GUIDELINES FOR THE PRUDENT USE OF ANTIMICROBIALS IN COMPANION ANIMALS

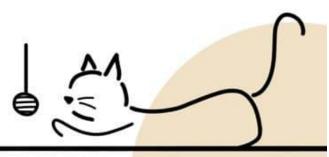
NATIONAL PARKS BOARD, ANIMAL AND VETERINARY SERVICE, SINGAPORE VETERINARY ASSOCIATION

Foreword by Dr Teo Boon Han Prudent Use Working Group Co-Chairperson

Antimicrobial resistance (AMR) has emerged to be one of the most serious threats to human health on a global scale and has been declared by the World Health Organisation (WHO) as one of the top 10 global public health threats. Aside from endangering human health and prolonging illnesses, AMR also threatens the health and welfare of companion animals and livestock; consequently, food safety and food security could also be impacted.

Combatting AMR requires a transdisciplinary collaboration spanning across all levels of society, with buy-in and action across different sectors in a holistic 'One Health' approach. At a national level in Singapore, this 'One Health' approach is embodied by the formation of the One Health Antimicrobial Resistance Workgroup in January 2017, and the subsequent publication of the National Strategic Action Plan on AMR.

The publication of these guidelines, jointly developed by members of the Singapore Veterinary Association and the Animal and Veterinary Service, is timely and well-aligned with the National Strategic Action Plan on AMR. I hope that the guidelines will be a practical and useful reference for veterinary practitioners as we safeguard animal health and welfare on a day-to-day basis. The guidelines also remind us that the veterinary profession continues to play a key role in this fight to protect human health, animal health and welfare, and the environment. I look forward to the continued contributions of the veterinary profession as we work together to continue advancing veterinary practice in Singapore.



Foreword by Dr Yap Him Hoo

Director General (Animal and Veterinary Services)

Antimicrobial resistance is a global threat to people, animals and the environment. When our currently available antimicrobial medications are no longer effective in treating infections, it will undermine years of medical progress and advancement that have been achieved thus far in treating humans and animals. A coordinated and synergistic One Health approach is essential in tackling this issue. This would cut across boundaries of public health, animal health, food and environment health.

Veterinarians play an integral role in the One Health effort to combat antimicrobial resistance. Amongst their numerous responsibilities, veterinarians are responsible for adhering to good prescribing practices and are an important interface with pet owners, farmers, and other animal caregivers in raising awareness on judicious antimicrobial use in animals. NParks/AVS has partnered with the Singapore Veterinary Association to produce Singapore's first Antimicrobial Prudent Use Guidelines for Companion Animals, in consultation with the local veterinary community. These guidelines provide updated, practical recommendations on prudent antimicrobial use, together with relevant resources on antimicrobial resistance and antimicrobial stewardship. I look forward to further collaborations amongst the veterinary profession, animal-related industries, and One Health partners in our combined effort to tackle antimicrobial resistance.



WORKING GROUP CONTRIBUTORS LIST

National Parks Board/Animal and Veterinary Service members:

Dr Kelvin Lim, BSc, BVMS, MPH-VPH, MS, MANZCVS (Vet Epidemiology), DACVPM Prudent Use Working Group Co-Chairperson

Dr Juline Chua, BVSc (Hons) Prudent Use Working Group Secretariat

Dr Suria Fabbri, BSc (Vet Bio), DVM Prudent Use Working Group Secretariat

Dr Christine Lee, BVetMed (Hons), MRCVS

Dr Denyse Khor, DVM (Distinction), CertAqV

Dr Grace Yam, BVSc

Singapore Veterinary Association members:

Dr Teo Boon Han, BVetMed, MRCVS, PG(Animal Nutrition), PGVetEd, FHEA Prudent Use Working Group Co-Chairperson

Dr Han Zi Yang, BVSc (Hons)

Dr Amelia Ho, BSc (Vet Bio), DVM

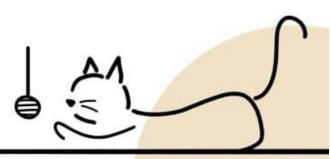
Dr Brian Loon, BSc. BVMS (Hons) (Murdoch), CVA (IVAS)

Dr Daphne Ang, BPharm, BVSc (Hons), MRCVS

Dr Denise Poh, BSc BVMS PgCert MVS MVetClinStud MSAECC

Dr Laurent Fillon, DVM, CESOpthalmology

Dr Simon Quek, BSc BVMS, MRCVS



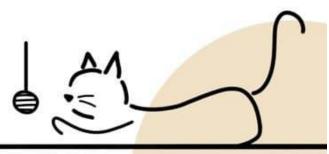
ACKNOWLEDGEMENTS

We would like to thank the following veterinarians for providing chapters or editorial reviews for the guidelines:

Dr Alfonso Lopez (Chapter 4: Exotics- Fish) Dr Komsin Sahatrakul (Chapter 4: Exotics- Fish) Dr Heng Yirui (Chapter 4: Exotics- Small Mammals) Dr Frederic Chua (Chapter 4: Exotics- Fish) Dr Patrick Maguire (Chapter 4: Abdominal; Musculoskeletal)

We would like to give a special thanks to Ms. Jocelyn Ng Sze Hui for her dedication and creativity in illustrating and formatting these guidelines, and the students from Ngee Ann Polytechnic, Ms Chong Yu Qian and Mr Michael Tejas Johnson, and Temasek Polytechnic, Ms Tessa Lee, for their contributions in data analysis.

We would like to thank "Asia Veterinary Diagnostics" (AVD) laboratory for providing microbial identification, antimicrobial susceptibility testing data from veterinary patient samples seen in Singapore. We would also like to acknowledge the AVD team for interpretation of the antimicrobial susceptibility data used to prepare this guideline. The AVD team who worked hard on this portion of the guideline included: Ms Praveena Jayarajah, M James Leung, Ms Jessica Yu Min Sing, Ms Brenda Kwek, Ms Kat Chew, Ms Rena Tan, Dr Myriam Baranger-Ete and Dr Véronique Bachy.



PRINCIPLES

The Working Group acknowledges the critical problem of AMR and recognises the urgent need for a collaborative effort within the veterinary community in slowing and preventing further development and spread of AMR in Singapore. The Working Group strongly believes that as veterinarians, we play a vital role in this cause through the following:

- Optimise therapeutic efficacy with an appropriate choice, duration, and administration of antimicrobial(s) therapy for a given specific medical condition.
- Educate owners/clients with up to date, evidence-based and accurate information on the determinants of AMR and the measures required to prevent it (i.e., adherence to treatment course and infection prophylaxis).
- Identify where owner or patient compliance is likely to be an issue and take appropriate measures to achieve compliance.
- Prioritise patient care, infection prevention and control. Simultaneously, diagnostic and therapeutic intervention(s) that may help prevent development of AMR are also strongly supported.
- Support the 'One Health' approach to ensure appropriate and judicious use of antimicrobials.
- Commit to aid the introduction, integration and implementation of new initiatives into daily practice as part of Antimicrobial Stewardship Programmes (ASP).



PRUDENT USE TIPS

- When prescribing antimicrobials, the most appropriate drug, shortest effective treatment period, lowest effective dose and most appropriate route of administration should be considered.
- 2. Ideally, the choice of antimicrobials should be based on culture and sensitivity (C&S) results. In cases where C&S testing is not available, practical, or feasible, first-line selection of antimicrobial(s) should be based on the most likely pathogen(s) associated with a particular infectious disease and/or available susceptibility profiles.
- 3. Avoid empirical or first-line use of critically important antibiotics (CIA) without C&S testing [Annex VI]. If first-line CIA has been instituted and has failed, C&S testing is strongly recommended. If financial constraints preclude C&S testing, another class of antimicrobial agent likely to be effective against the putative pathogen should be chosen.
- 4. Combination or 4-quadrant antimicrobial therapy should be avoided unless a lifethreatening infection is evident.
- 5. Antimicrobial treatment regimens should be regularly assessed during therapy and de-escalation should be considered whenever possible
- 6. Antimicrobial therapy should be discontinued once there is clinical and microbiological evidence that an infection has been eliminated, or once an alternative diagnosis has been made.
- 7. Develop and implement infection control and ASP protocols, especially when handling potential MDR infected animals.





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ABBREVIATIONS

- **AMR:** Antimicrobial Resistance
- AMU: Antimicrobial Use
- ASP: Antimicrobial Stewardship Programme
- **AST:** Antimicrobial Susceptibility Testing
- AVS: Animal and Veterinary Service
- C&S: Culture and Sensitivity
- MIC: Minimum Inhibitory Concentration
- MDR: Multi Drug Resistance
- NParks: National Parks Board
- **OIE**: World Organisation for Animal Health
- SVA: Singapore Veterinary Association
- WHO: World Health Organisation

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1. INTRODUCTION, SCOPE AND OBJECTIVE OF GUIDELINES

INTRODUCTION

Antimicrobials, including antibiotics, antivirals, antifungals and antiparasitic have been used to treat infections in humans, animals and plants. Today, antibiotics are one of the most commonly used drugs in human and veterinary medicine, not only for the treatment and prevention of infectious diseases of bacterial origin, but also for ensuring the safety and success of other important medical procedures and interventions such as surgeries. This ensures the health and welfare of animals and protect public health.

The development and spread of AMR has been increasingly observed globally. This is accelerated through the misuse and overuse of antibiotics. In Singapore, this trend is observed as well. The emergence and increase in the number of resistant bacteria reported in local veterinary practices threatens our ability to treat animal infections, the health of veterinary staff and companion animal owners and caregivers, and on a larger scale, public health. Infection with resistant pathogens result in higher morbidity and mortality in both people and animals. They are also more costly to treat due to prolonged hospital stays, overall causing greater burden on healthcare systems. AMR is a growing threat to modern medicine and our ability to treat common infections.

The Code of Ethics for Veterinarians states that a veterinarian is responsible for choosing the treatment regimens for his/her patients, based on sound, evidencebased science and practice and/or diagnostic test results. The Singapore veterinary profession should understand the importance of judicious and responsible use of antimicrobials, actively promote prudent use of antimicrobial drugs, as well as educate pet owners and animal caregivers on AMR.

To aid in this effort, NParks/AVS and SVA formed a working group to develop a set of guidelines for the prudent use of antibiotics in companion animals. Members of the working group consist of private practice and specialist veterinarians with substantial clinical experience in working with exotics and small animals, as well as government veterinarians experienced in animal and public health, ecology, surveillance and epidemiology of AMR.

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1. INTRODUCTION, SCOPE AND OBJECTIVE OF GUIDELINES

SCOPE

These guidelines contain recommendations on prudent use of antibiotics for companion animal species, which include dogs and cats, as well as select exotic animal species such as small mammals, avian species and fish.

The guidelines are intended to provide quidance for veterinarians practising in Singapore and aid prescription decisionmaking for individual patients based on clinical assessments by a veterinarian. The Working Group consolidated therapeutic recommendations for a list of common medical and surgical conditions seen in general and referral veterinary practices in Singapore for small animals and exotic animal species, based on available references and international guidelines familiar to local veterinarians. The Working Group recognises that the list of conditions with recommendations are not completely exhaustive and acknowledges that recommendations need to be updated over time and may not be applicable to all cases, particularly complex/complicated cases. Clinician discretion is strongly advised in such cases and the rationale for treatment be documented. Where new peer-reviewed or credible evidence is updated, they should be referred to as well. These recommendations are also not intended to be extrapolated to other uses.

The guidelines specifically refer to antibiotic use only. The Working Group may consider the addition of recommendations for other antimicrobial agents such as antifungal agents, if necessary or appropriate, in subsequent review of the guidelines.

OBJECTIVE

The primary objectives of these guidelines are to provide evidence-based recommendations to guide veterinarians in Singapore to practise judicious and responsible use of antimicrobials, and to improve antimicrobial stewardship in veterinary practice in Singapore.

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2. ANTIMICROBIAL RESISTANCE AND ANTIBIOTIC USE

HISTORY OF ANTIMICROBIALS

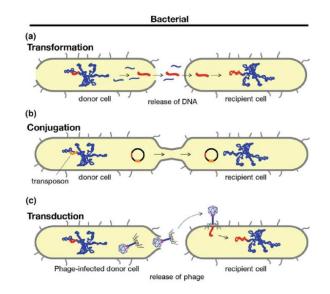
Antibiotics are used to treat or prevent the onset of bacterial infections in humans, plants and animals. Their discovery, development and use has underpinned modern medicine since the 1940's, including treating once lethal infections, allowing routine surgeries and supporting treatment of cancers.

Contrary to the common belief that antibiotics have been in existence only since the 19th Century, traces of antibiotics found in skeletal remains dating back to 350-550 CE show evidence of ancient antibiotic exposure. However, antibiotics were only discovered and gradually developed for use as medicines after the 1930s.

Today, antibiotics are used widely in human and veterinary medicine and dentistry both to treat and to prevent infections. Antibiotics are also an important tool in safeguarding global food supply and safety – the use of antimicrobials in treating and preventing disease alongside scientific and technological developments such as improvements in genetics, biosecurity, husbandry, veterinary medicine, etc. have allowed for marked increases in food animal production to meet consumer demand.

ANTIMICROBIAL RESISTANCE

Bacteria and other microorganisms naturally develop resistance to antibiotics over time through genetic changes via genetic mutations and/or acquisition of foreign DNA segments.



Mechanisms of horizontal gene transfer in bacteria³: (a) Uptake of naked DNA from the environment (transformation)

- (b) Transfer of plasmid genetic material through the mating-pore pilus from a donor to a recipient bacterial cell (conjugation)
- (c) Transfer of genetic material from a donor to a recipient bacterial cell through a bacteriophage intermediate (transduction)

2. ANTIMICROBIAL RESISTANCE AND ANTIBIOTIC USE

Widespread, inappropriate use of antibiotics has resulted in an alarming increase in antibiotic-resistant infections as it has accelerated the changes to the bacteria that allow resistance to develop and flourish. Examples of inappropriate use include taking antibiotics for viral infections (colds and flu), prescribing when not genuinely required and overuse and misuse in animals and food production, such as for growth-promoting purposes.

As a result, standard medical treatments such as broad-spectrum antibiotics become ineffective, infections persist and spread to others. Compounded with no new antibiotic discoveries being made in the past 2-3 decades, resistance has become a significant One Health issue – medical and veterinary professionals are left with limited or, in some instances, no available treatment options.

Intentional and increased efforts to decrease or eliminate inappropriate use can have a big impact on patient safety and the problem of AMR. The most critical issue is in the resistance of highly infectious strains of bacteria to antibiotics. In the companion animal realm, inappropriate antibiotic prescribing often occurs because of both veterinarians and their clients. Veterinarians may face limitations in antibiotic usage by factors such as the availability of antibiotics in their clinics, influence from pharmaceutical companies, client demands and satisfaction, personal values, beliefs and practice habits. Veterinarians are expected to strike a balance between providing medical advice, managing clients' expectations, achieving effective communication with clients, and staying competitive in the veterinary business.

Nonetheless, veterinarians play a critical role in combating AMR, promoting responsible AMU, and reducing the impact of resistant pathogens.

It is important to ramp up efforts to decrease or eliminate inappropriate AMU to optimise clinical outcomes while minimising unintended consequences, including the emergence and spread of resistance. Veterinarians need to take action to improve the knowledge and understanding of AMR and conserve the effectiveness of existing treatments by developing sector-specific prescribing guidelines and promoting responsible use practices.

Aminov R. I. (2010). A brief history of the antibiotic era: lessons learned and challenges for the future. Frontiers in microbiology, 1, 134. https://doi.org/10.3389/fmicb.2010.00134

The New Zealand Veterinary Association. (2021) Antimicrobial Resistance (AMR).

<https://www.nzva.org.nz/resource/general/amr/>

Vernikos, George & Medini, Duccio. (2014). Horizontal Gene Transfer and the Role of Restriction-Modification Systems in Bacterial Population Dynamics. 10.1007/978-3-319-07623-2_8.



CATEGORISATION OF ANTIBIOTICS

- Antibiotic class, which is typically determined by mode of action or chemical structure and properties
- 2. Effect on bacteria, which can be bacteriostatic or bactericidal
- Pharmacological properties, which can be time-dependent or concentrationdependent

ANTIBIOTIC CLASSES

The commonly encountered classes of antibiotics in companion animal medicine are listed in Table 1 below, together with some examples of antibiotic compounds that belong to each class.

4. Spectrum of activity

Antibiotic Class	Examples
Aminoglycosides	Amikacin, framycetin, gentamicin, neomycin, tobramycin
Amphenicols	Chloramphenicol
Carbapenems	Meropenem
Cephalosporins, 1 st and 2 nd generation	Cephalexin, cefazolin
Cephalosporins, 3 rd and 4 th generation	Cefovecin, cefotaxime, ceftriaxone
Fluoroquinolones	Ciprofloxacin, enrofloxacin, marbofloxacin
Fusidane	Fusidic acid
Lincosamides	Clindamycin
Macrolides	Clarithromycin, spiramycin, tylosin
Monoxycarbolic acid	Mupirocin
Nitroimidazoles	Metronidazole, tinidazole
Penicillins	Amoxicillin, ampicillin, penicillin
Polypeptides	Bacitracin, polymyxin B
Sulfonamides	Sulfacetamide, sulfadiazine, sulphamethoxazole
Tetracyclines	Chlortetracycline, doxycycline, oxytetracycline

Table 1: Antibiotic Classes and examples of compounds used across animal species

MUSCULOSKELETAL

EYE

INTEGUMENT

AURAL

ABDOMINAL THORACIC



EFFECT ON BACTERIA

Antibiotics can be

further categorised based on their effect on bacteria, which can be bacteriostatic or bactericidal.

Bacteriostatic

antibiotics (e.g., tetracyclines, chloramphenicol, macrolides and lincosamides) temporarily inhibit bacterial growth, although the effect is reversible once the antibiotic is no longer present. Antibiotic concentration at the site of the infection should be maintained above the minimum inhibitory concentration (MIC) throughout the dosing interval for the antibiotic to be effective. Bacteriostatic antibiotics also depend on a functional immune system for effective elimination of bacteria by the infected host and are typically not recommended for the sole use in patients that are immunocompromised or that have severe and acute infections.

Bactericidal

antibiotics (e.g., aminoglycosides, cephalosporins, fluoroquinolones, metronidazole, penicillins, potentiated sulphonamides) cause the death of the bacteria, which is preferred in infections that cannot be adequately controlled or eradicated by host mechanisms, due to factors such as the nature or site of the infection or host immunocompetency.

It is worthwhile to note that most antibiotics can potentially be both bacteriostatic and bactericidal, depending on the drug concentration achieved at sites of infection, the duration of drug action, and state of the invading bacteria [Annex I].

PHARMACOLOGICAL PROPERTIES

Antibiotics can be further divided into timedependent or concentration-dependent antibiotics.

Time-dependent antibiotics (e.g., penicillins and cephalosporins) are slowly bactericidal and require bacteria to be multiplying for them to be effective. Ideally, these antibiotics should not be given in combination with bacteriostatic antibiotics. Adherence to dose timings is important as plasma levels should be maintained above MIC for as long as possible during each 24hour period. It is also recommended that plasma levels be above MIC for 80% of the 24-hour period to reduce the risk of resistance emerging.

Concentration-dependent antibiotics (e.g., aminoglycosides and fluoroquinolones) kill a greater proportion of target bacteria and have a longer post-antibiotic effect as peak plasma concentration rises. It is therefore important that such antibiotics are administered in sufficiently high doses to ensure therapeutic efficacy. These antibiotics are also effective against dormant bacteria and can be given in combination with bacteriostatic drugs.

ORAL



SPECTRUM OF ACTIVITY

Antibiotics can also be categorised by their activity against certain groups of bacteria. One practical grouping of bacteria, as well as the types of antibiotics effective against each group, in companion animal medicine is listed in Table 2 below.

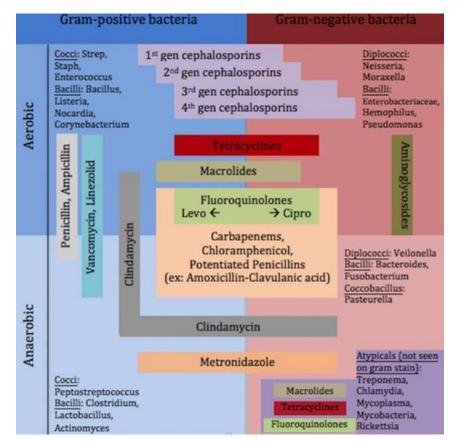
Adequate understanding of the spectrum of activity of antibiotics and the bacterial groups of likely pathogens involved in infections is essential, as this will allow veterinarians to choose appropriate empiric therapies for their patients. Information on the likely pathogens in common infections found in companion animals, together with their antibiotic recommendations, are found in Chapter 5.

Bacterial Group	Examples of Antibiotics with Excellent Activity
Gram positive aerobic bacteria (and facultative anaerobes)	Ampicillin, amoxicillin, cephalosporins, lincosamides/macrolides
Gram negative aerobic bacteria (and facultative anaerobes)	Aminoglycosides, fluoroquinolones
Obligate anaerobes, both gram negative and positive	Amoxicillin-clavulanic acid, clindamycin, metronidazole
Penicillinase- producing <i>Staphylococcus</i> species	Amoxicillin-clavulanic acid, 1 st and 2 nd generation cephalosporins, fluoroquinolones
Atypical bacterial species (which do not or are difficult to Gram stain), e.g. <i>Rickettsia, Mycoplasma,</i> <i>Chlamydia, Borrelia,</i> <i>Bartonella,</i> and <i>Mycobacterium</i> species	Fluoroquinolones, tetracyclines

Table 2: Bacterial groups and examples of antibiotic choices with excellent activity

EXOTICS

3. ANTIBIOTIC CLASSES AND LEVEL OF PRIORITY



⁽Figure from J Vet Emerg Crit Care. 2019;1-12. Antibiotic use in critical illness. Samuel D. Stewart, Sarah Allen)

CATEGORISATION OF ANTIBIOTICS BY PRIORITY

The categorisation of antimicrobials by priority allows for targeting of AMR risk management measures, e.g. the imposition of additional requirements for prescribing and use, and prohibition of use in specified circumstances.

There are several lists currently available, and some are designed for international use while others are created for national use that take into consideration factors that are relevant to that country. Two of the more important international lists include those from the World Organisation for Animal Health (OIE) and the World Health Organisation (WHO).

OIE LIST

The OIE list of antimicrobial agents of veterinary importance was published following consultation with its Member Countries. The list, which is regularly reviewed and updated, addresses antimicrobial agents authorised for use in food-producing animals and does not include antimicrobial classes/subclasses only used in human medicine or those only used as growthpromoters in animals. While antimicrobial classes and subclasses used only in human medicine are not included in the OIE list, careful consideration should still be made before use (including extra-label/off-label use) in animals. 눒

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3. ANTIBIOTIC CLASSES AND LEVEL OF PRIORITY

The list is divided into 3 classes based on the following 2 criteria-

- 1. Majority of the OIE Member Countries identified the importance of the antimicrobial class, and
- 2. Compounds within the class were identified as essential against specific infections and there was a lack of sufficient therapeutic alternatives.

WHO LIST

The WHO has similarly published a list of critically important antimicrobials for human medicine. The list is divided into 3 classes based on the following 2 criteria -

- 1. The antimicrobial class is the sole, or one of limited available therapies, to treat serious bacterial infections in people, and
- 2. The antimicrobial class is used to treat infections in people caused by either: a. bacteria that may be transmitted to humans from non-human sources, or b. bacteria that may acquire resistance genes from non-human

sources.

The class of highest importance, the Critically Important Antimicrobials (CIA), is further divided into 2 categories to determine which antimicrobials require urgent intervention and risk management strategies, based on the following 3 prioritisation factors –

- 1. Large number of people in the community or in certain high-risk populations (e.g., patients with serious infections in health care settings), who are affected by diseases for which there are very limited antimicrobial choices,
- 2. High frequency of use of the antimicrobial class for any indication in human medicine or in certain high-risk groups (e.g., patients with serious infections in health care settings), and
- The antimicrobial class is used to treat ς. infections in people for which there is already extensive evidence of transmission of resistant bacteria (e.g., non-typhoidal Salmonella spp. and Campylobacter spp.) or resistance genes (high for E. coli and Enterococcus spp.) from non-human sources.

The CIA which are considered "highest priority" are those that meet all 3 prioritisation factors, and the CIA which are considered "high priority" are those that do not.

3. ANTIBIOTIC CLASSES AND LEVEL OF PRIORITY

In addition to identifying the antimicrobials to be prioritised in risk management strategies for containing AMR in human medicine, the WHO list also identifies the antimicrobials used in animals that present potentially higher risks to human populations, and whose use should be managed to minimise antimicrobial resistance in both public and animal health. The combined use of the WHO and OIE lists allow for prioritisation of risk management strategies in the human sector, the animal sector, in agriculture (crops) and horticulture, through a coordinated multi sectoral One Health approach.

Several antimicrobials are listed in the categories of highest importance in both the OIE and WHO lists. These include fluoroquinolones, third and fourth generation cephalosporins, and colistin. The OIE has made the following recommendations for such antimicrobials in food animals:

- They are not to be used as preventive treatment applied by feed or water in the absence of clinical signs in the animal(s) to be treated;
- They are not to be used as a first line treatment unless justified, when used as a second line treatment, it should ideally be based on the results of bacteriological tests;

- Extra-label/off label use should be limited and reserved for instances where no alternatives are available.
 Such use should be in agreement with the national legislation in force; and
- 4. Use as growth promoters should urgently be prohibited.

While food animals are not within the scope of these guidelines, the above gives private veterinarians an understanding of the importance of the individual antibiotic classes.

World Organisation for Animal Health (OIE). Accessed 16 February 2021, <https://www.oie.int/scientificexpertise/veterinary-products/antimicrobials/> World Health Organisation (WHO) Accessed 16 February 2021, <https://www.who.int/foodsafety/publications/antimicrobials-sixth/en/>

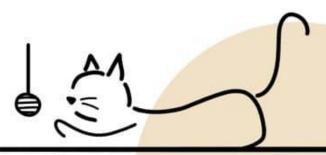
General Preamble to the Prescribing Guidelines

The recommendations set out in these guidelines are based on currently available information at the date of the drafting and are subject to change as new studies/information is published. The information provided is intended for use as a guide of a general nature only and is not intended to be exhaustive on the subject matter. The attending veterinarians should use these guidelines as a supporting tool when they exercise their own independent skill and clinical judgement, or seek professional third-party advice in relevant sections where deemed necessary, to handle individual cases.

The guidelines are directed to veterinary professionals with the appropriate qualifications and skills in ascertaining and discharging their professional duties, and should not be regarded as clinical advice, in particular, it is no substitute for a full clinical examination and thorough diagnostic work-up taking into consideration medical history.

The Singapore Veterinary Association, Animal and Veterinary Services and collaborating contributors would like to encourage proactive sourcing of up-to-date information for use in conjunction with these guidelines. Veterinarians are welcome to reach out privately to the authors or species experts and specialists via the SVA website link below.

https://sva.org.sg/veterinaryspecialists/





BACKGROUND

The most common conditions are stomatitis, gingivitis, periodontitis, and tooth root abscess. Predisposing factors include dental plaque or calculus, viral infections or immunosuppression.

Gingivitis is characterised by localised inflammation of the gingiva, often caused by dental plaque or calculus.

Periodontitis is characterised by inflammation of the periodontium leading to irreversible tissue loss around the tooth.

Stomatitis is characterised by inflammation of the oral mucosa, often with by secondary bacterial infection. Chronic stomatitis is more often seen in cats than dogs and is usually idiopathic.

DIAGNOSIS

- Review clinical signs (such as presence of tartar/calculus, gingivitis, halitosis, hypo-/anorexia, pain on chewing), and thorough examination of oral cavity.
- Radiographs may be of assistance, especially for tooth root abscesses.



Figure 1: A dog with periodontal disease and build-up of tartar on teeth. Photo courtesy of Vet Practice Pte Ltd

EXOTICS



KEY ISSUES

Predisposing factors can contribute (dental plaque or calculus, viral infections, immunosuppression).

TREATMENT

After removal of plaque and calculus, treatment with topical therapy is sufficient for many cases of gingivitis and periodontitis. Antimicrobials are only indicated when there are signs of severe periodontal disease.

