Chapter 1

General introduction
Aspects of *Toxocara* epidemiology,
Toxocarosis in dogs and cats

*P.A.M. Overgaauw*

*Virbac Nederland B.V, P.O. Box 313,
3770 AH Barneveld, The Netherlands*
Introduction

*Toxocara canis* and *Toxocara cati*, roundworms of dogs and cats, are probably the most common gastrointestinal helminths of domestic canids and felids world-wide (81). The reported infection rates in Western Europe vary from 3.5% to 17% for *T. canis* in dogs and 8% to 76% for *T. cati* in cats. In the USA the figures are between 2% - 79% and 10% - 85% respectively (1, 25, 31, 79). The prevalence of patent *Toxocara* infections is highest in young dogs and cats and much less common in adult animals. *Toxocara* infection is the (covert) infection following ingestion of *Toxocara* eggs, or ingestion of larvae that can lead to (overt) clinical disease, which is presently called toxocarosis. The former name for toxocarosis was toxocariasis.

A good understanding of the epidemiology is required so that effective prevention of infection in man, dogs and cats is possible. In this review, the mode of transmission, clinical symptoms, diagnosis, prevention and control of toxocarosis in dogs and cats will be discussed, together with a critical appraisal of some of the less well-known issues.

Mode of transmission

**Infectious agents**

The life cycles of *T. canis* and *T. cati* are complex. Adult worms in the intestinal tract of infected dogs and cats shed large numbers of eggs via the faeces into the environment where they are ingested by natural hosts as well as paratenic hosts (Figure 1). In the intestine the larvae hatch and migrate via blood vessels all over the body. This is called visceral larva migrans (VLM). In young animals a tracheal migration occurs via the lungs and trachea and after swallowing, the larvae mature in the intestinal tract. In paratenic hosts and most adult dogs and cats that have some degree of acquired immunity, the larvae undergo somatic migration to remain as somatic larvae in the tissues. After predation of *Toxocara* infected paratenic hosts by dogs or cats, larvae will be released and develop in most cases directly to adult worms in the intestinal tract.

In the pregnant bitch and queen, ‘dormant’ tissue larvae are reactivated and migrate in the bitch across the placenta to infect the foetuses. New-born puppies and kittens also acquire infection through ingestion of larvae in the milk. (81, 96, 97).
Contamination of the environment with Toxocara eggs

Toxocara eggs are unembryonated and not infectious when passed in the faeces of dogs and cats into the environment. Within a period of between 3 - 6 weeks to several months, depending on soil type and climatic conditions such as temperature and humidity, eggs will develop to an infectious stage that can survive under optimal circumstances for at least one year. No larval development occurs at temperatures below 10° C and larvae die below temperatures of –15° C (81). The 2nd larval stage or somatic larvae in the tissues has always been considered to be the infective stage; it has become clear that the infective stage is in fact the 3rd stage, reached after two moults in the eggshell (56).

Several studies from all over the world demonstrated high rates (10% - 30%) of soil contamination with Toxocara eggs in parks, playgrounds, sandpits and other public places (34).

Differentiation between eggs of T. canis and T. cati has not often been attempted (43, 71, 84, 105), but T. canis eggs are reported to be more commonly found in soil (35). Scanning electron microscopy (106) or microscopic differentiation of the fine pitting of the superficial layer of T. cati eggs compared to T. canis eggs (80) can be used to identify individual eggs reliably.

The source of the investigated soil, however, will certainly influence these findings. In a survey in the Netherlands, the presence of T. canis eggs in public parks was comparable with reports from other European cities, but most of the investigated sand-boxes were polluted with T. cati eggs. This was explained by the fact that cats prefer a quiet place with sandy material to defecate, while dogs only defecate in such places if owners force or educate them to do this (54). The same conclusion was drawn in a study where the defecation habits of cats were observed. Only 11 (1%) of the total 972 defecating animals in 3 sandpits during a 4.5 months observation period were dogs, the remainder were cats. Almost all of the cats were stray cats and between 25% (1/4) and 67% (8/12) of the cats that defecated in the different sandpits were infected with T. cati. Eighty per cent of the defecations occurred at night (106).
Infection with Toxocara larvae: 4. Transplacental infection. 5. Transmammary transmission. 6. Through paratenic hosts.
Infection of dogs and cats with *Toxocara* eggs

