Is it time to re-evaluate anti-parasitic use in companion animals?

Anti-parasitics are very frequently used in companion animals for both prevention and treatment of parasites. When compared with practices related to parasite control in farmed animals, strategic, risk-based use of anti-parasitics in pet dogs and cats instead of precautionary and calendar-based treatment, is not a mainstream approach. Evidence of growing drug resistance in parasites of these hosts and a realisation of the potential adverse environmental consequences of anti-parasitics used in pets provide reasons to re-evaluate the use of anti-parasitics in companion animals. In order to achieve this, consultation and dialogue with industry stakeholders, as well as animal owners, is required.

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Anti-parasitics for companion dogs and cats are routinely used for prevention as well as treatment of parasites, and there has been a rapid evolution in the ease of use and choice available to prescribers and pet owners in this regard (Zajac, 1993; Epe, 2009; Becskei et al, 2020). While specific recommendations for preventive use vary from one geographical region to another (for example, depending on the occurrence of highly pathogenic parasites such as *Dirofilaria immitis*), veterinarians generally recommend at least some prophylactic use of anti-parasitics. Until relatively recently, the need for restraint in use of companion animal parasitics, in view of concerns over development of resistance in parasite populations and eco-toxicity, has not been widely discussed. This is in contrast to attitudes on use of anti-parasitics in farmed animals. However, there is now evidence to suggest that a renewed consideration of the strategic use of anti-parasitics in pets is warranted, in order to provide optimum protection against parasite-mediated pathogenic effects, while preventing both development of resistance and environmental damage.

The scope of anti-parasitic use in pet dogs and cats

Parasites for which prophylactic and/or therapeutic drug use is common range across the spectrum of protozoa, helminths and arthropods. A non-exhaustive summary of common parasites, their geographic range and the drug classes commonly used to treat them is shown in *Table 1*. Specific recommendations for parasite control will vary according to the presence of particular threats, such as *D. immitis*, in individual regions.

Current practice

Use of anti-parasitics in neonatal dogs and cats

Early intervention to prevent or reduce environmental contamination with ascarid eggs (Toxocara canis, Toxocara cati) is universally recommended, and can be considered appropriate strategic use of anthelmintics given the very high prevalence of transplacental (T. canis) and/or transmammary (T. canis, T. cati) transmission of these parasites, and the known zoonotic importance of the Toxocara genus. Recommendations for prevention of environmental contamination with these parasites also include treatment of pregnant/lactating females, given the likelihood of reactivation of hypobiotic larvae from somatic tissues, as well as the potential for patent infections developing as a result of grooming of puppies or kittens and consumption of neonatal faecal matter by their mothers. Neonates can also show clinical signs because of protozoan infections, a range of ectoparasites and other nematodes including hookworms. While reduction, not elimination, of pre-natal transmission of T. canis to puppies following treatment of the bitch has been reported (Payne-Johnson et al, 2000), treatment of the bitch with moxidectin at 1 mg/Kg bodyweight at days 40 and 55 of gestation has been shown to completely eliminate vertical transmission (Krämer et al, 2006). However, early and frequent treatment of pups, as opposed to aiming to reduce prenatal transmission and thus patent infections and environmental contamination, forms

Table 1. Major parasites of dogs and cats for which anti-parasitics are commonly used for prevention and/or treatment

