heard more about antibiotic resistance are more likely to see it as a big problem: 68 percent of people who have heard "a great deal" about antibiotic resistance say it is a big problem and 27 percent of those who have heard nothing at all say it's a big problem.[18]

While this recent study indicates that concerns regarding antibiotic use and antimicrobial resistance isn't viewed as a pressing issue across the spectrum, the consumers who view it as a "big problem" are vocal, gaining attention and turning to legislators to address their concerns. Documentaries such as "Meet Your Meat" and "Food Inc." and media proliferation where anyone can say or write anything, mix facts and inaccurate information and cause the issue to gain additional momentum amplified through social media creates an environment where constructive dialogue is difficult.

As a result of what they read and hear, U.S. consumers are placing more focus on what goes into their food. They deserve facts about human medicine and food animal use of antibiotics and the facts about antimicrobial resistance.

The problem is not an animal or human issue per se. It's about using the antibiotics as judiciously as possible in situations where they are needed.[19]

The 13 animal health, human health and environmental health scientists and other experts speaking at the symposium were asked to share the latest, science-based information so open and honest dialogues could occur. Through panel discussions, participants asked questions of the presenters to better understand the antibiotics use and resistance issue. Adding to the dynamics of the symposium were the four interactive small group discussions where symposium participants exchanged perspective to further dissect the issue and provided real-time input to questions posed by the moderator.

The end goal of the symposium was: 1) to obtain the scientific facts regarding antibiotic use within animal health, human health and environmental health; 2) to better understand the "how" and "why" antimicrobial resistance occurs; 3) to look at alternatives to antibiotics in agriculture; 4) lead and engage participants in open conversations; 5) to build relationships with other sectors and gain better understanding of other perspectives; 6) to begin to find common ground and formulate a path forward; and 7) focus on continuous improvement and commitment to long-term health.

Symposium Planning Committee Co-Chairs:
Leah C. Dorman, DVM, Ohio Farm Bureau Federation
Jennifer Koeman, DVM, MPH, DACVPM, National Pork Board

Planning Committee Members:
Leonard Bull, PhD, PAS, Professor Emeritus, North Carolina State University
James McKean, DVM, JD, Iowa State University
Nevil Speer, PhD, Western Kentucky University

Symposium Topics and Speakers

"One Health Approach to AMR and Use: A Dialogue for Common Purpose" – **Dr. Lonnie King**, Dean, *The Ohio State University College of Veterinary Medicine*

"An Overview of Antimicrobial Use"

- **"Antimicrobial Use in Veterinary Medicine Today and Tomorrow"** – **Dr. Ron DeHaven**, Executive Vice President, *American Veterinary Medical Association*
- **"An Overview of Antimicrobial Use in Human Health" – Dr. Kurt Stevenson**, Division of Infectious Diseases, *Wexner Medical Center, The Ohio State University*

"Antimicrobial Use in Plant Agriculture" – Dr. George Sundin, *Michigan State University*

"What is Antimicrobial Resistance? How Does it Develop? Where Does it Come From?" – Dr. Randall Singer, *University of Minnesota, College of Veterinary Medicine*

"Antimicrobial Resistance Surveillance in Hospital and Community-Issues for Human Population Medicine" **– Dr. Kurt Stevenson**, Division of Infectious Diseases, *Wexner Medical Center, The Ohio State University*

"The Impact of Public Health of Environmental Contamination with Antimicrobial Residues" **– Dr. Randall Singer**, *University of Minnesota, College of Veterinary Medicine*

"Sources, Sinks and Other Conundrums: The Ecology of Antimicrobial Resistance" – Dr. Stuart Reid, *Royal Veterinary College, University of London*

"Antimicrobial Resistance Surveillance"

- **"The National Antimicrobial Resistance Monitoring System" – Dr. Patrick McDermott**, *U.S. Food & Drug Administration, Center for Veterinary Medicine, Office of Research*
- **"A Pilot Study for Animal Sampling in NARMS" – Dr. Mary Torrence**, National Program Leader, Food Safety, *U.S. Department of Agriculture/Agricultural Research Service*

"Pharmaceutical & Livestock Industry Perspective of the Impacts of the Regulatory Environment"

- **"Animal Health and Antibiotic Research, Development, Stewardship and Perspective" – Dr. Rick Sibbel,** Director, U.S. Cattle, *Merck Animal Health*
- **"Antimicrobial Restrictions: Swine Industry Perspective" – Dr. Harry Snelson,** Director of Communications, *American Association of Swine Veterinarians*