**Tracheal migration**

After ingestion of infective *Toxocara* eggs by young dogs, a tracheal migration of larvae occurs through the liver, the vascular system and the lungs. The larvae break out into the alveoli and migrate to the trachea and pharynx. After swallowing, they complete their development in the stomach and small intestine. Eggs first appear in the faeces 4 to 5 weeks post-infection (22, 23, 35, 81). In a survey among dogs and cats in the USA (60), the highest prevalence of patent *Toxocara* infections was found in 2-week to 2-month old dogs and in 2- to 6 month-old cats.

**Age resistance**

By the time a puppy has reached the age of one to two months, the probability that newly hatched *T. canis* larvae will develop into adult ascarids falls to a very low level, while the probability of somatic migration progressively increases (38). The failure to produce patent infections in older dogs is termed age resistance and is not ‘all or nothing’ in nature, but rather a gradual decrease in the recovery rate of adult ascarids as the age of the dog advances (76).

A significant contribution of acquired immunity to this phenomenon has been exclusively demonstrated in several studies (7). The mechanism of resistance in mature dogs may operate partly within the lungs, perhaps as a delayed-type hypersensitivity response (23, 36). The difficulty in development experienced by the infective stage larvae to the next stage suggests that the resistance is directed against the infective stage of the parasite (76).

Development of immunity was shown in mice infected with embryonated *T. canis* eggs and described as immunosuppression after one *T. canis* infection, whereas two or three infections seemed to cause immunoprotection (19). To determine the origin of the immune response, parasite naïve mice were injected with lymph cells, serum or both from mice infected with *T. canis* on days 1 and 100. Control mice received similar material but from parasite naïve mice. Comparison of the larvae after experimental infection revealed a significant reduction in the number of larvae in liver and lungs after cell transfer, whereas serum transfer decreased the number of parasites in brain and carcass. The combination of serum and cells showed a synergistic action in lungs and brain but an antagonistic activity in liver and carcass (7).

Löwenstein (66) infected one group of helminth-free bitches with infective *T. canis* eggs on the day of conception, followed by fenbendazole treatment (100 mg/kg) daily from day 30.
until parturition to remove somatic larvae. A further challenge with infective eggs was performed during lactation. Control dogs received only the infective eggs during lactation. It was found that previous exposure to infection resulted in significantly fewer larvae being shed in the milk and fewer migrating to organs and tissues compared with control animals. Re-infection resulted in diarrhoea in all sensitised bitches; this suggested an allergic inflammatory reaction, tending to limit larval infection.

Similar results were reported from twice-infected mice showing a 27% reduction in the total larval recovery rate compared with non-sensitised controls. A significant number of larvae were retained in the liver and less larvae were recovered from the brain. An inflammatory reaction was seen in the gut wall of sensitised mice but not in the controls, again suggesting a role played by the intestine in the development of resistance to T. canis infection (3).

The reason why the host’s immunity does not eliminate all tissue parasites is not understood; two mechanisms of evasion of the host’s immunity by the larval stages have been suggested. One is hypobiosis of the tissue larvae that presumably reduces the production of protection-inducing antigens, thus rendering the parasite less susceptible to interference from the metabolism of the host. The other is immunosuppression by interference with the function of T-helper cells which inhibits the response to protective parasite antigens and the production of specific antibodies to these antigens (7).

Large and sustained doses of corticosteroids were able to break the resistance of a 6-month-old dog and allow development of patent infection (62). This increased susceptibility to infection was associated with decreased lymphocyte responsiveness in vitro to phytomitogens and T. canis antigens and suppression of eosinophilia in a study on periparturient bitches (64). The authors formulated the hypothesis that the immunosuppressive effect of pregnancy and lactation may permit tissue larvae, or larvae from a newly acquired infection, to undergo tracheal migration and subsequent intestinal development. In general, new infections of the lactating bitch will occur also by ingestion of immature fourth-stage larvae from vomit or faeces from the puppies. Larvae can develop to adults without a tracheal migration; this could also be the explanation for finding egg-producing Toxocara worms in the intestine. The finding of Toxocara eggs in the faeces of a bitch one week after parturition and prior to the detection of eggs in the faeces of her puppies leads to the hypothesis of tracheal migration of activated somatic larvae in the bitch. However, this bitch was experimentally infected during pregnancy with 10,000 eggs, representing a very high dose of infective eggs which may have caused immunosuppression or simply overcome the resistance.
Scothorn (94) found no evidence of intestinal infection with \textit{T. canis} on necropsy examination of bitches at different times during gestation.