For cats with gingivostomatitis/faucitis associated with feline calicivirus, following treatments may be considered:

- Extraction of all teeth for cases of marked inflammation or tooth resorption
- Anti-viral strategies such as omega interferon (topically, intra-lesion or subcutaneously) and topical antiviral agents such as lactoferrin

Immunomodulators such as corticosteroids and cyclosporine.

ROUTINE DENTAL PROPHYLAXIS

For routine dental cleaning without surgical intervention, antibiotic prophylaxis is not indicated, since "healthy animals are able to overcome (transient) bacteremia (from dental scaling) without the use of systemic antibiotics" (American Veterinary Dental College Policy Statement 2005).

In dogs and cats with severe periodontal disease, treatment of pre-existing infection prior to definitive dental procedures may be indicated to decrease tissue inflammation and bleeding at the time of oral surgery.

Heart Disease and Dental Prophylaxis

For dogs with heart murmurs caused by myxomatous mitral valve disease, there is virtually no risk of endocarditis, so prophylactic antibiotic treatment for dental procedures is not needed in these cases. One potential exception is for dogs with moderate to severe subaortic stenosis, which have an increased lifetime risk of infective endocarditis. It is reasonable to pre-treat these patients with prophylactic antibiotics prior to dental procedures.



ANTIBIOTICS USED

PERIODONTAL DISEASE

First Line:

Doxycycline monohydrate (5 mg/kg q12h), Clindamycin (5-11 mg/kg q12h), or

Second Line:

Metronidazole (10 mg/kg q12h)

Cefovecin (8 mg/kg SC once) is suitable for cases where there are concerns of compliance, or there are difficulties with oral dosing, but is not appropriate for shortterm prophylaxis of bacteraemia during dental procedures, and should only be used for cases where there is residual infection that requires specific treatment.

Treatment Duration:

Ideally, start therapy a few days prior to anaesthesia for dental radiography, extractions, scaling, polishing, and continue for 2 weeks following the procedure or until there is good healing of the periodontal tissues. Cases of Osteomyelitis usually require 21-28 days of treatment.

Australasian Infectious Disease Advisory Panel 2013, Antibiotic prescribing detailed guidelines, viewed 01 October 2021 https://www.ava.com.au/siteassets/resources/fighting-antimicrobial-resistance/aidap-prescribing-guidelines.pdf

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Kittleson, M.D. & Rishniw, M 2017 'Teeth and Hearts', Veterinary Information Network Medical FAQs, viewed o1 October 2021

The University of Melbourne, Australian veterinary prescribing guidelines: companion animal guidelines oral, gastrointestinal and pancreas, viewed o1 October 2021 https://vetantibiotics.fvas.unimelb.edu.au/medical-quidelines/oral-gastrointestinal-pacreas/> apanier L.A 2018, 'Rational use of pre-surgical antibiotics', proceedings of the Pacific Veterinary Conference 2018, San Francisco, knia, viewed o1 October 2021 <https://www.vin.com/members/cms/project/defaultadv1.aspx?id=8550659&pid=20885&>

FELINE GINGIVOSTOMATITIS/FAUCITIS

First Line:

Doxycycline monohydrate (5 mg/kg q12h), Clindamycin (5-11 mg/kg g12h), or Metronidazole (10 mg/kg q12h)

Second Line:

Amoxycillin (10–20 mg/kg PO g 8-12 hr) C&S in cases that do not respond to empirical therapy.

Treatment Duration:

Typically for 1-2 weeks, but longer in certain circumstances.



OPHTHAI MOLOGY BACTERIAL CONJUNCTIVITIS

BACKGROUND

Only a small number of conjunctivitis cases are primary bacterial infections.

In dogs and cat, bacterial conjunctivitis is more often superinfection by opportunistic pathogens from the conjunctival surface:

- Cocci Gram positive bacteria (Staphylococcus spp., Staphylococcus aureus et Staphylococcus pseudintermedius, Streptococcus spp.)
- Cocci Gram negative bacteria (Nesseria spp.)
- Bacilli Gram positive bacteria (Corynebacterium spp.)
- Bacilli Gram negative bacteria (Pseudomonas aeruginosa, Eschericha coli, Enterobacter spp., Proteus spp., Hemophilus spp., Moraxella spp., Bacillus cereus)
- Others like Actinomyces spp., Nocardia are possible.

In cats: Chlamydophila felis, Chlamydophila pneumoniae et Mycoplasma.

DIAGNOSIS

- Cytology is fast and inexpensive [bacteria in extra or intracellular position with non and degenerate neutrophils]. PCR testing is justified in cats.
- Bacterial culture and sensitivity testing should be performed. Normal conjunctiva is rarely sterile and contamination from eyelids should be avoided when sampling from conjunctival sac. Anaerobes are rarely seen.



OPHTHALMOLOGY

BACTERIAL CONJUNCTIVITIS

KEY ISSUES

Negative tests do not exclude the possibility of infection.

TREATMENT

Treatment with antimicrobials should be considered in the following situations:

- In the presence of purulent or mucopurulent ocular secretions [white, yellowish, or greenish].
- With underlying causes (such as decreased or low tear production, eyelid abnormalities, distichiasis, trichiasis, foreign bodies).
- In cats, with history of possible infection by *Chlamydophila* and *Mycoplasma*.
 When identified, systemic antibiotics can be used.
- With corneal ulcer associated with conjunctivitis.
- With a nasolacrimal system infection.

Conjunctival lavage with saline prior to antibiotic treatment is advised.

Treating underlying causes is mandatory.

ANTIBIOTICS USED

First line:

Chlamydia felis and *Mycoplasma* species:

Topical oxytetracycline OR erythromycin

Chlamydia felis specifically:

Oral doxycycline (5-10 mg/kg q12h to q24h for 3-4 weeks)

Zirofsky D, Rekers W, Powell C, et al. Feline herpesvirus 1 and Mycoplasma spp. conventional PCR assay results from conjunctival samples from cats in shelters with suspected acute ocular infections. Top Companion Anim Med. 2018;33(2):45-48.

EVE

INTEGUMENT

AURAL



OPHTHAI MOLOGY ULCERATIVE KERATITIS

BACKGROUND

Acute corneal ulceration may result from trauma, exposure keratitis, a foreign body, or eyelid abnormalities such as distichiasis, entropion, trichiasis, ectopic cilia, particularly in younger patients. Chronic ulcers, in which the corneal epithelium heals poorly and with reduced adherence to the underlying stroma, are seen more commonly in older patients. Corneal ulcers infected with Pseudomonas spp. or beta-haemolytic streptococci can develop into 'melting' ulcers due to production of proteinases and collagenases by these bacteria.

DIAGNOSIS

- Cytology is fast and inexpensive. Care should be taken to focus on ulcer margins and avoid perforation, Local anaesthetic is mandatory.
- Bacterial culture and sensitivity testing is advised especially with stromal infection.



Figure 2: Clinical photograph of a fluoresceinstained anterior stromal corneal ulcer associated with a superficial yellow fungal plaque. (Ledbetter & Starr, 2015)

EXOTICS



OPHTHALMOLOGY
ULCERATIVE KERATITIS

KEY ISSUES

Systemic antibiotics should not be use unless associated with surgical treatment for perforated to deep ulcers.

Never use local anaesthetic as part of treatment plan. It will suppress the blinking reflex and is toxic for epithelium.

If the patient exhibits miosis and pain then topical atropine is indicated, possibly supplemented by systemic analgesics.

Ointments should not be used with deep stromal lesions where there is a risk of perforation due to intra-ocular toxicity risk.

TREATMENT

For complicated ulcers secondary to keratoconjunctiva sicca:

Ciprofloxacin 0.03% ophthalmic solution

OR other ophthalmic fluoroquinolones used alone

OR Tobramycin 0.03% ophthalmic solution AND cefazolin (33mg/ml in artificial tear solution) To be applied q 2h to infected ulcer until cornea stabilizes.

Consider conjunctival graft placement in addition to KCS therapy and frequent antibiotic therapy for deep ulcers.

For superficial, uncomplicated ulcers with severe, mucopurulent discharge suggestive of secondary bacterial infection:

Triple antibiotic ointment (Neomycin/bacitracin/polymyxin B) q6-8h for 14 days.

If empirical treatment fails to resolve the discharge, perform culture and sensitivity.

Kaswan RL, Salisbury MA. A new perspective on canine keratoconjunctivitis sicca. Treatment with ophthalmic cyclosporine. Vet Clin North Am Small Anim Pract 1990; 20(3):583-613.

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OPHTHALMOLOGY

BACKGROUND

Although uveitis has many potential causes, local bacterial infection is rarely to blame unless there is perforation of the cornea or sclera. Toxaemia, systemic disease, glaucoma, trauma, bleeding, neoplasia, lens protein leakage and immunological conditions can all cause uveitis. Idiopathic uveitis accounts for a large proportion of cases.

Infection with *Borrelia, Anaplasma, Leptospira*, herpesvirus, canine distemper, Leishmania, Toxocara, Toxoplasma, or septicaemia of any cause, can result in uveitis . In cats, uveitis may be seen due to FIP, FeLV and toxoplasmosis. Idiopathic lymphoplasmocytic uveitis is commonly seen .



Figure 3: Moderate corneal edema obscures visualization of the hyphema present in the eye of a dog with uveitis secondary to immunemediated thrombocytopenia. (Townsend, 2008)

DIAGNOSIS

Classic signs of uveitis include:

- Blepharospasm
- Miosis
- Opacity of the anterior chamber (due to cells and protein)
- Vascular injection of the ciliary body
- Conjunctival hyperaemia
- Corneal oedema
- Hypopyon
- Hyphaema
- Iridal oedema
- Cataracts

Laboratory investigations can be useful and include:

- Haematology
- Urinalysis
- Serology
- Bacterial culture, possibly in combination with diagnostic imaging ^[6]

Hypotonia will be observed provided that the corneal oedema permits intraocular pressure measurement.



TREATMENT

Therapy should be directed at the primary cause, if identified, and topical and systemic analgesics administered. Systemic antibiotics should be given if infection, perforation, or systemic infection can be demonstrated.

The choice of antibiotic depends on the diagnosis. Mydriatics (atropine) should be considered if blepharospasm, miosis and/or photophobia are observed, provided there are no contra-indications (e.g., glaucoma).

ANTIBIOTICS USED

Dependent on whether infectious element is present.

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Townsend, W.M. (2008) Canine and Feline Uveitis. Veterinary Clinics: Small Animal Practice. [Online] 38 (2), 323–346. Available from: doi:10.1016/j.cvsm.2007.12.004 [Accessed: 18 October 2021].

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OPHTHAI MOLOGY RETROBULBAR ABSCESSESS & ORBITAL CELLULITIS

BACKGROUND

Cause is frequently difficult to identify, but foreign bodies,

haematogenous spread and local spread of infection from the nasal cavity or dental roots are likely causes. Typical bacteria include Staphylococcus spp., E. coli, Pasteurella spp. and anaerobes.

DIAGNOSIS

Patient usually presents acutely with:

- Unilateral exophthalmos
- Protrusion of the nictitating membrane
- Conjunctival hyperaemia
- Pain on opening the mouth

Ultrasound-guided fine-needle aspirates or biopsies can recover material for cytology and bacterial culture. CT scanning is likely useful.

Figure 4A: Clinical appearance of a 6-year-old male castrated Swiss mountain dog that was presented to the Ophthalmology Service for ocular (right exophthalmos with periorbital swelling) and oral (ptyalism, vocalizing when eating) clinical signs.

Figure 4B: CT scan contributed to a diagnosis of retrobulbar abscess secondary to plant foreign material. Post intravenous contrast administration transverse CT image shows right exophthalmos (white *), enlargement of the right zygomatic salivary gland (**) compared to the left (*), and a mass effect surrounding the right zygoma (dashed line). Surgical exploration and drainage of the abscess, followed by medical management, allowed for resolution of the primary retrobulbar infection. (Winer et al., 2018)

EXOTICS



OPHTHALMOLOGY RETROBULBAR ABSCESSES & ORBITAL CELLULITIS

TREATMENT

Drainage should be established, if possible. Systemic analgesics should be given along with antibiotics.

ANTIBIOTICS USED

First line:

Amoxicillin/clavulanate may be used until sensitivity results are available.

Amoxicillin/clavulanate (12.5-25mg/kg q12h)

Chavkin, M.J., Lappin, M.R., Powell, C.C. 1992. Seroepidemiologic and clinical observations of 93 cases of uveitis in cats. Prog Vet Comp Ophthalmol. 2: 29-36.

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INTEGUMENT

CELLULITIS, ABSCESS, TRAUMATIC WOUNDS

BACKGROUND

Bacterial species that are often involved in these conditions include Staphylococcus, Streptococcus, Escherichia coli, Pasteurella, Anaerobes. A thorough history will need to be taken and clinical examination is required to determine the severity of the lesion. In non-pyrexic animals with minor isolated lesions, systemic antibiotic treatment can be foregone.

DIAGNOSIS

- History, clinical presentation, cytology
- Culture and sensitivity if there are lack of response to antimicrobial therapy
- If no response, consider underlying



Figure 5: A dog with abscess caudal to left front limb. Photo courtesy of Vet Practice Pte Ltd

EXOTICS



TREATMENT

No antibiotics unless fever, systemically impaired patients, deep lacerations or contaminated/ dirty wounds.

Surgical debridement, drainage and lavage alone usually suffice.

Systemic antimicrobials if:

- Systemically unwell
- Diffuse tissue involvement
- Potential joint involvement
- Immunosuppressed patient

ANTIBIOTICS USED

First Line:

Amoxicillin-clavulanate (12.5 mg/kg q12h) or

Doxycycline monohydrate (5 mg/kg q12h);

Clindamycin (5-11 mg/kg q12h) and Metronidazole_(10 mg/kg q12h)

Treatment Duration:

7-10 days

Antimicrobials used for surgical prophylaxis by companion animal veterinarians in Australia. Veterinary Microbiology 203: 301-307.

<https://www.bsavalibrary.com/content/chapter/10.22233/9781910443644.app7#html_fulltext> Australasian Infectious Disease Advisary Panel (AIDAP) Antibiotics Prescribing Detailed Guidelines Bray, J (2011), How to use antibiotics in surgical patients. BSAVA Companion 10: 15-19.

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BACKGROUND

Wounds resulting from cat fights occur encountered in veterinary practice. The nature of these wounds range from minor lacerations to deep tissue destruction, so a proper physical examination is necessary. In cats, bacterial infections can arise from microbial biofilm from gingival cleft. Often it comprises of a combination of anaerobic and facultative anaerobic bacteria which can include:

- Bacteroides spp
- Porphyromonas spp
- Fusobacterium spp
- Prevotella spp
- Pasteurella multocida
- Streptococci
- Nocadia spp
- Corynebacterium spp
- Rhodococcus equi

DIAGNOSIS

- History and clinical examination
- Cytology
- Culture & Sensitivity





Figure 6A: Anaerobic cat fight abscess on the side of a cat's face, before surgical drainage and insertion of a latex drain. (Malik et al., 2006)

Figure 6B: Anaerobic cat fight abscess on the side of a cat's face after surgical drainage and insertion of a latex drain. (Malik et al., 2006)



KEY ISSUES

IV fluid therapy in anaesthetic and/or SC fluid therapy to re-establish and maintain hydration.

NSAIDs to be used with caution in potentially dehydrated cats subjected to sepsis and general anaesthesia. These drugs are more safely given in day 2 once cat has resumed eating and drinking normally.

TREATMENT

Depending on nature of lesion, consider the following treatments:

- Aeration
- Copious saline lavage
- Surgical debridement
- Drainage

Provide sufficient analgesia (opioids in select cases)

ANTIBIOTICS USED

First Line:

Amoxycillin-clavulanate (12.5mg/kg q12h)

Doxycycline monohydrate (5mg/kg q12h)

Clindamycin (5-11mg/kg q12h) and Metronidazole (10mg/kg q12h)

(in severe/extensive cases Amoxicillinclavulanate + Metronidazole OR Clindamycin)

Treatment Duration: 7-10 days

R., Norris, J., White, J. & Jantulik, B. (2006) 'Wound cat'. Journal of Feline Medicine and Surgery. [Online] 8 (2), 135– hable from: doi:10.1016/j.jfms.2005.10.001 [Accessed: 7 October 2021].



BACKGROUND

Similarly to cat fight wounds, dog bite wounds may appear minor on external examination but reveal a more extensive damage on closer investigation. Bacterial infection arising from microbial biofilm from oral cavity and gingival cleft, as well as skin, mucous membranes, and environment (soil). Often it comprises of a combination of anaerobic and facultative anaerobic bacteria which can include:

- Enterococcus/Escherichia coli
- Staphylococcus pseudintermedius, Streptococcus spp

DIAGNOSIS

- History and clinical examination
- Cytology
- Culture & Sensitivity



Figure 7: A dog with a deep dog bite wound on the abdomen. Photo courtesy of Vet Practice Pte Ltd



INTEGUMENT DOG BITE WOUNDS

KEY ISSUES

Antibiotic therapy should be reserved for contaminated/dirty wounds, deep lacerations, or systemically impaired patients (fever or severe systemic infections).

TREATMENT

- Debridement
- Copious lavage with saline or 2-4% chlorhexidine
- Drainage
- Wound reconstruction

ANTIBIOTICS USED

Antibiotic recommendations are mainly against Gram-positive cocci

First Line:

Initially by injection (SC, IM) then orally Amoxicillin-clavulanate 12.5mg-25mg/kg q12hr OR Cephalexin 15-30mg/kg

More Severe Cases:

Alternative IV combinations: Ampicillin/amoxicillin+ gentamicin ticarcillin clavulanate 1st generation cephalosporin + gentamicin

Treatment Duration:

7-10 days

EXOTICS



INTEGUMENT **PYODERMA**

BACKGROUND

Pyodermas can vary from moderate infections to severe infections and are triggered by underlying factors such as allergic skin disease, ectoparasites and endocrinopathies.



Figure 8: Widespread deep pyoderma involving Pseudomonas aeruginosa in a young Dalmatian dog with juvenileonset demodicosis; there was no evidence of pyoderma on cytology after 3 weeks of systemic antibacterial therapy. (Loeffler & Lloyd, 2018)

DIAGNOSIS

- Cytology adhesive tape/direct smears/FNA for pustules or nodules
- Culture and susceptibility
 - Recommended in all cases of bacterial pyoderma in which systemic antimicrobials are being considered
 - Rods are present on cytology
 - Lack of response to antimicrobial therapy
 - New lesions develop during treatment
 - Chronic or recurrent pyoderma



INTEGUMENT **PYODERMA**

KEY ISSUES

Consider underlying disease such as atopic dermatitis, food allergies, hormonal problems such as Cushing's, hypothyroidism.

ANTIBIOTICS USED

First Line:

Cephalexin 22-30mg/kg BID

Amoxycillin/clavulanic acid 12.5-25mg/kg q12h

TREATMENT

Topical treatment of mild superficial pyodermas surface with antiseptic shampoo is generally recommended (topical chlorhexidine).

In cases where large areas of the body are affected or when hair follicles & surrounding skin is involved, consider treatment with systemic antimicrobials.

Treatment Duration:

At least 3 weeks (3-6 weeks, and 1-week past resolution of clinical signs)

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J.F.; Hendricks, A.; Brodbelt, D.C. Prescribing practices of primary-care veterinary practitioners in dogs diagnosed with bacterial pyoderma. BMC Vet. Res. 2014, 10, 240



BACKGROUND

The bacteria most commonly isolated from ear canals of dogs affected by otitis are *Staphylococcus* spp.

Other bacteria commonly associated with otitis include Pseudomonas, Proteus, Enterococcus,

Streptococcus, and Corynebacterium. Som e bacteria such

as Staphylococcus and Pseudomonas may produce biofilm, which can lead to persistence of infection despite adequate therapy, as the biofilm needs to be disrupted for any antimicrobial therapy to be effective in clearing the infection.

Malassezia yeast is another common component of otitis externa in dogs. Some dogs appear to develop an allergic response to Malassezia spp., leading to significant discomfort and pruritus.

DIAGNOSIS

- Otoscopy
- Cytology
- Culture and sensitivity
- If rods are present on cytology
- Lack of response to antimicrobial therapy
- Chronic otitis



Figure 9: Contact hypersensitivity reaction to topical otic medication during treatment for otitis externa. (Bajwa, 2019)



KEY ISSUES

Ensure tympanic membrane intact - if perforated consider ear flushing and nonototoxic cleaners, avoid topical antimicrobials. Avoid cleaning agents containing propylene glycol.

Ear flushing under GA may be necessary. Collect specimens before flushing.

Recurrent underlying disease should be investigated (foreign body, atopy, anatomical anomaly).

TREATMENT

Ear flushing (under GA if necessary): warm sterile saline under controlled pressure

- Ototoxic agents: polymyxin B, aminoglycosides, propylene glycol, all acids in ear cleaning solutions
- Non-ototoxic agents: 0.15% chlorhexidine and below, triz-EDTA, squalene

ANTIBIOTICS USED

First Line (Cocci only or cocci & rods):

Topical fusidic acid and framycetin/neomycin combination or gentamicin

First Line (Rods only):

Topical polymyxin, gentamicin or marbofloxacin

Treatment Duration:

5-14 days; recheck every 2 weeks to confirm cytological resolution

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THORACIC: UPPER RESPIRATORY TRACT ACUTE BACTERIAL UPPER RESPIRATORY INFECTION (CATS)

BACKGROUND

Acute upper respiratory tract (URT) disease in cats (≤ 10 days duration) is primarily caused by viral disease in most cases, with Feline herpesvirus-1 (FHV-1) being the responsible pathogen in the majority of cases, and less commonly Feline calicivirus (FCV). Secondary bacterial infection with normal flora of the sino-nasal cavity is common, such as *Staphylococcus* spp., *Streptococcus* spp., *Pasteurella multocida*, *Escherichia coli*, and anaerobes.

Primary bacterial infection with Chlamydophila felis, Mycoplasma felis and Bordatella bronchipseptica has also been suggested in some cats, but with ocular disease being predominant for the first two organisms, and naso-ocular disease less commonly so. Cryptococcal pathogens can also be a primary cause of URT disease in cats, but this is mostly detected only when the disease is at a chronic stage.

The presence of purulent or mucopurulent nasal or ocular discharges might increase the suspicion that primary or secondary bacterial infection is present, but there is no definite proof of this association because viral or fungal agents can also induce mucopurulent discharges.

DIAGNOSIS

- History and physical examination
- Cytology on nasal discharge (limited benefit)
- Need to check for Feline Leukaemia virus and feline immunodeficiency virus

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OTHERS

THORACIC: UPPER RESPIRATORY TRACT ACUTE BACTERIAL UPPER RESPIRATORY **INFECTION (CATS)**

KEY ISSUES

Culture and sensitivity is not recommended for the acute disease as interpretation of culture and sensitivity results from nasal discharge are difficult as some pathogens are difficult to grow, and positive culture is often with commensal organisms of no significance.

TREATMENT

Serous nasal discharge or lacks a mucopurulent or purulent component:

No antibiotics recommended.

Mucopurulent or purulent nasal discharge:

- No antimicrobial therapy if have history • of contact with shelter, or in-contact humans or animal contact with shelter (increased risk of infection by B. bronchiseptica).
- Consider antimicrobial treatment if patient is presenting signs consistent with pyrexia, lethargy, and anorexia.

Most cats rapidly improve within 10 days with or without antimicrobial therapy.

THORACIC: UPPER RESPIRATORY TRACT ACUTE BACTERIAL UPPER RESPIRATORY INFECTION (CATS)

ANTIBIOTICS USED

First Line:

Doxycycline (5 mg/kg PO q 12 hr or_10 mg/kg PO q 24 hr) if there is fever, lethargy, or anorexia OR

Amoxicillin (10–22 mg/kg PO q 8–24 hr) when *Chlamydia felis* and *Mycoplasma* are not highly suspected.

Concurrent treatment with Famciclovir (30-40 mg/kg q8-12h) for at least two weeks should be considered when FHV-1/FCV is the likely primary pathogen, as is the case with most presentations of acute feline URT disease.

Treatment Duration: 7-10 days.

Most cats rapidly improve within 10 days with or without antimicrobial therapy. If no response to therapy in 7-10 days, further diagnostics should be performed. Only if these are refused by the owner should antimicrobial therapy be changed empirically.

Australasian Infectious Disease Advisory Panel 2013, Antibiotic prescribing detailed guidelines, viewed of October 2021 <https://www.ava.com.au/siteassets/resources/fighting-antimicrobial-resistance/aidap-prescribing-guidelines.pdf>. Lappin, M.R., Blondeau, J., Boothe, D., Breitschwerdt, E.B., Guardabassi, L, Lloyd, D.H., Papich, M.G., Rankin, S.C., Sykes, J.E., Turnidge, J. & Weese, J.S. 2017, 'Antimicrobial use Guidelines for Treatment of Respiratory Tract Disease in Dogs and Cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases', Journal of Veterinary Internal Medicine, vol. 31, no. 2, pp. 279-294

The University of Melbourne, Australian veterinary prescribing guidelines: companion animal guidelines - respiratory, viewed o1 October 2021 [https://vetantibiotics.fvas.unimelb.edu.au/medical-guidelines/respiratory/].

VIN Veterinary Drug Handbook, Veterinary Information Network, viewed o1 October 2021 https://www.vin.com/members/cms/project/defaultadv1.aspx?pld=13468>. OTHERS

THORACIC: UPPER RESPIRATORY TRACT CHRONIC BACTERIAL UPPER RESPIRATORY **INFECTION (CATS)**

BACKGROUND

Chronic feline URT disease (>10 day duration) is considered to be a sequela to viral rhinitis, and in the vast majority of cases it is thought to be caused by FHV-1. Most cases first present in younger cats, but occasionally it is seen as a first presentation in older cats.

FHV-1 is an epitheliotropic virus, causing chronic lymphoplasmacytic inflammation and necrosis, eventually resulting in destruction of normal turbinate structures. Normal drainage pathways are impaired, leading to accumulation of mucus and exudate. Anatomic pockets not cleared by normal mucociliary clearance mechanisms develop, and eventually scarring and web formation within the nasal cavity and nasophaynyx (nasopharyngeal stenosis) occurs. Distortion of normal anatomy interferes with defence against commensal bacteria (including Mycoplasmas, Pasteurella spp., obligate anaerobes and Bordetella) and sometimes other infectious agents including fungi (Cryptococcus spp. complex, Aspergillus spp., Neosartorya spp.) and also filamentous bacteria (Actinomyces, Streptomyces).

DIAGNOSIS

- History and physical examination
- Rhinoscopy with histopathology (+/-• immunohistochemistry and PARR for lymphoma) and culture and sensitivity of biopsy samples
- For a complete evaluation of the nasal 0 cavity, sinuses and nasopharynx, also consider head and dental radiographs and head CT/MRI

Prescribing Guidelines and Investigative Process

THORACIC: UPPER RESPIRATORY TRACT CHRONIC BACTERIAL UPPER RESPIRATORY **INFECTION (CATS)**

KEY ISSUES

Antimicrobials should be selected on the basis of culture and sensitivity.

There is no evidence that 3rd generation cephalosporins and fluoroquinolones are more effective than doxycycline and amoxycillin for the treatment of chronic bacterial upper respiratory infection.

Azithromycin is not as effective as doxycycline for treating ocular chlamydiosis, so it should be reserved for situations where chlamydiosis is not suspected and amoxicillin and doxycycline are not viable options.

TREATMENT

Antimicrobial therapy is considered a critical component to controlling secondary opportunistic bacterial infection. Therapy should be continued for as long as there is progressive clinical improvement (usually for many months) and for two to three months past resolution of clinical signs.

There is anecdotal evidence that concurrent treatment with famciclovir (30-40 mg/kg q8-12h) is helpful in some cases, especially when there is bony erosion within the nasal cavity, or when FHV-1 associated ocular disease or dermatitis is also present.

Empirical antimicrobial therapy can be reinstated if there is recurrence of disease once. It is recommended to avoid frequent courses of antimicrobial therapy as the risk of resistance developing is high. Further diagnostics such as rhinoscopy and nasal debridement should be considered at this point.

