What Canadian veterinarians need to know and explain about AMR: A take-home tool-kit

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Major changes are underway in how agricultural use of antibiotics is regulated in food animals in Canada. All such use will become veterinary prescription only, growth promotion use of medically important antibiotics and Own Use Importation will stop, and compounding will be more strictly regulated. Veterinarians will need to understand more about antimicrobial resistance (AMR) so that they can explain to clients what resistance is and why it's important that these changes have been made, and the national and international context in which they have been made.

Although the international and national focus has been on agricultural use of antibiotics, the "post-antibiotic era" is more likely to emerge in companion animal medicine, and has actually already arrived in the form of the ESKAPE pathogens. There has been considerable blaming of agriculture for the AMR crisis in medicine, but a more balanced view is emerging with the general (but not totally accepted) embrace of a "One Health" approach. This is a "we're-all-in-this-together (rather than blaming) approach" but this demands that everyone using antimicrobials accepts responsibility for their stewardship. In agriculture, a stewardship approach will be a partnership of owners with veterinarians, although ultimately the legally mandated responsibility for stewardship has shifted to veterinarians.

There is a now an overwhelming amount of material on the AMR crisis and on the response to the crisis. It's a fast moving field that's hard to stay up with. This talk will provide veterinarians with a "tool kit" of the tools and resources, including a PowerPoint, successfully to start engaging with the era of antimicrobial stewardship and the changes in attitudes, behaviors and practices that this will require. The intent is to provide access to some of the best freely downloadable resources about the issue, so that veterinarians may both understand the dimensions of the issue and defend successfully some of the regulatory changes that position them to help address the issue in the food animal sector.

What is antimicrobial resistance, how does it develop and spread?

There's a large YouTube resource on AMR, including full feature documentaries, on the development and spread of antimicrobial resistance. Some good short ones are referenced.

Antibiotic resistant bacteria often have numerous other traits that make them "fit" as pathogens, and the "clonal" nature of successful high-risk AMR pathogens, and their global spread, is increasingly recognized. This spread highlights continuing issues of poor infection control in numerous health settings.

The Antibiotic Apocalypse Explained: https://www.youtube.com/watch?v=xZbcwi7SfZE

What causes antibiotic resistance? https://www.youtube.com/watch?v=znnp-Ivj2ek&t=31s

What is the resistance crisis?

AMR is one of the greatest global challenges of our time. Modern medicine is built on, and inconceivable without, the ability to control bacterial infections. Without this ability, numerous medical and surgical procedures now regarded almost routine will become impossible; even infections following minor cuts may become life-threatening.

The AMR resistance crisis is the emergence of difficult-to-treat infections because of the development and spread of AMR. The most difficult, and in some cases impossible to treat, infections are associated with hospitals (the "ESKAPE pathogens": ***E****nterococcus faecium*, methicillin-resistant ***S****taphylococcus pseudintermedius* (and *S. aureus*), ***K****lebsiella pneumoniae*, ***A****cinetobacter baumanii*, ***P****seudomonas aeruginosa*, and ***E****nterobacter* species) but resistance is increasingly a problem in "community acquired" infections. This crisis of resistance in human medicine is occurring across a broad range of pathogens and in a broad range of settings. It is a **global** problem because of the ready, non-prescription, availability of antibiotics in many countries, the rapid movement of peoples, and for other reasons. This *tsunami* of resistance has developed when the approval of new systemic antibiotics has declined to virtually nil in the last 30 years. Unless we act now, AMR bacterial infections are predicted to become the biggest single killer of humans by 2050.

Veterinary medicine has an increasing resistance problem across all fields of its activities, with impacts on human health. The emergence of livestock-associated MRSA and of MRSP in companion animals is just one example of the emergence and spread of resistance, with human health significance, but there are many more.