Another group that is reported to be at higher risk of \textit{Toxocara} infection is the bitch during metoestrus. Three times as many bitches in this phase of the Oestrous cycle had patent \textit{T. canis} infections as those in other groups (27). This comprised a pilot survey of 181 dogs during routine visits to a veterinary practice, but nothing was mentioned about the history of the dogs. The author assumed that prolactin is the major triggering factor for stimulation of somatic larvae. In addition to this, prolactin suppresses the immune response which enables the acquisition of new infections (28). Similar evidence supporting this hypothesis were not found in the literature.

\textit{Patent infection of adult dogs}

Although the prevalence of \textit{T. canis} is highest in young dogs, a certain proportion of the adult canine population can also be infected (72, 79, 88, 97, 104). Adult \textit{Toxocara} worms may occur as a result of suppressed immune response, ingestion of low numbers of infective eggs (23) or following ingestion of infected paratenic hosts (110). Fully susceptible adult dogs have also been described, despite repeated egg exposure and development of antibodies (68). This could be related to certain breeds, e.g. Greyhounds in this particular survey, and the size of the dose of \textit{T. canis} eggs. Since natural exposure of the canine population to infective \textit{T. canis} eggs is more likely to be similar to the low-dose levels described by Maizels and Meghji (68), it was concluded that it may well be that the overall susceptibility of dogs developing a patent \textit{Toxocara} infection is at a higher level than is currently accepted.

\textit{Toxocara infection and gender}

Patent \textit{T. canis} infection tends to be found more often in adult male dogs than female dogs (18, 33, 47, 48, 49, 68). A suggested explanation for this phenomenon is that female dogs harbour mainly resting larval stages in their somatic tissues which infect their offspring in the future, while continuation of \textit{Toxocara} infection via male dogs can only take place by the spread of eggs from adult worms in their intestinal tract. The remaining, albeit theoretical survival route of somatic larvae would be if male dogs were themselves predated thus acting as paratenic hosts. Nothing is published, however, regarding significantly different findings on somatic tissue larvae between female and male dogs to give substantive support to this hypothesis.
In one survey *T. canis* was more frequently found in females than males (73). This was explained by the assumption that females were exposed to *T. canis* larvae passed out by their puppies.

Castrated males and spayed females had a lower prevalence of infection, compared to their respective entire counterparts, probably because they are less likely to roam and more likely to be better cared for (60, 109).

**Tracheal migration in the cat**

Following a tracheal migration after oral infection with infective *T. cati* eggs, adult worms are present by day 28 and eggs can be first observed in the faeces 56 days after infection (96). In contrast to the dog, the tracheal migration following *T. cati* egg infection in cats remains high even in older cats (72, 81) but less frequent than in young cats (72, 109). In neutered cats a significant decrease in prevalence of infection was found, compared to their respective entire counterparts (109).

**Somatic migration**

Adult dogs and cats can be infected by ingestion of infective *Toxocara* eggs from the environment, mainly contaminated soil. Larvae will hatch in the intestine and invade the mucosal layer. Migration occurs either passively via lymph and blood or actively by penetration of the tissues and invasion of all parts of the body. Gradually somatic larvae accumulate in the tissues (somatic migration), persisting for long periods in a manner similar to that seen in paratenic hosts (97). Larvae of *T. cati* prefer to migrate to the muscles (93), while *T. canis* larvae were more found in the central nervous system (97). In mice, it was found that more than half of the embryonated eggs appeared to be discharged without hatching in the intestine. The emptying time of the gastrointestinal tract appeared to be one of the important factors. If eggs remained longer in the intestine, e.g. with a full stomach, 15 to 20 per cent more eggs hatched (74).