THORACIC: UPPER RESPIRATORY TRACT CHRONIC BACTERIAL UPPER RESPIRATORY **INFECTION (CATS)**

TREATMENT (CON'T)

Therapeutic nasal flushing and necrotic nasal turbinate debridement is very useful to flush out nasal discharge which is often too thick and ropey for the patient to expectorate easily, and remove necrotic tissue which serve as anatomic pockets and niduses for continued infection. This is done ideally under endoscopic guidance and small endoscopic biopsy/alligator forceps and can significantly improve the subsequent response to antimicrobial and antiviral treatment.

Concurrent corticosteroid treatment (oral +/- inhalant) is also considered in some cases, especially when lymphoplasmytic rhinitis has been diagnosed with histopathology that is refractory to antimicrobial and antiviral treatment after nasal flushing and endoscopic debridement.

ANTIBIOTICS USED

First Line:

Doxycycline monohydrate (5 mg/kg g12h)

Second Line:

Clindamycin (11 mg/kg q12h)

Anti-Pseudomonas drugs (such as enrofloxacin, marbofloxacin and pradofloxacin) are usually reserved for cases where there is a pure heavy growth of P. aeruginosa from deep nasal washing or nasal biopsy specimens.

Australasian Infectious Disease Advisory Panel 2013, Antibiotic prescribing detailed guidelines, viewed of October 2021 < https://www.ava.com.au/siteassets/resources/fighting-antimicrobial-resistance/aidap-prescribing-guidelines.pdf>. Lappin, M.R., Blondeau, J., Boothe, D., Breitschwerdt, E.B., Guardabassi, L, Lloyd, D.H., Papich, M.G., Rankin, S.C., Sykes, J.E., Turnidge, J. & Weese, J.S. 2017, 'Antimicrobial use Guidelines for Treatment of Respiratory Tract Disease in Dogs and Cats: Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases', Journal of Veterinary Internal Medicine, vol. 31, no. 2, pp. 279-294

Robertson, E 2018 'Clinical Approach to Chronic Upper Respiratory Tract Disease in Cats—How Rhinoscopy Can Help', proceedings in World Small Animal Veterinary Association Congress Proceedings 2018, Singapore.

The University of Melbourne, Australian veterinary prescribing guidelines: companion animal guidelines - respiratory, viewed of October 2021 https://vetantibiotics.fvas.unimelb.edu.au/medical-quidelines/respiratory/>



THORACIC: I OWER RESPIRATORY TRACT **BACTERIAL BRONCHITIS**

BACKGROUND

Acute lower respiratory tract (LRT) disease, including bronchitis, is a common condition in dogs and cats, and the presentation may be acute and severe. In animals presenting with dyspnoea and coughing, alternative diagnoses must also be considered, such as pulmonary oedema, aspiration pneumonia, allergic or hypersensitivity disease, haemorrhage, neoplasia, lungworm, heartworm, toxoplasmosis (in cats), viral infection and fungi. The long list of noninfectious causes of acute respiratory disease makes definitive diagnosis of acute LRT disease difficult. Furthermore, secondary pneumonia may occur in the setting of prior LRT disease due to a noninfectious cause.

Clinical signs suggesting infection might include a moist cough, harsh breath sounds, fever, purulent appearing expectorant and sometimes purulent nasal discharge.

DIAGNOSIS

- Diagnostic imaging
- Airway washings (bronchoalveolar lavage, or transtracheal wash in larger dogs)
- Cytology
- Culture and sensitivity (aerobic C&S and Mycoplasma culture)
- Bronchoscopy, where indicated
- Similar tests should be carried out in cases of chronic cough with or without respiratory distress.

AURAL



THORACIC: LOWER RESPIRATORY TRACT BACTERIAL BRONCHITIS

KEY ISSUES

Careful clinical examination to rule out noninfectious respiratory diseases. Although infectious LRTI occurs in cats, allergic lower airway disease is more common, and at some level is a diagnosis of exclusion.

Bordetella bronchiseptica is a primary respiratory pathogen and clinical disease is most common in kittens.

TREATMENT

Generally, for mild cases, antimicrobial therapy is not recommended while awaiting culture and sensitivity results.

Empirical antimicrobial therapy is only recommended in cases of severe clinical disease.

ANTIBIOTICS USED

DOGS: Non-life-threatening Infections First Line: Doxycycline (5 mg/kg q12h)

Second Line:

Amoxicillin-clavulanate (12.5 mg/kg q12h)

DOGS: Severe Infections

Four quadrant parenteral coverage with amoxicillin clavulanate, [enrofloxacin (5 mg/kg q24h) or gentamicin (6 mg/kg q24h IV/SC in a well hydrated patient)] and metronidazole (10 mg/kg q12hrs).

CATS: Acute life-threatening Bronchopneumonia

Empiric therapy with ampicillin (20 mg/kg IV every 8 hours) and gentamicin (5-6 mg/kg IV once daily) while receiving IV fluid therapy, plus nebulisation with saline and thoracic percussion and coupage. Change agents on the basis of C+S from BAL specimens.



ANTIBIOTICS USED (CON'T)

CATS: Chronic LRT

Empiric treatment with doxycycline monohydrate (5 mg/kg q12h). Change therapy based off C+S data if available.

Re-assess drug choices in the light of the response to therapy.

Notes:

As mycoplasma lacks a peptidoglycan cell wall, they are resistant to all beta-lactam drugs.

Treatment Duration:

7-10 days

Australasian Infectious Disease Advisory Panel 2013, Antibiotic prescribing detailed guidelines, viewed of October 2021 < https://www.ava.com.au/siteassets/resources/fighting-antimicrobial-resistance/aidap-prescribing-guidelines.pdf> The University of Melbourne, Australian veterinary prescribing guidelines: companion animal guidelines - respiratory, viewed of October 2021 < https://vetantibiotics.fvas.unimelb.edu.au/medical-guidelines/respiratory/>.

EXOTICS



THORACIC: LOWER RESPIRATORY TRACT **PNEUMONIA**

BACKGROUND

Pneumonia is an inflammation of the lungs which results in fluid accumulation within alveolar air sacs. Patients may present with mild to life-threatening conditions. The most common cause of pneumonia in small animals is due to a bacterial infection. Other causes include viruses (rare), fungi, aspiration, parasites, ventilator-induced, chemical or smoke inhalation.

Common bacterial organisms isolated include Escherichia coli, Pasteurella spp., Streptococcus spp., B. Bronchiseptica, Enterococcus spp., Mycoplasma spp., S. pseudintermedius and other coagulasepositive Staphylococcus spp., and Pseudomonas spp.

DIAGNOSIS

- Physical examination 0
- Complete Blood Count
- **Diagnostic imaging (Thoracic** radiographs)
- Airway washings
- Cytology
- Culture and sensitivity (including aerobic C&S and mycoplasma culture)



THORACIC: LOWER RESPIRATORY TRACT **PNEUMONIA**

KEY ISSUES

Investigations should include a search for an underlying disease process that predisposed to pneumonia.

Consult with a microbiologist in interpretation of laboratory results as airway contaminants are common.

TREATMENT

Following sample collection antimicrobials should be started as soon as possible, especially if signs of sepsis are present.



Figure 10: Thoracic radiographs from case 2 highlight a focal soft tissue opacity in the left caudal lung fields along with a diffuse bronchial pattern and a scant pneumothorax. A left lateral radiograph was not obtained. (Dear, 2014)

P

THORACIC: LOWER RESPIRATORY TRACT PNEUMONIA

ANTIBIOTICS USED

Mild Pneumonia

Doxycycline (5 mg/kg p.o. q12h)

Aspiration Pneumonia (Mild)

Supportive treatment OR

Amoxycillin (10–22 mg/kg PO q 8–24 hr),

Ampicillin (10–20 mg/kg IM, PO, SC q 8 hr) OR

1st generation cephalosporin (E.g., Cephalexin: Dogs: 25–45 mg/kg PO q 8 hr, Cats: 35 mg/kg PO q 6–8 hr).

Pneumonia and Sepsis

Dogs:

Enrofloxacin (5–20 mg/kg PO q 24 hr or divided q 12 hr, 2.5 mg/kg IM, 5–20 mg/kg IV q 24 hr or divided q 12 hr, diluted in 2x volume of saline and infuse over 15–20 min)

Cats:

Enrofloxacin (5 mg/kg PO q 24 hr or divided q 12 hr, 2.5 mg/kg IM) and Amoxycillin (10–22 mg/kg PO q 8–24 hr))

OR

Ampicillin (10–20 mg/kg IM, PO, SC q 8 hr) OR

Clindamycin (3–10 mg/kg IV, SC, PO q 8 hr)

Australasian Infectious Disease Advisory Panel 2013, Antibiotic prescribing detailed guidelines, viewed 01 October 2021 < https://www.ava.com.au/siteassets/resources/fighting-antimicrobial-resistance/aidap-prescribing-guidelines.pdf>.

Dear, J.D. (2014) Bacterial Pneumonia in Dogs and Cats. The Veterinary Clinics of North America. Small Animal Practice. [Online] 44 (1), 143–159. Available from: doi:10.1016/j.cvsm.2013.09.003 [Accessed: 7 October 2021].

Newfield, A 2019, 'Pneumonia in the dog and cat', in proceedings Ontario Association of Veterinary Technicians Conference, Niagara Falls, Ontario.

The University of Melbourne, Australian veterinary prescribing guidelines: companion animal guidelines - respiratory, viewed o1 October 2021 https://vetantibiotics.fvas.unimelb.edu.au/medical-guidelines/respiratory/. VIN Veterinary Drug Handbook, Veterinary Information Network, viewed o1 October 2021 https://www.vin.com/members/cms/project/defaultadv1.aspx?pld=13468 >

EXOTICS



THORACIC: LOWER RESPIRATORY TRACT PYOTHORAX

BACKGROUND

Pyothorax is uncommon in dogs. Critically, there are some key differences compared with cats where the disease is observed more commonly – most notably, grass awn inhalation is a common cause of the disease in many dogs. Thus, surgical exploration may be warranted early in therapy, unless there is a prompt response to medical therapy.

In cats, the majority of pyothorax cases are polymicrobial infections caused by obligate and facultative anaerobic bacteria derived from the feline oral cavity. Possible routes of infection include extension from an adjacent structure (bronchopneumonia, para- pneumonic spread, oesophageal rupture, mediastinitis or sub-phrenic infection), direct inoculation (penetrating trauma, migrating foreign body, thoracocentesis or thoracic surgery) or haematogenous or lymphatic spread from a distant site (systemic sepsis). Common organisms isolated from cats include: Fusobacterium, Prevotella, Porphyromonas, Bacteroides, Peptostreptococcus, Clostridium, Actinomyces, Filifactor villosus, Pasteurella spp., Streptococcus spp., and Mycoplasma spp.

Common organisms isolated from dogs include: Mixed anaerobes (*Prevotella* spp., *Peptostreptococcus, Clostridium, Actinomyces*, and *Filifactor villosus*), Enterbacteriaceae (*E.coli, Klebsiella pneumoniae*)

Also implicated: *Streptococcus canis*, *Staphylococcus* spp., *Enterococcus* spp., *Corynebacterium* spp., *Bacillus* spp., *Trueperella* (formerly *Arcanobacterium*) *pyogenes*, *Pasteurella*, *Acinetobacter*, *Capnocytophaga* spp., *Enterobacter* spp., *Stenotrophomonas maltophila*, *Aeromonas hydrophilia*, *Achromobacter xylosoxidans*, *Serratia marcescens and Pseudomonas* spp., *Actinomyces* spp.

THORACIC: LOWER RESPIRATORY TRACT **PYOTHORAX**

DIAGNOSIS

- Physical examination
- Complete Blood Count
- Diagnostic imaging (Thoracic radiographs, ultrasonography, CT)
- Therapeutic thoracocentesis •
- Cytology
- Culture and sensitivity (including) aerobic and anaerobic; and *Mycoplasma* culture)

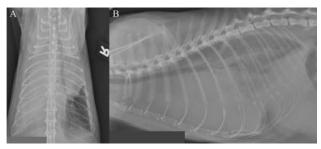


Figure 11: A. Dorsoventral and B. Right lateral thoracic radiographs of the cat of the second case, showing very severe pleural effusion, more pronounced in the left hemithorax. The cardiac silhouette is masked by the soft tissue opacity of the free fluid and the trachea is displaced dorsally. The lungs are severely displaced caudodorsally on the lateral projection. There is an alveolar pattern present in the right cranial lung lobe. (Gorris et al., 2017)

KEY ISSUES

In cats, infections typically begin in the lungs after aspiration of oropharyngeal microbiota and spread secondarily to the pleura and pleural space. Thus, pyothorax is often a complication some weeks after acute viral URT infection in cats. Rarely, infection occurs after penetrating cat bite injuries to the thoracic wall.

Aspiration of pleural fluid is crucial to provide adequate lung expansion and alleviate dyspnoea. This may be accomplished initially via needle aspiration followed by placement of indwelling thoracic drains, as deemed necessary, to facilitate daily drainage and lavage with warm crystalloid solutions. Unlike most cats, thoracic drains can often be inserted in larger dogs under local anaesthesia without a requirement for general anaesthesia.

Severe compartmentalisation of infection in the thorax and lung abscessation may require surgical intervention.



THORACIC: LOWER RESPIRATORY TRACT **PYOTHORAX**

TREATMENT

Empirical therapy should be initiated immediately and modified when culture and sensitivity results are obtained.

Treatment is recommended along with therapeutic drainage with/without lavage.

Treatment with an agent effective against anaerobes should continue regardless of culture results and anaerobic culture is not always successful for fastidious anaerobic bacteria.

Four quadrant antimicrobial therapy is warranted until results of antimicrobial susceptibility testing become available.

Because of the wide range of organisms that may be isolated from canine pyothorax cases, C&S testing is mandatory and cost effective, as it permits targeted therapy of the specific pathogen involved.

ANTIBIOTICS USED

First Line Empiric Therapy with Three Agents:

(i) Cefazolin (20 mg/kg q8h) or amoxicillin (10-20 mg/kg q6h),

(ii) Aminoglycoside (gentamicin 6 mg/kg q24h IV to a well hydrated patient) or

fluoroquinolone (enrofloxacin, 5 mg/kg q24h SC),

(iii) Metronidazole (10 mg/kg q12h) — four quadrant therapy

Treatment Duration:

Need for therapy should be reviewed after 10-14 days.

Australasian Infectious Disease Advisory Panel 2013, Antibiotic prescribing detailed guidelines, viewed o1 October 2021 < https://www.ava.com.au/siteassets/resources/fighting-antimicrobial-resistance/aidap-prescribing-guidelines.pdf> The University of Melbourne, Australian veterinary prescribing guidelines: companion animal guidelines - respiratory, viewed o1 October 2021 <https://vetantibiotics.fvas.unimelb.edu.au/medical-guidelines/respiratory



ABDOMINAL: GASTROENTERITIS ACUTE GASTROENTERITIS

BACKGROUND

There are many possible causes of acute gastroenteritis that are not bacterial in origin and therefore do not require antimicrobial therapy. The major bacteria implicated in the syndrome are as follows:

- Campylobacter- infection rarely causes clinical disease and the bacteria is frequently isolated from healthy animals. Clinical signs tend to be relatively mild. Concurrent infection with another pathogen is likely in animals with clinical signs.
- ۲ Salmonella - clinical salmonellosis is rare and asymptomatic carriers are common with international studies suggesting that up to 44% of healthy dogs and 14% of healthy cats may carry Salmonella. Infection can result in severe gastroenteritis with or without septicaemia.

- Clostridium difficile & C. perfringens- clinical signs are variable, from mild and self-limiting to potentially fatal acute haemorrhagic diarrhoea, and the clinical significance is unknown
- Escherichia Coli- the significance of enteropathogenic (EPEC) or enterotoxin-producing (ETEC) E. coli in diarrhoea in dogs and cats unknown. ETEC has been incriminated in diarrhoea in young dogs



ABDOMINAL: GASTROENTERITIS ACUTE GASTROENTERITIS

DIAGNOSIS

- History and physical examination
- Cytology: examining stained faecal smears
- Faecal PCR or culture

KEY ISSUES

Faecal culture reports should always be interpreted cautiously, since most bacteria can also be recovered from healthy animals.

Gastrointestinal infections are often selflimiting and antibiotic therapy is rarely required.

TREATMENT

Treatment is aimed at preventing and replacing fluid loss. Historically, antibiotics have often been used in acute gastroenteritis, but as majority of infections are self-limiting, supportive treatment will be sufficient in most cases.

Treatment with antibiotics should be carefully assessed as unnecessary use disrupts the normal flora and can result antimicrobial resistance. Antibiotics should be reserved for patients with severe mucosal damage secondary to parvovirus, which are severely ill, or which show signs of sepsis.



ABDOMINAL: GASTROENTERITIS ACUTE GASTROENTERITIS

ANTIBIOTICS USED

First Line

Campylobacter

Macrolides (Erythromycin)

OR Tetracycline

C. perfringens

Amoxicillin (Dogs: 15-22 mg/kg PO q 12 hr, Cats: 20-22 mg/kg PO q 12 hr) OR

Metronidazole (25 mg/kg PO g 12 hr or 50 mg/kg PO q 24 hr)

C. difficile

Metronidazole (25 mg/kg PO q 12 hr or 50 mg/kg PO q 24 hr)

E. coli

Antimicrobial therapy is controversial as the disease is generally self-limiting.

In severe cases with secondary sepsis:

Amoxicillin (Dogs: 22-30 mg/kg IM, IV, SC, PO q 6–8 hr, Cats: 22–30 mg/kg IV, SC, PO q 8 hr) OR

1st generation cephalosporins (E.g., Cephelexin: Dogs: 25-45 mg/kg PO q 8 hr, Cats: 35 mg/kg PO g 6-8 hr) are a reasonable choice.

Salmonella

Therapy should be based on culture and susceptibility testing. Empirical therapy: Amoxicillin (10–22 mg/kg PO q 8–24 hr) OR

Trimethoprim / sulphonamide (15 mg/kg PO, SC q 12 hr)

The University of Melbourne, Australian veterinary prescribing guidelines: companion animal guidelines - oral, gastrointestinal and pancreas, viewed of October 2021 < https://vetantibiotics.fvas.unimelb.edu.au/medicalguidelines/oral-gastrointestinal-pacreas/>

Companion Animal Group, Danish Veterinary Association, November 2018 Antibiotic use quidelines for companion animals, 2nd edn.

VIN Veterinary Drug Handbook, Veterinary Information Network, viewed 01 October 2021 <a>https://www.vin.com/members/cms/project/defaultadv1.aspx?pld=13468>.

ABDOMINAL: GASTROENTERITIS ACUTE HEMORRHAGIC DIARRHOEA SYNDROME (AHDS)

BACKGROUND

AHDS, formerly known as haemorrhagic gastroenteritis (HGE), is a specific disease characterised by a necrotising enteritis with an acute presentation of bloody diarrhoea and high risk for serious dehydration. AHDS can quickly become life-threatening. Most dogs with acute gastroenteritis and mildly bloody faeces do not have AHDS.

Patients with AHDS have reduced numbers of essential bacteria of the gut microbiota (Blautia spp., Faecalibbacterium spp., and Turicibacter spp.). This encourages growth of pathogenic bacteria, such as toxigenic Clostridium perfringens. A relationship between AHDS and C. perfringens enterotoxin has been found. Patients with AHDS represent a group in which empirical antibiotic therapy can be necessary for some, although most cases are self-limiting with supportive therapy and do not require antimicrobial therapy. Bacterial culture is always indicated in these patients, but clinical signs can worsen rapidly, and treatment may be needed before culture results are available. AHDS causes a breakdown of the mucosal barrier and patients are at risk of rapid deterioration and development of sepsis, which can be fatal and hospitalisation with intensive care is required. Close monitoring for signs of sepsis is necessary.

DIAGNOSIS

- History and physical examination
- Faecal culture and diagnostic panel for common pathogens such as Clostridium spp., Salmonella spp., Campylobacter spp., E. coli) is always indicated.

ABDOMINAL: GASTROENTERITIS ACUTE HEMORRHAGIC DIARRHOEA SYNDROME (AHDS)

KEY ISSUES

Acute haemorrhagic diarrhoea syndrome should only be treated with antibiotics if there is evidence of sepsis. ^[2] Other nonbacterial causes for haematochezia should be considered, such as viral (e.g., parvovirus), parasitic (giardia, coccidia, helminths) and GI neoplasia.

Figure 12: Giemsa staining of a duodenal section collected from Dog #2. A dense layer of large rod-shaped bacteria adherent to a necrotic villous tip (black arrow). (Unterer *et al.*, 2014)

TREATMENT

Treatment with amoxicillin / clavulanate does not reduce the duration of disease in patients without sepsis. Appropriate supportive care & close monitoring for signs of sepsis is recommended. Animals generally fall into one of 3 groups:

- Mild haemorrhagic diarrhoea with no evidence of hypovolaemia or other systemic effects: No antimicrobials indicated.
- Severe haemorrhagic diarrhoea with hypovolaemia but no evidence of sepsis: Supportive care and monitoring, no antimicrobials indicated.
- Severe haemorrhagic diarrhoea with hypovolaemia and signs of sepsis: Antimicrobials always indicated.

EYE

OTHERS

EXOTICS



ANTIBIOTICS USED

First Line: Intravenous ampicillin (10–20 mg/kg IV q 8 hr) or amoxicillin (22–30 mg/kg IV g 6–8 hr) is usually sufficient

Treatment Duration:

Dependent on pathogen,

Campylobacter & Salmonella: 10 days [1,3]

Clostridial diarrhoea: 5-7 days

Companion Animal Group, Danish Veterinary Association, November 2018 Antibiotic use quidelines for companion animals, 2nd edn.

The University of Melbourne, Australian veterinary prescribing guidelines: companion animal guidelines - oral, gastrointestinal and pancreas, viewed o1 October 2021 < https://vetantibiotics.fvas.unimelb.edu.au/medicalguidelines/oral-gastrointestinal-pacreas/>

Unterer, S., Busch, K., Leipig, M., Hermanns, W., et al. (2014) Endoscopically Visualized Lesions, Histologic Findings, and Bacterial Invasion in the Gastrointestinal Mucosa of Dogs with Acute Hemorrhagic Diarrhea Syndrome. Journal of Veterinary Internal Medicine. [Online] 28 (1), 52–58. Available from: doi:10.1111/jvim.12236 [Accessed: 18 October 2021]. VIN Veterinary Drug Handbook, Veterinary Information Network, viewed 01 October 2021 https://www.vin.com/members/cms/project/defaultadv1.aspx?pld=13468>.

EXOTICS



ABDOMINAL: GASTROENTERITIS **INFLAMMATORY BOWEL DISEASE**

BACKGROUND

This syndrome incorporates a group of chronic inflammatory conditions of the GI tract. Several types have been identified:

- Lymphoplasmocytic enteritis / colitis
- Eosinophilic enteritis / colitis
- Lymphangectasia
- Histiocytic (granulomatous) colitis

DIAGNOSIS

- ۲ History and physical examination
- Diagnostic imaging: abdominal ۲ ultrasonography. Important to rule out other differential diagnoses such as pancreatitis or gastrointestinal neoplasia which may not be diagnosed on endoscopy.
- Upper and lower gastrointestinal endoscopy with histopathology for definitive diagnosis.
- Histiocytic ulcerative colitis in Boxers ۲ can be diagnosed by histopathology (FISH test) of colonic biopsies.



ABDOMINAL: GASTROENTERITIS **INFLAMMATORY BOWEL DISEASE**

KEY ISSUES

Patients with inflammatory bowel disease should be treated with immunosuppressives and dietary management. Antibiotics should not be used unless a diagnosis of histiocytic/ granulomatous colitis has been made.

TREATMENT

Resistance development is widespread so therapy should be based on susceptibility testing rather than empirically. ^[1,2]

Prednisolone alone is as effective as prednisolone in combination with metronidazole, so solo therapy with prednisolone is recommended as first line treatment.

Histiocytic ulcerative colitis in Boxers can respond to long-term antimicrobial therapy.

ANTIBIOTICS USED

First Line:

Tylosin (12-20 mg/kg PO g8hr) OR

Oxytetracycline (8 mg/kg IM, SC q 24 hr (Australia label dosage) / 10 mg/kg IM once OR

Metronidazole (25 mg/kg PO g 12 hr or 50 mg/kg PO q 24 hr).

Treatment Duration:

2-8 weeks have been described

Companion Animal Group, Danish Veterinary Association, November 2018 Antibiotic use guidelines for companion animals, 2nd edn.

The University of Melbourne, Australian veterinary prescribing guidelines: companion animal guidelines - oral, gastrointestinal and pancreas, viewed o1 October 2021 < https://vetantibiotics.fvas.unimelb.edu.au/medicalquidelines/oral-gastrointestinal-pacreas/>

VIN Veterinary Drug Handbook, Veterinary Information Network, viewed 01 October 2021 <https://www.vin.com/members/cms/project/defaultadv1.aspx?pld=13468>



ABDOMINAL: GASTROENTERITIS SMALL INTESTINAL BACTERIAL **OVERGROWTH (SIBO) & ANTIMICROBIAL-RESPONSIVE DIARRHOEA (ARD)**

BACKGROUND

This syndrome usually has an underlying cause and identification of the primary disorder is recommended prior to antimicrobial therapy.

DIAGNOSIS

History and physical examination

TREATMENT

Resistance development is widespread so therapy should be based on susceptibility testing rather than empirically.

Prednisolone alone is as effective as prednisolone in combination with metronidazole50 so solo therapy with prednisolone is recommended as first line.

Histiocytic ulcerative colitis in Boxers can respond to long-term antimicrobial therapy.

ANTIBIOTICS USED

First Line:

Tylosin (12-20 mg/kg PO g8hr) OR

Oxytetracycline (8 mg/kg IM, SC q 24 hr (Australia label dosage) / 10 mg/kg IM once OR

Metronidazole (25 mg/kg PO g 12 hr or 50 mg/kg PO q 24 hr).

Treatment Duration:

SIBO: 2-4 weeks

ARD: 1-2 weeks

EXOTICS

The University of Melbourne, Australian veterinary prescribing quidelines: companion animal quidelines - oral, gastrointestinal and pancreas, viewed o1 October 2021 < https://vetantibiotics.fvas.unimelb.edu.au/medicalguidelines/oral-gastrointestinal-pacreas/>

VIN Veterinary Drug Handbook, Veterinary Information Network, viewed 01 October 2021 <https://www.vin.com/members/cms/project/defaultadv1.aspx?pld=13468>



ABDOMINAL: URINARY TRACT SPORADIC URINARY TRACT INFECTIONS

BACKGROUND

Previously called uncomplicated, sporadic bacterial infection of the bladder in an otherwise healthy animal with no underlying systemic, anatomic, neurologic, or functional problem. Uncomplicated cases are not recurrent and occur less than 3 times per year. In an animal has had an infection (with clinical signs) in the last 3 months, they should be approached like 'recurrent cystitis.' For cases with co-morbidities or 3 or more episodes per year see recommendations for recurrent urinary tract infections below.

DIAGNOSIS

- Urinalysis ۲
- Urine specific gravity
- Urine dipstick
- Cytology (stained and unstained) ۲
- Urine sediment
- Culture and sensitivity (aerobic)

AURAL

EXOTICS

Prescribing Guidelines and Investigative Process

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ABDOMINAL: URINARY TRACT SPORADIC URINARY TRACT INFECTIONS

KEY ISSUES

Leukocyte and nitrite results on dipsticks are not reliable for veterinary species so pyuria can only be diagnosed using cytology.

Sediment analysis alone is inadequate for diagnosis because of problems in the variable quality of interpretation, stain contamination and false positive results from bacteriuria in the absence of clinical infection.

Sample for C&S should always be collected by cystocentesis (unless there is a specific contraindication)

Culture should always be performed in cats presenting with signs of FLUTD.

There should be an adequate response to treatment within 48 hours (i.e., signs reduce/resolve) and if not, further investigation considered. DO NOT change antibiotics empirically (i.e., without culturing) if clinical signs persist.

TREATMENT

If it is unclear whether culture will be positive, consider giving pain relief (if there are signs of pain) and await culture results rather than starting empirical antimicrobials straight away, especially for cats (see delayed prescribing technique). For dogs, antimicrobials may be added three to four days later if clinical signs persist or worsen.

