

Antimicrobial stewardship in companion animals: Welcome to a whole new era

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Untreatable bacterial infections (“the post-antibiotic era”) are far more likely to emerge in companion animals than in food animals, and have already arrived in the form of the multi-drug resistant (MDR) ESKAPE pathogens, the scourge of hospitals. These highly resistant, and in some cases hospital-adapted pathogens, are *Enterococcus faecium*, methicillin-resistant *Staphylococcus pseudintermedius* (and *S. aureus*), *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species. There has however been a general increase in extended-spectrum beta-lactamase (ESBL) producing *E. coli* in companion animals which, like the ESKAPE pathogens, can be shared with their owners and escape into the veterinary clinic and hospital. We are moving rapidly from the antimicrobial era through the antimicrobial resistance (AMR) era into the era of antimicrobial stewardship (AMS). This shifting paradigm in our relationship with antibiotics is part of the global responsibility that all users have to preserve for the long term the rather small range of antimicrobial drugs available to treat bacterial infections.

We are unlikely to get the resistance genie back into the bottle but a stewardship approach will buy time until we eventually have new antibiotics and new approaches to controlling bacterial infections. **Antimicrobial stewardship** refers to an approach that promotes, improves, monitors and evaluates judicious antimicrobial use (AMU) to preserve the future effectiveness of antimicrobials and to promote and protect human and animal health. It is a term that is preferred to the previously used terms judicious or prudent use, since it includes the idea of not using 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. A combination of the multiple interventions and approaches embraced in the stewardship model has the potential to have a cumulative impact that will help control AMR. All veterinary users of antimicrobials are now inevitably part of the global “One Health” strategy to address AMR. This strategy, as endorsed in the 2017 pan-Canadian Framework for Action for Tackling Antimicrobial Resistance and Antimicrobial Use, includes surveillance, infection prevention and control, stewardship, and innovation.

Antimicrobial stewardship is a rapidly developing and evolving field, with greatest activity and leadership in large tertiary care human hospitals where AMR problems are most visible but with increasing engagement by national and international veterinary organizations and specialties. There is increasing focus in both human and veterinary medicine on primary care physicians and veterinarians,

since they are the major users of antimicrobials. There are an increasing array and depth of resources and it is hard to keep up with their pace of development. In Canada, the move to veterinary prescription only for antimicrobials in food animals is a major shift in responsibility for stewardship and GSP. It seems likely that, within a short time, provincial veterinary regulations will require all practices, including companion animal practices, to develop AMS policies and that regulators will monitor and evaluate AMU by veterinarians against agreed benchmarks. A program of AMS Certification could become required.

A practical approach to antimicrobial stewardship in companion animal medicine

The concept of AMS is of a dynamic process of continuous improvement in how we use antimicrobials and of reduction in their use to where the benefits are clear and substantial. Figure 1 is an illustration of some of the different elements of GSP.

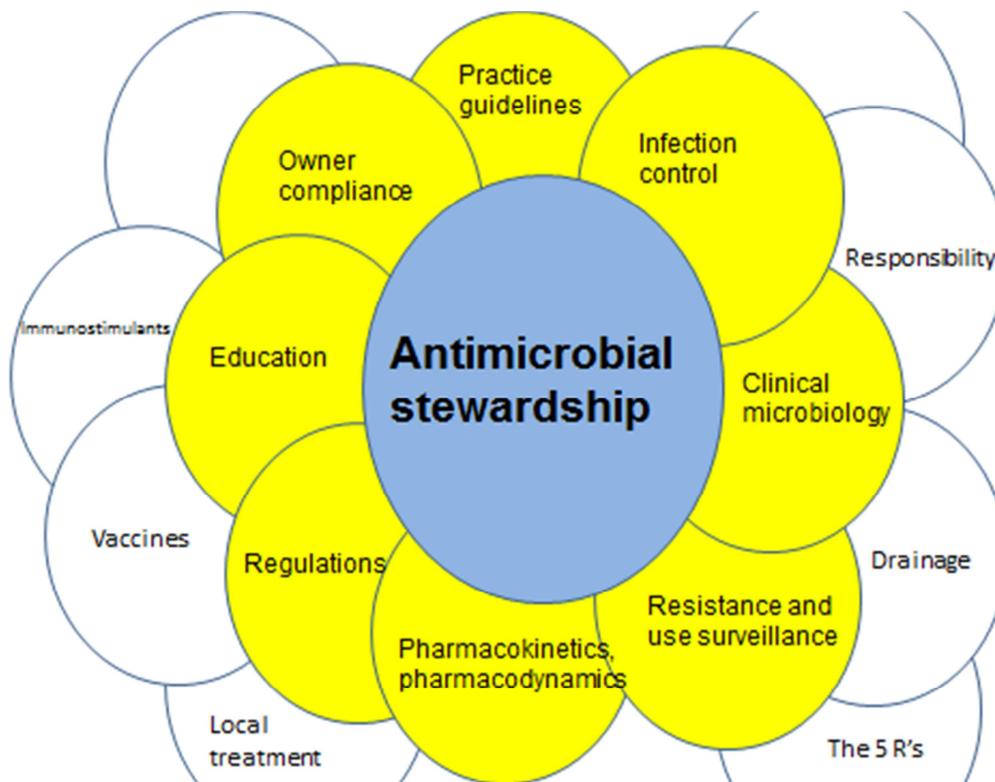


Figure 1: An approach to antimicrobial stewardship for companion animal practitioners. The inner circles are important major areas, and the outer circles are additional aspects. Some circles are deliberately blank so users can add their own ideas.