**Infection of dogs and cats with *Toxocara* larvae**

**Transplacental migration**

Several studies have shown that nearly 100% of puppies are infected in utero from day 42 of the gestation by somatic larvae (63, 94). This so called transplacental migration or
intra-uterine infection is the most important mode of transmission in dogs; 98.5% of activated larvae is reported (16). In cats, prenatal infection via the placenta does not occur (96, 103). The larvae in pregnant bitches are reactivated by one or more unknown factors; the changing hormonal status of the bitch during pregnancy has been suggested. Oshima (75) found that injections of the gonadotrophin prolactin led to a marked fall in the number of larvae in tissues of mice that were experimentally infected with *T. canis* and suggested that this hormone is involved in stimulating dormant larvae to resume their migration. Within hours of birth, the larvae that were present in the liver of the neonate, migrate to the lungs and undergo a tracheal migration. Adult worms can be found at two weeks of age (64) and large numbers of eggs may be passed in the faeces after a minimum period of 16 days (65, 88).

Little is known about the numbers of larvae which can be found in the tissues of the bitch, the proportion of tissue larvae activated in pregnancy and the survival time of larvae in the tissues (65). Transmission occurs in consecutive pregnancies, even in the absence of re-infection between each parturition (15).

**Transmammary transmission**

After activation somatic *Toxocara* larvae of dogs and cats will also be transmitted via the colostrum and the milk (transmammary transmission, lactogenic- or milk-borne infection). Following ingestion by the offspring, the larvae undergo development without tracheal migration. Larvae are found to pass in the bitch’s milk for at least 38 days after parturition (111).

This route is less important than intra-uterine transmission in the puppy, but it is the primary mode of infection in the kitten (103). In a study in puppies, only 1.5% of *T. canis* larvae were transmitted via the lactogenic route (16).

Kittens infected by lactogenic transmission will show faecal egg excretion 9 days earlier than in egg infected cats (by 47 and 56 days after infection respectively). After ingestion of an infected paratenic host this period is comparable with the period after transmammary infection (96).

**Infection of the dam by the offspring**

A nursing bitch or queen may acquire a patent *Toxocara* infection by ingesting intestinal larvae expelled in vomit or faeces of their offspring during nursing. A number of these larvae mature and become patent (98). Together with the ingested eggs from the faeces of their offspring, lactating dogs and cats can in this way disseminate large numbers of eggs into the
environment. Between 4 to 10 weeks after parturition, these infections will disappear spontaneously (64, 88).

Oshima (75) suggested that the suppression of resistance to infection during lactation and the subsequent development of *T. canis* in the intestine is explained by the special influence of lactation and the relationship with the secretion of prolactin. This seems to be confirmed by the finding that such infections are eliminated spontaneously within one week following the cessation of lactation (64).

Finally, *Toxocara* eggs shed in the faeces of puppies or kittens can be ingested by the mother, where they pass through the digestive tract, causing a false-positive diagnosis of *Toxocara* infection upon faecal examination.

**Transmission through paratenic hosts**

Paratenesis is the mode of infection of some larval nematodes like *Toxocara*, ensuring its continuing survival by its distribution in prey species (39).

This route of infection exists because of the development of somatic larvae in paratenic hosts, including vertebrates such as rodents and birds or invertebrates such as earthworms and insects (e.g. flies). Small mammals are suggested to play an important role as paratenic hosts in urban and rural localities. In the Slovak Republic, 22% of the investigated small mammals were found seropositive for *Toxocara*, most frequently in several species of mice (24).

A small fraction of the larvae in mice were found to migrate from the lungs to the intestine, following a tracheal migration. This resulted in an unexplained subsequent re-invasion of tissues by larvae after entering the intestine for the second time 5 days after infection (74).

