Antibiotic stewardship - A One Health approach

Lucas Pantaleon, DVM, MS, DACVIM (LAIM), MBA
DVM, One Health, Versailles, KY 40383; lucaspantaleon@gmail.com

Abstract

Antibiotic resistance is a complex emergent issue affecting not only public heath but veterinary medicine as well. As part of a holistic infection prevention and biosecurity plan, antibiotic resistance and stewardship should be addressed from a One Health point of view, where multidisciplinary collaboration is vital. In the US and other first world countries, animal agriculture is playing an important role controlling and improving the use of antibiotics in animal production systems; however, lower-income countries must further improve in this regard.

Key words: antibiotic stewardship, infection prevention, bacterial resistance, One Health

Introduction

One Health is a concept aiming at better understanding and addressing complex health problems arising from the intricate relationship between human, animal, and environment.[1,2] Examples of such complex problems are emerging zoonotic diseases, food safety, and the rise in antibiotic resistant bacteria.[2] One Health could be defined on 3 levels, that is the individual (human and animal), the population (human and animal), and the ecosystem. For the successful implementation of this concept, the need for interdisciplinary cooperation across complex systems (i.e. animal agriculture) with human and environmental health at the local, national, and global levels is key in order to tackle challenging health problems like antibiotic use.[1,2]

Advances in science have transformed our defenses against the threat of infectious diseases. Better hygiene, antibiotics, diagnostics, and vaccines have given people more effective tools for preventing and responding to outbreaks.[3] However, infectious pathogens continue to evolve and be a serious threat to human and animal health, and despite forward strides, emergent and endemic infectious disease outbreaks in humans and animals demonstrate that we cannot be complacent.[3] Outbreaks of infectious diseases could turn into epidemics and pandemics, causing massive loss of life and huge economic disruptions, as the world is currently experiencing with COVID-19.[3] There are approximately 1,461 human recognized diseases, of which 60% are multi-host pathogens and thus can move across species. Furthermore, approximately 75% of new human emerging diseases over the past 3 decades have been zoonotic in origin.[1] A large proportion of pathogens involved in emerging infectious disease events are of bacterial origin, chiefly antimicrobial resistant species.[4]

Veterinarians and producers must together play a fundamental role at improving population health through vaccination, parasite control, antibiotic stewardship, and client education. Furthermore, partnering with academia, industry and government agencies, animal agriculture must work cooperatively in order to continue to address the complex problem of antimicrobial resistance.

Infection Prevention and Biosecurity

Infection prevention and biosecurity could be defined as the implementation of strategies to protect human, animal, and environmental health against pathogenic microorganisms, thus it should be implemented as a One Health concept. Through infectious disease prevention, veterinarians are enhancing the quality of animal care and welfare by reducing infection rates, morbidity and mortality, and also improving personnel safety and reducing costs. The prevention of infectious diseases is done by a wide range of intertwined activities such as education, sanitation, disinfection, vaccination, surveillance, diagnostics, and antibiotic stewardship, all of which should be part of an infection prevention and biosecurity program at the farm.

Biosecurity refers to the measures used to prevent the entry of pathogens into a population.[23] As an example, a commercial swine operation implements very strict biosecurity measures in order to minimize the likelihood of infectious diseases entering the operation. On the other hand, infection prevention aims at limiting the impact of a disease introduction into a population, with the purpose of eliminating the source of potentially pathogenic microorganisms and disrupting disease transmission.[4,23]

A feedlot setting could be considered to be an "open" population with animals comingling from different sources in 1 place. This mixing of animals can lead to the spread of contagious infectious diseases in the feedlot, thus it is paramount that a comprehensive infection prevention plan is implemented. In "open" populations, we think more often in terms of limiting the effects that a disease introduction could have and how its impact could be minimized, that is, infection prevention. However, minimizing the probability for disease entry into a feedlot via biosecurity measures should also be part of protecting animals from diseases.

A comprehensive vaccination program is vital for the prevention of infectious diseases. However, there are limitations to vaccination because vaccines cannot fully protect the entire population, vaccines for many diseases are not available, and vaccination cannot be used to control emerging diseases.[15] Veterinarians use vaccination as a key tool to

maintain herd health, but by itself it will be less effective. Vaccination across species is a crucial element in maintaining herd immunity, which in turn helps lower the incidence of diseases. For example in dogs, using vaccination to control influenza is very important not just for the individual dog, but for the canine population as a whole. Furthermore, since dogs live in close contact with humans, vaccination aids with lowering the emergence of new viruses (i.e. influenza) in dogs with the potential of infecting humans, a zoonotic risk. This makes control of diseases such as canine influenza in the canine population not just important for dog health, but also for human wellbeing.[17] Regarding vaccination, the veterinary care team must play a crucial role establishing trust and educating producers and animal owners about the benefit of vaccination. Furthermore, proper vaccination can decrease the use of antibiotics by, for example, preventing respiratory diseases in cattle.