"Antimicrobial Resistance: Research and Priorities" – Dr. Mary Torrence, National Program Leader, Food Safety, *U.S. Department of Agriculture/Agricultural Research Service*

"The Future of Antimicrobials—An Industry Perspective" – Dr. Richard Carnevale, **Vice President, Regulatory, Scientific and International Affairs**, *Animal Health Institute*

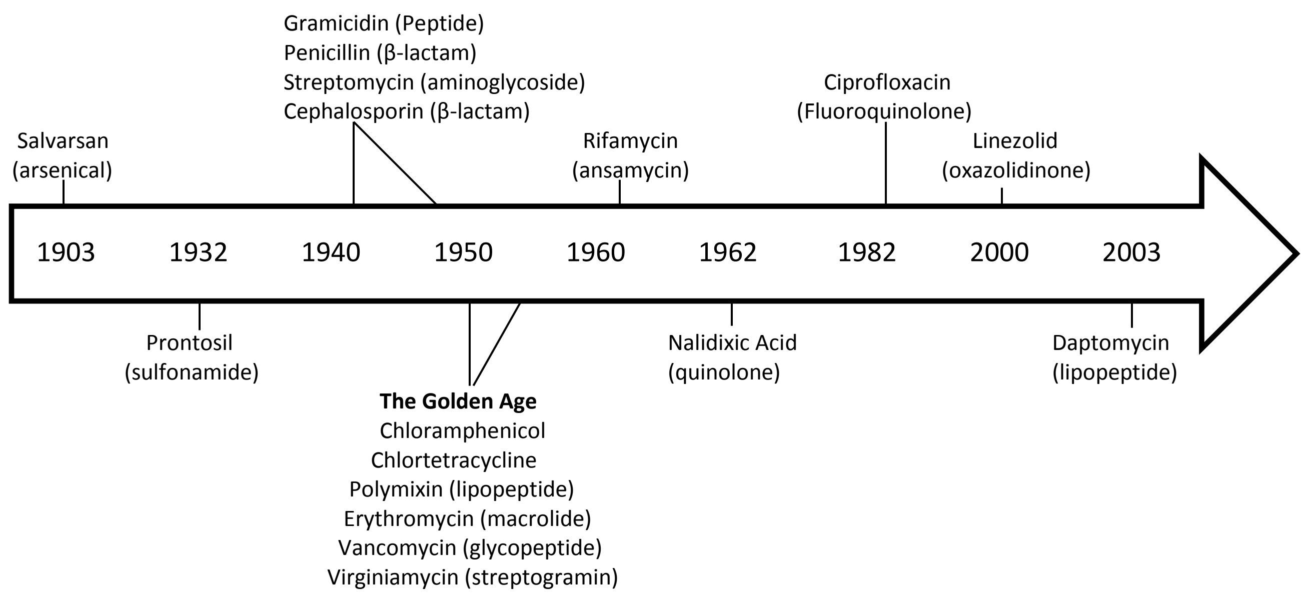
"Alternative to Antibiotics in Animal Agriculture" – Dr. Cyril Gay, Senior National Program Leader, Animal Production and Protection, *U.S. Department of Agriculture/Agricultural Research Service*

"Issues in Developing Alternatives to Antibiotics in Agriculture" – Dr. Aoife Corrigan, *Alltech Bioscience Center, Ireland*

PRESENTATION HIGHLIGHTS[20]

The search for antibiotics began in the 1800s with the growing acceptance of the germ theory of disease that linked bacteria and other microbes to the causation of a variety of ailments. The first antibiotic used in hospitals was in the 1890s but it later proved not to be effective. In the 1930s, a German chemist discovered Prontosil, the first sulfa drug, and in 1942 the manufacturing process for Penicillin G Procaine was invented by Howard Florey (1898–1968) and Ernst Chain (1906–1979).

Major classes of antimicrobials and the year of their discovery:[21]