Centers for Disease Control: Antibiotic Resistance Threats in the United States, 2013: https://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf

Center for Disease Dynamics Economics and Policy: The State of the World's Antibiotics, 2015. http://cddep.org/publications/state_worlds_antibiotics_2015#sthash.GDArpQGO.dpbs

O'Neill Report, 2014: Antibiotic resistance: Tackling a crisis for the health and wealth of nations. https://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations_1.pdf

Who's to blame for the resistance crisis?

The development and spread of resistance has many causes and influences, and is the cumulative effect of widespread use antibiotics for over 60 years for numerous purposes and in numerous settings. It's been estimated that 50% of antibiotic use in humans is unnecessary and of the other 50% the antibiotic chosen is inappropriate; it seems likely that similar figures would be true for animals, but agriculture also has a special feature of the use of medically-important antibiotics for growth promotion and "subtherapeutic" purposes. We've become so used to antibiotics as part of the modern world that we've taken them for granted. Most of the "blame" however lies in the ability of many bacteria to survive antibiotics through the ability to adapt and also to spread resistance genes through mobile genetic elements, such as plasmids. Adaptation is what many successful pathogens do naturally. Resistance itself can be infectious. Rather than assign blame (agriculture, medicine) the consensus view is that we have to totally change the way we use antibiotics, and in other ways. A **"One Health" approach** to AMR is increasingly being adopted.

What is the global response to the resistance crisis?

There has been a massive global response to the AMR crisis. The G8 countries are addressing it politically as an issue on a par with climate change and international terrorism. The World Health Organization has shown considerable leadership in this area, and is a good source for downloadable

materials. The mobilization of different national and international groups in medicine, public policy, veterinary medicine, and agriculture has been unprecedented, and is continuing, with considerable media and public attention to the issue. All agree on the scale, complexity and multidimensional nature of AMR, but there is increasing focus on the multiple international, national and local actions, including the coordination and resource allocation, required to address the issue.

UK Government: UK 5 year antimicrobial resistance strategy:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/244058/20130902_UK_5_year_AMR_strategy.pdf
World Health Organization: Global action plan on antimicrobial resistance, 2016:
http://apps.who.int/iris/bitstream/10665/193736/1/9789241509763_eng.pdf?ua=1

What is agriculture's role in the resistance crisis?

There is overwhelming evidence that antibiotic use in animals selects for AMR in animal bacterial pathogens and commensals; a strong causal relationship has been shown between antimicrobial use (AMU) and AMR in commensal enteric bacteria in food animals. There is also overwhelming evidence that antibiotic use in animals (companion, food) can lead to spread of resistant pathogens or their resistance genes to humans and that this can make these infections more difficult to treat. Examples include resistant *Campylobacter jejuni*, extraintestinal pathogenic *Escherichia coli* (ExPEC), *Salmonella*, methicillin-resistant *S. aureus* or *S. pseudintermedius*, vancomycin-resistant enterococci, and others.

The ways in which these infections, or resistance genes from animal-derived bacteria, can reach people is shown in the Figure. What is unclear, and what has been highly contentious, is **the scale** of this contribution. It is hard to get an overall sense of this, and new data are still emerging, in part because agriculture has been sometimes been the whipping boy for AMR issues in human medicine and in part because AMU issues have been a way to attack aspects of modern agriculture that some groups don't like. It is however generally now accepted that most AMR in human pathogens is the result of AMU in humans, but it is also accepted that there is a contribution from animals (especially farm animals) to AMR in selected important human pathogens. Continuing to argue about this misses the point that the resistance genie is out of the bottle and won't be got back in, and the train has left the station long ago. Given the mobile nature of many resistance genes, **resistance anywhere is potentially resistance everywhere.**