Parasite group	Geographic range	Available anti-parasitics
Ascarids – *Toxocara canis, Toocara cati, Toxascaris leonina*	Worldwide	Pyrantel, fenbendazole, macrocyclic lactones, endomepsides
Heartworm – *Dirofilaria immitis*	Warmer areas suitable for development and transmission of the microfilarial stages through the mosquito intermediate host. Habitat growing.	Avermectins/macrocyclic lactones
Lungworm – *Angiostrongylus vasorum*	Endemic in much of Europe. Foci in parts of Canada and Brazil, emerging parasite in other parts of the Americas	Macrocyclic lactones, fenbendazole
Tapeworms – *Dipylidium caninum*, *Taenia* spp, *Echinococcus granulosus, Echinococcus multilocularis*	Worldwide, but some areas are certified free from *E. multilocularis*	Praziquantel
Hookworms – *Ancylostoma caninum, Uncinaria stenocephala*	*A. Caninum* dominates in warmer areas, *U. stenocephala* in temperate regions	Pyrantel, benzimidazoles, macrocyclic lactones
Whipworms – *Trichuris vulpis*	Worldwide	Pyrantel, benzimidazoles, macrocyclic lactones
Apicomplexan protozoa – *Cystoisospora spp, Cryptosporidium Neospora caninum, Toxoplasma gondii*	Worldwide	Paromyocin, azithromycin, clindamycin, sulphonomides/ potentiated sulphonomides
Other protozoa – *Giardia spp, Leishmania*	*Giardia* worldwide, *Leishmania* in warmer climates suitable for the intermediate sandfly hosts	Fenbendazole and metronidazole for *Giardia*, allopurinol plus miltefosine/ meglumine for *Leishmania*
Fleas – *Ctenocephalides felis, Ctenocephalides canis*, occasionally other species	Worldwide	Imidoclopramid, macrocyclic lactones, insect growth regulators, fipronil, pyrethroids
Mange mite – *Sarcoptes scabiei, Otodectes cynotis, Demodex* spp, *Cheyletiella* spp, *Neotrombicula autumnalis*	Worldwide	Macrocyclic lactones, isoxazolines
Lice – *Trichodectes, Felicola* and *Heterodoxus* spp	Worldwide	Imidoclopramid, fipronil, macrocyclic lactones
Ticks – *Ixodes, Dermacentor, Rhipicephalus, Amblyomma Haemophysalis* spp	Distribution depending on species	Isoxazolines, macrocyclic lactones pyrethroids

the cornerstone of veterinary advice. The standard recommendation is to worm pups at 2, 4, 6 and 8 weeks of age, followed by monthly worming until 6 months of age (Overgaauw and Knappen, 2013). Recommendations for kittens are similar, but the first dose can be given slightly later at 3 weeks of age because lactogenic, but not prenatal, transmission occurs.

Use of anti-parasitics beyond the neonatal stage

Preventive treatment for heartworm is one of the most widely used anti-parasitic strategies in areas where the intermediate mosquito hosts are capable of maintaining transmission. Guidelines aimed at dog owners in North America (for example the Companion Animal Parasite Council) recommend annual testing for *D. immitis* antigens and microfilariae, year-round preventive medication and prompt treatment of dogs in which infection is diagnosed (https://capcvet.org/guidelines/heartworm/). Drugs used in prophylaxis are usually macrocyclic lactones in a variety of formulations, often combined with products to treat other parasites.

In more temperate areas, preventive treatment for *Angiostrongylus vasorum* infection in dogs is widely, although not universally, recommended, typically for monthly treatments. Added to this are universal recommendations for control of ectoparasites, which, in view of spot-on and persistent options, are usually also used preventively. The presence of fleas on a dog or cat usually also means the presence of the tapeworm *Dipylidium caninum*, and tapeworm treatments are more often given if there has been a recognised flea infestation in the absence of complete flea prevention. Because of their zoonotic potential, ascarids in both dogs and cats are clearly top of the list in terms of the need for regular anthelmintic treatments, as far as pet owners and the general public are concerned. However, evidence suggests that the point prevalence of ascarid infections in owned dogs is relatively low (Hon et al, 2022). This is logical, given the low prevalence of patent infections of adult non-pregnant animals (Overgaauw and Nijisse, 2020). Hence, there is scope for revision and restraint in the use of periodic anthelmintics in adult dogs and cats. An exception applies in the specific requirements of pet dogs in relation to travel within Europe, when moving from an area in which the zoonotic tapeworm *Echinococcus multilocularis* is endemic to an area free of this parasite; in these circumstances, administration by a veterinarian of a drug effective against *E. multilocularis* is mandated between 1 and 5 days before travel (Goodfellow et al, 2006). Monthly treatments of dogs living in endemic areas are also advised.