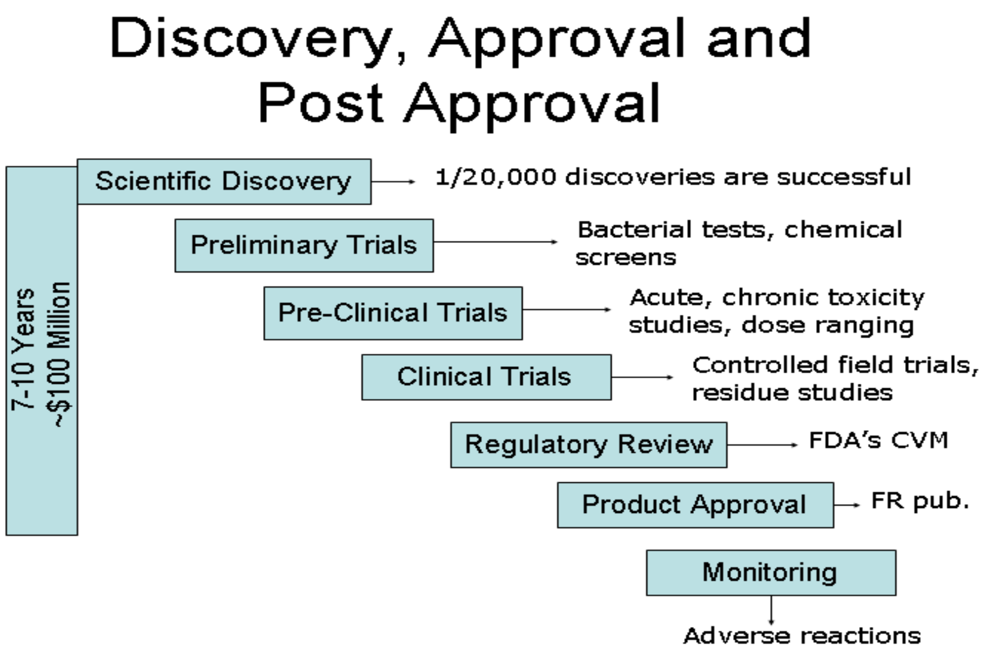


As more and more antimicrobials entered the market and have been used by human medicine and food animal medicine, the focus today has shifted to judicious antimicrobial use and the polarizing topic of antimicrobial resistance. These are not black-and-white issues.

Antimicrobial resistance is complex and is more than science and evidence. It's about politics, behavior, economics and conflicting opinions. And it's not merely a consequence of use; it's a consequence of use and misuse, with each community—animal health, human health and environmental health—responsible for antimicrobial stewardship.

Antimicrobials and Food Animals

Developing an approved antimicrobial for food animal use takes seven to 10 years and upwards of $100 million. In addition to efficacy and quality, each drug is assessed for animal, environmental and human food safety.[22]



The Food and Drug Act currently approves antimicrobials for food animals for treatment, control, prevention and growth promotion/feed efficiency. The benefits of antimicrobials include animal welfare, food safety—healthy animals produce safer food, economic/efficiency and environmental.

Thirty-five percent of antimicrobial use in food animals are compounds not used in human medicine, thus minimizing potential interference with effectiveness of antimicrobials used to treat human disease.[23]

While those opposing the use of antimicrobials in food animals advocate discontinuing use—either eliminating antimicrobials altogether or reducing their use—in food animals, this practice could jeopardize human health. The degree of risk associated with the discontinuing of antimicrobials in food animals is unknown and could lead to significant challenges. All scientific risk assessments published to date have shown a negligible risk to humans.[24]

The animal health industry is researching novel anti-infectives that address human health cross-resistance concerns while focusing on the health of the animal and the need to provide safe, affordable food to a growing population.

The American Veterinary Medical Association (AVMA) advocates the judicious use of antimicrobials and supports veterinary involvement in any use of antimicrobials. The AVMA maintains that any decision to allow or curb the use of antimicrobials in food animals should be based on risk assessments and available scientific research rather than on emotions and non-scientific information. The benefits to animal health and well-being, as well as the potential human health benefits, should be considered when making decisions about the use of antimicrobials in food animals.

The term "antimicrobial growth promoter" or AGP is used to describe an antimicrobial that is administered, usually in feed, to increase growth rates and improve feed efficiency.[25]

The statistics are unclear regarding the amount of AGPs being used in the production of food animal. The federal government collects data by the quantities of antimicrobials sold for use in animals and does not collect data by type of use: disease prevention, disease control, disease treatment and growth promotion. The statement often repeated that 80 percent of antimicrobials in the United States are used in healthy animals is not accurate as the 80 percent figure was deduced from comparing two sets of data that are not comparable. The number for animal use collectively used an entirely different methodology than the estimate presented for human use.[26] Further studies have not been conducted since 2000.

In March 2011, Rep. Louise Slaughter (D-NY) reintroduced the Preservation of Antibiotics for Medical Treatment Act (PAMTA – HR 965). The purpose of the Act is to preserve the effectiveness of medically important antibiotics used in the treatment of human and animal diseases by reviewing the safety of certain antibiotics for nontherapeutic purposes in food-producing animals. While this proposed legislation has not been referred out of Committee, this act raises questions and concerns because it intends to eliminate three of the four Food and Drug Administration's approved uses for antibiotics in food animals. PAMTA is not supported by science, lacks risk-based assessments and has animal welfare implications.

