Using antibiotics responsibly in companion animals

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Antibiotics are regularly prescribed in practice and it is not uncommon for veterinary surgeons to prescribe them without having first documented an infection. As such, antibiotics are not always prescribed appropriately. In contrast to many drugs prescribed, the more frequently antibiotics are used, the less effective they become, due to the selection of resistant bacteria. It is, therefore, important that clinicians understand the implications of the overuse of antibiotics and the principles of optimal prescribing. This article aims to review the concerns regarding antibiotic resistance, the role of antibiotics in the development of resistant bacteria, and to provide guidance on how practitioners can refine their prescribing.

The problem of emerging multi-resistant bacteria is well recognised in human medicine. The proportion of meticillin-resistant *Staphylococcus aureus* (MRSA) among all *S aureus* bacteraemias remained under 3 per cent until 1992, but by 2002 this had risen to 43 per cent (Griffiths and others 2004). In the second volume of her annual report for 2011, the Chief Medical Officer (CMO), Dame Sally Davies, chose to focus on the rise of antibiotic resistance, calling for this 'very real threat' to be placed on the national risk register (Department of Health 2013a). The British Society for Antimicrobial Chemotherapy is currently highlighting the slow development of new antibacterial agents and is actively petitioning the government to increase research in this area (www.antibiotic-action.com).

In this article the term 'antibiotic' will be used as a synonym for antibacterials (World Health Organization 2011). Antimicrobials include antivirals, coccidiostats, antimycotics and antibacterials; because this article focuses on treatment of bacterial and their resistance to therapy, the term antimicrobials will not be used.

How does antibiotic resistance impact on our patients and their owners?

The impact of antibacterial resistance is encountered in all types of veterinary practice. For farm animal species, there are welfare implications if treatments become ineffective, concerns regarding resistant bacteria entering the food chain and economic consequences. In small animal practice, maintaining treatment efficacy is also important for patients but responsible antibiotic prescribing is also part of the strategy to minimise hospital-acquired multi-resistant bacterial infections.

MRSA is a well-publicised multi-resistant bacteria with relevance to human health. There are documented cases of MRSA infection in companion animal practice; the multi-drug resistant strains of meticillin-resistant *Staphylococcus pseudointermedius* (MRSP) (previously *S intermedius*) are, however, more of a concern (Duquette and Nuttall 2004, Lloyd 2012). Hospitalisation and antibiotic treatment are risk factors for MRSP carriage in dogs (Nienhoff and others 2011). A UK laboratory reported that in 2008 MRSP accounted for 14 per cent of coagulase positive staphylococci isolated from dogs (Steen 2010). Worryingly, in this study, the MRSP resistance profiles were more extensive than those for MRSA.

In small animal practice, the close relationship between pets and owners has raised concerns regarding transmission of resistant bacteria (Guardabassi and others 2004a). Dogs can acquire MRSA from humans and, conversely, domestic animals can act as a vehicle for MRSA transmission to humans. The significance of this interspecies transmission of MRSA is not yet clear, but its incidence is believed to be low (Morris and others 2006).

In the case of MRSP, although *S pseudointermedius* rarely colonises humans, carrier rates are increased among individuals exposed to dogs (Guardabassi and others 2004b). There is, therefore, the possibility of a clinically significant MRSP infection developing in a human carrier (Bond and Loeffler 2012). Furthermore, MRSP could be considered a potential source of genetic material encoding resistance, which could transfer to staphylococcal strains that colonise or cause disease in humans and vice versa (Van Duijkeren and others 2011).

The impact of veterinary antibiotic prescribing on human health is an area attracting attention. The Royal College of Veterinary Surgeons, the Royal College of Pathologists and the Royal College of Physicians held an open meeting in October 2012 to debate the current opinions based on available evidence (the presentation slides are available [RCVS 2012]). The complex interaction between animals, humans and the environment, eg, sewage and soil, means that this is not a simple relationship to assess comprehensively, so work in this area continues.

In the author's opinion, veterinary surgeons have a responsibility to preserve antibiotic efficacy for veterinary patient welfare but also, given the theoretical concerns, for human health. This view is further strengthened by the slow development of new antibacterial agents.

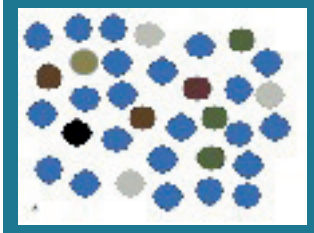
Are the veterinary profession's antibiotic prescribing privileges under threat because of implications for human health?