It is inevitable that despite the implementation of infection prevention and biosecurity measures, some animals will become sick. In this case stringent surveillance in order to identify early, isolate and treat the affected animal or group of animals is important for judicious antibiotic use.

Antibiotic Resistance

Antibiotics are a shared limited resource, and their administration to people or animals carries the risks for development of bacterial resistance, which is a global problem affecting everyone.[16]

Infection prevention practices, antibiotic stewardship, and innovation of drugs and therapies are important to combat and control the emergence of microbial resistance and contagious infectious diseases.[21] But, the limited prospect for newer, safer, and affordable antimicrobials and vaccines to cure and prevent disease, along with the emergence of multi-resistant microbes, make infection prevention strategies essential.[20,21] Implementing infection prevention tools as a One Health approach should lead to improved cooperation and collaboration, increased chances for success and reduced need of antibiotic use, lowering costs, and saving lives. Antimicrobial use must not be a "cover up" for poor management or suboptimal infection prevention practices. In low-to-middle income countries, investment in water and sanitation will be key to preventing diseases and improving antibiotic use in humans and animals.[6]

In the United States, more than 2.8 million people per year are affected by antibiotic resistant infections.[5] The burden on health care associated with multidrug-resistant organisms in the US remains high, with an estimated 622,390 cases among hospitalized patients annually and 35,000 people dying as a result of multidrug-resistant bacterial infections per year.[5,8] Despite this, a study showed that the trend in some antibiotic resistant bacteria has decreased between 2012 and 2017 in the US, thus it is likely that prevention measures adopted by the US health care system in combating this threat could be having a positive impact.[8]

The prevalence of hospital acquired infections (HAIs) in privately owned veterinary hospitals is poorly understood.[12] Outbreaks of HAIs in veterinary teaching hospitals reported economic loses from thousands of dollars to $ 4.12 million per outbreak, these costs were likely conservative and much likely greater in the long term.[7,13] A study that investigated HAIs in companion animals revealed that out of 1,535 dogs and 416 cats, 16.3% and 12%, respectively, had at least 1 nosocomial event. The most common reported syndrome in that study was surgical site inflammation.[18] A survey of veterinary teaching hospitals revealed that 82% of the institutions had reported an outbreak of an infectious disease. Agents most commonly detected were *Salmonella enterica* (65%), followed by methicillin-resistant *Staphylococcus aureus* (MRSA) (42%), and *Escherichia coli* (16%). Fifty-eight percent of these institutions had to restrict patient admissions while 32% had to close in order to control the outbreak. *Salmonella enterica* has been the agent most often (77%) involved in restricting admissions.[3] In large animal hospitals, importance of nosocomial salmonellosis lays on the fact of its high mortality rate of 30 to 60%, and carries antibiotic resistance genes.[14]

Contagious infectious diseases in a hospital and livestock environment not only are a risk for the animal resident population, but some zoonotic diseases pose a risk for the human caregivers. In a reported study, 50% of the surveyed institutions reported a zoonotic infection, and attack rates during an outbreak can be as high as 20 to 50%.[3,14] The 3 microorganisms more commonly involved in zoonosis were *Cryptosporidium parvum* (68%), MRSA (16%), and *Salmonella enterica* (16%).[3]

Some researchers argued that the increase in demand for animal protein around the world, which in turn has resulted in larger intensive and complex animal production operations, has in some instances increased the use of antibiotics.[24] Hence it is vital to invest resources into improving our understanding of disease transmission and prevention in animal agriculture, ultimately leading to improvement of animal, human, and environmental health.

Significant advances have been made in reducing antibiotic use in agriculture, especially in high income countries.[6] The evidence suggests that, with the right policies, the cost to producers of transitioning to low antibiotic use can be relatively small or negligible if compensated by improvements in animal hygiene, herd management, and biosecurity.[6] However, low and middle income countries have more work to do on implementing better systems to prevent and control infectious diseases in people and livestock in order to improve antibiotic use.[6] In those countries where less regulation exists, producers are prone to use antibiotics as they move towards more intensive farming practices.[6]

Antibiotic resistant bacteria can move across international borders, having a global impact on people, animals, and the environment. If ignored, the threat of antimicrobial resistance will have devastating consequences around the world by causing 10 million deaths, as well as accumulated costs for the global economy of $100 trillion by 2050.[6]

