**Introduction**

The control of nematode infestations is an important aspect of preventative canine and feline medicine. Anthelmintics are used in UK dogs and cats for the prevention of potentially serious clinical disease, reduction of zoonotic risk and to avoid owner revulsion induced by the presence of worms. *Toxocara* spp. eggs in the faeces of cats and dogs represent a significant zoonotic risk. Anthelmintic treatment remains central to limiting environmental contamination. The frequent use of parasiticides effective against roundworms has, however, led to concern that drug resistance may develop against the products being used, as has been the case for equine and livestock parasites. This article considers drug resistance in intestinal roundworms, heartworm and *Angiostrongylus vasorum*. The routine treatment of canine and feline nematodes presents a difficult balance between limiting the development of resistance and maximising animal and human health.

**Key words:** Drug resistance, nematode, anthelmintic, *Angiostrongylus vasorum*, *Dirofilaria immitis*

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and is heritable” (Bowman 2012). When drug resistance occurs, the consequences in terms of animal welfare and zoonotic risk can be severe. Parasite drug resistance must therefore be carefully monitored and should also be considered when developing control programs. This article discusses drug resistance in intestinal roundworms, heartworm and A. vasorum as well as the influence resistance has upon parasite control in UK cats and dogs.

Intestinal nematodes

Although high burdens of intestinal nematodes can cause ill thrift and morbidity in cats and dogs, particularly puppies and kittens, it is the zoonotic potential of Toxocara canis and Toxocara cati that represent the greatest concern. Whilst it has been proposed that people can be infected by eating the undercooked meat of paratenic hosts such as wild game (Struchler et al. 1990), the most common route of human infection is by the ingestion of embryonated eggs. It was originally thought that T. canis alone was the source of human infection by this route but there is now strong evidence to suggest that T. cati is significantly involved as well (Fisher 2003). Prevalence of patent Toxocara spp. infection varies significantly. In Western Europe the prevalence of T. canis varies between 3.5 and 34% and T. cati between 8 and 76% (Overgaard and Van Knapen 2013, Wright et al. 2016). Puppies and kittens provide the largest source of potential infection with a prevalence close to 100% due to transplacental and transmammary infection. Untreated adult cats and dogs can also potentially intermittently shed eggs throughout their lives. A number of strategies need to be employed to reduce environmental contamination with Toxocara spp. eggs including anti dog fouling campaigns, limiting access of cats and dogs to children’s play areas, covering sandpits to avoid faecal contamination and humane stray cat control. However, regular deworming of cats and dogs remains central to reducing zoonotic risk. The potential for this to result in anthelmintic resistance is therefore a concern as it is inevitable that parasites will adapt in response to increased anthelmintic exposure.

Drug resistance to benzimidazoles and macrocyclic lactones is an increasingly common phenomenon among intestinal nematodes of livestock and horses (Matthews 2014, Geurden et al. 2015). This limits treatment options and results in outbreaks of parasitic disease despite routine preventative treatment. In these cases, resistance is selected by the repeated treatment of all animals, placing significant selection pressure on the populations within the intestine of the hosts. The worms that survive treatment exposure are the only worms left to produce eggs, therefore selecting potential drug resistant individuals that will be over-represented in subsequent infecting populations of worms. Confirmed cases of anthelmintic resistance in cats and dogs are, however, rare, an example being hookworm resistance in urban Australian dogs (Kopp et al. 2007). Even in this case, intense deworming regimes were applied over a prolonged period of time. There are several possible reasons why resistance has been slow to develop in intestinal nematodes of cats and dogs:

• **Large wildlife reservoirs** – Foxes have a high prevalence of both hookworm and T. canis infection, neither of which are routinely exposed to anthelmintics. Similarly, hookworms and T. cati infections in stray and feral cats will have a dilutional effect on the proportion of parasite life stages that have been exposed to anthelmintic.

Statistical models, including a study conducted in the Netherlands (Nijssen et al. 2015), have demonstrated stray cats to be the greatest contributors of T. cati egg environmental contamination in urban areas. Their dilutional effect on resistant parasitic life stages is therefore likely to be significant. In addition, Toxocara spp. infect large numbers of paratenic hosts including rats and birds which will not be exposed to anthelmintics.

• **Arrested larval stages** – A proportion of Toxocara spp. larvae migrating through infected dogs and cats will become arrested in the host organs and muscle tissue rather than developing into adult worms in the intestine. Periodically these larvae will reactivate and resume their life cycle, particularly during pregnancy and lactation. Arrested worms form a population which is relatively protected from anthelmintic exposure.

**Widespread environmental refugia** – Resistance is most likely to occur when entire local populations of cat and dog nematodes are exposed to anthelmintic in isolated groups such as kennelled situations (Kopp et al. 2007). Varying the product and timing of treatment within these populations of cats and dogs will help to limit this effect. The increased urbanisation of foxes will also have a dilutional effect as new worm populations are introduced to urban areas.

These factors may have limited the development of resistance. However, if sufficient treatment pressure is put on the domestic cat and dog parasite populations, the potential remains for resistance to develop. Allowing Toxocara life stages into the environment to act as refugia and reduce selection pressure, carries zoonotic risk and is hard to justify. Deworming frequencies should therefore be risk based allowing resistance to be limited and minimising pet and human health risks. It is, however, important to acknowledge that leaving uninfected animals untreated does not limit resistance: if worms are not present they cannot contribute to refugia. On the other hand, allowing limited shedding by animals that represent a low zoonotic risk and are at low health risk from parasite infection will reduce resistance. These factors all need to be considered when deciding on worm treatment regimes.

**Recommendations for treatment regimes**

Treatment of puppies should start at two weeks of age, repeated at two weekly intervals until two weeks post weaning and then monthly until six months old. This is to eliminate T. canis egg shedding from trans-placental and trans-mammary infection and prevent significant populations establishing in the intestine. Kittens should be treated in the same way but the first treatment can be given at three weeks old as there is no trans-placental transmission. It has been demonstrated that the use of an effective anthelmintic every three months significantly reduces Toxocara spp. ova shedding (Wright and Wolfe 2007) and there is no evidence that less frequent deworming protocols will have any effect on egg output. Therefore, this frequency