Treatment of intact male dogs with no evidence of prostatitis or animals with comorbidities not involving the urinary tract (e.g., pets with clinical UTI that receive immunosuppressives, are obese or have endocrinopathies) and with non-recurrent cystitis are included in the above recommendation.



ABDOMINAL: URINARY TRACT SPORADIC URINARY TRACT INFECTIONS

ANTIBIOTICS USED

First Line:

Amoxycillin (11–15 mg/kg PO q8–12h), Amoxycillin clavulanic acid (12.5–25 mg/kg PO q12h), OR Trimethoprim / sulphonamide (15-30 mg/kg PO q12h)

Second Line:

Based on C&S

<u>Treatment Duration:</u> 3-5 days





Figure 13: Cystocentesis performed with palpation of the urinary bladder in the standing cat (a) and the cat in lateral recumbency (b) through the lateral abdominal wall. (Dorsch, Teichmann-Knorrn & Sjetne Lund, 2019)

Dorsch R, Teichmann-Knorrn S, Sjetne Lund H. Urinary tract infection and subclinical bacteriuria in cats: A clinical update. J Feline Med Surg. 2019 Nov;21(11):1023-1038. doi: 10.1177/1098612X19880435. Epub 2019 Oct 10. PMID: 31601143; PMCID: PMC6826873.

Granick, J. & Beaudoin, A. 2019 'A practical approach to antimicrobial stewardship for practices and practitioners', from proceedings ACVIM 2019, Saint Paul, Minnesota.

The University of Melbourne, Australian veterinary prescribing guidelines: companion animal guidelines – urinary tract, viewed o1 October 2021 https://vetantibiotics.fvas.unimelb.edu.au/medical-guidelines/urinary-tract/

Weese, J.S., Blondeau, J., Boothe, D., Guardabassi, L.G., Gumley, N., Papich, M., Jessen, L.R., Lappin, M., Rankin, S., Westropp, J.L., Sykes, J 2019, 'International society for companion animal infectious diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats', The Veterinary Journal, vol. 247, pp. 8-25.

EVE

EXOTICS

17. D

ABDOMINAL: URINARY TRACT RECURRENT URINARY TRACT INFECTIONS

BACKGROUND

Any infection that occurs in the presence of an anatomic or functional abnormality or in an animal that has a comorbidity that predisposes to persistent infection, recurrent infection, or treatment failure. Recurrent infections (3 or more episodes of infection during a 12-month period) can be further categorised as:

Reinfection: Recurrence of infection within 6 months of cessation of previous, apparently successful treatment and isolation of a different microorganism

Relapse: Recurrence of infection within 6 months of cessation of previous, apparently successful treatment and isolation of the same microorganism

Refractory: Similar to a relapse except that it is characterised by persistently positive culture results during treatment.

DIAGNOSIS

- Orinalysis
- Urine specific gravity
- Urine dipstick
- Oytology (stained and unstained)
- Orine sediment
- Culture and sensitivity (aerobic)

EXOTICS



ABDOMINAL: URINARY TRACT RECURRENT URINARY TRACT INFECTIONS

KEY ISSUES

Co-morbidities that should be considered:

- Endocrinopathy
- Kidney disease
- Obesity
- Abnormal vulvar conformation
- Congenital abnormalities of the urogenital tract (e.g. ectopic ureter, mesonephric duct abnormalities)
- Prostatic disease
- Bladder tumour
- Polypoid cystitis
- Urolithiasis
- Immunosuppressive therapy
- Rectal fistula
- Urinary incontinence/retention

Anecdotal evidence suggests that in mixed infections including Enterococcus spp., infection with this isolate will often resolve with effective treatment of other isolates, however ideally an antimicrobial that is effective against both pathogens should be selected. Note, there is no evidence that some drugs (i.e., clarithromycin) are effective at breaking down biofilms, these should be avoided as they are not excreted in the urine in active forms.

The presence of bacteriuria post-treatment should be approached as described under 'Subclinical bacteriuria'. If client compliance is deemed to have been adequate, referral to a specialist should be considered to explore reasons for microbial persistence or rapid re-infection.



ABDOMINAL: URINARY TRACT RECURRENT URINARY TRACT INFECTIONS

TREATMENT

Treatment should be based on culture and susceptibility results.

Consider pain relief whilst awaiting culture results, in lieu to starting antimicrobials empirically straight away. If empirical therapy is started, first choice is as for sporadic cystitis.

ANTIBIOTICS USED

First Line:

Amoxycillin (11–15 mg/kg PO q8–12h), Amoxycillin clavulanic acid (12.5–25 mg/kg PO q12h), OR Trimethoprim / sulphonamide (15-30 mg/kg PO q12h

Treatment Duration:

Treatment length may vary depending on the clinical signs/comorbidities; goal of treatment is clinical cure (i.e., no clinical signs) and no adverse effects (including antimicrobial resistance). Microbiological cure (i.e., negative culture) is desirable but not necessarily achievable.

Short duration (3-5 days) should be considered, particularly if infection appears to be a reinfection (not relapse/persistence) and/or the animal has comorbidities that relate to organs other than the urinary tract

Recommendation for longer courses has now shortened to 7-14 days (used to be 4 weeks); these to be considered if there are urinary tract abnormalities (e.g., bladder mucosa abnormalities).

The University of Melbourne, Australian veterinary prescribing guidelines: companion animal guidelines – urinary tract, viewed of October 2021 https://vetantibiotics.fvas.unimelb.edu.au/medical-guidelines/urinary-tract/ Weese, J.S., Blondeau, J., Boothe, D., Guardabassi, L.G., Gumley, N., Papich, M., Jessen, L.R., Lappin, M., Rankin, S., Westropp, J.L., Sykes, J 2019, 'International society for companion animal infectious diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats', The Veterinary Journal, vol. 247, pp. 8-25.

Prescribing Guidelines and Investigative Process

ABDOMINAL: URINARY TRACT SUBCLINICAL BACTERIURIA

BACKGROUND

Subclinical bacteriuria (SBU) is defined as evidence of positive urine culture in the absence of clinical signs. Note that urinalysis results (pyuria, haematuria, bacteriuria) may not correlate with culture results and poorly correlate with clinical signs. Attempts must be made to differentiate between SBU and clinical UTI based on history and clinical examination findings (not clinicopathological findings, e.g., urinalysis).

A patient that has pyuria and a positive culture but no clinical signs is considered to have SBU, not clinical infection.

A patient with heavy growth of bacteria on culture, but no clinical signs is considered to have SBU, not clinical infection.

SBU is a common finding particularly in animals with comorbidities (15-74% of these can have SBU), but may also happen in otherwise healthy dogs/cats (up to 13% of these can have SBU). SBU may not have clinical consequence, i.e., animals with SBU may not be at high risk of developing clinical disease however studies are limited.

DIAGNOSIS

- History and clinical examination
- Culture and sensitivity (aerobic). Culture of urine is NOT recommended when the animal does not have clinical signs (and there is no intention to treat), even if the animal has co-morbidities that predispose to bacteriuria (e.g., Diabetes Mellitus). [1,2]
- Retesting to assess whether SBU resolves is NOT recommended.

ABDOMINAL: URINARY TRACT SUBCLINICAL BACTERIURIA

TREATMENT

Treatment of SBU with antimicrobials is discouraged, even if there is evidence of pyuria or the isolated organism is multidrug resistant. If it is unclear whether the animal has SBU or clinical UTI a short course of treatment (3-5 days, as for sporadic cystitis) is recommended – if there is no discernible clinical improvement further treatment is discouraged.

In rare circumstances, treatment of SBU may be considered if there is concern of high risk of ascending or systemic infections. By extrapolation of data from humans, not many animals may be at risk of developing ascending or systemic infections when SBU is present.

In animals that cannot display clinical signs (e.g., paralysed) judgement must be made whether treatment is indicated.

If Corynebacterium urealyticum or Staphylococci are isolated short course treatment may be considered because of their associations with encrusting cystitis and struvite urolith formation, respectively. Because of the potential difficulties in treating these conditions, consideration of a single short course (3-5 days duration) of treatment, as per 'Sporadic bacterial cystitis', could be considered after confirming that bladder wall plaque or uroliths are not present. However, it is unknown whether this is a necessary or effective approach. Continued treatment of subclinical bacteriuria with these strains is likely not warranted. [1,2]

There is currently no evidence that adjunctive treatment (e.g., cranberry extract) is effective but there is no contraindication to the use of supplements that are known to be safe.

If an animal subsequently develops clinical UTI or pyelonephritis, it must not be assumed that this is caused by the SBU strain. Approach these cases is as mentioned in other categories (i.e., recurrent cystitis, pyelonephritis).



ANTIBIOTICS USED

First Line: Amoxycillin (11–15 mg/kg PO q8–12h),

Amoxycillin clavulanic acid (12.5–25 mg/kg PO q12h), OR

Trimethoprim / sulphonamide (15-30 mg/kg PO q12h)

<u>Treatment Duration:</u> 3-5 days

Granick, J. & Beaudoin, A. 2019 'A practical approach to antimicrobial stewardship for practices and practitioners', from proceedings ACVIM 2019, Saint Paul, Minnesota

The University of Melbourne, Australian veterinary prescribing guidelines: companion animal guidelines – urinary tract, viewed o1 October 2021 https://vetantibiotics.fvas.unimelb.edu.au/medical-guidelines/urinary-tract/

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ABDOMINAL: URINARY TRACT **PYELONEPHRITIS**

BACKGROUND

Definitive diagnosis of pyelonephritis is challenging. A diagnosis of acute pyelonephritis can be suspected based on positive aerobic bacterial urine culture when accompanied by systemic signs such as fever, lethargy, and/or polyuria/polydipsia; renal pain on abdominal palpation; laboratory findings of azotemia, cylindruria, and peripheral neutrophilia with or without left shift (in the absence of another identifiable cause). However, animals with acute pyelonephritis may be oliguric or anuric or have vague clinical signs.

Imaging findings such as renal pelvic dilation and/or blunting of the renal papilla on ultrasound examination may be noted but are non-specific. Care should be taken not to over-interpret the relevance of renal pelvic dilation, since it can be present in normal animals and those with other renal diseases.

DIAGNOSIS

- Urinalysis ۲
- Urine specific gravity ۲
- ۲ Urine dipstick
- ۲ Cytology (stained and unstained)
- Urine sediment ۲
- Culture and sensitivity (aerobic)
- Complete Blood Count + Biochemistry ۲
- ۲ Imaging
- Serum creatinine + SDMA



ABDOMINAL: URINARY TRACT PYELONEPHRITIS

KEY ISSUES

Culture and susceptibility testing should always be performed. Cystocentesis specimens should be used for culture. Obtaining a urine specimen for cytology and culture by pyelocentesis should be considered, particularly if results of culture of a cystocentesis specimen are negative, or when a cystocentesis specimen cannot be obtained. Blood cultures are recommended at the same time as urine cultures in immunosuppressed or febrile animals.

Evaluation for leptospirosis should be considered in culture-negative dogs by use of serological testing and PCR.

A diagnosis other than bacterial pyelonephritis should be considered if there is no improvement in systemic signs, haematology or serum biochemistry (e.g., azotemia, acute phase proteins) within 72 hours of antimicrobial therapy and the results of culture and susceptibility indicate susceptibility to the antimicrobial used and there is confidence in client compliance. At that time, consideration should be given to a diagnosis of subclinical bacteriuria (with discontinuation of antimicrobial therapy) or for the presence of uncontrolled underlying factors (e.g., ureteroliths, neoplasia) that would need to be addressed to resolve the underlying infection.

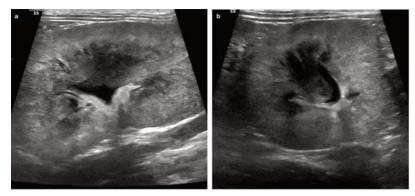


Figure 14: Longitudinal (a) and transverse (b) ultrasound images of the left kidney of a cat with bilateral renomegaly and acute (grade V) kidney injury. The kidney is enlarged, there is poor corticomedullary differentiation, the cortex is patchy hyperechoic, and the medulla has lost its typical hypoechogenic to anechoic appearance. The renal pelvis is dilated to 4 mm. Post-mortem examination of this cat revealed severe pyelonephritis. (Dorsch, Teichmann-Knorrn & Sjetne Lund, 2019)

EVE

INTEGUMENT

AURAL

ABDOMINAL THORACIC



ABDOMINAL: URINARY TRACT **PYELONEPHRITIS**

TREATMENT

Treatment should be based on culture and susceptibility results.

Consider pain relief whilst awaiting culture results, in lieu to starting antimicrobials empirically straight away.

If ascending infection is suspected, recently obtained urine culture results should be the basis of initial therapy (remembering that serum breakpoints must be considered). If hematogenous spread is suspected, initial therapy should be based on cultures of blood or the infected site, whenever available.

Oral antimicrobial therapy is recommended in animals that otherwise appear systemically well and have normal appetite. Intravenous therapy is recommended for animals that are dehydrated, hyporexic or anorexic, or lethargic.

A recheck examination that includes physical examination, serum creatinine concentrations, urinalysis and aerobic bacterial urine culture is recommended one to two weeks after cessation of antimicrobials. However, if clinical signs and azotaemia have resolved, consideration has to be given to the clinical relevance of microbiological failure, as it may represent subclinical bacteriuria and not indicate a need for treatment.

Re-isolation of the same bacterial species as that identified initially should stimulate consideration of reasons for potential persistence, including antimicrobial resistance, urolithiasis, anatomic defects or immune deficiency. Management of positive urine cultures in animals that have responded clinically and hematologically should be as per 'Subclinical bacteriuria'.



ABDOMINAL: URINARY TRACT

ANTIBIOTICS USED

Initial treatment should involve antimicrobials drugs with local or regional efficacy against Enterobacteriaceae. If regional data are supportive, the following antimicrobials are reasonable first line treatments:

Fluoroquinolones

e.g., Enrofloxacin (5-20 mg/kg q24h), Marbofloxacin (2.7-5.5 mg/kg PO q24h) or Cefpodoxime (5-10 mg/kg PO q24h),

For IV Administration:

Cefotaxime (dogs: 10–30 mg/kg IM, IV, SC q 8 hr x \leq 7 d, 20–80 mg/kg IM, IV q 6 hr) or Ceftazidime (dogs: 20–40 mg/kg IM, IV, SC q 8 hr, cats: 25–30 mg/kg IM, IV, IO q 8 hr)

Treatment Duration:

10-14 days

Culture and sensitivity data should be reviewed when results are received:

a) If combination therapy was initiated empirically and the isolate is susceptible to both drugs, one might be discontinued if supported by evidence of clinical response.

b) If resistance is reported to one of the drugs, that antimicrobial should be discontinued. A second drug to which the isolate is susceptible should be substituted if the patient has not responded sufficiently; substitution is not necessary if patient response has been sufficient.

c) If resistance is reported to both antimicrobials and clinical evidence of improvement is not evident, antimicrobial treatment should be changed to a drug to which the offending organism is susceptible in vitro.

d) If resistance to the drug(s) that are used is reported but there has been good clinical response, continuation with the initial therapy could be considered, provided there are no other reasons (such as fluid therapy) that might explain clinical improvement. Otherwise, a change in antimicrobial is indicated.

Dorsch, R., Teichmann-Knorrn, S. & Sjetne Lund, H. (2019) Urinary tract infection and subclinical bacteriuria in cats: A clinical update. Journal of Feline Medicine and Surgery. [Online] 21 (11), 1023–1038. Available from: doi:10.1177/1098612X19880435 [Accessed: 7 October 2021]

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VIN Veterinary Drug Handbook, Veterinary Information Network, viewed 01 October 2021

<a>https://www.vin.com/members/cms/project/defaultadv1.aspx?pld=13468>

Weese, J.S., Blondeau, J., Boothe, D., Guardabassi, L.G., Gumley, N., Papich, M., Jessen, L.R., Lappin, M., Rankin, S., Westropp, J.L., Sykes, J 2019, 'International society for companion animal infectious diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats', The Veterinary Journal, vol. 247, pp. 8-25.



ABDOMINAL: URINARY TRACT BACTERIAL PROSTATITIS

BACKGROUND

Consider bacterial prostatitis in every entire male dog.

Various bacteria can be involved, including a range of Gram-negative (e.g., *E. coli, Klebsiella, Pseudomonas, Pasteurella*) and Gram-positive (e.g., *Streptococcus, Staphylococcus*) species. *Brucella canis* is a potentially important zoonotic pathogen that can also be involved.

DIAGNOSIS

- Physical examination, per rectum palpation of the prostate
- Complete Blood Count
- Biochemical profile
- Urinalysis and urine culture (collected by cystocentesis
- Ultrasonographic evaluation of the prostate is recommended to characterise the size and structure of the prostate, to identify changes consistent with neoplasia (e.g., mineralisation) or abscessation.

- Cytological examination
- Aerobic bacterial C&S should be performed on the third fraction of the ejaculate, fluid collected by urethral catheterisation or per-rectum prostatic massage, or prostatic fluid collected by fine needle aspiration. The latter is particularly helpful when there is strong suspicion for prostatitis and the urine culture is negative for bacterial growth.



Figure 15: Prostatic abscess. Note the presence of a large cavity with a thick wall and the presence of a fine needle for aspiration (hyperechoic). (Lévy et al., 2014)



ABDOMINAL: URINARY TRACT **BACTERIAL PROSTATITIS**

KEY ISSUES

Isolation of Brucella canis at any level of growth is significant, but serological testing is recommended if *B. canis* infection is possible because of laboratory biosafety hazards associated with isolation of this bacterium and the potential for false negative cultures.

Castration should be recommended in dogs that are not intended for breeding. Castration does not alter the recommended antimicrobial drug choice or duration, but should be performed as early as is possible.

TREATMENT

Prostatic abscesses should be drained because of the low likelihood of resolution with medical treatment alone. Surgical or ultrasound-guided percutaneous drainage can be performed. This should be performed after culture results are available, whenever possible, to facilitate proper peri-operative antimicrobial therapy. Concurrent with drainage, treatment as for chronic prostatitis should be administered. Empirical treatment should target Enterobacteriaceae.



ANTIBIOTICS USED

First Line:

Trimethoprim-sulfonamide (Dogs and Cats: 15 mg/kg PO q 12 hr; Cats: 30 mg/kg PO q 24 hr)

If brucellosis suspected:

Fluoroquinolone (e.g., Enrofloxacin: Dogs: 5-20 mg/kg PO q 24 hr; Cats: 5 mg/kg PO q 24 hr/ Marbofloxacin: 2.0-5.5 mg/kg PO q 24 hr)

Second Line:

Based on C&S

Clindamycin (3–10 mg/kg IV, SC, PO q 8 hr) and macrolides

Treatment Duration:

4-6 weeks

The University of Melbourne, Australian veterinary prescribing guidelines: companion animal guidelines – urinary tract, viewed o1 October 2021 https://vetantibiotics.fvas.unimelb.edu.au/medical-quidelines/urinary-tract/

Weese, J.S., Blondeau, J., Boothe, D., Guardabassi, L.G., Gumley, N., Papich, M., Jessen, L.R., Lappin, M., Rankin, S., Westropp, J.L., Sykes, J 2019, 'International society for companion animal infectious diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats', The Veterinary Journal, vol. 247, pp. 8-25.

VIN Veterinary Drug Handbook, Veterinary Information Network, viewed o1 October 2021 https://www.vin.com/members/cms/project/defaultadv1.aspx?pld=13468.

Lévy, X., Niżański, W., von Heimendahl, A. & Mimouni, P. (2014) Diagnosis of Common Prostatic Conditions in Dogs: an Update. Reproduction in Domestic Animals. [Online] 49 (s2), 50–57. Available from: doi:10.1111/rda.12296 [Accessed: 7 October 2021].

ORAL



ABDOMINAL **HEPATOBILIARY**

BACKGROUND

Controversy surrounds the presence of normal hepatic bacterial flora.

While Kupffer cells are known to remove of bacteria and endotoxin delivered to the liver from the gut, a resident bacterial population has been suggested by some studies.

Various organisms have been isolated from the normal canine liver including strict anaerobes, strict aerobes and facultative anaerobes.

Multiple bacterial isolates (more so in dogs than cats) are common.

Bacteria has been isolated from up to 60% of dogs with gall bladder mucoceles and 60% of cases of bile peritonitis.

The use of peri-operative antibiotic therapy for major hepatobiliary surgery is considered appropriate as a means of prophylaxis.

If there is a high index of suspicion of bacterial infection it may be prudent to withhold peri-operative antibiotic therapy until after sample collection to reduce the incidence of a false negative cultures.

DIAGNOSIS

- Liver biopsy
- Bile collection via ultrasound or intraoperative cholecystocentesis
- Anaerobic/aerobic culture
- Results of culture interpreted together with clinical signs and cytology



ABDOMINAL HEPATOBILIARY

KEY ISSUES

TREATMENT

metronidazole

clavulanate

Antibiotic dose adjustment required in the presence of icterus or hepatic damage.

1. Fluroquinolone, penicillin, and

2. Fluroguinolone and amoxicillin-

3. Fluroquinolone and clindamycin

ANTIBIOTICS USED First Line

E. coli:

Ampicillin (10mg/kg/12hr) OR

Amoxicillin (11-22mg/kg/12hr)

Streptococcus spp:

Ampicillin (10mg/kg/12hr) OR

Amoxicillin (11-22mg/kg/12hr) OR

Amoxicillin + clavulanate (12.5-25mg/kg/8 to 12hr)

Anaerobes (Bacteroides, Clostridium):

Ampicillin (10mg/kg/12hr) OR

Amoxicillin (11-22mg/kg/12hr) OR

Clindamycin (5.5-11mg/kg/12hr)

Treatment Duration:

Until clinical improvement (On average 6-8 weeks)

Australasian Infectious Disease Advisary Panel (AIDAP) Antibiotics Prescribing Detailed Guidelines

Bray, J (2011), How to use antibiotics in surgical patients. BSAVA Companion 10: 15-19.

CEVA- Gram book- Guidance for the rationale use of antimicrobials. Recommendations for dogs and cats https://vetantibiotics.fvas.unimelb.edu.au/surgery-guidelines/

Herdefeldt LY, Browning GF, Thursky K, Gikerson JR, Billman-Jacobe H, Stevenson MA, Bailey KE (2017). Antimicrobials used for surgical prophylaxis by companion animal veterinarians in Australia. Veterinary Microbiology 203: 301-307. https://www.bsavalibrary.com/content/chapter/10.22233/9781910443644.app7#html_fulltext.

Tufts University (2021). https://vetmed.tufts.edu/foster-hospital-small-animals/policies-foster/use-of-antibiotics-in-dogs-and-cats-having-surgery/



ABDOMINAL

ROUTINE DESEXING PROCEDURES

BACKGROUND

Perioperative use of antimicrobials is considered unnecessary in routine short surgical procedures (<1 hour in duration) such as ovariohysterectomy and castrations conducted under sterile conditions.

Antibiotic use should be reserved for specific indications, such as a pre-existing infection or a break in surgical asepsis.

Nature of infection: Most potential contaminants arise from the skin of the or the veterinary staff. Organism involved: Staphylococcus pseudintermedius or Staphylococcus aureus.

Although in cats, Pasteurella multocida is also a common endogenous organism and surgical site infection isolate.

Emphasis should be placed on maintaining a sterile operating environment in order to reduce the reliance on antibiotics. The most well-established strategies to reduce the impact of surgical site infections are mostly preventative, focusing on strengthening host immunity while decreasing wound contamination during surgery.

Factors affecting surgical wound infection:

- Host risk factors (e.g., systemic conditions, endocrinopathies, geriatric, severe malnutrition, infection elsewhere in the body, obesity)
- Patient preparation (inadequate skin preparation, rough clipping prior to induction causing increased numbers of bacteria to grow on the surface)
- Surgical time (90 minutes has a twofold increase compared to 60 minutes, with each additional hour of surgery doubling the risk)

Surveillance protocols are critical to identify systematic breaks in surgical asepsis, inadequate perioperative care protocols, and patterns of antimicrobial resistance. Ideally, one member of the hospital team should take responsibility for ensuring thorough and regular monitoring of sterilisation procedures, assessment and control of environmental contamination within the hospital and monitoring the incidence of surgical site infections. Please refer to Chapter 9.



ABDOMINAL

ROUTINE DESEXING PROCEDURES

KEY ISSUES

Prolonged surgery times and an increased number of personnel at the time of the surgery poses a greater risk of infection.

If antibiotics are to be used, they should be administered prior to surgery or as soon as a break in surgical asepsis or other indications are recognised

TREATMENT

The use of antibiotics with higher efficacy for Staphylococcus spp. can be considered in the event of prolonged desexing operation or a breach in asepsis.

ANTIBIOTICS USED

A single injection of amoxicillinclavulanate or a 1st generation cephalosporin (e.g., cefazolin) can be considered.

- Amoxicillin/Clavulanate Acid (13.75-25mg/kg PO BID)
- Cephalexin(22mg/kg PO BID)

If perioperative antimicrobial agents are required, the first antimicrobial dose should begin within 60 minutes before surgical incision.

Prophylactic antimicrobial agents should be administered within 24 hours of the end of surgery.

Bowater RJ, Stirling SA, Lilford RJ. Is antibiotic prophylaxis in surgery a generally effective intervention? Testing a generic hypothesis over a set of meta-analyses. Ann Surg. 2009 Apr;249(4):551-6. doi: 10.1097/SLA.ob013e318199f202. PMID: 19300236.

Bratzler, Dale W., and Peter M. Houck. "Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project." Clinical Infectious Diseases (2004): 1706-1715.

Eugster, Simone, et al. "A prospective study of postoperative surgical site infections in dogs and cats." Veterinary surgery 33.5 (2004): 542-550.

National Research Council's Risk Index for Surgical Infection, Surgical-site infections and the NNIS SSI Risk Index: Room for Improvement. InfectionControl and Hospital Epidemiology (2000)

Rational Use of Presurgical Antibiotics, WSAVA World Congress Proceedings, 2013

Surgical Wound Infection and Antibiotic Prophylaxis, WSAVA/FECAVA/BSAVA World Congress 2012

Maintaing a Sterile Operating Environment WSAVA World Congress Proceedings, 2014

- <a>https://www.vin.com/apputil/content/defaultadv1.aspx?id=7054771&pid=12886&print=1>
- Surgical Wound Infection and Antibiotic Prophylaxis WSAVA/FECAVA/BSAVA World Congress 2012 13.

<https://www.vin.com/apputil/content/defaultadv1.aspx?pld=11349&catld=34738&id=5328375>

The Association of Shelter Veterinarians' 2016 Veterinary Medical Care Guidelines for Spay-Neuter Programs https://vetantibiotics.fvas.unimelb.edu.au/surgery-guidelines/

Tufts University. (2021) https://vetmed.tufts.edu/foster-hospital-small-animals/policies-foster/use-of-antibiotics-in-dogs-and-cats-having-surgery/

MUSCULOSKELETAL

ORAI



ABDOMINAL SEPTIC PERITONITIS

BACKGROUND

The most common origin of septic peritonitis is leakage from the gastrointestinal tract.

The pancreas, genitourinary tracts, hepatobiliary system, and percutaneous penetrating objects are other potential sources.

The stomach and proximal small intestine contain low numbers of acid-resistant microorganisms and no anaerobes. The colon is very densely populated with obligate anaerobes.

Septic peritonitis is most typically polymicrobial, E. coli and Bacteroides fragilis are overrepresented.

Therapy should be instituted on the basis of patient history, examination, findings of preliminary tests while awaiting bacterial culture results.

DIAGNOSIS

- History and physical examination
- **Complete Blood Count**
- **Biochemistry**
- Imaging
- Abdominocentesis (most useful test and should be conducted prior to initiation of therapy)



ABDOMINAL SEPTIC PERITONITIS

KEY ISSUES

Antibiotic therapy without appropriate surgical management and drainage is rarely successful and is not recommended. Surgical intervention should be considered over medical management when a diagnosis of septic peritonitis is made.

Bacteria isolated from aseptically collected abdominal fluid can confirm sepsis, however abdominal sepsis requires urgent intervention and other forms of fluid testing should take place while awaiting culture results.