Practice guidelines: 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; Cytology and culture; Treat 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. Using downloadable PROTECT templates, practices can develop policies on empirical antibacterial use for commonly encountered bacterial infections, for surgical prophylaxis, and for when not to use antibacterial drugs. A Guide to PROTECT is available on the website. I don't think the PROTECT site has the brilliance of the British Equine Veterinary Association PROTECT ME approach since, although it requires practices to think through their AMU approaches, it doesn't engage the entire veterinary team in the same way and misses out the important ME (**M**onitor use, compliance and resistance; **E**ducate) aspect. Assignment of responsibility in the clinic for developing, implementing, monitoring and evaluating an AMS program is essential for success. Nevertheless, PROTECT is a well-organized, well-supported, systematic and thoughtful way on which to build.

An excellent downloadable guideline resource is the Danish Small Animal Veterinary Association's Antibiotic Use Guidelines for Companion Animal Practice. Other relevant guidelines (superficial bacterial folliculitis, urinary tract infections) are referenced.

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 increasing reports surveying AMU in companion animals, some through capture of digital records through commonly used practice software. Not unexpectedly, the majority of AMU in dogs and cats is with AMs classified as "critically important" for humans using the World Health Organization (WHO) criteria, and up to about one-third of cats are with AMs of the WHO "highest importance" classification. In Canada, Murphy and others (2012) found that there was overuse of cefovecin and of fluoroquinolones for the treatment of cat and dog diseases for which antibiotics were either not indicated or for which first line antimicrobials were quite appropriate. A focus on use is important since reducing AMU will be one of the drivers of reduced AMR. Thus reliable "benchmark" data fed back to the prescribers has great potential future value in AMS.

Infection control: There are many reports of the remarkable clonal spread of resistant pathogens in companion animals, both ESBL-producing *Enterobacteriaceae* in Europe and, most importantly, of methicillin-resistant *S. pseudintermedius* (MRSP) globally. The increasing prevalence of canine MRSP globally, including in Canada, is well documented, as is the higher frequency of MRSP infections in cats and dogs that have been hospitalized or have visited veterinary clinics. The reason for the dramatic emergence in the last decade of MRSP, of which there are five major lineages globally, and which are often MDR, is unclear but they demonstrate why good infection control is an important part of AMS. Human infections or colonization with MDR MRSP, the majority of which are apparently transmitted from dogs, have been identified in Canada. The close proximity of dogs and cats with people is one reason for the spread of different MDR bacteria between them, and veterinary clinics or hospitals are recognized to be a potential source for further dissemination between animals (and from them to people).

Companion animal practitioners are sources of MRSA or MRSP and hand and other hygiene practices in companion animal medicine often leaves a lot to be desired. In a video observational study in Canada, **median contact time for soap and water handwashing in companion animal practices was just two seconds** (Anderson and others, 2014). As noted by others, resolving the issue of MDR endemic bacterial infections will not be through development of new antibiotics if current hygiene practices remain and if we don't undertake good stewardship practices to preserve our existing drugs. In Ontario, no companion animal practices surveyed in 2009 had an infection control program (Murphy and others 2010). Good infection control is fundamental in reducing the spread of infections, including of resistant bacteria.

Clinical microbiology : Greater use of clinical microbiology data to guide selection of antimicrobials is an obvious approach to GSP, but is currently hampered by delays in obtaining data and cost. There is considerable effort being made to speed the process, particularly through rapid DNA-based approaches. PROTECT suggests such testing before the use of Category 1 antimicrobials, those of critical importance in human medicine (fluoroquinolones, third-generation cephalosporins).

Resistance and use surveillance: On-going monitoring of resistance and use is an important part of the “continuous improvement” mindset of GSP. Resistance data can be misleading as a measure of population resistance since it is often derived from antibiotic-treated but unresponsive infections but will help identify if there is an infection control problem at the veterinary clinic level (as well as at the country, continental, or global level). Development of practice policies based around PROTECT provides an excellent framework to integrating resistance data into practice policy around stewardship.

Pharmacokinetics and pharmacodynamics: Knowing the difference between concentration- (aminoglycosides, fluoroquinolone) and time-dependent antimicrobial drugs is an important pharmacokinetic consideration both in optimal dosing and in the prevention of the emergence of resistance. One survey found that inappropriate dosing generally was common in equine medicine.

Regulations: Regulations should be followed. They are particularly important in relation to human health considerations. It may eventually become illegal to prescribe the “last resort drug” vancomycin and carbapenems for animals.

Education

Client education posters around antibiotic use in companion animals are readily available for download and display. As society increasingly expects responsible antibiotic use, clients might expect to see such posters in the clinic, including those promoting compliance.

<https://www.avma.org/PracticeManagement/ClientMaterials/Pages/clinic-posters-be-careful-antibiotics.aspx>

Summary

Companion animal practitioners are on the front line of the fight against AMR and need to engage now before it is too late. Many aspects of AMS, including regulatory monitoring, evaluation and certification are in their infancy and concepts and practices are evolving rapidly.

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