Antibiotic Stewardship

Injudicious prescription and use of antibiotics are thought to be the main driver for the increase in antimicrobial resistance (AMR) in human and veterinary medicine around the globe.[11,22] Therefore, the central focus in human and animal health to address the AMR is to implement stewardship programs.[11]

Antimicrobial stewardship refers to the actions veterinarians take individually and as a profession to preserve the effectiveness and availability of antimicrobial drugs through conscientious oversight and responsible medical decision-making while safeguarding animal, public, and environmental health. Stewardship involves maintaining animal health and welfare by implementing a variety of preventive and management strategies to prevent common diseases, using an evidence-based approach in making decisions to use antimicrobial drugs, and then using antimicrobials judiciously, sparingly, and with continual evaluation of the outcomes of therapy, while respecting the client's available resources.[1]

In animal agriculture systems, antibiotics are prescribed for disease treatment, control, and prevention. In the past few years in the US, significant effort has been made to decrease and improve the use of medically important antibiotics.[22] In the US, regulatory agencies have banned the use of medically important antibiotics as growth promoters and increased veterinary oversight for the use of medically important antibiotics for disease prevention in livestock and poultry.[22]

There is an urgent need to generate data that would accurately reflect antibiotic use in production animal medicine. This information will be important in guiding regulation and other interventions aimed at improving antibiotic use. Furthermore this data, coupled with the large animal veterinarian's perceptions and attitudes about antibiotic resistance, will improve training and education aimed at mitigating the emergence of resistance and discouraging unnecessary use of antibiotics.[22]

The Consumer

The agriculture sector has struggled with accurate consumer communication of information regarding antibiotic use, antibiotic resistance, and mitigation in a positive manner.[16] A large proportion of the consumers in the US are removed from the farm, hence they have no direct link to agriculture.[16] Pressure and changes in consumer habits and demands are having an impact on the use of antibiotics in production animal medicine.[6] However, some of those pressures by consumers and large retailers could inadvertently have a negative effect on animal welfare.

Proper communication and education with consumers, in a manner that captivates their attention about the advances that animal agriculture has made on improving antibiotic use in livestock, are key. Accurate communication will, in turn, improve the consumer's knowledge about the positive impact animal agriculture in the US is having on issues such as bacterial resistance, environmental sustainability, and food safety.

Conclusions

The rising antimicrobial resistance is a threat to global health.[11] Infection prevention, along with judicious antibiotic use, should play a key role as part of the One Health initiative since both concepts share the ultimate objective of safeguarding human, animal, and environmental health from infectious diseases.

Recent studies revealed that the majority of veterinarians surveyed (81%) consider antibiotic prescription practices in veterinary medicine to be a contributing factor to antimicrobial resistance.[22] However, a larger percentage (94%) of responders consider antibiotics used and prescribed in human medicine to be a more important contributor to the emergence of resistance.[22] Ultimately it is paramount to recognize that this is a problem that affects humans and animals, and rather than finger pointing, collaboration and cross-learning in a multidisciplinary way to better implement strategies aimed at preventing the spread of bacterial resistance will be what ultimately leads to success.

Veterinarians need to be aware that there is a recognizable standard of care with regard to infection control, meaning measures geared towards minimizing the spread of contagious infectious diseases and education, must be part of the care provided by veterinarians to their patients and clients. Not meeting these standards constitutes malpractice and represents a failure to meet the ethical responsibilities to patients and clients.[14,15] Neglecting infectious disease control is unethical, constitutes malpractice, and can be very costly in the short and long term. Veterinarians are concerned about antibiotic resistance, and they believe that by implementing the right strategies it can be addressed. For example, veterinarians believe that efforts geared towards environmental modifications that improve management practices could reduce antibiotic use.[22] This highlights the importance for the implementation of a robust infection prevention and biosecurity program.

In a spirit of One Health, the research efforts around characterization of antimicrobial resistance in feedlots, strategies for metaphylaxis in high-risk animals, improving consumer communication and education or alternatives to tylosin administration to treat liver abscesses are some of the ongoing endeavors to improve how the complex system of animal agriculture tackles antimicrobial resistance.[2,16]

Efforts by different government agencies, combined with those of private industry and the global community, are making great strides towards antimicrobial stewardship and towards understanding and combating antimicrobial resistance in animal agriculture. Continuation of these efforts is of paramount importance, as is the clear communication of the science to the consumer.[16]