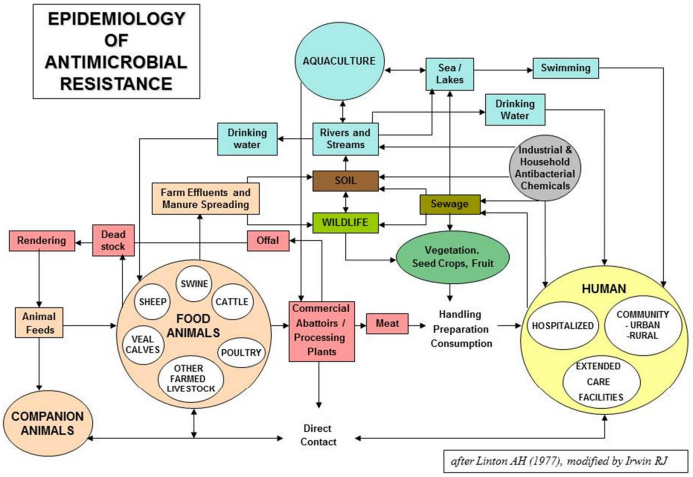


Figure. Epidemiology of antimicrobial resistance and movement of resistant bacteria (and resistance genes) between humans and animals. The figure illustrates the complexity of the interaction and the idea that "resistance anywhere is potentially resistance everywhere". After Linton (1997) as modified by Rebecca Irwin, PHAC.

Alliance for Prudent Use of Antibiotics: Antibiotics in agriculture: The risk to human health. http://emerald.tufts.edu/med/apua/about_issue/antibiotic_agri.shtml

Antimicrobials in agriculture and the environment: Reducing unnecessary use and waste. O'Neill Report, 2015: https://amr-review.org/sites/default/files/Antimicrobials%20in%20agriculture%20and%20the%20environment%20-%20Reducing%20unnecessary%20use%20and%20waste.pdf

Chataziaras I, et al: Correlation between veterinary antimicrobial use and antimicrobial resistance in food-producing animals: a report on seven countries. J Antimicrob Chemother 2014;69:827. (Free through PubMed).

Collignon P, et al: Human deaths and third-generation cephalosporin use in poultry, Europe. https://wwwnc.cdc.gov/eid/article/19/8/12-0681_article. (Free through PubMed).

Landers TF, et al: A review of antibiotic use in food animals: perspective, policy, and potential. Pub Hlth Rpt 2012;127:4 (Free through PubMed).

Manges AR: *Escherichia coli* and urinary tract infections: the role of poultry-meat. Clin Microbiol Infect. 2016;22:122. (Free through PubMed).

Van Boeckel TP, et al: Global trends in antimicrobial use in food animals. Proc Nat Acad Sci USA 2015; 112:5649. (Free through PubMed).

What is Canada's response to the resistance crisis?

Early response: The Canadian Integrated Program for Antimicrobial Resistance Surveillance, CIPARS

Following the 1997 Health Canada Consensus Conference on antimicrobial resistance in Montreal, an early response was the report to HC in 2002 on Uses of antimicrobials in food animals in Canada: Impact on resistance and human health. Still a very useful document, one of the very few recommendations acted on, and that was probably underway anyway, was the development of the Canadian Integrated Program of Antimicrobial Resistance Surveillance (CIPARS), modelled partly on the US NARMS program. CIPARS, which is highly respected internationally, integrates national resistance surveillance data in selected enteric pathogens in animals and humans, and monitors resistance in selected enteric "indicator" bacteria such as *E. coli* from animals at slaughter and animal products at the retail level. CIPARS is moving from resistance surveillance to use surveillance in animals. CIPARS became well known internationally through its work on ceftiofur resistance in *Salmonella* Heidelberg in chicken hatcheries and the impact on serious infection in humans with an organism resistant to the drug of choice (Dutil et al., 2010).

CIPARS published quarterly and annual surveys of resistance in selected pathogens, focused on the human-agricultural use, and on use in humans and farm animals: http://www.phac-aspc.gc.ca/cipars-picra/index-eng.php

Dutil L, et al: Ceftiofur resistance in *Salmonella enterica* serovar Heidelberg from chicken meat and humans, Canada. Emer Infect Dis 2010; 16:48. (Free through PubMed).