As UK veterinary surgeons, our privilege to prescribe antibiotics without restrictions has not gone unnoticed and came under the spotlight in the annual report for 2008 of the then CMO, Sir Liam Donaldson (Department of Health 2009). This report recommended a ban on the use of fluoroquinolones and 3rd and 4th generation cephalosporins in animals due to a perceived risk of antibiotic resistance development to these agents and the potential impact on human health. The CMO's report for 2011 acknowledges that current evidence suggests antibiotic use in veterinary species is not a major cause of resistance in bacteria affecting human health. However, it argues that, because veterinary use provides a vehicle for resistance transmission, the national approach to the problem of antibiotic resistance should be jointly managed by the Department of Health and Defra. The UK's five-year antimicrobial resistance strategy published in September 2013 advocates a coordinated 'one health' approach (Department of Health 2013b).

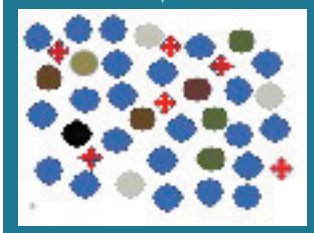
In January 2013, members of the European Parliament adopted a resolution by the European Parliament's Public Health and Food Safety committee which argued that the key to tackling antibiotic resistance involved maintaining the effectiveness of currently available drugs through responsible use. Part of this resolution called for guidelines on the prudent use of antimicrobials, in particular the restricted use in veterinary species of fluoroquinolones, and 3rd and 4th generation cephalosporins, classified by the World Health Organization as critically important for human use (Anon 2013).

It is, therefore, vitally important that the veterinary profession adopts a responsible and unified approach on antibiotic usage to demonstrate that restrictions on our prescribing privileges are not required.

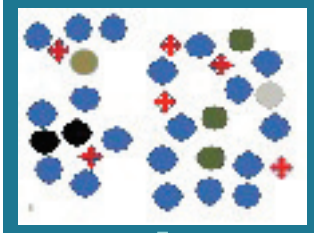
Box 1: Effects of prolonged antibiotic treatment on a bacterial population



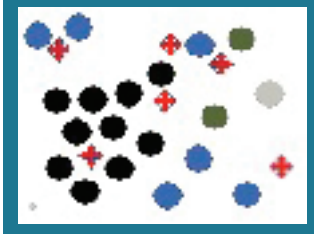
In this example, the pathogen bacteria which we want to eliminate are brown. The other bacteria are commensals



We introduce a broad spectrum antibiotic (red cross). Most of the bacteria are sensitive to the antibiotic except the black bacteria which is a multi-resistant strain



The antibiotic has eliminated a number of bacteria including our target brown bacteria. The reduced numbers of commensals reduce competition with the black bacteria allowing it to proliferate. Ideally, therapy should be stopped at this point



With long courses of antimicrobials, commensal numbers continue to decline, competition is reduced further and the number of resistant black bacteria start to increase

How does antibiotic usage influence the development of resistance?

Bacterial resistance can be categorised as follows:

- **Inherent resistance**. The absence of a cell wall in some bacterial species, eg, mycoplasmas, render agents which inhibit cell wall synthesis, such as ß lactams, ineffective. Similarly, anaerobic bacteria are inherently resistant to aminoglycosides as drug uptake mechanisms are oxygen dependent.
- **Spontaneous chromosomal mutation**. It is estimated that once in approximately 10 million bacterial divisions, a mutation occurs. Each mutation may or may not result in a survival advantage. If the mutation is not detrimental to the bacteria then it is passed on to future generations. Such a mutation might confer resistance to antibiotics.
- **Transferred resistance**. An example of transmissible genetic elements are plasmids which can be transferred between individuals of the same or different bacterial species. If a plasmid encodes antibacterial resistance this can be transferred and disseminated among a bacterial population.

Mutations which encode resistance do not require the presence of antibiotics for their generation. In fact, genes encoding for resistance to ß lactam and tetracycline antibiotics have been identified in bacterial DNA found in permafrost sediments which were 30,000 years old (Lloyd 2012). Following Darwin's principles of natural selection, the introduction of selection pressure (an antibacterial) will preferentially select the strain that bears an advantageous genotype and the longer the exposure to the antibacterial the more rigorous the selection process (see Box 1). Therefore, the presumption that long courses of antibiotics prevent resistance is incorrect; prolonged courses eliminate the sensitive bacteria and exert positive selection pressure favouring resistant strains (Department of Health 2013a). Furthermore, since plasmids may encode resistance to several antibiotic classes, use of one antibiotic may result in selection for stains with resistance to multiple antibiotic classes (Livermore 2003).