After ingestion of a paratenic host infected with *T. canis* larvae by the dog (97) or *T. cati* larvae by the cat (81, 96, 103), the larvae develop directly in the intestine because the larvae have already migrated in the preceding host, and presumably have reached an appropriate stage of maturity such that they can develop into adults in the intestine. In contrast with these conclusions, Warren (110) reported that *T. canis* larvae undergo a tracheal migration to adults by 19 days in dogs following their ingestion via an experimental paratenic host (mice tissues). The difference between the two experiments however, was the time of infection of the mice which were fed to the dogs. Infection of these mice in Sprent’s study (97) was two to six weeks before, whereas they were infected only four days before being fed to the dogs in Warren’s experiment. It can be assumed that four days is too short for developing the stage of maturity that is responsible for direct development in the intestine of the dog after ingestion.
Publishing different conclusions of similar experiments without giving possible reasons such as the time of infection of the fed mice can create confusion. The paratenic route seems to play a significant role in certain wildlife populations like foxes (81) and might be of importance for hounds (8). In cats infected with *T. canis*, disseminated eosinophilic and granulomatous disease with marked pulmonary artery and airway lesions as a visceral larva migrans (VLM) like syndrome was seen (83).

**Clinical symptoms, haematological findings and pathology**

The clinical symptoms depend on the age of the animal and on the number, location and stage of development of the worms. *Toxocara* infection is highest in puppies (94, 108) and kittens up to 6 months of age (96, 109).

**Dogs**

**Puppies**
Prenatal infection of puppies is suggested to be responsible for stillbirths and early deaths (94), but this has never been reported in other studies. After birth, puppies can suffer from pneumonia associated with the tracheal migration and die within 2 to 3 days. At an age of 2 to 3 weeks, puppies can show emaciation and digestive disturbances, caused by mature worms in the stomach and intestine. Diarrhoea, constipation, vomiting, coughing and nasal discharge can be found at clinical examination. Distension of the abdomen (‘potbelly’) can occur, probably as result of gas formation caused by dysbacteriosis. Mortality is possible due to obstruction of the gall bladder, bile duct, pancreatic duct and rupture of the intestine (81). After superinfection with *Toxocara* the eosinophil count is raised with a peak on the 8th day that may last for more than 50 days. The average peak level was indicated as high (0.5 - 1 x $10^9$), but this falls between the limits (0.1 - 1.25 x $10^9$) and cannot be considered as an eosinophilia. The rise in eosinophils was suggested to be indicative of an allergic reaction by the host (76).

**Adult dogs**
A low infection rate of patent *T. canis* infections of adult dogs is the reason that clinical symptoms are rare. During somatic larval migration, dogs seldom manifest signs of clinical
disease (9). Migrating larvae induce high levels of liver enzymes (AST, ALT) with a peak 3 days after infection with embryonated eggs. The total IgG levels in serum double during 20 days post infection and lymphocyte responses to T-cell (phytohem agglutinine, PHA) and T and B cell (pokeweed mitogen, PWM) mitogens have been markedly suppressed for at least 10 days (99). The larval titre, established by the ELISA test using TES (*Toxocara* excretory-secretory) antigens, and the number of eosinophils increase (111). Larval migration to the eyes (OLM) of *T. canis* larvae is described (45, 55).

**Cats**

**Kittens**
The situation in kittens is different from puppies, because primary infection is only by transmammary infection. Kittens are older when worms are maturing (adult from day 28 and egg producing from day 49 after birth); tracheal migration with related symptoms is not present. Therefore, kittens have a better chance to grow and in the meantime develop better bodily condition before problems may be seen. For this reason clinical symptoms similar to those in puppies are usually inapparent and occur at an older age than in puppies.

**Adult cats**
The cat with more severe intestinal infections can show a potbelly, rough coat and signs of dehydration in cases of diarrhoea (42). Parsons et al. (82) described a disseminated granulomatous disease caused by migrating *T. canis* larvae in a cat; this can be assumed to be comparable with a *T. cati* infection.