Uses of antimicrobials in food animals in Canada: Impact on resistance and human health, Report 2002. https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/veterinary-drugs/uses-antimicrobials-food-animals-canada-impact-resistance-human-health-health-canada-2002.html

Recent response: The pan-Canadian Framework for Action

Canada has responded relatively late to the AMR crisis but has been spurred to action by a 2015 report from the Auditor-General that criticized the Public Health Agency of Canada (PHAC) and Health Canada (HC) for lack of a national strategy to address AMR. The Federal government released a federal Framework for Action on AMR and AMU (antimicrobial use) in Canada in 2014, addressing the issue in three pillars: Surveillance, Stewardship and Innovation, and committing PHAC, HC, Agriculture and

AgriFood Canada (AAFC), the Canadian Food Inspection Agency (CFIA), and the Canadian Institute of Health Research (CIHR) to addressing AMR. The 2015 Federal Action Plan committed the government to leadership on AMR. HC announced a process to remove the growth promotional use of medically important antibiotics, to bring antimicrobials used in food animals under veterinary prescription, to closing down the "own use importation" loophole, and to tightening up regulations around use of active pharmaceutical ingredients. Since medicine, veterinary medicine and pharmacy are provincial responsibilities, subsequently, PHAC has worked with the provinces and territories, and numerous stakeholders, to develop a pan-Canadian Framework for Action (draft May 2014) based on Surveillance, Infection Prevention and Control, Stewardship and Innovation which requires to be endorsed by all the provincial and territorial Ministers of Health and Ministers of Agriculture. Once it is, then these groups will work on the **pan-Canadian Action Plan**. The pan-Canadian Framework is taking a "One Health" approach (minus the environmental piece) to AMR.

Report of the Auditor General: Antimicrobial Resistance. http://www.oag-bvg.gc.ca/internet/English/parl_oag_201504_01_e_40347.html

Antimicrobial Resistance and Use in Canada: A Federal Framework for Action. https://www.canada.ca/en/public-health/services/antibiotic-antimicrobial-resistance/antimicrobial-resistance-use-canada-federal-framework-action.html

Antimicrobial Resistance and Use in Canada: A Federal Action Plan. http://healthycanadians.gc.ca/alt/pdf/publications/drugs-products-medicaments-produits/antibiotic-resistance-antibiotique/action-plan-daction-eng.pdf

What is antimicrobial stewardship?

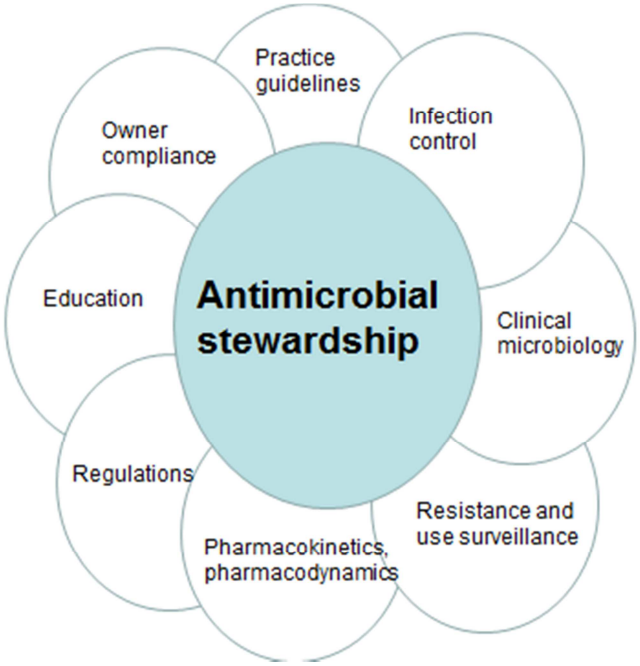
Antimicrobial stewardship is a coordinated program that takes a multifaceted approach to sustaining the efficacy of antibiotics and minimizing the emergence and spread of resistance. It promotes the appropriate use of antimicrobials (by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration), improves patient outcomes, reduces microbial resistance, and decreases the spread of infections caused by multidrug-resistant organisms. It's an evolving concept that replaces the older terms of "prudent use" or "judicious use" since it. Aspects are illustrated in the Figure below.