Rep. Henry Waxman (D-CA) is prepared to introduce the Delivery Antibiotic Transparency in Animals (DATA) Act that would mandate that the Food and Drug Administration "improve" the data it collects on agricultural antibiotics use, requiring feed mills and drug manufacturers to provide extensive reports. Feed mills will not be able to readily provide information on how drugs are used, and drug manufacturers will not be able to provide estimates of use based on species, indication or quantity.

The Food and Drug Administration is working with drug sponsors to voluntarily phase out AGP uses of "medically important" antimicrobials used in feed over the next three to five years, depending on regulatory timelines. Medically important antimicrobials include penicillins, tetracyclines, macrolides, lincosamides, streptogramins and potentiated sulfas. In addition, the marketing status will change from over-the-counter to Veterinary Feed Directive or prescriptions for approved new animal drug applications (NADAs), with more than 200 NADAs affected.

With controversy surrounding the use of growth promoters for animals destined for meat production and antimicrobial use in general for food animals, agribusinesses and government are looking to alternatives. A 2012 "Alternatives to Antibiotics" international symposium[27] organized by USDA's Agricultural Research Service and hosted by the World Organization for Animal Health (OIE) brought forth several key items. Among them: 1) a need to conduct scientific studies to determine the efficacy and safety of alternative products; 2) a need to conduct studies under field conditions; 3) a need to integrate nutrition, health and disease research; 4) alternatives to antibiotics need to be regulated as a drug, a biologic, a feed additive or possibly all; 5) alternatives to antibiotics must be developed according to national and international standards and meet requirements for efficacy, safety and quality; 6) need to engage regulatory agencies early in the process; 7) need to link academia, government researchers, feed industry, pharmaceutical industry, regulatory agencies and livestock industries; and 8) stakeholders and the scientific community need to define the scope of the research, development and applications of alternatives to antibiotics.

Human Medicine

In a Feb. 25, 1966 issue of Time magazine, an article stated that "Nearly all experts agree that (by the year 2000) bacterial and viral diseases will have been wiped out."[28] Instead, bacterial and viral diseases exist today, with 200 million to 300 million antibiotic prescriptions written annually to treat these infections.

Twenty-five percent to 40 percent of hospitalized patients receive antibiotics, with 10 percent to 70 percent deemed unnecessary or sub-optimal. With physicians having significant freedom in use of antibiotics, inappropriate uses occur.[29]

There is a debate among infectious disease physicians regarding how to measure antimicrobial usage in human medicine. The basic defined daily dose of an antimicrobial within human medicine is the "assumed average maintenance dose per day for a drug used for its main indication in adults."[30] Research shows that defined daily dose and days of antimicrobial therapy have a correlation regarding total antimicrobial usage. However, not all physicians follow the World Health Organization's basic defined daily dose. For example, while the defined daily dose for cefepime is 1 gram every 12 hours, one hospital gives 2 grams every eight hours. The same hospital may give 6-10 mg/kg of daptomycin daily while the defined daily dose is 4 mg/kg daily. Physicians tend to follow protocol that has worked for them.[31] Other difficulties with defined daily dose measurement is that defined daily doses are weight-based (assuming 70 kg), apply only to adults and cannot be used for pediatric populations.

Examples of emerging antimicrobial resistance for important antimicrobials in human medicine are methicillin-resistant *Staphylococcus aureus* (MRSA), multi-drug resistant gram-negative bacilli, epidemic strains of *C. difficile*, vancomycin-resistant *Enterococcus ssp.*(VRE), vanomycin-intermediate *Staphylococcus aureus* (VISA), and vanomycin-resistant *Staphylococcus aureus* (VRSA).

The National Healthcare Safety Network (NHSN) is a surveillance system that integrates and expands legacy patient and healthcare personnel safety surveillance systems managed by the Division of Healthcare Quality Promotion (DHQP) at the Centers for Disease Control. NHSN collects standardized data on healthcare-associated infections and is launching a module for collecting antimicrobial use and resistance data.