Observations have also shown that, in the presence of an antibacterial, bacteria can become hypermutable through inactivation of the proofreading and DNA mismatch repair systems that normally correct DNA copying errors. The transient induction of a hypermutable state adds a further

Table 1: Examples of physical examination and laboratory findings in canine and feline patients that may be found with bacterial infection. The findings are non-specific for bacterial infection, so alone may not be an indication to prescribe antibiotics

Presenting clinical sign	Differential diagnoses in which antibiotics are not required
Fever	Infection – viral, protozoal, fungal Sterile inflammatory disease Immune-mediated disease Paraneoplastic Metaphyseal osteopathy Stress
Neutrophilia	Infection – viral, protozoal, fungal Stress leukogram Sterile inflammatory disease Paraneoplastic Immune-mediated disease Medication – steroids
Leucocytosis	Infection – viral, protozoal, fungal Stress leukogram Sterile inflammatory disease Paraneoplastic Immune-mediated disease
Proteinuria	Protein-losing nephropathy Feline lower urinary tract disease

GI disorder	Example bacterial isolate	Empirical Antibacterial choices
Diarrhoea Acute Uncomplicated Acute Complicated (e.g leukopenia,pyrexia, heamatochezia,shock)		No antibacterials indicated amoxicillin-clavulanate or 1st generation cephalosporin
Conditions in which antibiotics are not indicated		
Uncomplicated Acute Vomiting Chronic gastroenteritis unless other differentials have been excluded and part of Antibiotic Responsive Diarrhoea treatment trial Pancreatitis- unless bacterial translocation is a concern or a concurrent suppurative process is present e.g. bacterial cholangitis in the cat (C)		

Respiratory	Example bacteria isolates	Empirical antibacterial choice
Aspiration pneumonia	Mixed infections are frequently identified	ampicillin or amoxicillin/clavulanate +/- enrofloxacin or Metrondazole
Pyothorax	*Actinomyces spp* *Bacteroides spp* *Fusobacterium spp* *Actinomyces spp* *Pasteurella multocide* *Nocardia spp* *E.coli*	amoxicillin/clavulanate (cat) ampicillin/clindamycin/metronidazole + fluoroquinolone (dog)
K cough	*Bordetella bronchiseptica* *Mycoplasma sp* *Streptococcus sp*	No antibioticss trimethoprim/sulphomide tetracyclines
Conditions in which antibiotics are not indicated		
Chronic bronchitis/allergic airway disease unless BAL culture positive Congestive heart failure		

Urogenital	Examples of common isolates	Empirical Antibacterial
Bacterial Cystitis	*E.coli* *Enterococcus spp.* *Proteus*	amoxicillin/clavulanate potentiated sulphonamides
Struvite urolithasis (dog)	*Staphylococcus aureus* *Proteus spp.* *Ureaplasma spp.*	amoxicillin/clavulanate potentiated sulphonamides
Pyelonephritis	*E.coli* *Enterococcus spp.* *Proteus*	potentiated sulphonamides
Prostatitis	*E.coli* *Staphyloccus spp.* *Streptococcus spp.*	potentiated sulphonamides fluoroquinolones
Conditions in which antibiotics are not indicated		
FLUTD – unless urine culture positive Struvite urolithasis – cat PUPD (unless pyogenic focus suspected) Urinary Incontinence		

Fig 1: An example of a practice prescribing policy and recommendations. The antibacterial choices have been taken from the BSAVA PROTECT poster (see Fig 3)

twist to the selection pressure exerted by antibiotics and may explain why multiple mutations have emerged more rapidly than predicted (Livermore 2003).

Antibacterial resistance is a complex and dynamic process, and for further information on resistance development see Livermore 2003, Martinez and Silley 2010 and Department of Health 2011.

What factors should veterinary surgeons consider when prescribing antibiotics?

Prescribing antibiotics is an everyday occurrence in veterinary practice. It may seem relatively straightforward, but using these drugs appropriately to ensure a good clinical outcome and at the same time reduce selection of resistant bacteria requires some thought. The following text reviews some of the principles that can help achieve these aims.

Are antibiotics really indicated in this patient?