The practices of antimicrobial stewardship are perhaps best developed in human hospitals, originally as a cost saving measure, but the area is exploding as stewardship becomes a requirement for hospital licensing. Nevertheless, there is increasing focus in both human and veterinary medicine on primary care physicians and veterinarians, since they are the major users of antimicrobials. The general mindset of **good stewardship practice (GSP)** is a "**5R" approach**: Responsibility, Reduction, Refinement, Replacement, and Review. A **5R stewardship approach is an active, dynamic, process of continuous improvement** in AMU, a pragmatic ethic with many steps of different sizes. The Figure is an illustration of some of the different elements of GSP, many of which are discussed in the two other talks given at this conference. It seems likely that, within a short time, provincial veterinary regulations will require all practices to develop AMS policies and that regulators will monitor and evaluate AMU by veterinarians against agreed benchmarks.

Practice guidelines: The British Equine Veterinary Association (BEVA) has developed an award-winning approach to AMS, Protect ME, and is the best veterinary stewardship approach currently available: www.beva.org.uk/protectme.The British Small Animal Veterinary Association (BSAVA) has developed a practical and accessible approach to AMS, called PROTECT: https://www.bsava.com/Resources/Veterinary-resources/PROTECT. PROTECT offers a comprehensive approach for a practice to develop its AMS policies and practices: the acronym stands for **P**ractice policy; **R**educe prophylaxis; **O**ther options (eg, lavage, topical use); **T**ypes of drug and bacteria (drug properties, likely bacterial agents); **E**mploy narrow spectrum; **C**ytology and culture; **T**reat effectively; For example,

under Practice policy it recommends making a list of **first-line, second-line and third-line drugs**, where culture and sensitivity is used for second- and third-line drugs, and the latter are only used for life-threatening infections where first- and second-line drugs are not appropriate.

Infection control: Since AMR is essentially an infection control issue, infection control is an essential part of GSP. See comments on important AMR infections in the other two talks.



National Institute for Animal Agriculture, 2015: Antimicrobial stewardship: From metrics to management; http://www.animalagriculture.org/resources/Documents/Conf%20-%20Symp/Symposiums/2015%20Antibiotics/2015%20NIAA%20ABX%20White%20Paper-Final.pdf

Resistance and Use Surveillance: Benchmarking: "Benchmarking", the quantitative determination of norms for antibiotic use by veterinarians or at the farm level has been a powerful driver in reduction of antibiotic use in agriculture in countries which has significantly reduced AMU. There are also increasing reports surveying AMU in companion animals, some through capture of digital records through commonly used practice software. Benchmarking of AMU by veterinarians and at the farm level has been important in the reductions of AMU achieved in Denmark, where it forms the basis of the "Yellow card" system, and in Holland, where it has been an integral part of the 65% reduction in AMU on farms between 2009 and 2016. It seems likely that there will be farm and food animal veterinarian benchmarking in Canada as part of the pan-Canadian Antimicrobial Resistance Action Plan.

Danish Veterinary and Food Administration: The Yellow Card initiative on Antibiotics: https://www.foedevarestyrelsen.dk/english/Animal/AnimalHealth/Pages/The-Yellow-Card-Initiative-on-Antibiotics.aspx

European Commission Directorate-General of Health and Food Safety: Fact-finding mission to The Netherlands on Prudent Use of Antimicrobials in Animals, 2016: file:///C:/Users/Desktop/Downloads/Final%20report%20NL%202016-8889.pdf

Will making antimicrobials in food animals in Canada veterinary-prescription-only have any impact on resistance?