Given the societal value of antimicrobials, the Infectious Diseases Society of America (IDSA) which represents physicians, scientists, and other health care professionals who specialize in human infectious disease is taking steps to address antimicrobial misuse through an antimicrobial stewardship program. The Centers for Disease Control has implemented a “Get Smart for Healthcare” that focuses on improving antimicrobial use in inpatient healthcare facilities, starting with hospitals, then expanding to long-term care facilities.[32]

Environment

Research by a German scientist has shown that after passing through wastewater treatment, pharmaceuticals and other compounds are released directly into the environment.[33] While residues will decrease with time in the environment, the rate of decay will vary depending on various factors.

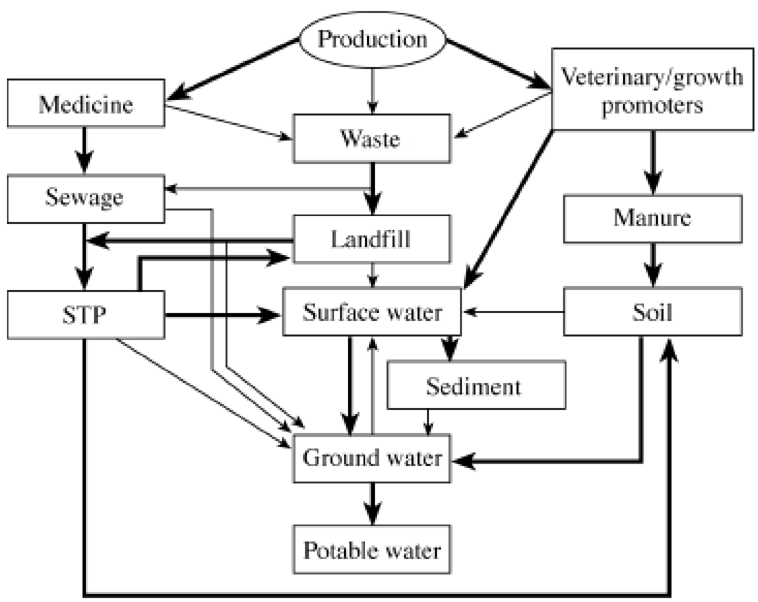
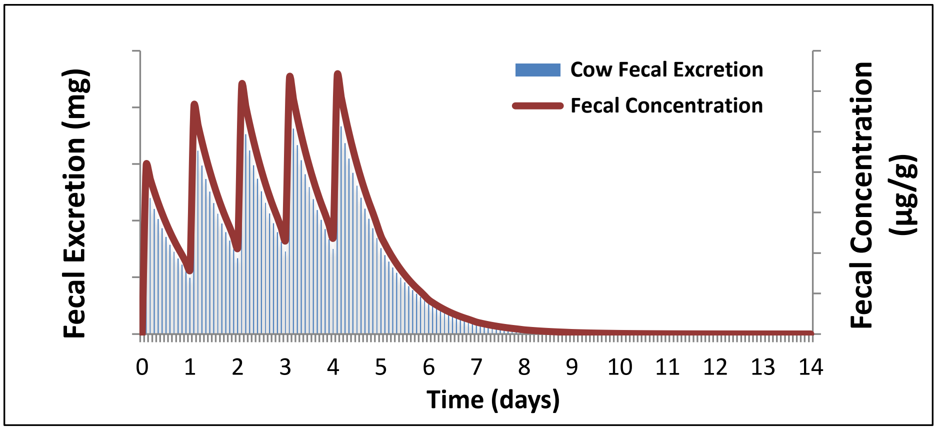


Figure 1. Sources and distribution of pharmaceuticals in the environment[1] (STP: sewage treatment plant).

Research shows that antimicrobials used in hospitals and private households may be released into effluent and municipal sewage, potentially causing a selection pressure on bacteria. It is recommended that hospitals and private users take steps to reduce the risk of environmental selection pressure by properly handling antimicrobials.[34]

Accurate estimates of environmental loading of antimicrobials excreted in animal agriculture are not only lacking but are extremely difficult to obtain.[35]



Other potential contributions to environmental residue include antimicrobial use in aquaculture and plant agriculture. Aquaculture contributes to the environmental challenge as medicated pelleted feed is used in aquaculture.