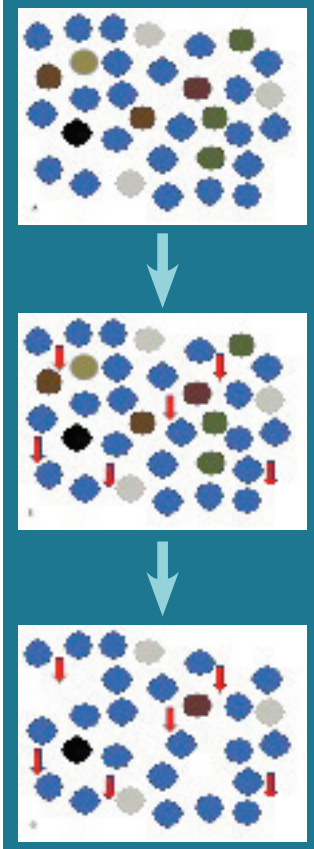
This is the first and most important question to consider when deciding whether to prescribe antibiotics. It could be an easy decision in cases with an obvious bacterial aetiology (eg, pyothorax) but less clear cut in others. Consider the following points before starting treatment:

- **Consider the specificity of your physical examination and laboratory findings for bacterial infection**. The presence of bacteria, seen on cytology or culture, in the presence of an appropriate inflammatory response (seen cytologically or histologically) is a specific indication of infection. Elevated temperature or the presence of a neutrophilia may prompt antibiotic administration but both these findings are not specific for bacterial infection (see Table 1). As such, the presence of a fever alone does not necessarily mean antibiotics should be prescribed.
- **If a patient fails to respond to an initial course of antibiotics, should a second course be prescribed?** If empirical therapy fails it is important to question if the initial diagnosis was correct, or if an inappropriate drug was chosen (see sections below on spectrum and pharmacokinetics). Changing antibiotic should only be considered following a review of the diagnosis, confirmation of infection and exclusion of factors that may affect treatment efficacy. A second antibiotic should be prescribed based on culture and sensitivity findings. Examples would include a dog with a fever (Table 1) or a cat with bronchopneumonia. In the latter, failure to respond to initial treatment may be due to presence of an inhaled foreign body. Further antibiotics of any kind will not result in resolution unless the foreign body is removed.
- **Owner expectations**. Owners may expect antibiotics to be prescribed for a condition that is likely to resolve without them, eg, acute uncomplicated diarrhoea. Owners are increasingly aware of bacterial antibiotic resistance and are now more open to discussion about the overuse of antibiotics. If antibiotics are not indicated then there are no circumstances in which a veterinary surgeon should feel compelled to prescribe them.

Selecting of the most suitable antibiotic

There are a number of factors that must be considered when selecting an antibiotic. These include the site of

Box 2: Narrow spectrum versus broad spectrum antibiotics on selection of resistance



This is the same bacterial population as described in Box 1. The black bacterium has the genetic potential for multi-drug resistance

Instead of a broad spectrum antibiotic, this time we introduce a narrow spectrum antibiotic. Only the brown bacteria (our target) and the beige commensal bacteria are sensitive to the antibiotic

As the antibiotic has a narrow spectrum we eliminate our target but a smaller number of commensals (only the beige). This leaves higher numbers of commensals to out compete the black multi-resistant bacteria

infection, the most likely pathogen (if culture results are not available), the spectrum of activity of the drugs available and their pharmacokinetic properties. Additional considerations include potential side effects, route of administration, drug interactions and the prescribing cascade. To aid such decisions, a practice prescribing policy can be developed (discussed later). Some of the principles and strategies to minimise selection of resistance are as follows:

Spectrum of activity and target organism

An understanding of which pathogens are likely to be encountered in specific infections (Fig 1) can aid the clinician when prescribing empirically, particularly if a Gram stain can be performed and antibacterials can be selected which are likely to be efficacious. The spectrum of activity of a given drug can be found in reference texts, eg, the BSAVA Formulary (Ramsey 2010). To simplify the process, most clinicians adopt the four quadrant approach for the drugs they most commonly use (eg, Gram-positive aerobes, Gram-negative aerobes, anaerobes and ß lactamase producing *Staphylococcus* species) (Maddison and others 2008).

When considering the available drugs, selection of one with the narrowest spectrum of activity possible will minimise the selection of resistant organisms (Department of Health 2013a) (Box 2). Generally, antibiotics used in veterinary medicine are broad spectrum; however, some have a wider range of activity than others (see Table 2). Combination therapy can increase the spectrum of activity in polymicrobial infections and, in some situations, there is synergism which improves efficacy (eg, trimethoprim sulfonamides). Combination therapy is not effective at preventing antibiotic resistance except in very few situations (Cunha and others 2012) and, with the potential for drug antagonism, monotherapy is preferred to combination therapy for the majority of infections. Combination therapy should not be instigated without the support of culture and sensitivity testing, given the potential impact on selection for resistance (Cunha and others 2012).

It is important to minimise the use of second line antibiotics and those reserved for life threatening human conditions – see Table 3 and the practice policy section below.