In Canada, the move to veterinary-prescription-only for antimicrobials in food animals is a major shift in responsibility for stewardship and GSP from agriculture to veterinarians. There would seem to be considerable scope to reduce the quantities of antimicrobials used in food animal production to where the benefits are clear and substantial, a process that is now underway. The increased emphasis on documenting use rather than simply resistance is appropriate, since use drives resistance and use is more easily managed than resistance. In Holland, which has intensive animal agriculture generally similar to that of Canada, there has been a 65% reduction in AMU on farms between 2009 and 2016. There will likely be a pan-Canadian process that will need to monitor and report AMU provincially, nationally and international as part of the process of prescription filling and the requirements for benchmarking. If you can't measure AMU, you can't manage AMR. Major food retailers are now making changes in AMU requirements for farms from which they obtain animal products, and may become ahead of veterinary and other regulatory bodies. However, failure of veterinarians to rise to the challenge will result in loss of self-regulation in this regard.

What's the role of the Canadian Veterinary Medical Association (CVMA) and the provincial veterinary regulators?

The CVMA continues to take a major leadership role on AMR on behalf of the veterinary profession in Canada. It is revising and expanding prudent use guidelines and developing numerous other resources including educational material around stewardship. One very important initiative around AMR has been the development by CVMA, together with the Council of Canadian Veterinary Registrars, of a pan-Canadian Framework of Professional Standards for Veterinarians on Veterinary Oversight of Antimicrobial Use. It is expected that these will become the common standard adopted by all the veterinary licensing bodies.

All provincial licensing bodies are engaging with AMR issues, and will do so more in the future, particularly in relation to development of the pan-Canadian Action Plan. Québec has the most experience, since veterinary prescription only of antimicrobials in food animals has been a provincial requirement for at least 20 years.

Canadian Veterinary Medical Association: Veterinary Oversight of Antimicrobial Use in Animals in Canada. https://www.canadianveterinarians.net/policy-advocacy/veterinary-oversight-of-antimicrobial-use-in-canada.

College of Veterinarians of Ontario: Use of Antibiotics in Food Animals, 2015. https://cvo.org/CVO/media/College-of-Veterinarians-of-Ontario/Resources%20and%20Publications/Reports/GF2DiscussionSummary.pdf

CVMA, 2016. Veterinary Oversight of Antimicrobial Use: pan-Canadian Framework of Professional Standards for Veterinarians. https://www.canadianveterinarians.net/documents/pan-canadian-framework.

What's the role of specialty veterinary groups?

All specialty veterinary groups nationally and internationally are engaging with antimicrobial stewardship, including development of practice guidelines. It is beyond the scope of this review to list examples because they are too numerous.

What's the role of Canadian farmers and the farm organizations?

Major Canadian farm groups (aquaculture, beef feedlots, dairy, poultry, pork) are engaged with AMR and stewardship issues through the different national on-farm food safety and quality assurance (FSQA) programs. The smaller farm groups (eg smaller cow-calf operations) are probably less engaged and less accessible to educational initiatives. They will be forced to engage further with AMR as a result of the move to prescription only of antibiotics for food animals and what will almost certainly to

documentation of AMU and benchmarking initiatives. All groups will benefit by educational actions by veterinarians. The move to stewardship standards in animal agriculture that reaches international standards will have to be an on-going partnership between veterinarians and farmers, and will require monitoring by regulatory groups.

The Chicken Farmers of Canada have developed the most rigorous antibiotic stewardship programs of all the major farm groups, a response to the problems identified ceftiofur resistance in *Salmonella* Heidelberg and *E. coli* through extra-label use of ceftiofur in hatcheries, as well as market demand for poultry raised without preventive use of medically-important antibiotics.