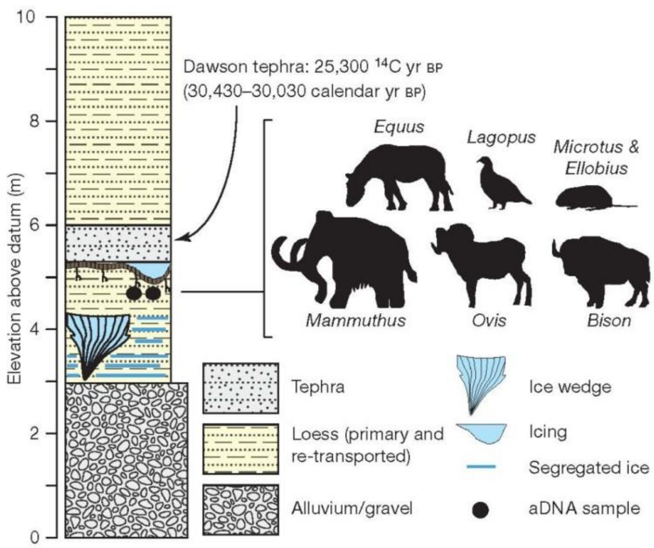
Streptomycin has been utilized in plant disease management since the early 1950s.[36] Other antimicrobials used in plant agriculture include oxytetracycline and kasugamuycin. While estimates from a U.S. Geological Survey and from the National Agricultural Statistics Service show that plant use of antimicrobials is less than 0.5 percent of 22.6 million kilograms of annual U.S. production of antimicrobials, antimicrobial use in plant agriculture enters the antimicrobial resistance equation.

Antimicrobial Resistance

The debate continues regarding whether or not resistant bacteria in humans can be linked to antimicrobial use in food animals. Some studies suggest a relationship between such use in food animals and human resistance trends, and other studies and risk analyses find no such relationship.[37]

Antimicrobial resistance isn't a new problem.[38] Research supported by the Canada Research Chairs program, a Canadian Institutes of Health Research Operating Grant, the National Science Foundation Microbial interactions and Processes Program and a Canadian Institutes of Health Research Frederick Banting and Charles Best Canada Graduate Scholarship states: "A growing body of evidence implicates environmental organisms as reservoirs of these resistance genes; however, the role of anthropogenic use of antimicrobials in the emergence of these genes is controversial. We report a screen of a sample of the culturable microbiome of Lechuguilla Cave, New Mexico, in a region of the cave that has been isolated for over 4 million years. We report that, like surface microbes, these bacteria were highly resistant to antimicrobials; some strains were resistant to 14 different commercially available antibiotics. Resistance was detected to a wide range of structurally different antibiotics including daptomycin, an antibiotic of last resort in the treatment of drug resistant Gram-positive pathogens. Enzyme-mediated mechanisms of resistance were also discovered for natural and semi-synthetic macrolide antibiotics via glycosylation and through a kinase-mediated phosphorylation mechanism.

Sequencing of the genome of one of the resistant bacteria identified a macrolide kinase encoding gene and characterization of its product revealed it to be related to a known family of kinases circulating in modern drug resistant pathogens. The implications of this study are significant to our understanding of the prevalence of resistance, even in microbiomes isolated from human use of antibiotics. This supports a growing understanding that antibiotic resistance is natural, ancient, and hard wired in the microbial pangenome."[39]



Research carried out by the University of Glasgow (in partnership with the Scottish Salmonella Shigella and Clostridium difficile Reference Laboratory at Stobhill Hospital, Health Protection Scotland, the Public Health Agency of Canada and the University of Guelph in Canada) exploited long-term surveillance data of *Salmonella Typhimurium DT104* and demonstrated how animal and human DT104 populations differ significantly in several ways, including prevalence, linkage, time of emergence and diversity.[40]

The study found significantly more human-only types of resistance than expected if the animal and human microbial communities were well-mixed and discovered that, in the majority of resistances common to both animals and humans, the resistances appeared first in humans.

While direct or indirect contact between animals and humans will lead to some transmission of disease and resistance in both directions, this study indicates that it is unlikely that the animal population is the major source of resistance diversity for humans. The study underscores that policies should not disproportionately impact antimicrobial use in food animals without considering the medical use of antimicrobials as well as imported foodstuffs and animals abroad.

From a scientific aspect, a unified definition of resistance is needed. Data on antimicrobial resistance in isolates from human cases are typically interpreted using clinical breakpoints while the quantitative data on antimicrobial resistance in isolates from food and animals are typically interpreted using epidemiological cut-off values to define the microbiologically resistant isolates. The epidemiological cut-off values discriminate between the wild-type (susceptible) bacterial population and the non-wild type populations which have a decreased susceptibility towards a given antimicrobial. While this may enable the early detection of developing resistance, the use of different thresholds, clinical breakpoints and epidemiological cut-off values means that resistance data in isolates from humans and in isolates from animals and food are, in most cases, not directly comparable. Likewise, there is lack of agreement on the definition of cut-off values across countries, regions and time. In addition, epidemiological cut-off values may have no predictive power in treatment success for animals or humans.