Topical/local versus systemic therapy

The application of an antibacterial topically or locally can result in higher drug levels at the target site compared to systemic administration. Cultures and in-vitro resistance testing can offer a guide to the sensitivity of bacteria to a given drug based on anticipated serum or tissue levels following standard dosing (Nuttall 2013). Topical therapy can achieve much higher local concentrations of antibiotics and can overcome apparent in vitro resistance.

A further benefit of topical therapy is minimising exposure of commensals to antibacterials. For example, prescribing a systemic antibacterial for a skin problem may select a resistant organism in the bowel.

Pharmacokinetics and optimising drug penetration and treatment

Although some perceive certain antibacterials to be 'stronger' than others, the efficacy of the drug is determined by multiple factors including lipid permeability, environment of the target tissue (eg, tissue pH, necrosis or presence of a foreign body), and the spectrum of activity of the drug, in addition to antibacterial resistance. The pharmacokinetics of specific antibiotics can be obtained from a reference pharmacology text. However, a few of the key considerations are listed in Box 3.

These factors mean that the sensitivity of a bacterium to drugs in vitro does not guarantee success in vivo. Conversely, apparent resistance in vitro may be overcome in vivo by achieving higher antibacterial concentrations using topical therapy or by considering the pharmacokinetics of the drug, eg, ß lactams achieve very high concentrations in the urine.

Table 2: Examples of antibacterials classified by their spectrum of activity

Type of spectrum	Examples
Narrow spectrum	Penicillin Metronidazole Aminoglycosides
Moderate spectrum	Macrolides or macrolide-related Lincosamides (lincomycin, clindamycin)
Broad spectrum	Amoxicillin ± clavulanate, ampicillin Cephalosporins Tetracyclines Potentiated sulfonamides Fluoroquinolones*

*Third generation fluoroquinolone pradofloxacin has a wider spectrum of activity than marbofloxacin and enrofloxacin

Table 3: Example of a veterinary classification of antibiotics

Classification	When to use	Examples
Topical		Chlorhexidine Fusidic acid
First tier (or empirical)	Initial therapy with known or suspected bacterial infection or while culture and sensitivity results pending	Penicillins Clindamycin 1st and 2nd generation cephalosporins Potentiated sulfonamides
Second tier	Antibacterials reserved for use when supported by culture and sensitivity results or if other factors determine that 1st tier choices are ineffective	Amikacin Fluoroquinolones 3rd and 4th generation cephalosporins
Classed as critically important for life-threatening infections in humans and restricted use guidelines for humans. Loss of efficacy would have serious implications for human health	Strong arguments that should never be used in veterinary medicine	Imipenin Vancomycin Linezolid Teicoplanin

Box 3: Some basic pharmacokinetic principles to consider when prescribing antibiotics. More detailed information can be obtained from Maddison and others (2008)

Distribution

Many of the antibiotic classes are well distributed around the body. It is also important to be aware of some of the specifics of distribution:

Aminoglycosides not absorbed from the gastrointestinal tract.

Hydrophilic drugs that have low lipid solubility include ß lactamase inhibitors, cephalosporin, aminoglycosides, polymixins and penicillins. These drugs do not readily attain adequate concentrations in the cerebrospinal fluid and other transcellular fluids, but adequate concentrations may be achieved in joints, pleural and peritoneal fluids.

Lipid barriers prevent drug permeability to the central nervous system, eye, bronchial secretions, prostate and mammary glands. Lipid-soluble basic antibacterials such as the macrolides and lincosamides become ion trapped (concentrated) in sites such as the prostate and the mammary gland. Other lipid-soluble drugs include potentiated sulfonamides, fluoroquinolones, metronidazole and tetracyclines.

During severe inflammation, the lipid barrier may become more leaky which allows most drugs to penetrate. However, as the inflammation resolves, the barrier efficacy returns and bacteria can sequester within the tissue unless a lipid soluble drug is used.

Due to the high renal excretion of the ß-lactam drugs (penicillins and cephalosporins), high concentrations (up to x200 that in plasma) can be achieved in the urine. As a consequence, in some cases of urinary tract infection ß-lactams may still be effective in the face of an apparent in-vitro resistance.

Local environment

Pus/necrotic environments inactivate aminoglycoside and trimethoprim sulfonamides.

Metronidazole can work in low oxygen tensions.

Low pH significantly reduces the activity of fluoroquinolones and clindamycin.

Pus, necrotic tissue and foreign material can reduce the chances of achieving adequate tissue concentrations at the target tissue and act as a nidus of infection.

Bacterial considerations

Penicillins rely on bacterial division because they act on cell wall synthesis. So, if bacterial growth is slow, drug efficacy will be reduced.