Indicators for tentative diagnosis of sepsis:

- Identification of high total nucleated cell count in abdominal fluid
- identification of degenerate neutrophil populations
- decreased abdominal glucose and ۲ increased abdominal lactate levels

Specific isolates or certain disease states (such as pancreatic necrosis) may warrant longer courses.

Empirical recommendations for antimicrobial therapy are listed below based on the most commonly observed pathogens.

There is a current trend towards shorter duration of antimicrobial therapy and, when coupled with appropriate surgical intervention, duration of therapy of 5-7 days is considered appropriate.

TREATMENT

If abdominal effusion is observed, proceed with paracentesis followed by sampling (cytology, peritoneal/abdominal glucose ratio; FNA/biopsy; C&S.

Stabilise patient prior to surgery and proceed with surgical exploration/correction if deemed necessary (+/- drainage/lavage/tissue sampling).



ABDOMINAL SEPTIC PERITONITIS

ANTIBIOTICS USED

First Line

Gram Negative (*E. coli, Pasteurella, Klebsiella*):

Amoxicillin + clavulanate (12.5-25mg/kg/8 to 12hr)

Gram Positive (*Enterococcus, Staphylococcus*):

Amoxicillin (20-25mg/kg/8 to 12hr)

Ampicillin (10-20mg/kg/6 to 8hr) OR

Clindamycin (5.5-11mg/kg/12hr)

Obligate Anaerobes (*Clostridium*, *Bacteroides*, *Fusobacterium*):

Amoxicillin (20-25mg/kg/8 to 12hr PO; 20mg/kg/6hr)

Ampicillin (10-20mg/kg/6 to 8hr PO; 20mg/kg/6 to 8hr IV) OR

Clindamycin (5.5-11mg/kg/12hr) OR

Metronidazole (10-15mg/kg/12hr PO; 10mg/kg/8hr IV)

Treatment Duration:

2-4 weeks; In mixed infections 4 weeks minimum (2 weeks after clinical resolution)

Australasian Infectious Disease Advisary Panel (AIDAP) Antibiotics Prescribing Detailed Guidelines

Bray, J (2011), How to use antibiotics in surgical patients. BSAVA Companion 10: 15-19.

CEVA- Gram book- Guidance for the rationale use of antimicrobials. Recommendations for dogs and cats https://vetantibiotics.fvas.unimelb.edu.au/surgery-guidelines/

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Tufts University (2021).<https://vetmed.tufts.edu/foster-hospital-small-animals/policies-foster/use-of-antibiotics-in-dogsand-cats-having-surgery/>



MUSCULOSKELETAL OSTEOMYELITIS

BACKGROUND

Often based on clinical suspicion with presenting signs such as lameness and diagnostic imaging.

DIAGNOSIS

- History and physical examination
- Imaging bone lysis, sequestration, periosteal reaction, loosening of implants, fistula tracts)
- Culture and sensitivity

KEY ISSUES

- *Staphylococcus* is most commonly isolated.
- 30% of mixed infections associated with anaerobes (*Bacteroides*, *Fusobacterium*) and aerobes (*Pasteurella*, *Klebsiella*) when osteomyelitis was secondary to bites.
- If implant-associated, the infection may not resolve until implant is removed.
- If no clinical improvement is observedrevise antimicrobial therapy, surgical debridement and re-sample (tissue, infected implant) for C&S.

TREATMENT

Empirical therapy (Amoxicillin+/clavulanate/cefelaxin/cefadroxil/clindamyci n) while awaiting culture and sensitivity results.

Removal implant if possible.



MUSCULOSKELETAL **OSTEOMYELITIS**

ANTIBIOTICS USED

First Line

Gram Negative (*E. coli*): Amoxicillin + clavulanate (12.5-25mg/kg/8 to 12hr) OR

<u>1st generation cephalosporin:</u>

Cephalexin (15-30mg/kg/12hr PO)

Cefadroxil (10-20mg/kg/12hr PO)

Gram Positive (Streptococcus,

Staphylococcus):

Amoxicillin + clavulanate (12.5-25mg/kg/12hr PO) OR

Clindamycin (11mg/kg/12hr PO) OR

1st generation cephalosporin:

Cephalexin (15-30mg/kg/12hr PO)

Cefadroxil (10-20mg/kg/12hr PO)

dogs-and-cats-having-surgery/>

Treatment Duration:

Administer antimicrobials intravenously for 2-3 days then orally

Treat for 6-8 weeks OR

Up to 2 weeks beyond clinical and radiographic resolution of the infection

Remove implant if possible/ replace with antibiotics impregnated implant

Australasian Infectious Disease Advisary Panel (AIDAP) Antibiotics Prescribing Detailed Guidelines Bray, J (2011), How to use antibiotics in surgical patients. BSAVA Companion 10: 15-19. British Small Animal Veterinary Association. (2018) BSAVA/SAMSoc Guide to Responsible Use of Antibacterials: PROTECT ME https://www.bsavalibrary.com/content/chapter/10.22233/9781910443644.app4#html_fulltext CEVA- Gram book- Guidance for the rationale use of antimicrobials. Recommendations for dogs and cats Herdefeldt LY, Browning GF, Thursky K, Gikerson JR, Billman-Jacobe H, Stevenson MA, Bailey KE (2017). Antimicrobials used for surgical prophylaxis by companion animal veterinarians in Australia. Veterinary Microbiology 203: 301-307University of Melbourne (2021). Surgery Guidelines. https://vetantibiotics.fvas.unimelb.edu.au/surgery-guidelines/ > Tufts University (2021). < https://vetmed.tufts.edu/foster-hospital-small-animals/policies-foster/use-of-antibiotics-in┢

INTEGUMENT

AURAL

ABDOMINAL THORACIC



MUSCULOSKELETAL

BACKGROUND

Often based on clinical suspicion with presenting signs such as lameness and joint effusion.

DIAGNOSIS

- History and physical examination
- Joint effusion (Joint fluid >40% neutrophils and bacteria visible intra- and extracellularly)
- Arthrocentesis
- Cytology
- Imaging

KEY ISSUES

In the absence of improvement after 2 weeks, lavage and a C&S is required.

TREATMENT

Empirical therapy (Amoxicillin+/clavulanate/cefelaxin/cefadroxil/clindamyci n) while awaiting culture and sensitivity results. Consider joint lavage.



Figure 16: The joint was lavaged with lactated Ringer's solution using 16 and 18 gauge needles. (Hewes & Macintire, 2011)



MUSCULOSKELETAL

ANTIBIOTICS USED

First Line

Gram Negative (*E. coli*): Amoxicillin + clavulanate (12.5-25mg/kg/8 to 12hr) OR

1st generation cephalosporin:

Cephalexin (15-30mg/kg/12hr PO)

Cefadroxil (10-20mg/kg/12hr PO)

Gram Positive (Streptococcus,

Staphylococcus):

Amoxicillin + clavulanate (12.5-25mg/kg/12hr PO) OR

Clindamycin (11mg/kg/12hr PO) OR

1st generation cephalosporin:

Cephalexin (15-30mg/kg/12hr PO)

Cefadroxil (10-20mg/kg/12hr PO)

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British Small Animal Veterinary Association. (2018) BSAVA/SAMSoc Guide to Responsible Use of Antibacterials: PROTECT ME https://www.bsavalibrary.com/content/chapter/10.22233/9781910443644.app4#html_fulltext

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Tufts University (2021). https://vetmed.tufts.edu/foster-hospital-small-animals/policies-foster/use-of-antibiotics-in-dogs-and-cats-having-surgery/

Treatment Duration:

4 weeks minimum (2 weeks after clinical resolution of effusion or until synovial fluid <3% neutrophils)



MUSCULOSKELETAL DISCOSPONDYLITIS

BACKGROUND

Often based on clinical suspicion with presenting signs such as lameness and joint (Aspergillus spp, Blastomyces) effusion.

DIAGNOSIS

- History and physical examination
- Joint effusion (Joint fluid >40% neutrophils and bacteria visible intraand extracellularly)
- Arthrocentesis
- Cytology
- Imaging

KEY ISSUES

Rule out possible fungal infection

TREATMENT

Empirical therapy (Amoxicillin+/clavulanate/cefelaxin/cefadroxil/clindamyci n) while awaiting culture and sensitivity results. Consider joint lavage.



Figure 17: Lateral spinal survey radiograph. Notice the areas of osteolysis and osteoproliferation involving the T13 and L1 vertebrae (arrow). The radiographic changes are consistent with discospondylitis and vertebral osteomyelitis.

ORAL



MUSCULOSKELETAL DISCOSPONDYLITIS

ANTIBIOTICS USED

First Line

Gram Negative (*E. coli***):** Amoxicillin + clavulanate (12.5-25mg/kg/8 to 12hr) OR

Clincamycin (11mg/kg/12h PO)

1st generation cephalosporin:

Cephalexin (15-30mg/kg/12hr PO)

Cefadroxil (10-20mg/kg/12hr PO)

Brucella spp: Minocycline/Doxycyline (25mg/kg/24hr PO) – for 4 weeks OR

Tetracycline (30mg/kg/12hr PO) + Gentamicin (5mg/kg SC for 7 days) (Administered week 1 and 4) OR

Streptomycin (20mg/kg/24hr IM, SC for 7 days) (Administered week 1 and 4)

Gram Positive (Streptococcus,

Staphylococcus):

Amoxicillin + clavulanate (12.5-25mg/kg/12hr PO) OR

Clindamycin (11mg/kg/12hr PO) OR

1st generation cephalosporin:

Cephalexin (15-30mg/kg/12hr PO)

Cefadroxil (10-20mg/kg/12hr PO) OR

Trimethoprim/sulfadiazine (15mg/kg PO, SC q12hr)

Antimicrobial therapy to be administered intravenously if severe neurological compromise or signs of sepsis.

Treatment Duration:

Minimum of 8 weeks (based on clinical response)

Australasian Infectious Disease Advisary Panel (AIDAP) Antibiotics Prescribing Detailed Guidelines Bray, J (2011), How to use antibiotics in surgical patients. BSAVA Companion 10: 15-19.

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INTEGUMENT

AURAL

ABDOMINAL THORACIC

OTHERS



BACKGROUND

Antimicrobial therapy is NOT INDICATED in clean (elective surgery, no entry into hollow viscus) surgical procedures.

In instances where antimicrobial therapy is indicated, comprehensive guidelines for type, dose and duration of treatment remain lacking for veterinary medicine.

The Surgical Care Improvement Project (SCIP) for human medicine has outlined three core strategies, which may be useful in veterinary medicine.

- Antimicrobials should be selected to combat the organisms expected at the surgical site.
- Antimicrobial administration should be timed such that peak drug concentration is present at the time of the incision.
- 3. Prophylactic antibiotics should be discontinued within 24 hours.

Prophylactic/ perioperative antimicrobial(s) are indicated in (comorbidities)

- Prolonged clean surgery (>90mins)
- Surgery involving an implant
- Surgery involving entry into hollow viscus
 (qastrointestinal tract, urinary tract)
- Obvious break in asepsis causing contamination of wound
- Contaminated wounds
- Presence of pre-existing infection
- Debilitated or immunosuppressed patients
- Potentially catastrophic infections (e.g., in CNS)
- Hypotension
- Obese dogs
- Bacterial dermatitis
- Endocrine disorder



OTHERS

GENERAL SURGERY

Surgery Type	Choice of Antimicrobial Agent	Timing/ Duration of Therapy
Clean A (No co-morbidities) - No entry into hollow viscus - Elective surgery - Castration/OVH - Simple skin mass removal - Splenectomy - Umbilical hernia repair - Short clean procedures (<gomins)< td=""><td>None</td><td></td></gomins)<>	None	
Clean B (co-morbidities) - Entry into hollow viscus - Minor break in asepsis - Clean procedures with drain placement	Amoxicillin-clavulanate OR 1 st generation cephalosporin (e.g., Cefuroxime, cefazolin)	IV 30-60 minutes BEFORE SC 2hrs BEFORE Thereafter EVERY 90 minutes until end of surgery Stop within 24hrs (except dermatitis – treat until cure)
Contaminated (+anaerobic involvement) - Entry into hollow viscus with intraoperative contamination of surgical site - Pyometra - Prostatic abscess significant bowel leakage - Fresh traumatic wounds (<6hr) - Major break in asepsis	Amoxicillin-clavulanate OR 1 st generation cephalosporins (e.g., Cefuroxime) (+ gentamicin + metronidazole)	IV 60 minutes BEFORE SC 2hrs BEFORE Thereafter EVERY 90 minutes until end of surgery Cefazolin every 4hrs; Amoxicillin every 2hrs Stop within 24hrs (except dermatitis/septic peritonitis – treat until cure)
Dirty (Bacterial Infection Present) - Abscess - Septic peritonitis - Traumatic wound incurred >6hr prior to surgery - Chronic wound or faecal contamination	Based on C&S Use appropriate antimicrobials based on infection	As above Treatment until clinical resolution



KEY ISSUES

NB: DO NOT CONTINUE antimicrobials after surgery unless there is a therapeutic indication as this will select for resistance.

Australasian Infectious Disease Advisary Panel (AIDAP) Antibiotics Prescribing Detailed Guidelines Bray, J (2011), How to use antibiotics in surgical patients. BSAVA Companion 10: 15-19. British Small Animal Veterinary Association. (2018) BSAVA/SAMSoc Guide to Responsible Use of Antibacterials: PROTECT ME <https://www.bsavalibrary.com/content/chapter/10.22233/9781910443644.app4#html_fulltext> CEVA- Gram book- Guidance for the rationale use of antimicrobials. Recommendations for dogs and cats Herdefeldt LY, Browning GF, Thursky K, Gikerson JR, Billman-Jacobe H, Stevenson MA, Bailey KE (2017). Antimicrobials used for surgical prophylaxis by companion animal veterinarians in Australia. Veterinary Microbiology 203: 301-307 University of Melbourne (2021). Surgery Guidelines. <https://vetantibiotics.fvas.unimelb.edu.au/surgery-guidelines/ > Tufts University (2021). <https://vetmed.tufts.edu/foster-hospital-small-animals/policies-foster/use-of-antibiotics-indogs-and-cats-having-surgery/>



BACKGROUND

Defined as a controlled rise in body temperature when the hypothalamic thermostat is reset to a higher core temperature. The two main causes for this are presence of exogenous pyrogens or generation of pyrogenic cytokines. It is important to note that not all fevers are associated with infections, as there are a wide range of non-infectious diseases that can also cause fever. The main differentials for fever should include infectious, inflammatory, immune-mediated and neoplastic conditions.

Generation of fever is an adaptive response of the body and arises in a physiologically regulated manner such that it may be beneficial to the body. Treatment and management strategies should be aimed towards determining the underlying cause for the fever, and not dropping the patient's body temperature. Mild to moderate body temperature elevations are rarely fatal, and there is little to no danger of a fever getting dangerously high to result in cellular dysfunction and death in most patients. However, if a fever exceeds 41.6°C, there is significant risk of developing disseminated intravascular coagulopathy and permanent organ damage. It is thus important for clinicians to distinguish fever from hyperthermia as the approach to diagnostics and treatments differ greatly between the two. [Annex III]



Common differential diagnosis for fever in dogs and cats

Cause	Dogs	Cats
Infectious	Aspiration pneumonia	Feline infectious peritonitis
	Pyothorax	Feline leukemia
	Fungal pneumonia	Feline immunodeficiency virus
	Ehrlichia, Babesia, Anaplasma	Cellulitis/otitis (media)
	Leptospirosis	Pyothorax
	Pyelonephritis	Upper and lower respiratory tract
	Prostatitis	infections (Mycoplasma felis,
	Pyometra	calicivirus, herpes virus)
	Lower urinary tract infection	Bronchopneumonia
	Parvoviral enteritis	Mycoplasma haemofelis
	Cholangiohepatitis/cholangitis	Neutrophilic cholangiohepatitis
	Septic peritonitis	Pyelonephritis
	Brain empyema	Lower urinary tract infection
	Infectious meningitis	Septic peritonitis
	Discospondylitis	Panleukopenia
	Osteomyelitis	Brain empyema
	Cellulitis	Infectious meningitis
	Severe	Hepatic abscess
	pyoderma/furunculosis/panniculitis	Severe
		pyoderma/furunculosis/panniculitis



Inflammatory	Pancreatitis	Pancreatitis
	Pulmonary embolism	Pulmonary embolism
	Meningitis/meningoencephalitis/m	Lymphocytic cholangiohepatitis/ cholangitis
	eningoencephalomyelitis	Sterile peritonitis
	Juvenile cellulitis	Sterile lymphadenitis/panniculitis/cellulitis
	Nodular panniculitis	Inflammatory lower airway disease
		Lymphocytic cholangiohepatitis/ cholangitis
		Inflammatory CNS disease
		Myocarditis
Immune-	Immune-mediated haemolytic	Immune-mediated haemolytic anaemia
mediated	anaemia	Immume-mediated polyarthritis
	Immume-mediated polyarthritis	
Neoplasia	Lymphoma	Lymphoma
	Haemangiosarcoma	Squamous cell carcinoma
	Osteosarcoma	Mammary carcinoma
	Mast cell tumours	Fibrosarcoma
	Melanomas	Pulmonary carcinoma
	Transitional cell carcinomas	Leukemia
	Pulmonary carcinoma	Pulmonary metastasis
	Leukemia	Gastrointestinal adenocarcinoma
	Pulmonary metastasis	
	Gastrointestinal adenocarcinoma	
	Anal sac adenocarcinoma	

Please note that this list is not exhaustive



DIAGNOSIS

Initial Diagnostics

Diagnostic tests should be chosen based on clues provided from patient's signalment, history and presenting signs. All samples for bacterial culture should be collected prior to empiric antibiotic use.

- Haematology, biochemistry, urinalysis
- Blood and urine cultures
- Thoracic radiographs
- Point-of-care ultrasonography

Further Diagnostics

In no particular order. Again, choice of diagnostics should be prioritised based on results of previous initial diagnostic tests, signalment, history and presenting signs.

- **Tissue biopsies**
- Cerebrospinal fluid analysis
- Joint fluid analysis
- Echocardiography
- Culture or PCR for specific infectious diseases
- Radiographs of long bones

KEY ISSUES

Early empirical antibiotic use will interfere with subsequent diagnostics and should be reserved for cases with a high index of suspicion for an infectious cause.

Empirical antibiotic use is recommended in patients with signs of sepsis, or if they are determined to be at high risk of becoming septic.

**All samples for bacterial culture should be collected prior to empiric antibiotic use.



TREATMENT

If an underlying bacterial infectious disease is suspected, choice of broadspectrum antibiotic should be based on likely pathogenic bacteria, pending culture results. The exception is in patients showing clinical signs of sepsis, 'fourquadrant' therapy should be instituted immediately (and no more than 1h after hospital admission) after collection of appropriate samples for diagnostic testing.

ANTIBIOTICS USED

All dosages listed are for both dogs and cats, except when indicated otherwise.

Duration of antibiotic therapy should be based on patient's clinical progression, typically a minimum of 5-7 days, to extend if required and to de-escalate when appropriate.

For febrile patients demonstrating clinical signs of sepsis;



ANTIBIOTICS USED

First Line

Ampicillin/sulbactam 22mg/kg IV q8h or

Amoxicillin/clavulanic acid 20-25mg/kg IV q6-8h

<u>Four-quadrant therapy (if</u> <u>indicated)</u>

Ampicillin/sulbactam 22mg/kg IV q8h or Amoxicillin/clavulanic acid 20-25mg/kg IV q6-8h, with enrofloxacin 10mg/kg (5mg/kg for cats) slow IV q24h

or Ampi

Ampicillin/sulbactam 22mg/kg IV q8h or Amoxicillin/clavulanic acid 20-25mg/kg IV q6-8h, with ceftazidime 30-50mg/kg IV q6-8h or

Clindamycin 8-10mg/kg IV q8-12h with enrofloxacin 10mg/kg slow IV q24h

For anti-pseudomonal coverage:

Pipericillin-tazobactam 50mg/kg slow IV q4-6h or Amikacin 15-20mg/kg IV q24h or Ceftazidime 30-50mg/kg IV q6-8h or

Meropenem 24mg/kg q24h SC or 12mg/kg SC q8-12h, OR imipenem 5-10mg/kg q6-8h (last resort)

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BACKGROUND

Heartworm Disease (Dirofilaria imminitis) Transmitted by mosquitos

Clinical Signs (Dogs)

Weakness, lethargy, heart murmur, pulmonary oedema, ascites, dyspnea and coughing, haemoptysis

Clinical Signs (Cats)

Tachypnea, coughing, haemoptysis, acute death due to hypersensitivity

Antibiotics Used (Dirofilaris Canis)

Doxycycline (10 mg/kg BID for 28 days)

Ehrlichia (Ehrlichia Canis)

Transmitted by brown dog tick (Rhipicephalus sanguineus)

Clinical Signs

Lethargy, anorexia, weight loss, pyrexia, lymphadenomegaly and organomegaly

Bleeding

Pale mucous membrane, petechiae, hyphema, epistaxis

Ocular Anterior uveitis

Neurological Seizures, ataxia, vestibular signs

Polyarthritis Shifting lameness, joint pain

Antibiotics Used

Doxycycline (10 mg/kg PO g24h for 28 days) OR

Imidocarb diproprionate 5 mg/kg IM given 15 days apart



OTHERS

VECTOR-BORNE DISEASES

Babesia (Babesia canis/gibsoni)

Transmitted by brown dog tick (Rhipicephalus sanguineus)

After initial parasitemia, the immune system does not totally eradicate the infection, and a chronic carrier state remains. Relapses may occur months to years later.

Infection may be subclinical and produce no clinical signs.

Clinical Signs

Depression, weakness, pallor, icterus, lethargy, palpable splenomegaly, petechiation, epistaxis, recumbency, hypersalivation, arrhythmias, weak peripheral pulses, ataxia, paresis, dyspnea, dribbling urine, hemoglobinuria, lymphadenopathy, and fever may be noted on physical examination.

Antibiotics Used

Imidocarb diproprionate (5 to 6.6 mg/kg IM or SC, repeat in 2 weeks)

Atovaquone (13.3 mg/kg PO g8h for 10 days) with azithromycin (10 mg/kg PO q 24 h for 10 days) OR

Buparvaquone (5 mg/kg IM twice with 48 hr intervening) and azithromycin (10 mg/kg PO q24 h for 10 days) OR

Clindamycin 30mg/kg PO g12h, Diminazene aceturate 3.5mg/kg IM on the day of starting treatment, imidocarb diproprionate 6mg/kg SC once on the day after diminazene is administered OR

Clindamycin (25 mg/kg body weight, per os, q 12 hours for 14 days and Metronidazole (25-50 mg/kg PO g24h for 7 days) and Doxycycline (10 mg/kg PO BID for 7–10 days)

Anaplasma spp. (Anaplasma. phagocytophilum/Anaplasma platys)

Transmitted by brown dog tick (Rhipicephalus sanguineus) for Anaplasma platys.

Most infected dogs will have symptoms for 1 to 7 days, however, some will have no or only minor symptoms.

Infection with the more common form of anaplasmosis, A. phagocytophilum, often causes lameness, joint pain, fever, lethargy, and anorexia (lack of appetite).

Infection with A. platys can cause cyclic thrombocytopenia. Clinical disease is often mild, but some dogs may develop bruising or bleeding (including nosebleeds), especially during the early stages of infection when platelet counts may be at their lowest.

Antibiotics Used

Tetracycline (22 mg/kg given every 8 hours) or doxycycline (5 mg/kg every 12 hours)

Duration of treatment: 28 days

ORAL

EVE

INTEGUMENT



Leptospirosis

Caused by bacterial spirochetes of the genus *Leptospira*.

Leptospires can penetrate mucous membranes, wet or macerated skin, and broken skin.

Animals can become infected through contact with infected urine; via venereal or placental transfer; through bite wounds; and ingestion of infected tissues. Indirect transmission can occur through exposure to water sources, soil, food, or bedding that are contaminated with infected urine or tissues.

Antibiotics Used

Doxycycline (5 mg/kg q 12 hrs PO, IV for 2-3 weeks) OR

Penicillin G (25,000-40,000 units/kg q 12 hrs IV, SC, IM for 3 weeks) OR

Ampicillin (22 mg/kg q 6-8 hrs IV for 3 weeks)

Mycoplasma haemofelis

Caused by *Mycoplasma* spp. Mycoplasma spp. are common cell wall deficient bacteria that colonise cats. May be transmitted by fleas with *C. felis* being a possible vector.

Some Mycoplasma spp. reside on the surface of mucous membranes and are frequently isolated from the mouth, pharynx, airways and conjunctiva of cats.

Clinical Signs

Anaemia

Antibiotics Used

Doxycycline 5 mg/kg q 12 hrs PO \leq 28 days



Figure 18: Attachment sites of Rhipicephalus sanguineus. A: three adults on the ear of a dog. B: two females attached to the axilla of a dog. C: an engorged nymph on the interdigital region of a dog. (Dantas-Torres, 2010)



DIAGNOSIS

- Antigen/ antibody testing (screening tests, often used as a first line during diagnosis.
- PCR (higher specificity, usually to confirm a true infection)

based off clinical suspicion following history and physical examination.

KEY ISSUES

Selection of appropriate diagnostic tests is

- Cytology (direct smear)
- **Complete Blood Count**
- Urinalysis
- Additional tests: Knott's test, filer test



TREATMENT

A large part of managing these diseases is to prevent infection by the vector organisms. This is achieved by working with owners to ensure that the animal is on regular preventatives.

Flea/Tick Preventives with the following: imidacloprid, fipronil, selamectin, indoxacarb, pyrethrin, permethrin, fluralaner, spinosad, nitenpyram, afoxolaner, sarolaner Heartworm Prevention: Macrocyclic lactones such as Ivermectin, Milbemycin, Moxidectin Oxime, and Selamectin

Once a diagnosis has been confirmed, proceed with antimicrobial therapy where indicated. Antimicrobial therapy should not be administered as sole therapy for positive cases, rather in conjunction with other therapeutic treatments.

American Heart Work Society Recommended Heartworm Management Protocol Current Canine Guidelines for the Prevention, Diagnosis, and Management of Heartowrm (Dirofilaria immitis) Infection in Dogs by the American Heartworm Society

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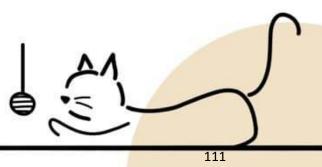
INTEGUMENT

AURAL

Preamble to Chapter 4: Exotics

The recommendations set out in Chapter 4: Exotics of the guidelines are based on information that is subject to regular amendments as new studies/information is published. The information provided is intended for use as a guide of a general nature only and may or may not be relevant to patients or circumstances, nor is it intended to be exhaustive on the subject matter. We leave it to the discretion of the attending veterinarian to use these guidelines in conjunction with exercising their own independent skill and clinical judgement, or seek third-party professional advice in relevant sections where deemed necessary. In particular, we strongly encourage sourcing of updated information with regards to species-specific dosages, routes of administration and treatment durations for each individual patient, taking into consideration medical, dietary and environmental factors.

Compliance with any recommendation within the guidelines does not guarantee discharge of duty of care owed to the patients from the attending veterinarian.





INTRODUCTION

As the majority of antimicrobial research in aquatic animals has been focused more on food aquaculture than companion aquatic species, there is a paucity of information relating to the levels and patterns of antimicrobial use in companion aquatic species.

Currently, there is a notable challenge in the ornamental fish industry where medications with antibiotics are marketed either as part of or the main component of off-the-shelf treatments, without requiring veterinary examination and prescription [Annex VII]. For example, erythromycin, which is listed under Critically Important Antimicrobials under the WHO's document on Critically Important Antimicrobials in human medicine is sold as a commercial product marketed as a remedy for broad spectrum treatment and control of bacterial disease in fish. It comes along with a chart to guide owners on which treatment to administer based on clinical signs of the fish alone. This means that, when the owner does come to seek the veterinarian's opinion, the veterinarian should bear in mind that they might have already tried several over-the-counter treatments and are coming in to the clinic because their over-the-counter treatments are no longer working.

It is important to note that AMR can be transmitted through the aquatic environment, and that ornamental fish and their carriage water can act as reservoir for resistance bacteria and genes.



GENERAL PRINCIPLES

The general principles of antimicrobial use in aquatic animals are similar to that for other species. A diagnosis is achieved based on history, clinical presentation, in combination with culture and sensitivity.