The U.S. government closely tracks antimicrobial resistance through the National Antimicrobial Resistance Monitoring System (NARMS), a cooperative program among the Food and Drug Administration, the Centers for Disease Control and the USDA's Agricultural Research Service. The FDA coordinates the program and monitors resistant bacteria in retail meats; the Centers for Disease Control collects samples from public health laboratories to monitor the emergence of antimicrobial-resistant foodborne pathogens in humans; and the USDA's Agricultural Research Service conducts susceptibility testing for animal isolates collected from diagnostics, healthy farm animals and from slaughter. USDA's National Veterinary Service Laboratory oversees the serotyping. Both USDA's Food Safety and Inspection Service and USDA's Animal Plant and Health Inspection Service provide samples.

Resolution

The time has come when academia, government researchers, the scientific community and stakeholders within animal agriculture, human medicine and the environment seek resolution on the polarizing and the often misunderstood issues of antimicrobial use and resistance.

Finding resolution to antimicrobial resistance must begin with the end in mind: improving human and animal health. Individuals within animal agriculture, human medicine and the environmental field will be best served to think in bigger and broader dimensions and to focus on collective interests and not positions. Common ground should be defined, with mutual satisfaction a priority. Based on scientific bodies of information, the facts should be separated from perceived facts. Reactions, emotions and distrust should be suspended. Reaching resolution also requires acceptance that the issues of antimicrobial use and resistance are not personal.

The scale and complexity of animal and human medical problems embedded in a changing environment demand that scientists move beyond the confines of their own disciplines and explore new organizational models for team science.[41] One solution is to use a One Health mindset and perspective. One Health is a collaborative effort of multiple disciplines—working locally, nationally and globally—to attain optimal health of humans, animals and the environment.

INTERACTIVE SESSIONS, RESULTS

With consensus a high priority of the symposium, individuals attending the symposium were assigned to tables where they gathered with individuals from other disciplines to address questions posed by a moderator. Disciplines at the conference included animal health, 43.3%; production agriculture, 18.7%; other, 14.9%; pharmaceutical industry, 14.2%; and 9% public health. The "other" category was comprised of individuals from government, academia, food animal production industry, commodity organizations, media, private practice and support industries.

A facilitator assigned to each table led the discussions, kept the group on task, saw that speaking time was shared and entered ideas into computers which then distilled overarching themes and "gems." Once overarching themes were identified, attendees voted in private using individual keypads to anonymously place their votes and determine priorities.

Interactive Session #1

Questions posed during Interactive Session #1

- What are the three to four most important issues that need to be addressed?
- What is your vision for what we hope to achieve in addressing these issues?

The Top 4 most important issues identified by attendees were:

1. Effective communication – between consumers and producers; between animal health and human health professionals; messages delivered through mass media
2. Research needed to define the antimicrobial use and resistance problem
3. Stakeholder consensus
4. Education on judicious use of antimicrobials

Four vision themes emerged from Interactive Session #1:

1. Consensus and collaboration building
2. Improved communication and education
3. Redirect how we approach medicine
4. Science-driven decision process

Attendees were asked "What is your vision for what we hope to achieve in addressing these issues?" A qualifier explained that a vision is the change we would like to see if we are successful at addressing the issues. Attendees brainstormed a list of visions and then, via their keypad, voted on their favorite vision, with the top vision being "Consensus and collaboration" at 36 percent.

Verbatim comments under consensus and collaboration included: a) producers getting out of the "defensive mode" and engaging the other stake holders proactively; b) to have an agreed-upon list of pathogens of importance with respect to antimicrobial resistance; c) international standards, with this being a global issue; d) legislation/regulation; and e) the future of these discussions/meetings should include people in disciplines beyond just animal experts.

"Science-driven decision process" was voted second at 26 percent. Comments that emerged included: a) science-driven rather than perception-driven process; b) actual risk to humans, animals, environment; c) we need to have the answers to consumer and producer questions.

"Improved communication and education" was the third vision, at 25 percent. Attendee comments included: a) early education; b) consumer education; c) consistent message among stakeholders to public; d) communication needs to include the producers' story; e) allow transparency; f) positive and pre-emptive.

Interactive Session #2

During the second interactive session, attendees at each table were asked to identify three or four factors they consider most important when addressing each of four "most important issues"—factors that require attention so the vision of consensus and collaboration can become a reality.