Intracellular pathogens require a drug that will penetrate into cell rather than those that remain in the extracellular space. These drugs include tetracyclines and fluoroquinolones

The distinction between bactericidal and bacteriostatic agents is clear using in vitro techniques but is inconsistent for a particular agent against all bacteria (Parnkey and Sabeth 2004). For most infections, bacteriostatic and bactericidal agents inhibit organisms at the same rate and should not be a factor in antibiotic selection (Cunha and others 2012). Bactericidal antibiotics have an advantage in certain infections, such as endocarditis and bacterial meningitis (Cunha and others 2012), but bacteriostatic agents have still been used to treat these infections successfully in humans (Parnkey and Sabeth 2004).

The status of the host's immune system should also not be forgotten. Antibiotics have a role in killing and curing an infection; however, they assist the immune system to control an overwhelming infection. Treatment failure can occur when using appropriate antibiotics in patients with immunodeficiency due to chronic debilitation or malnutrition.

Duration of treatment course: as short as possible . . .

Unfortunately, to date, the data to determine the shortest effective period of therapy for veterinary species are very limited. In human medicine, there has been a shift towards much shorter courses of antibiotics (typically shorter than those used in veterinary species, see Table 4).

Until studies in veterinary patients are performed comparing different treatment durations of the same antibiotic for a specified condition, production of evidence-based guidelines is not possible. Although there will, no doubt, be species differences, the author encourages readers to consider the shift in human medicine towards a shorter course and whether, as vets, we have a tendency to prescribe longer courses than might be necessary.

Antibiotic stewardship and developing a practice prescribing policy

Antibiotic stewardship is designed to ensure cost-effective therapy and improve patient outcome while minimising selection for bacterial resistance. Stewardship can be instigated at multiple levels, which may include national awareness campaigns, hospital guidelines, or the implementation of restricted antibiotic usage. The Department of Health Advisory Committee promotes the 'Start Smart – Then Focus scheme', which offers guidance for antibiotic stewardship in hospitals in England (Department of Health 2011b). The scheme assists hospitals to produce guidelines based on regional bacterial resistance profiles.

Veterinary examples of prescribing guidelines include the poster produced by British Veterinary Association (Fig 2) and the 'Are you PROTECTing antibiotics' poster (Fig 3) developed by Small Animal Medicine Society and the British Small Animal Veterinary Association. The latter also lists a number of common conditions encountered in practice and makes suggestions for treatment. The user can then select one of the suggestions as the standard empirical treatment for the practice.

A practice policy should also include a list of conditions for which antibiotics are not indicated (Fig 1) and guidelines on perioperative and postoperative antibiotic prescribing (see Box 4). Following implementation of a practice policy, monitoring of culture profiles within the practice allows adjustments to the policy if trends are identified.

Table 4: Examples of studies performed in the human medical field which have indicated that the duration of antibiotic treatment can be reduced

Condition	Summary of outcome
Uncomplicated lower urinary tract infection in females[a]	No difference between 3 days of treatment and 5 to 10 days
Pyelonephritis (non-hospitalised patients)[b]	Meta-analysis indicated no difference between 7 to 14 days treatment and 14 to 42 days.
Septic arthritis in children[C]	No difference in outcome between 10 days and 30 days treatment

a Milo and others 2005, b Kyriakidou and others 2008, c Peltola and others 2009

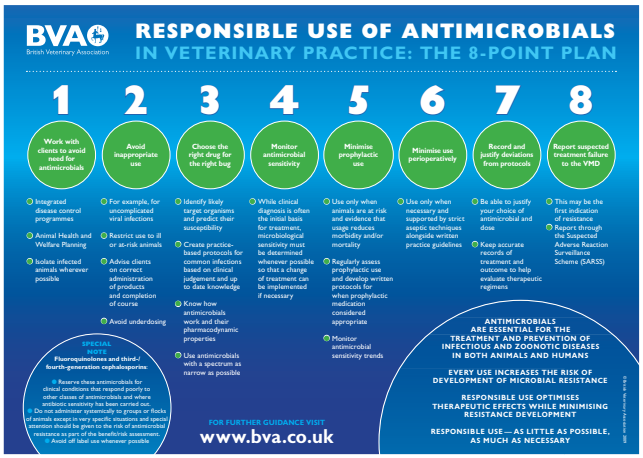


Fig 2: A poster from the British Veterinary Association on the responsible use of antibiotics. This can be downloaded from www.bva.co.uk/public/documents/bva_antimicrobials_poster.pdf