National Farmed Animal Health and Welfare Council: The NFAHWC is an advisory council of the Federal-Provincial-Territorial Regulatory Assistant Deputy Ministers of Agriculture Committee that works with industry, commodity groups and animal health organizations to develop advice on matters of national importance relating to animal agriculture. Addressing agricultures role in antimicrobial stewardship is a matter of active current interest to the Council and was the subject of a useful report in 2016 and of on-going activities.

Chicken Farmers of Canada: http://www.chickenfarmers.ca/what-we-do/antibiotics/

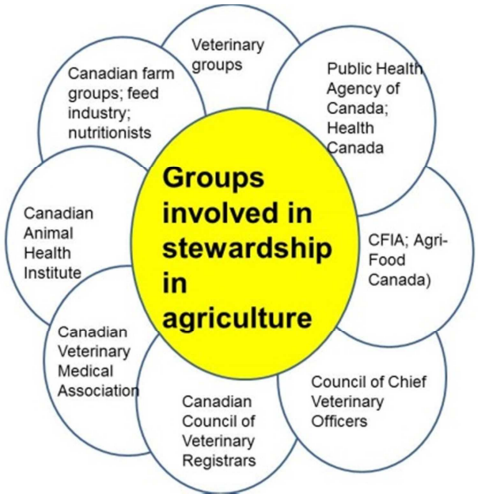
NFAHWC. Antimicrobial stewardship in food animals in Canada: http://www.ahwcouncil.ca/pdfs/council-updates/NFAHW%20Council_Recommendation_AMU_AMR_2016.pdf

Other groups involved in the changing nature of animal agriculture's antibiotic use

Canadian Animal Health Industry: The Canadian Animal Health Industry (CAHI has taken a critical and indispensable leadership role in supporting responsible changes in the use of antimicrobials in animal agriculture. This on-going work includes providing documentation of AMU in the provinces and by different user groups, as well as discussion of the logistics of the move to veterinary prescription only for food animals.

Canadian Animal Health Industry: Antimicrobials. https://www.cahi-icsa.ca/food-animal-health/antimicrobials.aspx

The complexity of leadership on animal AMR issues in Canada: Major changes will have been instituted in food animal use of antimicrobial once the federal action plan is implemented around or after December 2017. The pan-Canadian Framework for Action is setting the scene for development of a pan-Canadian Action plan to take a One Health approach to AMR. There are numerous issues to resolve, including notably the pan-Canadian leadership: Who do you phone to find out what's happening or discuss issues? Who's monitoring and reporting AMR and AMU, and to whom? How will antimicrobials be distributed to farms and farmers? Who's monitoring appropriate use, and benchmarks against which possible AMU and AMR problems can be identified? The Figure below shows the many actors involved and the complexity of the integration that will be required for an effective pan-Canadian approach to addressing AMR that meets international standards. We are underway but there's lots to be integrated.



What are the critically-important antibiotics for human medicine?

The World Health Organization (WHO), and Health Canada, categorize and prioritize antibiotics into different categories based on their importance in treating bacterial infections in human medicine. Those of the Very high importance (HC) are drugs regarded as critical for the treatment of very serious infections for which alternates are not available. The purpose of categorization is to assist in risk assessment for determination of the approval process for drugs used in veterinary medicine, for example restricting these in different ways. Health Canada's intention is that categorization is a dynamic process depending on changing circumstance. It's a somewhat contentious process with differences in the categories (and antimicrobials listed) between Health Canada and the WHO (and other groups). What is obvious is that humans and animals share the same antimicrobials and that there is a "hierarchy" of importance of antimicrobials, to some extent based on when they were first introduced. The general approach is an important part of the strategy to preserve antibiotics.