Four factors were identified for "effective communication":

1. Communication should be precise and not have any spin
2. Communication should have a collaborative approach and feature wording such as "This message was approved by…" and/or created and delivered by a panel of acknowledged experts from balanced backgrounds
1. Common interests/outcomes that would benefit all or most parties need to be identified and incorporated in messaging
2. Specific messages should be tailored for the various avenues of communication

The issue of "research needed" elicited six factors or key concerns:

1. Research should be meaningful and yield practical, implementable results
2. Who would fund the research and might certain groups have an inherent bias
3. Who should conduct the research: government, academia, industry, etc.
4. Who will determine research priorities
5. Are appropriate diagnostic tools available so meaningful research can be conducted
6. Is surveillance adequate to best identify priorities for emerging infectious diseases and research

Discussion of the "stakeholder consensus" theme brought forth six factors:

1. Stakeholders should represent a broad base and be comprehensive
2. An open dialogue is a must
3. Consensus at higher levels is needed
4. At this point, there is no single group to lead or initiate this task. Other concerns: Where would funding come from, and what single group would be viewed as unbiased so trust can be built and maintained

5. Is there low-hanging fruit where the process should begin
6. A clear goal must be identified

Attendees pinpointed seven factors when addressing "education on judicious use":

1. Target groups and their educational needs must be defined
2. The most effective educational tools need to be identified
3. Consumer education and increased public awareness should focus on judicious use of antimicrobials
4. Additional education and improved delivery of education programs for health professionals about existing judicious use guidelines is needed
5. On-farm training of employees/producers/suppliers about judicious use of antimicrobials would be beneficial
6. Educating people requires a clear, concise message
7. Education should be designed to motivate professionals/producers/consumers on the consequences of misuse and should focus on a global mindset, improving commitment to improve human, animal and environmental health

Interactive Session #3

Interactive Session #3 was conducted after all symposium presentations had been given and zeroed in on action items for each of the Top 4 most important issues.

Action that participants cited that can help work toward effective communication included:

- Commodity and producer groups should directly engage other stakeholders (i.e. human public health) to define specific problems before engaging lawmakers and the public. Relationships should be forged under the "One Health" umbrella
- Communications from commodity and producer groups should provide the media with research results so information shared with the public is fact based and not emotion based
- Market research to understand consumer perceptions on issues surrounding AMR and food animal position is warranted
- Animal agriculture would be wise to fully engage with federal agencies on the "Get Smart: Know When Antibiotics Work" campaign

Action themes identified to align with research included:

- International bodies (OIE, WHO) should clearly define research gaps so science can move forward productively
- Open communication regarding research needs should occur between producers and regulatory bodies
- Unbiased research should be promoted, and a One Health advisory board should be developed and leading the way
- Research should address the relationship between antimicrobial use, antimicrobial growth promoters and the health of animals

Participants identified four key actions they believe are needed to help stakeholders work toward reaching consensus:

1. Key stakeholders need to be identified and a recruitment plan developed
2. Concrete, measurable goals—and not just a vision—need to be specified
3. Steps must be taken to earn the trust of producers, consumers, leaders and stakeholders
4. Working relationships must be established

Symposium participants could not narrow key actions for the "Education on Judicious Use" issue down to the requested four and, instead, provided five actions:

1. Relationship between human health professionals and veterinary professionals should be established early in their careers (highest rated action)
2. A conference on antimicrobial use and AMR should be recurring and involve all stakeholders
3. Consensus from the veterinary, environment, OIE and medical communities should be developed
4. Continuing education about the judicious use for human health professionals and veterinary professionals should be required or at minimum increased
5. Building trust with the media and providing education about antimicrobial use and antimicrobial resistance is paramount

Interactive Session #4

The last session of the symposium was an interactive session where participants were asked "What is the headline you would like to send to the outside world about this conference?"

The Top 2 headlines emerging from in-depth discussions were:

1. Animal agriculture promotes a One Health approach to antimicrobial resistance
2. Animal agriculture calls for One Health summit to address the problem of antimicrobial resistance

Interactive Session Summary

The combination of interactive discussions and presentations took the complex subject of antimicrobial use and resistance and broke it down into issues that need to be addressed, factors that need to be considered and actions that need to be taken in order to improve human, environmental and animal health.

The last question posed to the attendees was "Given everything that's been discussed at this conference, what are you personally going to do to make a difference?" The consensus was that everyone is a stakeholder in this issue and wants effective antimicrobials to work when needed to protect both human and animal health. Stakeholders should continue to strive toward adopting a One Health mindset and engage in open dialogue with all stakeholders to learn from each other and move toward consensus on a path forward.

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