Reasons to think about a re-evaluation

There are two major reasons why a re-evaluation of the way parasiticides are used in pet dogs and cats is now timely. The first of these is increasing evidence of resistance in parasite populations, as has been the known in respect of parasites in farmed animals for much longer. The second is the actual or potential environmental harms caused by anti-parasitics for pets.

Resistance to anti-parasitics

It is not surprising, given the frequency of use, that drug resistance among parasite populations in companion animals should be documented. Evolutionary pressures will ensure that this trend will continue, with the speed of development of further resistance determined by the extent, frequency and patterns of use of anti-parasitics in companion animals.

The most alarming evidence has emerged in respect of multi-drug resistance in populations of the hookworm *Ancylostoma caninum*. Evidence of resistance in this hookworm was first reported in racing greyhounds in Australia (Marsh and Lakritz, 2023). Multi-drug resistant isolates were then characterised in the USA. They can now be found among *A. caninum* populations circulating in the general companion dog population (Cima, 2021). Whereas benzimidazole resistance in *A. caninum* populations has been mapped to a specific β-tubulin mutation (Venkatesan et al, 2023), the genetics of resistance to other drug classes remains incompletely defined. Initially, reports of chronic recurrent *A. caninum* infection in spite of repeated treatment were attributed to the well-known 'larval leak' phenomenon, which is also reported as having become more common (Cima, 2021).

Drug resistance is also an issue in *Dirofilaria immitis* populations where molecular markers of resistance to macrocyclic lactones have been defined (Ballesteros et al, 2018; Bourguinat et al, 2015). Where ectoparasites are concerned, flea populations have acquired resistance to pyrethroids (Bass et al, 2004; Erkunt Alak et al, 2020). There is ongoing surveillance of *Ctenocephalides felis* populations for resistance to the more recently introduced, but widely used, imidoclopramid, and similar surveillance will be important in monitoring any development of resistance to the even more recently introduced isoxazoline products, now widely used to control fleas and other ectoparasites in companion animals (Rust, 2020). To date, there are no published reports of resistance to this drug in *C. felis* populations. Fleas, of course, are intermediate hosts of the tapeworm *Dipylidium caninum*, in which resistance to praziquantel has been documented (Jesudoss-Chelladurai et al, 2018).

Environmental concerns

Ecotoxicity is of increasing concern in regard to a wide range of pharmaceuticals used in human and veterinary medicine, as well as in crop protection. With respect to anti-parasitics, persistence of avermectins and their binding to soil has been shown to adversely affect biodiversity on farmland when used for treatment of grazing animals (Liang et al, 2023). A high degree of concern also exists with respect to the use of neonicotinoids (Goulson, 2013), among which is imidoclopramid, widely used as a topical/spot-on product for treatment of fleas and other ectoparasites in companion animals. Because of the smaller size of companion animals, there was an assumption that use of anti-parasitics in these species did not represent a threat in respect of environmental residues comparable to that posed by use in ruminants and horses. However, this assumption has now been challenged (Perkins, 2020; Domingo-Echaburu et al, 2021).

The European Medicines Agency (2020) produced a reflection paper on environmental concerns relating to use of parasiticides in companion animals, outlining the need for review of the assumption that a lower degree of vigilance is required for evaluating the ecotoxicity of companion animal parasiticides when compared with those used in large animals. Reasons which support a re-evaluation include increasing use of parasiticides in companion animals and an overall increase in the number of companion animals in the European Union. Wastewater monitoring of potentially ecotoxic pharmaceutical residues is increasingly used, and data from this and other sources postulate quantifiable risks between residues left by dogs swimming in lakes and rivers following treatment (Hill, 2020), and hair from treated dogs used by songbirds in nests (Little and Boxall, 2020). Collection of further data to quantify the ecotoxicity of parasiticides used in companion animals is warranted.