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References

1. AABP judicious therapeutic use of antimicrobials in cattle. Available at: https://www.avma.org/resources-tools/avma-policies/aabp-judicious-therapeutic-use-antimicrobials-cattle.
2. AVMA. Researchers to study drug resistance in high-risk cattle. *J Am Vet Med Assoc* 2020;239.
3. Benedict KM. Characteristics of biosecurity and infection control programs at veterinary teaching hospitals. *J Am Vet Med Assoc* 2008;233:767-773.
4. Burgess BA, Morley PS. Managing Salmonella in equine populations. *Vet Clin North Am Equine Pract* 2014;30:623-640.
5. CDC. Antibiotic resistance threats in the United States. Available at: www.cdc.gov/DrugResistance/Biggest-Threats.html US Centers for Disease Control and Prevention, 2019;1-148.
6. Clift C. Review of progress on antimicrobial resistance. Available at: https://reader.chathamhouse.org/review-progress-antimicrobial-resistance#: Chatham House, the Royal Institute of International Affairs, 2019;1-18.
7. Dallap Schaer BL. Outbreak of salmonellosis caused by *Salmonella enterica* serovar Newport MDR-AmpC in a large animal veterinary teaching hospital. *J Vet Intern Med* 2010;24:1138-1146.
8. Jernigan JA, Hatfield KM, Wolford H, Nelson RE, Olubajo B, Reddy SC, McCarthy N, Paul P, McDonald LC, Kallen A, Fiore A, Craig M, Baggs J. Multidrug-resistant bacterial infections in U.S. hospitalized patients, 2012-2017. *N Engl J Med* 2020;382:1309-1319.
9. Jones K. Global trends in emerging infectious diseases. *Nature* 2008;451:990-993.
10. King L. One Health: A new professional imperative, American Veterinary Medical Association. *J Am Vet Med Assoc* 2008;1-76.
11. Kpokiri EE, Taylor DG, Smith FJ. Development of antimicrobial stewardship programmes in low and middle-income countries: A mixed-methods study in Nigerian hospitals. *Antibiotics (Basel)* 2020;9.
12. KuKanich KS, Ghosh A, Skarbek JV, Lothamer KM, Zurek L. Surveillance of bacterial contamination in small animal veterinary hospitals with special focus on antimicrobial resistance and virulence traits of enterococci. *J Am Vet Med Assoc* 2012;240:437-445.
13. Morley PS. Biosecurity of veterinary practices. *Vet Clin North Am Food Anim Pract* 2002;18:133-155, vii.
14. Morley PS. Evidence-based infection control in clinical practice: If you buy clothes for the emperor, will he wear them? *J Vet Intern Med* 2013;27:430-438.
15. Morley PS, Anderson ME, Burgess BA, Aceto H, Bender JB, Clark C, Daniels JB, Davis MA, Hinchcliff KW, Johnson JR, McClure J, Perkins GA, Pusterla N, Traub-Dargatz JL, Weese JS, Whittem TL. Report of the third Havemeyer workshop on infection control in equine populations. *Equine Vet J* 2013;45:131-136.
16. NIAA. Communicating the science of responsible antibiotic use in animals, in *Proceedings.* NIAA 9th Annual Antibiotic Symposium 2019;1-54.
17. Rodriguez L, Nogales A, Murcia PR, Parrish CR, Martinez-Sobrido L. A bivalent live-attenuated influenza vaccine for the control and prevention of H3N8 and H3N2 canine influenza viruses. *Vaccine* 2017;35:4374-4381.
18. Ruple-Czerniak AA, Aceto HW, Bender JB, Paradis MR, Shaw SP, Van Metre DC, Weese JS, Wilson DA, Wilson JH, Morley PS. Using syndromic surveillance to estimate baseline rates for healthcare-associated infections in critical care units of small animal referral hospitals. *J Vet Intern Med* 2013;27:1392-1399.
19. Sands P, Mundaca-Shah C, Dzau VJ. The neglected dimension of global security -- a framework for countering infectious-disease crises. *N Engl J Med* 2016;374:1281-1287.
20. Sattar SA. Allen Denver Russell Memorial Lecture, 2006. The use of microbicides in infection control: A critical look at safety, testing and applications. *J Appl Microbiol* 2006;101:743-753.
21. Spellberg B, Bartlett JG, Gilbert DN. The future of antibiotics and resistance. *N Engl J Med* 2013;368:299-302.
22. Taylor DD, Martin JN, Morley PS, Belk KE, White AE, Scallan Walter EJ. Survey of production animal veterinarians' prescription practices, factors influencing antimicrobial drug use, and perceptions of and attitudes toward antimicrobial resistance. *J Am Vet Med Assoc* 2020;257:87-96.
23. Weese JS. Infection control and biosecurity in equine disease control. *Equine Vet J* 2014;46:654-660.
24. Xie T, Liu W, Anderson BD, Liu X, Gray C. A system dynamics approach to understanding the One Health concept. *PLoS One* 2017;12:e0184430.