Aquatic animals depend greatly on their aquatic environment and their health is greatly influenced by water parameters ranging from oxygen. pH, temperature, hardness, chlorine and ammonia and their derivatives. As such, testing of water parameters of the water at home should be considered part of the workup of any fish or aquatic animal presenting to the veterinarian. Ideally, the client is aware and has the capacity of testing the water parameters at home. Ig not, bringing the samples to the clinic for testing is also an option, but some parameters such as temperature and dissolved oxygen may change because of transport conditions or over time.

The fish immune system is greatly affected by its environment, and hence, it is of even greater importance to consider the environmental factors that may contribute to lowered immunity. Overcrowding, fighting, handling and transport can also cause stress to the aquatic animal that can make them more susceptible to disease. Ectoparasites are common and can act as primary pathogens that break the epidermal barrier, allowing for secondary bacterial infection.

Many diseases that are commonly seen in aquatic animals are related to poor husbandry or are the result of ectoparasites or opportunistic bacterial pathogens that in some cases, respond to just correcting these husbandry factors, or salt bath or dip treatment instead of antibiotics.

Prescribing Guidelines and Investigative Process



EXOTICS ANTIMICROBIAL USE IN FISH

DECISION-MAKING ON ANTIBIOTIC USE

Systemic bacterial infection, depending on aetiology and severity, may involve the following clinical signs singly or in combination of two or more; degenerative lesions of the integument and associated structures (i.e., scales and fins), loss of control over buoyancy and righting reflex, exophthalmos, and abdominal distension ('dropsy'). In many cases, the initiating clinical problem may not be bacterial but ultimately becomes aggravated by an opportunistic bacterial pathogen.

Sahatrakul et al. (pers comm) have observed that >90% of bacteria isolated from lesions and/or clinical cases in both fresh and saltwater fish were gramnegative. Hence, the first line of antibiotic treatment is generally directed against gram-negative bacteria. However, for a more directed and "fine-tuned approach" to therapy, it is still prudent to perform microbiology including (but not limited to) Gram stain, species identification, and antimicrobial susceptibility test.

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Drug Name	Dose	Remarks		
Enrofloxacin	5-10 mg/kg PO, IM, ICe q24- 48h for 7-14 days	Enrofloxacin can cause muscle necrosis at injection site in certain species. Dilution with at least the equal volume of sterile water before intramuscularly injection is recommended.		
	5-10 mg/L, prolonged immersion for 7-14 days	Change 50 – 100% of the water between treatments.		
	o.1% feed PO, q24h for 7-14 days	Mix medication directly into the feed.		
Amikacin	5 mg/kg IM, IV q72h for 3-5 treatments	Aminoglycosides can be nephrotoxic in certain species.		

Some commonly used antimicrobials in fish



ANTIMICROBIAL USE IN FISH

Some commonly used antimicrobials in fish

Drug Name	Dose	Remarks
Gentamicin	2.5 mg/kg IM q72h for 3-5 treatments	Aminoglycosides can be nephrotoxic in certain species.
Ceftazidime	20 mg/kg IM, IV, ICe q72h for 3-5 treatments	None
Ceftiofur crystalline free (Excede®)	6.6 mg/kg IM q6d for 3 treatments	High volume can be irritating to the surrounding tissues at injection site. Dividing into two equal volumes and injection into two injection sites (left and right epaxial muscles) is recommended.
Neomycin	66 mg/L, prolonged immersion, q3d up to 3 treatments	Biological filtration must be removed during treatment to prevent killing nitrifying bacteria.
Tricide-NeoTM	Not more than 5 minutes dip in stock solution, q24- 48h, 1 week	Mix 5.80 g of Tricide-Neo powder to 1L of normal saline (0.85%) or distilled water thoroughly. Equilibrate the temperature with that of the exhibit tank water before administration.





ANTIMICROBIAL USE IN FISH

ROUTES OF ADMINISTRATION

Below is a summary of the routes of antimicrobial administration used in fishes; water-borne, injection, oral, topical. The ideal choice of delivery shall depend on the species of fish involved, its current state in the disease process, habitat or environment the fish would be kept during the treatment, the ability to monitor and manipulate water quality, and the chemical or physical stability of the antibiotics used at different preparations.

1. WATER-BORNE IMMERSION

Unit Dose: Mg/L (ppm) or g/L (ppt)

<u>Advantages</u>

- Most common treatment method
- Non-invasive

Disadvantages

- Often imprecise
- Most drugs are unstable and quickly degrade
- Repetitive dosing and/or removal of by-products of drugs with water changes
- Water quality should be monitored

Dip (0-15 minutes) Description

Concentrated drug solution for a short duration

Practical Considerations

- High concentrations can be stressful and even lethal if used for prolonged periods
- Harmful to biological filtration
- Treatment should be done in an isolated tank.
- Aeration required during treatment
- Monitor for signs of stress during treatment

Bath (>15 minutes to <24 hours) Description

Moderate drug concentration in moderate duration

Practical Considerations

- Treatment should be done in an isolated tank.
- Aeration required during treatment
- Monitor for signs of stress during treatment

Prolonged Immersion (>24 hours) Description

Low drug concentration in long term exposure <u>Practical Considerations</u>

- Reduced risk of toxicity and stress
- Can be done in an entire pond or tank
- Generally does not severely impair biological filtration
- Remove activated carbon during treatment
- Monitor water quality parameters (e.g., ammonia, nitrite, pH).

EVE

INTEGUMENT

AURAL

ABDOMINAL THORACIC

MUSCULOSKELETAL



2. INJECTION

Unit Dose: mg/kg body weight

<u>Advantages</u>

- Delivers a precise dosage
- Disinfection of the injection site is not necessary

Disadvantages

- Requires physical handling of fish
- Stress due to capture
- Invasive technique

IM

Description

Inject into flank (epaxial muscle) or posterior end of dorsal fin <u>Practical Considerations</u>

- Most favourable parenteral administration
- Insert needle underneath the scale to avoid damage
- Some drugs can cause skin discolouration and/or muscle necrosis

IP/ICe

Description

Inject at the ventral midline between vent and pelvic fins

Practical Considerations

- Fasting for 24 hours prior injections is recommended
- Peritonitis risk

IV

Description

Delivers drugs systemically via the caudal vein or caudal artery

Practical Considerations

- Sedation is required
- Least recommended

EXOTICS



3. ORAL ADMINISTRATION

<u>Unit Dose:</u> mg/kg body weight or % in feed

Advantages

- Easily administered by clients
- More economical method than water-borne administration

Disadvantages

- Palatability must be taken into consideration
- Regurgitation is possible after gavage or tube feeding

In-feeding Medication

Description

Feed ad libtum

Practical Considerations

- Least stressful method
- Not applicable for anorectic fish
- Uncontrollable amounts of actual intake
- Leaching of drug into the water

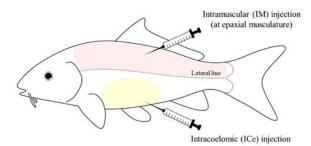
Gavage or Tube-feeding

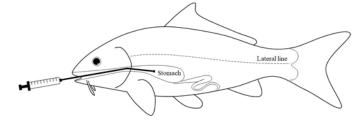
Description

A suspension of known amounts is administered directly into stomach

Practical Considerations

- Stressful procedure, light sedation recommended
- Observation of regurgitation
- Difficult in some species with pharyngeal teeth
- Risk of gills damage and/or oesophageal perforation





EYE

INTEGUMENT

AURAL



ANTIMICROBIAL USE IN SMALL MAMMALS

GENERAL PRINCIPLES

There are a limited number of antimicrobials approved for use in small mammals. Pharmacokinetic studies in small mammals are lacking, hence many dosage regimens used in these species are based on empirical data, observations and experience. When selecting an antimicrobial agent for use in small mammals, it is important to consider the patient's clinical status, the disease and organ system involved, the known or suspected pathogen and the antimicrobial most likely to be effective against the pathogen and potential adverse effects. Oral suspensions are normally easiest to administer to small mammals, and due to small patient size, some medications may need to be diluted at acceptable dosages to small patients. Rabbits and rodents metabolise many drugs rapidly, hence dosages may be higher or more frequently administered than that for other species. There are also species-specific sensitivities to certain antimicrobials that need to be taken into consideration.

It is noteworthy that one of the most common antimicrobial products used in small mammals is fluoroquinolones, which is listed as a Highest Priority Critical Antimicrobial by the World Health Organisation. Veterinarians have a responsibility to ensure that antimicrobials are use responsibly to minimise development of antimicrobial resistance in animals and minimise transmission of resistance to humans. Not all diseases are caused by pathogens susceptible to antimicrobials and many have underlying husbandry, nutrition and environmental factors that predispose to disease, and these need to be properly investigated prior to starting antimicrobial therapy. For example, environmental stressors can result in altered immune function, increasing predisposition to developing disease.

Lastly, the ability of the owner to comply with the selected treatment regimen needs to be considered. Rabbits and rodents may not be tolerant of handling and administration of antimicrobials need to be in a manner than allows delivery of the drug without overly stressing the patient and its owner. Mixing the drugs with palatable liquid or food may help encourage consumption.



ANTIMICROBIAL USE IN SMALL MAMMALS

DECISION-MAKING ON ANTIBIOTIC USE

As with other companion animal species, it is important to first establish if there is a microbial infection present. A detailed history and clinical examination are helpful in identifying underlying risk factors for infection, such as husbandry or nutritional factors resulting in predisposition to opportunistic bacterial or fungal infections. A diagnosis is achieved based on history, clinical presentation, in combination with culture and sensitivity testing.

Ideally, C&S testing should be performed prior to starting antimicrobial therapy to determine the susceptibility of the organism. However, most small mammals will not show obvious clinical signs of disease until their condition is advanced, hence in cases where the disease is acute or severe and infection is suspected, and treatment must begin before test results are known, empirical treatments can be started based on the suspected agent and the condition of the host. Samples for culture and sensitivity should be collected prior to starting antimicrobial therapy.

In small mammals, there are speciesspecific differences in their sensitivity to these antimicrobials, and some antimicrobials are tolerated better via parenteral routes than oral routes. Appropriate supportive care, such as fluid therapy, nutritional support, thermal support and analgesia as well as correcting underlying husbandry or environmental problems, are important adjuncts to antimicrobial therapy.



ANTIMICROBIAL USE IN SMALL MAMMALS

COMMONLY USED ANTIMICROBIALS IN SMALL MAMMAL SPECIES

Veterinarians treating small mammal companion species should consult the most up-to-date drug formularies and literature for species-specific drug doses. The following section lists a few unique considerations of common species, and commonly used antimicrobial dosages, and available drug formularies are listed in the references for this chapter.

RABBITS

The special digestive physiology of the rabbit requiring a delicate flora of bacteria in their gut for degradation of food makes them extremely sensitive to various kinds of antibiotics. Caution when using topical formulations as ingestion may occur. Owners should be advised to look out for signs of profuse, watery diarrhoea after medications have been administered. This is a medical emergency that needs immediate attention.

Veterinarians should make their clinical diagnosis and determine the presumptive or confirmed cause of bacterial infectious before administering the antibiotics. The table below presents common antibiotics used in rabbits.

Drug Name	Dose	Remarks
Antibiotics that are s	afe to use – least likely to cau	se gastrointestinal disease
Chloramphenicol	30-50 mg/kg SC, IM, IV q8-24h	
Enrofloxacin	5mg/kg PO, SC, IM, IV q12-24h	Dilute before giving parenterally
Gentamicin	5-8 mg/kg SC, IM, IV q8-24h	Decreased toxicity when given once daily; dilute in saline for IV use in slow bolus



Drug Name	Dose	Remarks			
Antibiotics that are safe	Antibiotics that are safe to use – least likely to cause gastrointestinal disease				
Metronidazole	5 mg/kg IV q12h 4omg/kg PO q24h X 3 days	Administer slowly			
Trimethoprim/sulfa	15 mg/kg PO q12h 30 mg/kg IM q12h	May cause tissue necrosis when given SC			
Antibiotics that should be used with caution – intermediate ability to incite gastrointestinal disease					
Procaine Penicillin	40000 U/kg IM q24h x 5-7 days	Effective against rabbit syphilis, do not give orally			
Ceftazidime	100 mg/kg IM q12h	Do not give orally			
Ceftriaxone	40 mg/kg IM q12h X 2-3 days	Do not give orally			
Tetracycline	50-100 mg/kg PO q8-12h				
Oxytetracycline	25 mg/kg SC q24h	Oral use ineffective; inactivated in gut			
Doxycycline	4 mg/kg PO q24h				



ANTIMICROBIAL USE IN SMALL MAMMALS

Drug Name	Dose	Remarks
	Other antimicrobial agents	5
	5-10 mg/kg PO q24h x 30 days	Dermatophytosis
Itraconazole	20-40 mg/kg PO q24h	Aspergillus pneumonia
Ketoconazole	10-40 mg/kg PO q24h x 14 days	Dermatophytosis

RODENTS

Due to the size of rodents, the dispensation of medications for treatment of various bacterial infections in rodents can be challenging. Some drugs can be obtained from a compounding pharmacy, which is an alternative to clinic dilution of various drugs.

Some rodents like the guinea pigs have sensitive gut flora and the use of wrong antimicrobials can cause enterocolitis, diarrhoea and eventually death.

Veterinarians should make their clinical diagnosis and determine the presumptive or confirmed cause of bacterial infectious before administering the antibiotics. The table below presents common antibiotics used in rodents.



ANTIMICROBIAL USE IN SMALL MAMMALS

Drug Name	Dose	Remarks
Amoxicillin/Clavulanic Acid	20 mg/kg PO q12h	Mice and gerbils only
Ciprofloxacin	10 mg/kg PO q12h	Avoid use in younger animals
Chloramphenicol	30-50 mg/kg PO q8-12h	
Clindamycin	7.5 mg/kg SC q12h	Can cause diarrhoea; use in mice and gerbils only
Doxycycline	5 mg/kg PO 12h	Do not use in young and pregnant animals
Enrofloxacin	5-10 mg/kg PO q12h 100 mg/L drinking water	
Itraconazole	2.5-10 mg/kg PO q24h	Dermatophytosis; use terbinafine in guinea pigs
Ketoconazole	10-40 mg/kg PO q24h x 14 days	Mycoses
Metronidazole	10-20 mg/kg PO q12h	Use with caution in chinchillas; may result in reduce appetite
Oxytetracycline	5 mg/kg IM q12h	
Procaine Penicillin	22000 IU/kg SC, IM q24h	Do not give orally; do not use in mice
Terbinafine	20 mg/kg PO q24h	Dermatophytosis in guinea pigs
Trimethoprim Sulfas	30 mg/kg SC q24h	
	15 mg/kg PO q12h	



RODENTS: TOXIC DRUGS

The following lists antimicrobials which are toxic to rodents and should be avoided.

Chinchillas

Penicillin, bacitracin, cephalosporins, clindamycin, erythromycin, lincomycin

Guinea Pigs

Penicillin, cefazolin, clindamycin, erythromycin, lincomycin, streptomycin, bacitracin, chlortetracycline, oxytetracycline, tylosin

Hamsters

Penicillin, bacitracin, cephalosporins, clindamycin, erythromycin, lincomycin, vancomycin, streptomycin, tylosin

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ANTIMICROBIAL USE IN COMPANION BIRDS

GENERAL PRINCIPLES

Selection of appropriate antimicrobials for companion birds should follow the same guidelines as for dogs and cats, taking into consideration pathogen susceptibility, severity of illness, pharmacokinetics and pharmacodynamics of the drugs, and route of administration. The ability of the owner to comply with the selected treatment regimen also needs to be considered. Use of antimicrobials in a responsible manner maximises therapeutic success and minimises the development of antimicrobial resistance.

There is a paucity of pharmacokinetic, pharmacodynamic and safety data in avian species and many dosage regimens are based on empirical evidence or extrapolated from other species, hence veterinarians seeing avian species should understand drug pharmacology when choosing the optimal drug and dosage regimen to meet the patient's individual needs. Not all diseases are caused by pathogens susceptible to antimicrobials and there are often underlying husbandry, nutrition and environmental factors that predispose to disease which need to be thoroughly investigated prior to starting antimicrobial therapy.

Companion birds may display non-specific signs of illness, and it is imperative to ensure that antimicrobial treatment is in fact necessary. For example, antimicrobials are indicated if a potential pathogen is present in large numbers and associated with clinical signs, or if laboratory test results indicate inflammation or infection. Appropriate supportive care, such as fluid therapy, nutritional support, thermal support, and analgesia as well as correcting underlying husbandry or environmental problems, are important adjuncts to antimicrobial therapy.



ANTIMICROBIAL USE IN COMPANION BIRDS

SELECTION OF ANTIMICROBIALS FOR EMPIRICAL TREATMENT

A detailed history and clinical examination are helpful in identifying underlying risk factors for infection, such as nutritional deficiencies resulting in predisposition to opportunistic bacterial or fungal infections. A diagnosis is achieved based on history, clinical presentation, in combination with culture and sensitivity. Evaluation of a blood smear is immediate and gives immediate results to guide the diagnosis and should be performed in all sick birds.

Ideally, culture and susceptibility testing should be performed prior to starting antimicrobial therapy to determine the susceptibility of the organism. However, in cases where the disease is acute or severe and infection is suspected, and treatment must begin before test results are known, empirical treatments can be started based on the suspected agent and the condition of the host. Samples for culture and sensitivity should be collected prior to starting antimicrobial therapy.

Escherichia coli, Klebsiella spp., and Pseudomonas aeruginosa are often identified as aetiologic agents responsible for respiratory, gastrointestinal and multiorgan infections, although other Gram-negative bacteria such as Salmonella spp., *Pasteurella* spp. and *Bordetella* spp. also occur. Staphylococcus aureus is the most common Gram-positive bacterial pathogen and is most frequently isolated from skin, upper respiratory and gastrointestinal infections. Anaerobes (such as Clostridia spp.) can cause severe intestinal infections. Mycobacterium and Chlamydia are common intracellular bacterial pathogens. For stable birds with a suspected bacterial infection, trimethoprim-sulfonamide or amoxicillinclavulanic acid are appropriate first line choices.



ANTIMICROBIAL USE IN COMPANION BIRDS

ROUTE AND FREQUENCY OF **ADMINISTRATION**

Capture and restraint of companion birds for the administration of oral or parenteral medications can be stressful and difficult for both the bird and the owner. Selecting liquid formulations with a low volume dose and less frequent dosing regimen is usually preferred. Compliance can be increased by adding flavouring to the medication or adding it to food or water, however the latter may achieve lower drug plasma concentrations than desired. Administration of antimicrobials via food or water should be reserved for when the susceptibility of the target organism is known, or where efficacy trials have demonstrated that effective drug concentrations can be achieved.

COMMONLY USED ANTIMICROBIAL IN AVIAN **SPECIES**

Veterinarians treating avian species should consult the most up-to-date drug formularies and literature for speciesspecific drug doses. The following section lists some of the commonly used antimicrobials and dosages, and available drug formularies are listed in the references for this chapter.



ANTIMICROBIAL USE IN COMPANION BIRDS

Drug Name	Dose	Remarks
Amoxicillin/Clavulanic Acid	125 mg/kg PO q6-8h	Avoid in ratites
Ceftazidime	50-100 mg/kg IM, IV q4-8h	For aerobic Gram-negative (including <i>Pseudomonas</i>) and Gram-positive bacteria, a few anaerobic bacteria
Ceftiofur	20 mg/kg IM q72-96h	Extended release
Chloramphenicol	35-50 mg/kg PO, IM, IV q8h	
Doxycycline	25-50 mg/kg PO q12-24h	
Enrofloxacin	15 mg/kg PO, IM, SC q12h	Dilute before giving parentally
Gentamycin	5 mg/kg q12h	Maintain hydration
Metronidazole	10-30 mg/kg PO q12h	
Trimethoprim/ sulfamethoxazole	20 mg/kg PO, SC, IM q12h	

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EYE

INTEGUMENT

AURAL

ABDOMINAL THORACIC

MUSCULOSKELETAL



5. LOCAL/GENERAL C&S TEST RECCOMENDATIONS AND RESULTS INTERPRETATION

Where the decision to use antibiotics as part of the treatment regime has been made, veterinarians should abide by guidelines as described in previous chapters to guide the choice and length of antibiotic treatment. Often, veterinarians and owners depend on clinical improvement or disease resolution as feedback on the success of the antibiotic treatment.

Culture and sensitivity testing is a particularly useful tool for veterinarians, providing clarity on the bacteria species that is causing the infection and the spectrum of antibiotics that the bacteria is susceptible to. The information provides veterinarians with more confidence in recommending more targeted treatment strategies and allows for de-escalation (switching to the use of narrow-spectrum antibiotics) where possible [Annex II].

GUIDELINES TO USE OF C&S TESTING:

 Culture appropriately: A sample for culture should be collected before starting antibacterial therapy, where possible. Collect samples aseptically (wear gloves). Sterile sampling equipment (e.g., swabs, containers) should be used. Samples collected should be sent for testing as soon as possible. If there is a delay of delivery to the laboratory for more than 24hours, store the sample at 2 to 8°C (normal refrigerator temperature) to avoid sample degradation (Exceptions apply for anaerobic culture samples). Do not freeze the samples.

2. Scenarios where performing a culture is particularly recommended when:

- Prolonged (>1 week) treatment courses are anticipated
- Resistance is likely (e.g., hospitalacquired infections)
- Dealing with life-threatening infections
- 3. If first-line treatment fails, avoid using alternative antibacterials without culture and sensitivity results.
- 4. Monitor culture results to inform clinic policy: Culture results across patients should be monitored to inform whether certain practices can be changed (e.g., improving aseptic techniques to prevent postoperative infection), to perform audits on antibiotic usage, or to customise the clinic's first-line antibiotic selection policy.

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5. LOCAL/GENERAL C&S TEST RECCOMENDATIONS AND RESULTS INTERPRETATION

TYPES OF ANTIBIOTIC SENSITIVTY TESTING METHODS

The most common AST methods that veterinarians are familiar with are the Disc Diffusion method, the Broth dilution method and the Agar dilution method. Commercial antibiotic gradient strips (aka Epsilometer test, E-test) are also available, though not widely used locally. For commercial laboratories, larger automated AST systems are now available to speed up sample processing times.

DISC DIFFUSION METHOD

Due to its convenience, cost and availability, disc diffusion methods are usually the choice of in-house AST carried out in a clinic setting. Commercially prepared disks impregnated with standard concentrations of antibiotic are placed on a growth medium with the isolate of interest plated. The antibiotics diffuses outward from the discs, creating a gradient of antibiotic concentration. The agar is incubated overnight before it is interpreted.

The zone of inhibition refers to the area of no growth around an antibiotic disc and its width is measured and compared to a reference standard which has interpretations on whether the measurement corresponds to the isolate being susceptible, intermediate or resistant to the antibiotics. Note on interpretation: The presence of a zone of inhibition does not automatically equate to susceptibility to the antibiotic.

Advantages: Low cost, ease in modifying antimicrobial discs choices, useful for screening against large number of isolates

Disadvantages: Manual measurement can be time-consuming, although automated zone-reading devices are available._

BROTH AND AGAR DILUTION METHOD

The aim of both the Broth and Agar dilution methods is to determine the lowest concentration of the assayed antimicrobial that inhibits the visible growth of the bacterium being tested.

The isolate is introduced into concentrations of antimicrobial that are serially diluted in either a broth or agar medium.

For both of these broth dilution methods, the lowest concentration at which the isolate is completely inhibited (as evidenced by the absence of visible bacterial growth) is recorded as the minimal inhibitory concentration or MIC.

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5. LOCAL/GENERAL C&S TEST RECCOMENDATIONS AND RESULTS INTERPRETATION

Note on interpretation: The 'true' Minimum Inhibitory Concentration (MIC) is a point between the lowest test concentration that inhibits the growth of the bacterium and the next lower test concentration.

Therefore, MIC determinations performed using a dilution series may be considered to have an inherent variation of one dilution.

Advantages:

- More reproducible and quantitative than disc diffusion method.
- Agar dilution methods can test multiple bacteria, except bacteria that swarm, on the same set of agar plates at the same time.

Disadvantages:

- MIC data are not usually exact due to the antibiotics dilutions factors used. Require a laboratory set-up to maintain reagents and antibiotic dilutions, with quality control process in place.
- More laborious and costly than disc diffusion methods. Commercial microdilution antimicrobial test panels may not offer flexibility in terms of antimicrobial choice.

COMMERCIAL ANTIBIOTIC GRADIENT STRIPS (AKA EPSILOMETER TEST, E-TEST)

These commercial test strips are impregnated with antibiotics of a gradually decreasing concentration. The test strips are placed on an agar plate inoculated with the bacterium. Following incubation, the zone of growth inhibition is interpreted. The MIC value is read from where the edge of the inhibition intercepts with the test strip.

Advantages:

• Convenient

Disadvantages:

 Can be expensive and studies have shown some discrepancies with agar dilution results.

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5. LOCAL/GENERAL C&S TEST RECCOMENDATIONS AND RESULTS INTERPRETATION

AUTOMATED AST SYSTEMS

Automated AST testing are usually found in commercial laboratories due to the high start-up and maintenance cost. These machines can process large volumes of samples in a short period of time (often in hours) and can conduct automated inoculation, reading and interpretation.

Some examples of these automated AST system include Thermo Scientific[™] Sensititre[™] ID/AST System and the VITEK system from bioMérieux.

Advantages:

• High throughput and fast. Less prone to human error.

Disadvantages:

• High start-up and maintenance cost.

LOCAL CULTURE AND SENSITIVTY TESTING SERVICES

Local laboratory services are available for the conduct of culture and sensitivity testing. Veterinarians may contact the individual laboratories on sampling and delivery instructions.

IN-HOUSE CULTURE AND SENSITIVTY TESTING DEVICES

In-house bacteria identification diagnostic test devices are emerging in the market to provide veterinarians with timely, point of care results to inform their antibiotic selection choices. Such tests are useful due to the quick turn-aroundtime and lower risks of sample degradation due to inadequate storage and transport conditions.

Products listed below are not representative of endorsement by the working group. Test validity and accuracy varies among products. Veterinarians are advised to study the product prior to using them

1. RapidBac™Vet

A lateral flow immunoassay for the detection of Gram-positive and Gram-negative bacteria in urine. The test utilizes a cocktail of monoclonal antibodies targeting a panel of bacterial surface proteins. Turn-around-time is about 20 minutes.

LexaGene's MiQLab™ Bacterial and AMR Rapid Molecular Testing System

The MiQLab system uses real-time qPCR to simultaneously detect a panel of common bacteria associated with infections in cats and dogs, including 7 pathogens and 13 antimicrobial resistance markers of therapeutic and public health significance. Turn-around time is about 1 hour.

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5. LOCAL/GENERAL C&S TEST RECCOMENDATIONS AND RESULTS INTERPRETATION

<u>Test Panel</u>

Bacteria	AMR Markers
E. coli Enterobacter Enterococcus Klebsiella	CMY (ESBL) CTX-M-1 (ESBL) CTX-M-9 (ESBL) KPC (carbapenemase) IMP (carbapenemase) mecA (methicillin resistance) NDM (carbapenemase)
Proteus Staphylococcus Streptococcus	OXA-48 (carbapenemase) SHV (ESBL) TEM (ESBL) vanA (vancomycin resistance) vanB (vancomycin resistance) VIM (carbapenemase)

Sample Types

Fluid: Urine, Cerebrospinal fluid, Synovial fluid, Exudates, Lavages

Swabs: Wound/abscess, Skin, Ear, Respiratory tract, Rectum, Body cavities

3. U-Treat

U-treat technology uses the principles of ATP bioluminescence to detect bacterial UTIs within 5 minutes. If a urine sample tests positive for bacteria, a further test can be run which identifies the most effective antibiotic for treatment within a further 30 minutes. Does not provide identification of bacteria. ORAL

6. LOCAL INFORMATION ON AMR, AMU, AND KAPS

Locally, a retrospective analysis of diagnostic reports from 2014 to 20161 revealed that almost half of the bacteria isolated from unwell companion animals were multi-drug resistant. Resistance to broad-spectrum antibiotics were also observed among individual bacterial species - 50% were methicillin-resistant Staphylococcus aureus, 40% were fluoroquinolone-resistant E. coli and 7% were carbapenem-resistant Klebsiella pneumonia.