Examples for Health Canada's categories of "Very high importance" are third and further generation cephalosporins, carbapenems, penicillin-beta-lactamase inhibitor combinations; fluoroquinolones; glycopeptides; polymixin. Examples of "High importance" are aminoglycosides, first- and second-generation cephalosporins, lincosamides, macrolides, penicillins, and trimethoprim-sulfamethoxazole. Examples of "Medium importance" are bacitracin, phenicols, sulfonamides and tetracyclines. Examples of "Low importance" are ionophores.

An alternative "unofficial" approach to categorization is of "First line", "Second line, and "Third line", and Restricted drugs. Primary or first line drugs are those used in initial treatment in advance of or in lieu of culture and susceptibility testing; such drugs are those less important for treating serious human infections. Examples include penicillins, first- and second-generation cephalosporins, trimethoprim-sulfonamides. Secondary or second line drugs are used when culture and susceptibility, plus patient and infection factors, indicate that no first line drugs are reasonable options. These drugs may be more important in treating serious human infections. Examples include fluoroquinolones and third- or fourth-generation cephalosporins. Tertiary or third-line drugs are those used for serious, life-threatening infections with support by culture and susceptibility, and where no first or second line drugs are indicated. An example is carbapenems. Restricted drugs are those that are either never used or only under the most dire circumstances. An example is vancomycin.

An example of the use of this categorization approach has been the voluntary ban on third-generation cephalosporins in swine production in Denmark (Agersø and Aarestrup, 2013).

Agerso Y, Aarestrup FM: Voluntary ban on cephalosporin use in Danish pig production has effectively reduced extended-spectrum cephalosporinase-producing *Escherichia coli* in slaughter pigs. J. Antimicrob. Chemother. 2013;68:569 (Free through PubMed).

World Health Organization, 2016: Critically important antimicrobials for human medicine: **http://apps.who.int/iris/bitstream/10665/255027/1/9789241512220-eng.pdf?ua=1**

Health Canada, 2012: Antimicrobial categorization: **https://www.canada.ca/en/health-canada/services/drugs-health-products/veterinary-drugs/antimicrobial-resistance/cover-page-categorization-antimicrobial-drugs-based-importance-human-medicine.html**

What's does the future look like?

The future is always hard to predict, but we are going to have a very different relationship with antimicrobial drugs in the future. The final O'Neill Report identifies the top ten approaches to addressing AMR globally, one of which is reduction of antibiotic use in agriculture and reducing antibiotic contamination of the environment. AMR will continue to adversely affect how we treat bacterial infections. Bacteria can readily change to resistance, but people, groups and institutions are highly resistant to change. We have however no choice.

World Health Organization: The evolving threat of antimicrobial resistance: Options for Action, 2012. http://apps.who.int/iris/bitstream/10665/44812/1/9789241503181_eng.pdf

O'Neill Report: Tackling drug resistant infections globally: Final report and recommendations. https://amr-review.org/sites/default/files/160525_Final%20paper_with%20cover.pdf

References available for purchase

Danish Small Animal Veterinary Association's Antibiotic Use Guidelines for Companion Animal Practice: http://www.fecava.org/sites/default/files/files/DSAVA_AntibioticGuidelines%20-%20v1-1_3(1).pdf. Free for download.

Giguere S, et al. Guardabassi L, Prescott JF. Antimicrobial stewardship in small animal veterinary practice: From theory to practice. Vet Clin N Am Small Anim Pract 2015:45:361.

Page S, et al. The 5Rs approach to antimicrobial stewardship Vet Rec 2014; 175:79.

Weese JS, et al: Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases. Vet Med Intern 2011;do:10.4061/2011/263768.

Weese JS, et al: Antimicrobial stewardship in animals, p. 117. In: Giguere S, et al (eds). Antimicrobial Therapy in Veterinary Medicine, 5th ed. 2013. Wiley.

Disclaimer: The perspectives expressed in this summary are mine alone, and almost certainly do not adequately acknowledge the effort or thought put into AMR by numerous different individuals and groups in Canada.