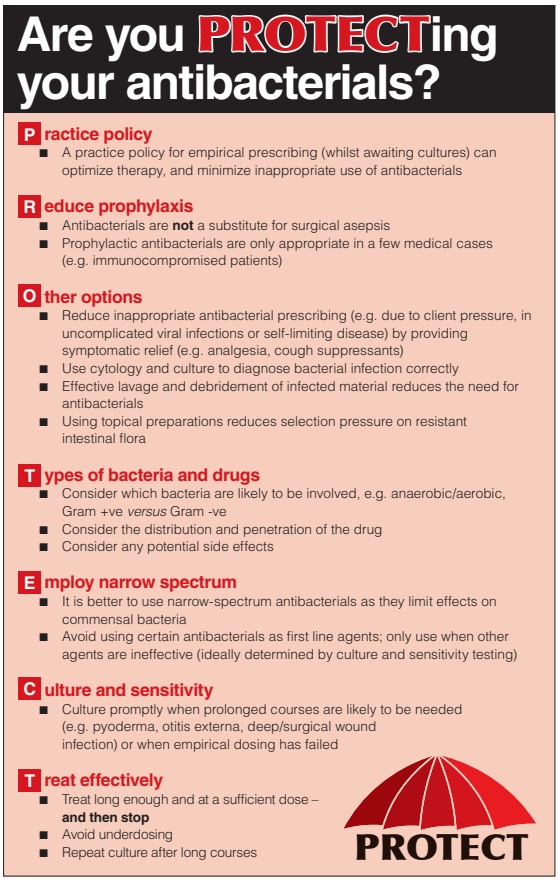


Fig 3: Poster advising on the British Small Animal Veterinary Association PROTECT acronym (published with permission of BSAVA *Companion* magazine). This can be downloaded from www.bsava.com/Portals/4/knowledgevault/resources/files/Protect_Poster.pdf

The positive impact of empirical prescribing guidelines on resistance profiles in hospitals has been highlighted in human medicine. Protocols normally involve multiple strategies, making accurate assessment of the antibiotic stewardship programmes challenging due to their complexity. Stewardship, in combination with other infection control protocols, has assisted in the reduction of hospital-acquired infections in England, which in 2011 had a prevalence of 6.4 per cent compared to 8.2 per cent in 2006 (Health Protection Agency 2012). Active involvement of staff in the development of the policy has shown to improve compliance and policies that involve the restriction of certain antibacterials have also proven effective (Mateus 2011). Such studies are rare in veterinary practice; nevertheless, those that have been performed have demonstrated a positive effect on prescribing habits. In 2006, for example, a Canadian teaching hospital demonstrated a reduction in the frequency of antibacterial prescribing, particularly of fluoroquinolones over a nine-year period (Weese 2006).

In human medicine, a first line (or empirical) treatment is usually chosen on the basis of its efficacy. In veterinary medicine, we adopt the definition that first-line antibiotics typically are older and less expensive drugs, eg, amoxicillin or potentiated sulfonamides (Table 3). As veterinary surgeons, we should minimise the empirical use of second line antibiotics, which should be reserved for cases in which culture and sensitivities indicate that first line choices are ineffective. There are strong arguments that antibiotics restricted for use in life-threatening infections in human medicine (eg, imipenem, linezolid, teicoplanin, vancomycin) should not be used in animals under any circumstances.

Minimising prophylactic and perioperative use of antibiotics.

Prophylactic use of antibiotics should be avoided, but there are specific situations where it is appropriate.

Surgery

Detailed discussion of surgical prophylaxis can be found in BSAVA (2011) and Knights and others (2012). Some of the important points are listed in Box 4.

Immunocompromised patients

In neutropenic patients, antibiotics may be given to control the gastrointestinal flora, which is the most common source of infection in these patients (through translocation). Trimethoprim sulfonamide is an appropriate first choice.

Dentistry

Prophylaxis is required in at-risk patients, eg, those with aortic stenosis or previous endocarditis. Options include metronidazole, clindamycin, and amoxicillin, +/- chlorhexidine mouthwash. For prophylaxis, a 24-hour course started the day before the dental procedure is sufficient. For gingivitis/stomatitis, a 10 to 14 day course is required; however, antibiotics should not be used alone, but in combination with scaling, polishing and extractions.

Summary

Antibiotic resistance affects all areas of veterinary medicine. In order to protect the efficacy of antibacterials for veterinary patients, and to protect the prescribing privileges that veterinary surgeons have, there must be a unified responsible approach to using these drugs and veterinary surgeons should promote responsible use where possible.