A qualitative study suggested gaps in antibiotic stewardship in animal health. In this study, animal health providers indicated pressure from pharmaceutical companies marketing the use of antibiotics and the lack of strict regulations on the import of new broad-spectrum antibiotics for animal use. However, respondents from veterinary clinics were limited.

Descriptive analysis of diagnostic reports of antimicrobial resistance in urine, ear and skin samples of dogs and cats in Singapore was conducted. Analysis of resistance profiles was made for urinary, ear and skin samples collected from veterinary clinics and sent to a private laboratory to be cultured and tested for antibiotic susceptibility from May to August 2021. E. Coli isolates from urinary samples showed significant resistance to various antibiotic classes including penicillin (up to 48.8%), and multidrug resistance (up to 24.3%) [Annex V]. The *Pseudomonas* isolates from ear samples showed variable resistance profiles. A high proportion of Staphylococcus isolates were methicillin-resistant (up to 33.6%) and multidrugresistant (up to 47.7%) [Annex IV].

These findings provide a snapshot of prevalence of antimicrobial resistance in companion animals in Singapore, and the importance of antimicrobial susceptibility testing to support clinical treatments of infections. Singapore is combatting AMR on various fronts including that in the companion animal sector, and prudent use guidelines are one step toward minimising the risks associated with AMR development and spread in companion animals.

Hartantyo SHP, Cau ML, Fillon L, et al. Sick pets as potential reservoirs of antibiotic-resistant bacteria in Singapore. Antimicrobial Resistance and Infection Control 2018; 7: 106.

Singh SR, Chua AQ, Tan SK, Tam CC, Hsu LY, Legido-Quigley H. Combating antimicrobial resistance in Singapore: a qualitative study exploring the policy context, challenges, facilitators, and proposed strategies. Antibiotics 2019; 8: 201.

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7. PUBLIC HEALTH INFORMATION, INCLUDING MANAGEMENT OF PATIENTS WITH MULTIDRUG RESISTANT INFECTIONS

PUBLIC HEALTH INFORMATION

Transmission of resistant bacteria or their resistance genes can occur between humans and animals via direct or indirect contact, through the following listed transmission routes. Transmission routes to be considered when developing standard operating procedures related to the prevention of hospital-acquired infections include:

- Direct contact transmission (physical transfer and entry of microorganisms though mucous membranes, open wounds or abraded skin; direct inoculation from bites or scratches); this poses the highest risk of pathogen transmission to patients and personnel.
- Fomite transmission (contamination of inanimate objects)
- Aerosol (airborne) transmission (aerosolisation of pathogens from infected individual)
- Oral (ingestion) transmission (ingestion of contaminated food/water or by licking/chewing contaminated objects or surfaces.
- Vector-Borne transmission (indirect transmission via an infected vector)

Despite the limited number of surveillance programmes dedicated to AMR prevalence in companion animals, several studies describe companion animals as potential reservoirs of antimicrobial resistance. This poses a significant concern relating to the spread of resistance mechanisms in humans due to the close proximity and shared environment in which companion animals and humans reside.

Recent studies have demonstrated the potential for horizontal transfer of resistance mechanisms for gram negative bacterial species that fall within the *Enterobacteriaceae* family in clinically healthy animals. This suggests that nonpathogenic gram-negative bacteria may play a role as a reservoir coding for resistance genes. This highlights the need for a prudent approach when dealing with clinically healthy animals and the importance of preventative measures such as barrier nursing, good animal husbandry and appropriate sanitisation measures- as well as client education to limit the potential for spread.

Multidrug resistant bacteria have and will continue to have debilitating effects on human, animal and environmental health and thus significant efforts should be taken to minimise the propagation and spread of resistance. This can be done with the prudent and judicious use of currently available antimicrobials, as well as by practicing good preventative medicine, barrier nursing and animal husbandry.

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7. PUBLIC HEALTH INFORMATION, INCLUDING MANAGEMENT OF PATIENTS WITH MULTIDRUG RESISTANT INFECTIONS

MANAGEMENT AND PRECAUTIONS

Every veterinary practice should develop a comprehensive Infection Control Plan to detect, prevent and control MDR infections.

- Minimise prescription of unnecessary antibiotics,
- General control precautions for staff, patient, and their owners.

The risk of transmission to and from animals may be affected by factors such as the health and hygiene of the animal, behavior of the animal, environment, and amount of contact with patients.

Risk can be reduced by simple preventive measures, such as hand washing after contact with the animal and preventing the animal from contact with the nonintact skin of the patient (e.g., surgical wounds and tube entry sites).

Colonisation with MDR organisms is frequently undetected and medical records of patient and also owners should mention identified MRD organism. Furthermore, veterinarians may not be aware of the immune status of a pet owner.

1. <u>Standard precautions</u>

- Hand Hygiene: Basic of infection control for centuries. Gloves are not a substitute for hand hygiene. Multiple products are now available which include waterless, alcohol-based antiseptic agents. Soap and water should be used when hands are visibly soiled.
- Enhanced Barrier Precautions:
- PPE: Gown / Mask / Eye and face protection (goggles, face shield) / Gloves
- Appropriate control measures must be used especially during transport / exposure to blood and body fluids.
- Education: Health Care Workers and Owners. It should be emphasized that hands should be washed after contact with secretions or excretions. Personal items contact should be minimized.

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7. PUBLIC HEALTH INFORMATION, INCLUDING MANAGEMENT **OF PATIENTS WITH MULTIDRUG RESISTANT INFECTIONS**

Contact precautions 2.

- The necessary duration of contact precautions for patients treated for infection with an MDRO, but who may continue to be colonised with the organism at one or more body sites, remains unfortunately an unresolved issue.
- Close interactions with pets (e.g., sleeping in beds with owners, face licking) should be avoid. Discourage licking the faces of young children and immunocompromised patients.
- Promptly wash bites and scratches inflicted by animals. Do not allow pets to lick open wounds, cuts or medical devices (e.g., intravascular catheters).

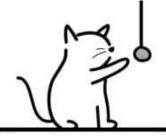
Environmental precautions 3.

The role of environmental reservoirs, such as surfaces and medical equipment, is now well known.

Keep cats indoors; change litter boxes daily; wear vinyl or household cleaning gloves during cleaning and wash hands immediately after

- Keep litter boxes away from kitchens or other areas where food preparation and eating occur
- Keep dogs confined when possible; walk on a leash to prevent hunting, coprophagia and garbage eating
- Feed only canned or dry commercial food or well-cooked home-prepared food; egg or meat products and treats should be cooked, and dairy-based products should be pasteurised.
- Routinely clean and disinfect animal contact surfaces (e.g., cages, feeding areas) and immediately after contact with high-risk species or raw animal-based food items; freshly mixed diluted household bleach (1 part bleach to 32 parts water) or similar household disinfectants (e.g., quaternary ammonium compounds) are adequate.
- Regularly (e.g., weekly) launder pet bedding and other items. Washing and dryer (>160F) is advised, and not allowed to air dry.

United States Environmental Protection Agency (2021) Selected EPA-registered disinfectants. Accessed:2021 <www.epa.gov/pesticide-registration/selected-epa-registered-disinfectants>



8. ANTIMICROBIAL STEWARDSHIP PROGRAMMES

INTRODUCTION

Antimicrobial stewardship (AS) refers to the organisation-wide effort to promote the use of antimicrobials to combat antimicrobial resistance with a conscientious and systematic approach while safeguarding animal, public, and environmental health. Antimicrobials are a critical tool in the veterinary practitioner's inventory for preventing and treating infections. The veterinary profession should put into practice dedicated and focused efforts to contribute to preserving the efficacy of these life-saving medications, while ensuring the best clinical outcome for patients.

Veterinarians can implement measures in their practice to measure and optimise the use of antimicrobials in the form of antimicrobial stewardship programs (ASPs), which can be adjusted to take into account factors such as available resources and size of the practice and can also be stepped up over time. The following recommendations are intended to be a guide for companion animal veterinary practitioners in setting up and implementing ASPs within their unique practice setting.

Outline of approach to setting up an ASP:

- 1. Form an ASP team
- 2. Identify priority areas and define interventions to achieve goals

3. Educate and brief the rest of the staff on implementation

4. Assess effectiveness of ASP and update interventions

1. FORM AN ASP TEAM

The core members of the ASP team of a veterinary practice should consist of at least one person from each of the following roles: veterinarian, veterinary technician/nurse, and practice manager. Involve personnel with special interest in topics related to AMR and AS, such as infectious disease and pharmacology. Allocate adequate resources to support the ASP team in their role, such as through further training. Ensure that roles and responsibilities are clearly defined within an ASP.

8. ANTIMICROBIAL STEWARDSHIP PROGRAMMES

The ASP team will decide on the initial AS priority areas, design protocols and guidelines to address those priorities, and establish a plan for educating all staff on AMR and AS interventions. The ASP team should meet regularly to assess priority areas, evaluate the effectiveness of the ASP and update implementation protocols.

IDENTIFY PRIORITY AREAS AND DEFINE INTERVENTIONS TO ACHIEVE GOALS

The priority areas selected will vary depending on the ASP team and the unique factors specific to the practice. Interventions should be backed by scientific evidence or existing recommendations and guidelines where possible. The goals that are set by the team should be clearly defined and reasonably achievable. Some priority areas and interventions that can be considered include:

- a. Evaluate antimicrobial use practices
- Develop an inventory of antimicrobials in the practice
- Monitor and evaluate antimicrobial use (AMU) practices and trends in the practice
- Explore factors that influence AMU and when they are not benchmarked against existing prudent antimicrobial use guidelines or recommendations

b. Encourage judicious use of antimicrobials

- Adopt existing prudent antimicrobial use guidelines or recommendations
- Identify opportunities for developing additional prescribing guidance
- Categorize antimicrobials and develop practice policies for their use (e.g., available for first-line use, use with caution, use as last resort, avoid all use)
- Target reduction of the use of certain specified antimicrobials prescribed for empiric treatment of patients
- Promote and develop protocols or workflows for the utilisation of diagnostic testing as part of medical decision-making, e.g., in-house cytology, culture and sensitivity testing, imaging
- Establish avenues to provide feedback and guidance to veterinarians on AMU practices in a supportive environment

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8. ANTIMICROBIAL STEWARDSHIP PROGRAMMES

c. Educate and advocate on AMR and AS

- Develop protocol for training new staff on AMR and AS practice policies
- Encourage and track staff training and continuing education on AMR and AS
- Educate clients with consistent messages on antimicrobial use and importance of preventive healthcare (e.g. vaccination)
- Use existing client-communication tools
- Provide support for clients on administration of medicines and antimicrobials (e.g., demonstration for clients during patient discharge, providing tips and resources on successful patient restraint and administration of medications, encouraging clients to have an open discussion on potential difficulties they may face in complying with administration or dosing of medications, reminding clients to raise any issues or concerns early instead of waiting till next visit)

3. EDUCATE AND BRIEF THE REST OF THE STAFF ON IMPLEMENTATION

Once an ASP intervention has been approved by the ASP team, it is vital to educate and brief the rest of the staff. Raise their awareness on the severity of the threat of AMR and the consequent importance of AS, explaining the crucial role each staff plays, and clearly explaining expectations and their contributions, are necessary to ensure the effective implementation of the ASP. This can be done in several ways:

- Introduce the idea to staff on the intervention using multiple approaches (e.g. ward round, briefings, clinic handouts, email bulletins, posters)
- Regularly disseminate and communicate information about AMU practices in the veterinary clinic
- Encourage peer review and sharing of learning and experiences on prescribing practices within the veterinary clinics

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4. ASSESS AND MONITOR EFFECTIVENESS OF ASP AND UPDATE INTERVENTIONS

The ASP team should meet regularly to assess and evaluate the progress of the ASP. When determining the priority areas and goals of the ASP, the ASP team should also have identified specific indicators that can be used to effectively evaluate the progress and success of the ASP. These indicators should be clear and measurable outputs that can be tracked easily over time and can accurately inform of the effectiveness of the ASP. In reviewing the effectiveness of the ASP, the ASP team will be able to identify opportunities for improvement of the ASP, for example adding new priority areas and coming up with new and more effective interventions. These changes should be based on valid reasons and have a scientific basis and should be adequately documented for recordkeeping purposes.

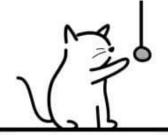
Basic	Intermediate	Advanced	Checklist
1. F	orm an ASP team		
	practice members to sponsible to lead the	form the ASP team and appoint an individual e team.	
	roles:	of at least one person from each of the following	
	Veterinarian, veter	inary technician/nurse and practice manager.	
		Make sure resources available and encourage the ASP team to develop expertise in AMR and AS and fulfilling their roles, such as through further training.	
Establish clear roles and responsibilities for each member of the ASP team.			
Develop clear Terms of Reference for the ASP team, to guide actions and define each of their roles.			
	Develop ASP team commitment statement or policy on practice stewardship plans.		
		Incorporate the ASP team responsibilities in the respective officer's job description to acknowledge their contributions and provide accountability.	
		Recognise the efforts of the ASP team and clinic's commitment to ASP (e.g., publicly display ASP team members, stating their roles and the clinic's commitment to ASP).	



8. ANTIMICROBIAL STEWARDSHIP PROGRAMMES

Basic	Intermediate	Advanced	Checklist	
2. Identify	priority areas ar	nd define interventions to achieve goals		
Identify cl	inic ASP prioritie	es, gaps, barriers to appropriate antimicrobial use, and		
set priorities for intervention in any of the following areas:				
-	te antimicrobial			
		ntimicrobial agents in the practice of all formulations		
	•	al, ocular and aural agents.		
	z	microbial use (AMU) practices and trends in the		
practice o				
	Identify condit	ions that are commonly treated with antimicrobials on		
		stewardship efforts.		
	Assess outcom	es of antimicrobial use in patients over time.		
		Explore factors that influence AMU and identify		
		barriers for when they are not benchmarked against		
		existing prudent antimicrobial use guidelines or		
		recommendations.		
B) Encour	age judicious us	e of antimicrobials		
Adopt exis	sting prudent AN	IU guidelines or recommendations.		
Identify op	oportunities for a	leveloping additional prescribing guidance for the		
practice.				
	Categorise ant	imicrobials and develop practice policies for their use		
		for first-line use, use with caution, use as last resort,		
	avoid all use).			
	Promote and d	evelop workflows for the utilisation of diagnostic		
	testing as part of medical decision-making, e.g., in-house cytology,			
	culture and ser	nsitivity testing, imaging.		
		Target reduction of the use of certain specified		
		antimicrobials prescribed for empiric treatment of		
		patients.		
		Establish avenues to provide feedback and guidance		
		to veterinarians on AMU practices in a supportive		
		environment.		
	e and advocate			
		ng new staff on AMR and AS practice policies.		
-		training and continuing education on AMR and AS,		
including	preventative hea			
		te clients with consistent messages on AMU and		
		preventive healthcare (e.g., vaccination, husbandry,		
	nutrition)			
		Provide client-communication tools to help clients		
		evaluate administration and storage of		
		antimicrobials, and work with clients to address gaps.		

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8. ANTIMICROBIAL STEWARDSHIP PROGRAMMES

Basic	Intermediate	Advanced	Checklist
		est of the staff on implementation	
		form to effectively inform all practice members of ASP	
interventio	•		
		larly engages all practice members on stewardship	
	5	practices and ASP intervention plans.	
		ASP team encourages peer review, analysing and	
		sharing of learning and experiences on prescribing	
		practices within the veterinary clinics.	
4. Assess a	4. Assess and monitor effectiveness of ASP and update interventions		
ASP meets regularly to assess and evaluate the progress of the ASP			
interventions.			
	ASP team deve	elops an ASP workplan to track and record progress of	
	ASP implemen	itation plans.	
		ASP team identifies specific indicators that can be	
		used to effectively evaluate the outcome of the ASP	
		interventions. These indicators should be clear and	
		measurable outputs that can be tracked easily over	
		time and can accurately inform of the effectiveness of	
		the ASP.	

Centers for Disease Control and Prevention. Core elements of antibiotic stewardship. Accessed 18 Feb 2021. <https://www.cdc.gov/antibiotic-use/core-elements/>

University of Minnesota. Handbook of Antimicrobial Stewardship in Companion Animal Veterinary Settings. May 2020. Accessed 20 Feb 2021. NICE (2021). NICE Guidance on Antimicrobial stewardship: systems and processes for effective antimicrobial

medicine use. https://nice.org.uk/guidance/NG15/chapter/1-Recommendations#all-antimicrobials

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9. CLIENT EDUCATION TOOLKIT

A VETERINARIAN'S ROLE IN IMPROVING CLIENT COMMUNICATION

One of the most common factors resulting in poor therapeutic outcome is a lack of client compliance. Veterinary practitioners have a key role to play in increasing awareness of AMR among animal owners to encourage compliance and curb further emergence and spread of drug-resistant infections. This chapter is intended to provide veterinary practitioners recommendations and resources on improving client compliance.

FACTORS AFFECTING CLIENT COMPLIANCE

The first step is to recognise and acknowledge the various challenges clients might face in administering medications to animals. In many cases, this lack of compliance may arise from multiple factors, such as the method of drug administration, patient characteristics, client lifestyle, lack of client understanding on the rationale for treatment, etc.

For example, owners may give medication at inappropriate doses and durations, leading to underdosing or dosing at suboptimum levels. Overdosing is also not uncommon as owners may attempt to make up for missed doses.

Key recommendations for veterinary professionals on improving client compliance

To boost understanding and awareness of antimicrobial therapy, and encourage responsible use of antimicrobials among clients, key recommendations include:

- Considering physical properties of medication before prescribing it (i.e., size and palatability of oral medication)
- Adjusting the frequency of the dosing and duration of the therapy to fit clients' lifestyle and routine (where possible)
- 3. Selecting for the least complicated treatment regimen possible
- Providing a clear explanation behind the rationale for prescribing specific medications, including possible side effects
- 5. Providing clear verbal and written dosing instructions, ensuring written instructions are precise and legible
- 6. Demonstrating administration and use of medication, including tips and resources on successful patient restraint and administration of medications

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7. Encouraging clients to have an open discussion on potential difficulties they may face in complying with administration or dosing of medications, including reminding clients to raise any issues or concerns early instead of waiting till next visit

8. Dedicating sufficient time to answer questions in consult, encouraging trust and nurturing understanding between clients and vets

Key points to advise when dispensing antimicrobials:

- Monitor the animals closely during the treatment period. If animal is showing any signs of adverse reaction to antimicrobial (vomiting, acute diarrhoea, inappetence), advise your client to return for a review. Remind them not to change the treatment plan without consulting you first.
- If no improvement is noted during the recommended period of treatment with an antimicrobial, advise your client to return for further investigation in which an antimicrobial culture and sensitivity test is recommended.

Ensure that your client do not share meditations between animals or humans as this may result in the spread of infection (in particular topical ear/aural preparations)

9. CLIENT EDUCATION TOOLKIT

- Discourage the use of left-over medications prescribed at previous visits as this might be inappropriate for the animal's current condition, expired or contaminated.
- Remind your client not to take antimicrobials from non-qualified persons.

Tips for pet owners on administering pills to dogs and cats:

Pet owners are responsible for providing for the day-to-day needs of an animal and for looking after their health and welfare. Therefore, they play a crucial role in ensuring the responsible and prudent use of antimicrobials by working closely with their veterinarian.

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Whether their pill is for prevention, or to treat a condition, it is important for pet owners to follow the instructions on the label and complete the full course as prescribed by a veterinarian. If not, bacteria have a higher chance to develop resistance. Overtime, this can render antimicrobials ineffective and making common infections difficult to treat.

Pets have many tricks up their sleeve to avoid taking their medicine. Some pets are able to tell if medicine is in their food and refuse to eat. Others may eat it first and spit out the tablet later. Here are some top tips for helping the medicine go down:

1. <u>Check with your vet if the medication</u> <u>can be crushed or given with food</u>

Try crushing the tablets up into your pet's food. It is best to give a small portion first with the tablet in while your pet is hungry, to make sure that they eat the whole dose. You can then follow this up with their main meal.

2. Give it with a treat

If your pet's tablets can be taken with food, you could also consider giving it in or with your pet's favourite treat. Make sure they eat it all to get the full dose.

Always give your pet with lots of praise or a healthy treat so that they learn to associate pills with a positive experience. (Advise owners to practice this in moderation as overly fatty treats may result in further health complications.)

9. CLIENT EDUCATION TOOLKIT

3. <u>"Pill" your pet with some extra help</u>

Get someone to hold your pet from behind and keep their body and head still. Consider wrapping cats in a towel or blanket to protect yourself from their claws.

Gently tilt the pet's upper jaw upwards and pull the pet's lower jaw down to open their mouth.

Gently place the tablet as far back on the tongue as possible. Close their mouth, and gently hold their muzzle so they don't spit out the pill and stroke the pet's throat in a gentle downward motion.

4. Give it with some water

Get a small syringe of water ready. Do step 3 above. Once you've managed to place the pill in your pet's mouth, syringe a small amount of water into the side of your pet's mouth to help them swallow.

5. Practice good hygiene

Always wash your hands before and after handling medication and your pet.

If you've tried these tips and they don't work or if you have concerns about AMR, speak to your vet for more advice.

AVS infographic/leaflet:<_https://www.nparks.gov.sg/avs/animals/animal-health-and-veterinarians/animal-diseases-and-antimicrobial-resistance/antimicrobial-resistance >

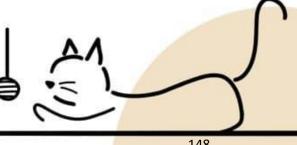
British Veterinary Association: Antibiotics – Your role as a pet owner:<<u>https://www.bva.co.uk/resources-support/client-guides/antibiotics-your-role-as-a-pet-owner/></u>

World Organisation for Animal Health (OIE): <https://oie-antimicrobial.com>

ANNEX/RESOURCES



Annex I - Chapter 3: Antibiotic Classes and Priority



Laboratory **Tests Available** Centre for Animal and Veterinary Sciences (AVS/NParks) Routine bacteriological culture For the latest tests and price list, please refer to: (antibiotic sensitivity https://www.nparks.gov.sg/avs/who-we-are/our-centres/aphc-cavs testing can be added) Service Booklet available online with instructions for sample submission. Specialised bacteriological culture 6 Perahu Road - please specify Singapore 718827 bacteria of interest Tel: (65) 63165168/(65) 63165188 upon sample Fax: (65) 63161090 submission. Opening Sample (antibiotic sensitivity testing can be added) hours submission hours 8.30 am - 5 8 am - 5.30 Mondays - Thursdays pm pm Fridays 8 am - 5 pm 8.30 am -4.30 pm Weekdays (lunch break) 12.30 pm -1.30 pm New Year's Eve, Chinese New Year 8 am - 12.30 8 am - 12 Eve, and Christmas Eve pm pm Saturdays, Sundays, and Public Closed Closed Holidays Aerobic Culture and Sensitivity Test ANTECH Anaerobic Culture and **Asia Veterinary Diagnostics** Sensitivity Test For the latest tests and price list, you may refer to: 1. https://avd.asia/microbiology/ **Blood Culture** 2. Latest Price List from AVD: Soft or Hard copy Brochure available upon request at sg@avd.asia Opening hours Urine Culture and 9.30 am to 6.30 pm, 7 days a week, including Public Holidays Sensitivity Test Call (or book sample pick-up via AVD Booking App or Online Portal) before 3 pm for same day collection by AVD's cour service. 3. Contact AVD laboratory

Annex II - Local/General C&S Test Recommendations and Results Interpretation

83 Genting Lane, #05-02A Genting Building, Singapore 349568 Tel: (65) 6291 5412 E-mail: sg@avd.asia

IDEXX

IDEXX For the latest tests, please refer to:

https://www.idexx.com/en/veterinary/referencelaboratories/tests-and-services/

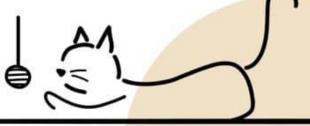
21 Biopolis Road, Nucleos (North Tower), Unit #03-06

Singapore 138567

Tel: (65) 68076288

Fax: (65) 63975279

*Please refer to IDEXX website for full range of available tests Aerobic Culture (ID and Susceptibility) Anaerobic Culture (ID only) Aerobic Ear Culture (ID and Susceptibility) Aerobic Eye Culture (ID and susceptibility) **Blood Culture** Environment Culture Fecal Enteric Pathogen Culture Fecal Culture Toxin Panels Fungal Culture (ID only) Methicillin-Resistant Staphylococcus (MRS) Screening Culture Necropsy Culture Pre-Breeding Culture Urine Culture and MIC Susceptibility



Annex III - Fever vs Hyperthermia

Hyperthermia is defined as excessive thermogenesis or inadequate heat loss and should be distinguished from a patient with a physiologically appropriate fever. As previously mentioned, the approach to diagnostics and treatments differ greatly between the two. For example, hyperthermic patients should be actively cooled, while cooling of febrile patients increases metabolic rate, oxygen consumption, water, and caloric requirements, and causes significant patient discomfort. In most patients, obtaining a comprehensive history and performing a thorough physical examination can provide an answer between both conditions.

	Fever	Hyperthermia			
History	Non-specific signs - Lethargy - Obtundation - Anorexia - Heat-seeking behaviour - Shivering	 Excessive thermogenesis: Seizures Muscle tremors Intense exercise/ activity Inadequate heat loss: Enclosed in a very hot environment Impaired ability to lose heat (Brachycephalics, laryngeal paralysis) 			
Clinical Signs	 Curl up Seek warm surfaces to lie on Shivering 	 Panting Sprawled out on cool surfaces Grooming (cats) Stertor (Brachycephalics) Stridor (Laryngeal paralysis) Generalised tremors Seizures 			



Annex IV - Descriptive Analysis of Antimicrobial Resistance from Bacterial Culture and Susceptibility Data on Ear and Skin Samples from Dogs and Cats in Singapore

Introduction

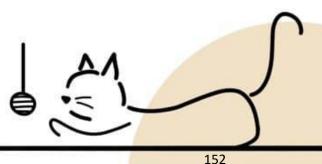
A preliminary descriptive analysis of diagnostic reports of antimicrobial resistance (AMR) in ear and skin samples of unwell dogs and cats in Singapore was conducted. Analysis of resistance profiles was made on isolates from ear and skin samples collected from veterinary clinics and sent to Asia Veterinary Diagnostics (AVD) to be cultured and tested for antibiotic susceptibility from May to August 2021.

Ear Samples

A total of 300 animals (260 dogs, and 40 cats) were tested, and 365 bacterial colonies were isolated for antibiotic susceptibility testing. AMR profiles of two common bacterial isolates from ear samples, *Staphylococcus* and *Pseudomonas*, were reviewed.

Staphylococcus isolates

There were a total of 161 *Staphylococcus* ear isolates, with *Staphylococcus schleiferi* being the most prevalent strain (51.2%, n=72). Of the 141 canine *Staphylococcus* isolates, 29.8% (n=42) were Methicillin-resistant *Staphylococcus* (MRS). The most common antibiotic resistance phenotypes of *Staphylococcus* isolates were Fluoroquinolones (FLQ) (39.0%, n=55), Penicillins (PEN) (31.2%, n=44), Carbapenems (CAR) (31.2%, n=44), Cephalosporins (CEP) (30.5%, n=43) and Lincosamides (LIN) (30.5%, n=43). However, Methicillin-resistant *Staphylococcus* (MRS) strains are intrinsically resistant to beta-lactam antibiotics, namely PEN, CEP, CAR, due to the presence of *mecA* gene in MRS strains.



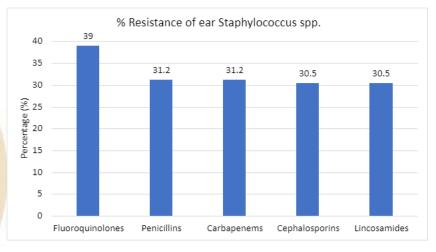
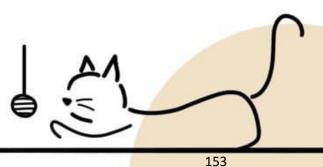


Figure 1. Antimicrobial resistance profiles of *Staphylococcus* isolates from ear samples of dogs in Singapore against FLQ, PEN, CAR, CEP and LIN antibiotics between May to August 2021.