Conversations around the risks of ecotoxicity following use of anti-parasitics in pets should also involve stakeholder consultation. It is likely that the level of awareness among both veterinarians and animal owners on this topic is even less than in relation to the risks of anthelmintics. Furthermore, anti-parasitics in pets or other domestic animals are only one of the sources of concern in this regard, with crop protection products also leading to potential environmental contamination. Some products may also be used to control parasites of populations adversely affected by the same products (treatment of *Varroa* mites in honeybees).

Envisioning future scenarios

The prudent use of anti-parasiticides in farm animals, encompassing strategies for targeted and/or selective use and maximising non-pharmaceutical control methods, has long been advocated, even if it is not universally applied. Concerns over ecotoxicity have also more recently been voiced in this area. It seems clear, from this vantage point, that those concerned with developing strategies to counter both of these concerns arising from the use of companion animal parasiticides, are already relatively late in stimulating debate and strategies for change. In planning how best to counter both resistance and ecotoxicity concerns in companion animals, it must be acknowledged that different cost-benefit ratios, concerns over zoonotic parasites, views of animal owners and relationships between owners and veterinary practitioners mean that it is not likely that strategies used in farm animals can be directly extrapolated to companion animals. So, where to start?

Whereas consistent efforts are made to inform owners of farmed animals about the existence of resistance to anti-parasitics and the factors which influence its development, the same cannot be said about communication with owners of pet dogs and cats thus far. While warranted, conversations with this category of veterinary client on this topic will need to be calibrated differently. Generally, the wishes of clients are to eliminate parasites from their pets, avoiding not only direct concerns but also those related to potential zoonotic transmission of parasites. This greater focus on individual animals rather than on populations, and potential future problems affecting them, is likely to influence how messages in relation to drug resistance are received. However, much can be learnt from the history of communicating the importance of drug resistance to those concerned with production animals. It has become abundantly clear that conflicting messages from various sources, information which is unclear and recommendations which are difficult or impractical to implement hinder changes in stakeholder behaviours aiming to slow the development of drug resistance. Proven approaches to changing behaviour, with involvement of social scientists and health psychologists, are now being employed to improve control of parasitic diseases in production animals (Coyne et al, 2020; Walshe et al, 2023). Evidence from these approaches also has much to offer in the companion animal field. With these approaches, it is key to consult stakeholders (in this context, animal owners and prescribing veterinarians/suitably qualified persons) on what their knowledge and perceptions of the situation are, on how receptive they are to change and their key concerns. Within such consultations, there should be opportunities for mutual exchange of information and education on the risks specific parasites pose to pets at various life-cycle stages, together with any zoonotic risks. Crucially, discussions should also involve information and exchanges of views on non-pharmaceutical interventions for reducing the risks of parasitic disease, including breaking the cycle of infection by removing faecal material before eggs or larvae develop, and avoiding exposure to arthropod vectors at peak host biting times (dawn and dusk).

Conclusions

Logically, it seems reasonable for veterinarians to be aware and conscious of avoiding the use of anti-parasiticides on an interval or calendar-based regimen, as opposed to one which is risk-based. Whereas *T. canis* tends to dominate the conversation around zoonotic parasites in the mainstream media, the nuance of differentiating between environmental risks posed by egg shedding in puppies as opposed to adult dogs is often not represented. Collaborations between clinicians, parasitologists and social scientists have begun to explore animal owners' behaviour and attitudes towards parasite control in ruminants and horses, along with the real and perceived barriers to adopting safer and more sustainable control methods. It is reasonable to suggest that such approaches would also prove fruitful in the area of companion animal parasite control. Veterinarians need to be prominent in this discourse. Finally, future planning should involve a renewed focus on the development of vaccines against parasites of pets. CA

Conflict of interest

The author declares that there are no conflicts of interest.

KEY POINTS

- Anti-parasitics are very frequently used for both prevention and treatment of parasites in companion animals in the interests of animal and human health.
- Drug resistance has been documented in populations of several common and important parasites of these species.
- The effects of companion animal anti-parasitics on the environment need to be further investigated and considered.
- In view of concerns in relation to both resistance and potential eco-toxicity, it is reasonable to consider whether more strategic and targeted use of anti-parasitics in companion animals is justified.

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