Box 4: Important points regarding perioperative and postoperative antibiotic use (ie, use during surgical operations and after surgery has been completed)

- The goal of prophylaxis is to reduce the incidence of postoperative wound infections and assumes use where contamination may occur. Prophylactic use of antibacterials is not a substitute for appropriate aseptic technique.
- There is good evidence to suggest that inappropriate use of perioperative antibiotics may increase the risk of surgical site infection with resistant organisms. This is because surgical site infections typically develop due to colonisation of the wound with bacteria from the patient's endemic flora or from human staff involved with care.
- Decontamination: reducing bacterial exposure is one of the most important ways to avoid future antimicrobial usage and resistance. This includes disinfection of the environment, effective hand washing, use of gloves and reducing exposure to contaminated areas by separating work areas.
- Clean surgical wounds (eg, not involving the gastrointestinal or respiratory tract) do not require prophylactic antibiotic therapy unless the consequences of infection are serious (eg, orthopaedic implants, involves central nervous system) for prolonged surgery (>1.5 hours) or where there has been a break in asepsis.
- Contaminated wounds (eg, bite wound or intestinal surgery with leakage) should be treated as infected and managed with pre- and post-surgical antibacterial therapy.
- If required, a dose of intravenous antibiotic is given at the time of anaesthetic induction and within one hour of the incision. If the surgery lasts longer than 2 to 3 hours, then an additional dose can be given during the procedure.
- Potentiated amoxicillin or first/second generation cephalosporins are good choices for surgical prophylaxis because they will cover the pathogens that are most likely to infect the surgical wound. If there is likely to be involvement of anaerobes (eg, surgery of the lower gastrointestinal tract) then metronidazole can be added.
- A single preoperative dose of antibiotic for an uncomplicated procedures is as effective as a five-day course of postoperative therapy.
- Postoperative antibiotics are not indicated in routine operations eg, neutering and 'lumpectomies' unless there is concern regarding intraoperative contamination.
- Use of a postoperative course of antibiotics may be recommended in some non-routine surgeries, eg, those involving implants. Readers should consult BSAVA (2011) and Knight and others (2012) for current recommendations.

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Quiz: Using antibiotics responsibly in companion animals

1. Which of the following statements is false?

a. Antibacterial usage can select for resistant strains of bacteria that have occurred through mutation.
b. In human medicine, to minimise the selection of antibiotic resistance, there is a trend towards longer courses of antibiotics.
c. Optimising treatment efficacy and drug delivery can reduce the length of treatment course necessary, which benefits the patient but also reduces the selection pressure for resistance.
d. Prescribing systemic antibiotics affects bacteria all over the body, in particular the bowel, which, given the numbers of bacteria present, is the most likely site of selection of resistant bacteria.
e. Plasmids containing DNA encoding for antibacterial resistance can be transferred between bacteria of the same species, but also across species. Plasmids can encode resistance for one or more than one class of antibiotic.

2. Which of the following statements are false?

a. Pyrexia is only caused by bacterial infection and, therefore, if present, antibacterials should always be prescribed.
b. In a cat with signs of dysuria and pollakuria, a urine dipstick indicates the presence of protein. Antibacterials are indicated in this situation without a culture.
c. Pyrexia can occur during infection. The infection may be bacterial, viral, fungal or protozoal so antibacterials may not always be indicated in the presence of an infection-induced pyrexia.
d. Pyrexia can occur secondary to infection, immune mediated disease or be paraneoplastic.
e. Antibiotics are always indicated in the presence of a neutrophilia.

3. Which are the following is true regarding meticillin-resistant *Staphylococcus pseudointermedius?*

a. Following a recent taxonomic change, *Staphylococcus intermedius* is now termed *S pseudointermedius*.
b. Genetic material encoding for resistance has the potential to pass between different staphylococcal species.
c. In recent non-peer reviewed data released by a UK laboratory, MRSP isolates accounted for 14 per cent of coagulase positive Staphs isolated. These isolates were resistant to more antibiotics than the MRSA isolated in the same period.
d. MRSP rarely colonises humans, but carrier rates are increased in individuals exposed to dogs.
e. All of above.

4. Which of the following statements is false ?

a. A practice prescribing policy should include a list of conditions in which antibacterials are not indicated and guidelines on perioperative prescribing in routine procedures.
b. A practice prescribing policy forms part of infection control measures and ideally should be implemented alongside policies on cleaning and staff hygiene.
c. A practice policy on prescribing enables standardised approaches to treatment which can improve patient outcome and improve responsible prescribing.
d. There is good evidence that inappropriate use of perioperative antibiotics may increase the risk of surgical site infection with more resistant organisms.
e. Not involving staff in designing a practice prescribing policy can improve compliance.

5. True or False?

To protect efficacy of antibacterials for veterinary patients and to protect our prescribing privileges, the veterinary professional must develop a unified responsible approach to responsible antibiotic prescribing.

Answers: (1) b, (2) a, b, e, (3) e, (4) e, (5) True

InPractice

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Notes