Staphylococcus felis was the most prevalent strain (70%, n=14) in cat ear samples. As resistance is low, further analysis is not reported.

Pseudomonas isolates

There were 61 *Pseudomonas* bacterial isolates, with *Pseudomonas aeruginosa* being the most common strain (95.1%, n=58). About 95.1% (n=58) were canine isolates and only 4.9% (n=3) were feline isolates. Gentamicin (GEN), FLQ and POL are commonly used for treatment of *Pseudomonas* infection. The *Pseudomonas* isolates were resistant to these antibiotics – Enrofloxacin (ENR) (54.1%), GEN (37.8%), other FLQ (27.9%), and POL (1.6%). Other fluoroquinolones refer to Ofloxacin (OFX), Marbofloxacin (MAR) and Ciprofloxacin (CIP).



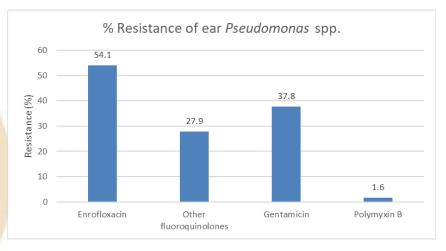


Figure 2. Antimicrobial resistance profiles of *Pseudomonas* isolates from ear samples of unwell dogs and cats in Singapore against FLQ, POL and GEN between May to August 2021. The other fluoroquinolones consist of CIP, MAR and OFX.

Skin Samples

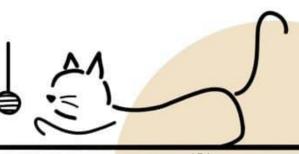
A total of 172 skin samples from 143 dogs and 29 cats were collected, and 263 bacterial colonies were isolated for antibiotic susceptibility testing. *Escherichia coli* or *E. coli* and *Staphylococcus* isolates were analysed.

E. coli isolates

Of the 24 E. coli skin infections reported, 87.5% (n=21) were canine isolates and 12.5% (n=3) were feline isolates. Within the small sample size, it was observed that the *E. coli* colonies were most resistant to PEN with 100% (n=24) resistance. It was also observed that 12.5% (n=3) of the isolates were resistant to CEP while 25% (n=6) were resistant to TET and FLQ, of which CEP and TET are commonly used to treat *E. coli* infections.

Staphylococcus isolates

There were 107 *Staphylococcus* skin infections, with 33.6% (n=36) of the isolates being MRS. Out of 107 isolates from the *Staphylococcus* genus, *Staphylococcus pseudintermedius* was the most prevalent strain (63.6%, n=68).



The most common antibiotic resistance phenotypes of *Staphylococcus* isolates were Ampicillin (AMP) (73.8%, n=79), TET (43.9%, n=47), MAC (35.5%, n=38), Amoxicillin/Clavulanic Acid and Ticarcillin/Clavulanic Acid (AMC/TCC) (33.6%, n=36), CEP and CAR equally (33.6%, n=36), and FLQ (30.8%, n=33). Fusidic acid (FUS) and Mupirocin (MUP), which are common topical antibiotics used to treat skin infections, appeared to be 100% or near 100% effective against the isolates in both MRS and non-MRS.

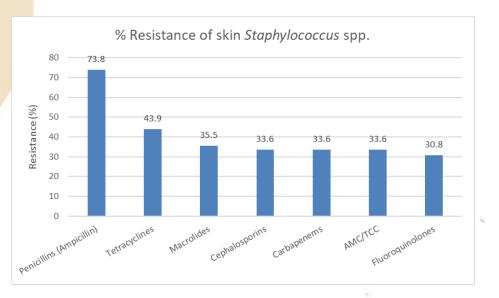


Figure 3. Antimicrobial resistance profiles of *Staphylococcus* isolates from skin samples of unwell dogs and cats in Singapore between May to August 2021 against various antibiotic classes.

Multi-drug resistance (MDR)

MDR is defined as antimicrobial resistance to three or more antibacterial classes, by the European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC). Focus is placed on acquired resistance by *Staphylococcus* below.

Of the *Staphylococcus* isolates from skin samples, 47.7% (n=51) of isolates were MDR, and their AMR profile showed resistance to several antibiotic classes including PEN, MAC and TET. About 36.0% (n=58) of the *Staphylococcus* ear isolates were found to be MDR, and included resistance to FLQ. 100% (n=78) of Methicillin-resistant *Staphylococcus* from skin and ear samples were MDR. All the *E. coli* isolates (n=24) from skin were found to be MDR, and macrolides (MAC). However, it is worthwhile to note that *E. coli* can have natural resistance to LIN and MAC *in vivo*.



Discussion

This discussion focuses on *Pseudomonas* and *Staphylococcus* as they are common pathogens of clinical significance in ear and skin infections. The *Pseudomonas* ear isolates showed variable resistance profiles. A high proportion of *Staphylococcus* isolates were MRS. Thus, the possibility of MRS isolates should be taken into account when treating a *Staphylococcus* infection to improve clinical outcomes.

Culture and sensitivity (C&S) testing would be useful to guide treatments of local *Pseudomonas* and *Staphylococcus* infections, considering the reported varied resistance profiles to different antibiotics. This assessment is confined to the data from diagnostic reports from veterinary clinics of unwell animals. Data on the pets' prior and current antibiotic use, presumptive diagnoses of infections and receipt of veterinary care are not available from the reports. These findings provide a snapshot of the prevalence of antimicrobial resistance in unwell companion animals in Singapore, and the importance of antimicrobial susceptibility testing to support clinical treatments of infections.

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Annex V - Descriptive Analysis of Antimicrobial Resistance from Bacterial Culture and Susceptibility Data on Urine Samples from Dogs and Cats in <mark>Sin</mark>gapore

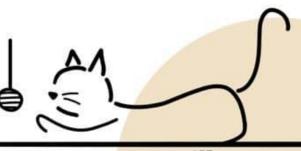
Introduction

A preliminary descriptive analysis of diagnostic reports of antimicrobial resistance (AMR) in urine samples of unwell companion animals in Singapore was conducted. Analysis of resistance profiles was made on isolates from urinary samples collected from veterinary clinics and sent to Asia Veterinary Diagnostics (AVD) to be cultured and tested for antibiotic susceptibility from May to August 2021.

A total of 684 animals (446 dogs, 286 cats, 10 rodents) were tested, and 742 bacterial colonies were isolated for antibiotic susceptibility testing. Rodent results were excluded in this study. In both dogs and cats, the most common type of bacterial isolates are *Escherichia coli* or *E. coli* (33.8%, n=78) in dogs and (49.3%, n=41) in cats; *Proteus*, (26.8%, n=62) in dogs and (20.5%, n=17) in cats, and *Enterococcus (ENTC)/Streptococcus*, (13.9%, n=32) in dogs and (13.3%, n=11) in cats.

E. Coli Isolates

The most common antibiotic resistance phenotypes of canine *E. coli* isolates included resistance to Penicillins (PEN) (38.5%, n=30), Cephalosporins (CEP) (23.1%, n=18), and Fluoroquinolones (FLQ) and Trimethoprim/Sulfonamides (SXT) equally (15.4%, n=12). The most common antibiotic resistance phenotypes of feline *E. Coli* isolates included resistance to PEN (48.8%, n=20), CEP (29.3%, n=12) and, FLQ and Tetracyclines (TET) equally (19.5%, n=8) (Figure 1).



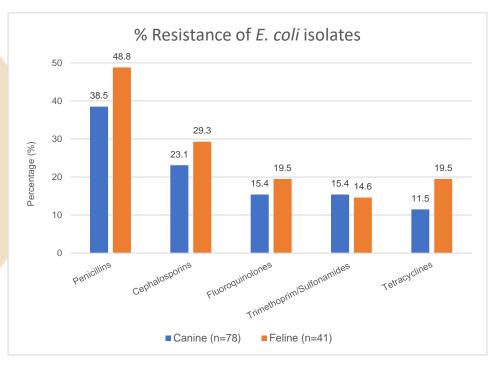
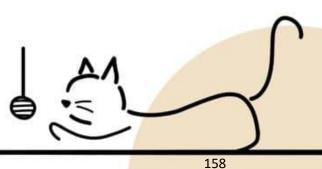


Figure 1. Antimicrobial resistance profiles of *E. coli* isolates from urine samples of unwell dogs and cats in Singapore between May to August 2021. Note: Penicillins refers to the penicillin class of antibiotics, which in this case included ampicillin, amoxicillin, and amoxicillin-clavulanic acid; and excluded penicillin G.

Proteus Isolates

Resistance of canine *Proteus* isolates was observed most often to PEN (65.6%, n=21), SXT (25.8%, n=16) and Amphenicols (CHL) (22.6%, n=14). Resistance of feline *Proteus* isolates was observed most often to PEN (23.5%, n=4), FLQ (17.6%, n=3), and CEP, CHL, and SXT equally (11.8%, n=2). (Figure 2). Nearly all the isolates are found to be resistant to TET, with 98.4% (n=61) of samples found resistant in dogs and 94.2% (n=16) in cats. All the isolates from both dogs (n=62) and cats (n=17) were resistant to Nitrofurans (NIT). However, selected species of *Proteus* are intrinsically resistant to PEN, CEP, TET, and NIT. These antibiotic classes are not represented in Figure 2.



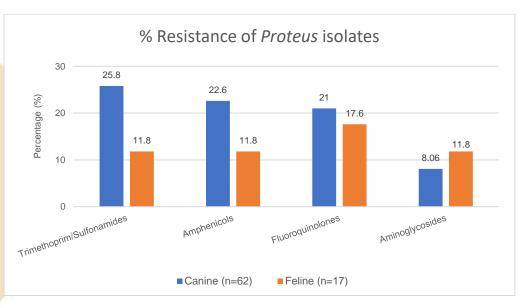
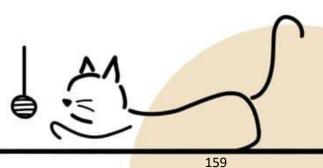


Figure 2. Antimicrobial resistance profiles of *Proteus* isolates from urine samples of unwell dogs and cats in Singapore between May to August 2021.

ENTC/Streptococcus* Isolates

The most common antibiotic resistance phenotypes of canine *ENTC/Streptococcus* isolates are CEP (78.1%, n=25), SXT (78.1%, n=25) and TET (40.6%, n=13). With regard to feline *ENTC/Streptococcus* isolates, the most common are CEP (72.7%, n=8), SXT (72.7%, n=8) and Carbapenems (CAR) (45.5%, n=5) (Figure 3.) All of the isolates were resistant against Aminoglycosides (AMG) (96.9% (n=31) in canines, 100% (n=11) for felines). This is likely because *ENTC/Streptococcus* are intrinsically resistant toward AMG.4 Only 3.23% (n=1) of positive isolates for *ENTC/Streptococcus* in canines and 9.09% (n=1) in felines are resistant to NIT. However, it is also to be noted that interpretation of the *ENTC/Streptococcus* data for CEP and SXT needs to be assessed in caution as ENTC is inherently resistant to CEP and SUlfonamides in SXT, while *Streptococcus* is not.

* ENTC and Streptococcus data was pooled and could not be split at the time of writing.



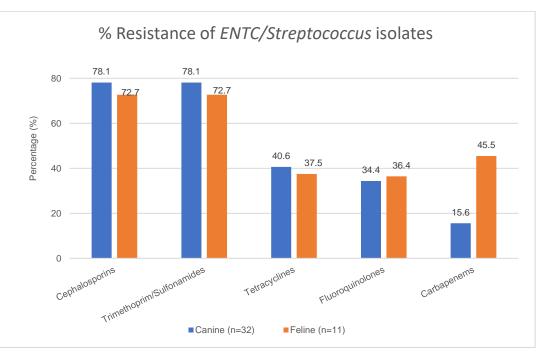
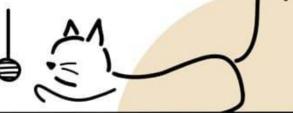


Figure 3. Antimicrobial resistance profiles of *ENTC/Streptococcus* isolates from urine samples of unwell dogs and cats in Singapore between May to August 2021.

Multi-Drug Resistance (MDR)

MDR is defined as antimicrobial resistance to three or more antibacterial classes, by the European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC). Focus is placed on acquired resistance by *E. coli* below.

MDR was found in 19.2% (15/78) of the *E. coli* isolates from canine samples and 24.3% (10/41) in feline samples. The most common MDR AMR profile of *E. coli*, comprising 60.0% (9/15) for dogs and 40.0% (4/10) for cats, includes resistance to CEP, FLQ and PEN. MDR was found in 14.5% (9/62) of the *Proteus* isolates from canine samples and 11.8% (2/17) for the feline samples. The most common MDR AMR profile of *Proteus*, comprising 100% (9/9) of the MDR canine samples are resistant to at least CHL, FLQ, SXT and 100% (n=2/2) of MDR feline samples resistant to at least AMG, CHL, FLQ and SXT. This could be because certain *Proteus* strains have MDR toward beta-lactams, AMG, FLQ, CHL, Streptothricin, TET and SXT. MDR was found in 18.8% (6/32) of the *ENTC/Streptococcus* isolates from canine samples and 18.2% (2/11) of the feline samples. The most common MDR AMR profile of *ENTC/Streptococcus*, comprising 66.7% (4/6) of canine samples were resistant to at least FLQ, PEN and TET, and 100% (2/2) of MDR feline samples and 18.2% CAR, FLQ, PEN.



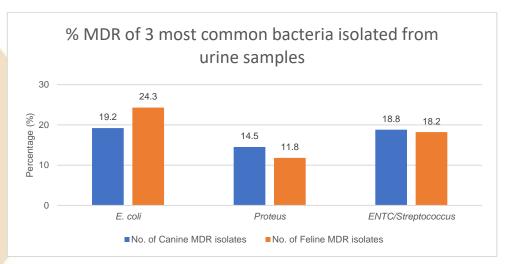


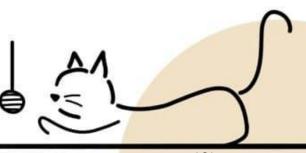
Figure 4. Percentage of MDR isolates from urine samples of unwell dogs and cats in Singapore between May to August 2021 from three most common bacteria.

Discussion

This discussion focuses on *E. coli* as they are considered good indicators of selective pressure. *E. coli* isolates displayed high proportions of PEN resistance. This needs attention as Amoxicillin-Clavulanic Acid and Amoxicillin, which belong to the penicillin class, are key antibiotics prescribed for cases of urinary tract infections – these are usually attributed to *E. coli*.

The proportion of MDR is higher in *E. coli* isolates compared to the other common bacteria types surveyed. *E. coli* can acquire resistance to different antimicrobials; thus, their resistance profiles can generally be used to reflect antimicrobial loads in their hosts. Studies have shown that the prevalence of MDR *E. coli* is increasing and is an area of clinical focus for veterinarians.

This assessment is confined to the data from diagnostic reports from veterinary clinics of unwell animals. Data on the pets' prior and current antibiotic use, presumptive diagnoses of infections and receipt of veterinary care are not available from the reports. These findings provide a snapshot of prevalence of antimicrobial resistance in unwell companion animals in Singapore, and the importance of antimicrobial susceptibility testing to support clinical treatments of infections.



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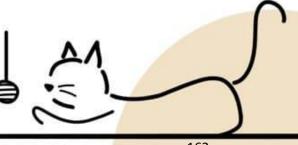
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Annex VI – WHO CIA List

WHO list of Critically Important Antimicrobials for Human Medicine (WHO CIA list)



WHO Critically Important Antimicrobials for Human Medicine 6th revision Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) November 2018

		Antimicrobial class			itization	factor (/es=●)				
	C	RITICALLY IMPORTANT ANTIMICROBIALS	C1	C2	P1	P2	P3 -				
t		HIGHEST PRIORITY						C1	Criterion 1		
	rity –	Cephalosporins (3 rd , 4 th and 5 th generation)	•	•	•	•	•				
	Pric	Glycopeptides	•	•	•	•	•	The antimicrobial class is the sole, or one of limited available			
	Highest Priority	Macrolides and ketolides	•	•	•	•	•		therapies, to treat serious		
	igh	Polymyxins	•	•	•	•	•	bacterial infections in people.			
tar	T	Quinolones	•	•	•	•	•	C2	Criterion 2		
o	HIGH PRIORITY Aminoglycosides		•	•		•		02	Untonon 2		
dr				•	•				The antimicrobial class is used		
	Ansamycins		•		•	•		to treat infections in peop caused by either: (1) bacter that may be transmitted			
ally	Carbapenems and other penems		•	•	•						
tic	Glycylcyclines		•	•	•			humans from nonhur	mans from nonhuman		
Critically Important	Lipopeptides Monobactams		•		•				urces, or (2) bacteria that av acquire resistance genes		
	Monobactams Oxazolidinones		•		•				from nonhuman sources.		
			•	•		•		P1	Prioritization factor 1		
		Penicillins (antipseudomonal)		•			•				
	Penicillins (aminopenicillins)		•						Large number of people in the community or in certain high- risk populations (e.g. patients		
	Penicillins (aminopenicillins with β-lactamase inhibitors)					-					
	Phosphonic acid derivatives		•	•	•	•			with serious infections in		
	Drugs used solely to treat tuberculosis / mycobacterial diseases		•	•	•				alth care settings), who		
	HIGHLY IMPORTANT ANTIMICROBIALS		C1	C2	P1	P2	P3	are affected by diseases for which there are very limited antimicrobial choices.			
	Amphenicols			•							
	Cepha	Cephalosporins (1 st and 2 nd generation) and cephamycins		•							
+		Lincosamides		•				P2	Prioritization factor 2		
an		Penicillins (amidinopenicillins)		•				High frequency of use of the			
b		Penicillins (anti-staphylococcal)		•				antimicrobial class for any			
d		Penicillins (narrow spectrum)		•				indication in human medicine or in certain high-risk groups			
E		Pseudomonic acids		•		NA		(e.g. patients with serious infections in health care settings), since use may favour selection of resistance.			
Ê		Riminofenazines Steroid antibacterials Streptogramins Sulfonamides, dihydrofolate reductase inhibitors and combinations									
Highly Important				•							
				•					Jui selection of resistance.		
	Sulfonam			•				P3	Prioritization factor 3		
	Sulfones Tetracyclines		•					The optimicrobial aloog is use	e antimicrobial class is used		
			•					to treat infections in people for			
	IMPORTANT ANTIMICROBIALS		C1	C2	P1	P2	P3	wh	ich there is already extensive		
+		Aminocyclitols Cyclic polypeptides		62	FI	r Z	F S	evidence of transmission of resistant bacteria (e.g. non-			
mportant					NA			typhoidal Salmonella spp. and Campylobacter spp.) or resistance genes (high for E. coli and Enterococcus spp.)			
ort											
ď	Nitrofuran derivatives										
2		Nitroimidazoles Pleuromutilins									

WHO CIA list 6th rev.:https://www.who.int/foodsafety/publications/antimicrobials-sixth/en/ AGISAR: http://who.int/foodsafety/areas_work/antimicrobial-resistance/agisar/en © World Health Organization 2019. Some rights reserved. This work is available under the CC BY-NC-SA 3.0 IGO licence WHO/NMH/FOS/FZD/19.1





Annex VII - FDA List of Approved Aquaculture Drugs

Immersion

CHLORAMINE-T

- HALAMID® AQUA NADA 141-423
 - Original FOI Summary 04.30.2014 (PDF-729KB) EA (PDF-4.77MB) FONSI (PDF-100KB)
 - For the control of mortality in freshwater-reared salmonids due to bacterial gill disease associated with *Flavobacterium* spp.
 - For the control of mortality in walleye due to external columnaris disease associated with *Flavobacterium columnare*.
 - For the control of mortality in freshwater-reared warmwater finfish due to external columnaris disease associated with *Flavobacterium columnare*.

FORMALIN

- FORMALIN-F[™] NADA 137-687
 - Original Approval 04.03.1986
 - Supplemental FOI Summary 11.25.2002 (PDF-281KB)
 - For the use of formalin to be expanded, as a parasiticide, to all finfish and penaeid shrimp, and, as a fungicide, to the eggs of all finfish.
- FORMACIDE-B ANADA 200-414
 - Original FOI Summary 07.17.2007 (PDF-143KB)
 - For use as a parasiticide for all cultured finfish and penaeid shrimp and as a fungicide for all finfish eggs.
- PARASITE-S NADA 140-989
 - o Original FOI Summary 07.31.1992 (PDF-22KB)
 - For the control of external parasites on cultured food fishes: salmon, trout, catfish, largemouth bass, and bluegill sunfish. Organisms controlled include the protozoa: *lchthyophthirius* spp. ("Ich"), *Chilodonella* spp., *Costia* spp., *Scyphidia* spp., *Epistylis* spp., and *Trichodina* spp. and monogenetic
 - trematodes: Cleidodiscus spp., Gyrodactylus spp., and Dactylogyrus spp.
 - For the control of fungi of the family *Saprolegniaceae* on salmon, trout, and esocid eggs.
 - Supplemental FOI Summary 09.30.1993 (PDF- 43KB)
 - For control of external protozoan parasites (*Bodo* spp., *Epistylis* spp., and *Zoothamnium*) on cultured shrimp.
 - <u>Supplemental FOI Summary 06.18.1998</u> (PDF-277KB) <u>EA</u> (PDF-1.13MB) <u>FONSI</u> (PDF-151KB)
 - For the use of formalin to be expanded, as a parasiticide, to all finfish, and, as a fungicide, to the eggs of all finfish.
 - <u>Supplemental FOI Summary 04.11.2019</u> (PDF-456KB)
 - For the control of mortality in freshwater-reared finfish due to saprolegniasis associated with fungi in the family *Saprolegniaceae*.

HYDROGEN PEROXIDE

- 35% PEROX-AID[®] NADA 141-255
 - Original FOI Summary 01.11.2007 (PDF-1MB) EA (PDF-7.06MB) FONSI (PDF-223KB)
 - For the control of mortality in freshwater-reared finfish eggs due to saprolegniasis.
 - For the control of mortality in freshwater-reared salmonids due to bacterial gill disease associated with *Flavobacterium branchiophilum*.
 - For the control of mortality in freshwater-reared coolwater finfish and channel catfish due to external columnaris disease associated with *Flavobacterium columnare* (*Flexibacter columnaris*).
 - o Supplemental FOI Summary- 07.26.2019 (PDF-413KB)
 - For the control of mortality in freshwater-reared coldwater finfish, fingerling and adult freshwater-reared coolwater finfish, and fingerling and adult freshwater-reared warmwater finfish due to saprolegniasis associated with fungi in the family Saprolegniaceae
 - For the treatment and control of *Gyrodactylus* spp. in freshwater-reared salmonids
 - For the control of mortality in freshwater-reared warmwater finfish due to external columnaris disease associated with *Flavobacterium columnare*

OXYTETRACYCLINE HYDROCHLORIDE

- OXY Marine™ NADA 130-435
 - Supplemental FOI Summary 12.24.2003 (PDF-117KB)
 - For the skeletal marking of finfish fry and fingerlings.
- Tetroxy[®] 343 ANADA 200-247
 - o Supplemental FOI Summary 09.15.2004 (PDF-358KB)
 - For the skeletal marking of finfish fry and fingerlings.
- *Pennox* 343[®] ANADA 200-026
 - Supplemental FOI Summary 12.06.2010 (PDF-86KB)
 - For the marking of skeletal tissues in finfish fry and fingerlings.
- Terramycin 343[®] NADA 008-622
 - o Supplemental FOI Summary 06.13.2005 (PDF-107KB)
 - For the skeletal marking of finfish fry and fingerlings.
- TETROXY[®] Aquatic ANADA 200-460
 - Original FOI Summary 04.20.2007 (PDF-52KB)
 - To mark skeletal tissues, most often the otoliths, of all finfish fry and fingerlings for subsequent identification.

TRICAINE METHANESULFONATE

- TRICAINE-S ANADA 200-226
 - o Original FOI Summary 11.21.1997 (PDF-34KB)

 For the temporary immobilization of fish, amphibians, and other aquatic, cold-blooded animals.

Injectable

CHORIONIC GONADOTROPIN

- CHORULON® NADA 140-927
 - o <u>Supplemental FOI Summary 08.06.1999</u> (PDF-270KB)
 - As an aid in improving spawning function in male and female brood finfish.

Medicated Articles/Feeds

FLORFENICOL

- Aquaflor[®] NADA 141-246
 - Original FOI Summary 10.24.2005 (PDF-432KB) EA (PDF-5MB) FONSI (PDF-284KB)
 - For the control of mortality in catfish due to enteric septicemia of catfish associated with *Edwardsiella ictaluri*.
 - Supplemental FOI Summary 03.19.2007 (PDF-262KB) EA (PDF-5.23MB)
 FONSI (PDF-239KB)
 - For the control of mortality in freshwater-reared salmonids due to coldwater disease associated with *Flavobacterium psychrophilum*.
 - Supplemental FOI Summary 10.26.2007 (PDF-127KB) | EA (PDF-1.64MB)
 | FONSI (PDF-296KB)
 - For the control of mortality in freshwater-reared salmonids due to furunculosis associated with *Aeromonas salmonicida*.
 - o Supplemental FOI Summary 04.04.2012 (PDF-680KB) EA (PDF-
 - 65KB) FONSI (PDF-131KB)
 - For an increase in the maximum florfenicol dose for the existing enteric septicemia indication for catfish, the addition of new species/classes, and the addition of indications for the control of mortality due to columnaris disease associated with *Flavobacterium columnare* in freshwater-reared finfish and for the control of mortality due to streptococcal septicemia associated with *Streptococcus iniae* in freshwater-reared warmwater finfish.
 - Supplemental FOI Summary 01.29.2014 (PDF-133KB) EA (PDF-844KB) FONSI (PDF-78KB)
 - For an increase in the maximum daily dose for freshwater-reared finfish other than freshwater-reared warmwater finfish to provide a dosage range of 10-15 mg/kg body weight/day and to change the conditions of use to permit the use of florfenicol in recirculating aquaculture systems.

OXYTETRACYCLINE DIHYDRATE

- Terramycin® 100 for Fish and Terramycin® 200 for Fish NADA 038-439
 - Original approval 09.23.1970, updated 07.16.2018
 - For the control of ulcer disease caused by Hemophilus piscium, furunculosis caused by Aeromonas salmonicida, bacterial hemorrhagic septicemia caused by Aeromonas liquefaciens (updated to A. hydrophila 07.16.2018) and pseudomonas disease in salmonids. For the control of bacterial hemorrhagic septicemia caused by Aeromonas liquefaciens (updated to A. hydrophila 07.16.2018) and pseudomonas disease in catfish. Supplemental FOI Summary - 06.30.2006 (PDF-80KB) 0 For the control of gaffkemia caused by Aerococcus viridans. Supplemental FOI Summary - 07.06.2008 (PDF-235KB) | EA (PDF- \cap 985KB) FONSI (PDF-349KB) For the control of mortality in freshwater-reared salmonids due to coldwater disease associated with *Flavobacterium psychrophilum*, the addition of an indication for the control of mortality in freshwaterreared Oncorhynchus mykiss due to columnaris associated with *Flavobacterium columnare*, removal of the limitation on treating salmonids in water temperatures below 9°C, and the addition to the label of the previously approved indication for marking of skeletal tissue in Pacific salmon. Supplemental FOI Summary- 11.21.2018 (PDF-367KB) For marking the skeletal tissue of freshwater-reared salmonids weighing

SULFADIMETHOXINE/ORMETOPRIM

up to 55 grams.

- Romet[®]-30 NADA 125-933
 - Original approval 11.26.1984 | <u>EA</u> (PDF-4.87MB) | <u>FONSI</u> (PDF-1.08MB)
 - For the control of furunculosis in salmonids (trout and salmon) caused by *Aeromonas salmonicida*.
 - Supplemental FOI Summary 05.23.1986 (PDF-85KB)
 - For the control of bacterial infections in catfish caused by *Edwardsiella ictaluri* (enteric septicemia of catfish).

SULFAMERAZINE

SULFAMERAZINE FISH GRADE - NADA 033-950
 Original approval 1967

For more information in FDA-approved aquaculture drugs, please visit: https://www.fda.gov/animal-veterinary/aquaculture/approved-aquacult