**Diagnosis**

**Patent infections**
Patent *Toxocara* infection in dogs and cats can be tentatively diagnosed from the medical history, particularly the use or otherwise of an appropriate anthelmintic schedule, and the clinical symptoms. Confirmation of the diagnosis can be obtained by finding dark brown coloured eggs with thick pitted shells in faecal samples. The direct faecal smear technique is not a sensitive test and generally should never be used for recovering eggs from faecal samples (61). Examination of faeces by a floatation technique is a useful method for detecting helminths (42). The specific gravity of floatation solution should be at least 1.18 and
centrifugation is preferred (22). The specifications of the floatation test for finding *Toxocara* eggs were calculated as 51% for the specificity, a sensitivity of 100%. The predictable value of a positive test is 100% and 81% for a negative test (79).

**Non patent infection**

The ELISA test, using TES antigens, is described as a sensitive technique for determining whether or not a bitch is carrying somatic larvae (91).

**Methods of control**

**Preventive measures**

There are two reasons for *Toxocara* control; to prevent human infection and to reduce the risk of infection to pets. *Toxocara* eggs are very resistant to adverse environmental conditions and remain infective for years. Since no practical methods exist for reducing environmental egg burdens, prevention of initial contamination of the environment is the most important tool. This can be achieved by taking measures such as eliminating patent infections in dogs and cats, preventing defecation by pets in public areas, hygiene, and education of the public (77, 37).

**Prevention of contamination of the environment**

High degrees of environmental contamination can be expected in places where dogs and cats are concentrated such as training schools, animal shelters and breeding kennels (49). No correlation could be established between pet ownership and the presence of *Toxocara* spp. eggs in suburban gardens (84). Household garden soil was found to be a potentially greater source of *Toxocara* infection than soil in public green areas (43).

A decrease in contamination can be achieved by methods including: restriction of uncontrolled dogs and cats, cleaning up faeces from soil and on pavements by dog owners, preventing access of dogs and cats to public places (especially children's playgrounds) and by use of strategic anthelmintic treatment of dogs and cats with emphasis on puppies, kittens, nursing bitches and queens (58, 90). *Toxocara* eggs are not destroyed by composting and can survive sewage treatment (65).

A complicating factor in the prevention of environmental contamination is the presence of infected wild and stray canines and felines. In Europe the wild fox is nowadays more common in urban areas and stray cats are familiar in every neighbourhood (87). In surveys in the
Netherlands, foxes (12) and stray cats (79) were found to be heavily infected with *Toxocara* (74% *T. canis* and 21% *T. cati* respectively). Stray dogs in Switzerland were found to be infected with *Toxocara* in 17% of cases (21). A high prevalence (75%) of stray dogs infected with *T. canis* is reported from the Slovak Republic (24).

**Anthelmintic treatment strategy**

The most serious and concentrated source of infection is the bitch nursing a litter and puppies aged between 3 weeks and 6 months (49). A major aim of long-term prophylactic treatment programmes is to suppress *T. canis* egg-output throughout the whole of puppyhood using a multidose schedule (51). Anthelmintic treatment should be started before the age of 3 weeks. Because milk transmission occurs continuously for at least 5 weeks post partum, repeated treatments are necessary. Larvae that reach the intestine need at least 2 weeks to mature and start passing eggs, therefore the treatment should be repeated every 14 days.

Re-infection can occur throughout the suckling period (30) and treatment should at least be continued until the time when the last larvae arrive through the milk in the puppies’ intestine at 7 weeks of age (8). Bitches should always be included in the treatment at the same time as the puppies.

Advice regarding the initial anthelmintic dose for kittens can cause confusion, because prenatal infection does not occur in kittens and egg excretion begins later than in puppies (96). Therefore, preventive treatment in kittens can usually be instituted effectively at 6 weeks of age.

Control in older dogs and cats can be achieved by periodic treatments with anthelmintics whose efficacy can be limited to the intestinal stages, or by treatments prescribed based on the results of periodic diagnostic faecal examinations (5).

In the Netherlands the following schedule to prevent egg output is advised: puppies should be dewormed every two weeks from 2 to 8 weeks of age and kittens from 4 to 8 weeks of age, followed by treatments every 2 months until 6 months of age. Nursing bitches and queens should be treated concurrently with their puppies and kittens respectively and every other dog and cat twice a year. This advice corresponds closely with the ‘Recommendations for Veterinarians’ of the American Association of Veterinary Parasitologists in 1994. Similar programmes were previously described in 1978 (58, 85).

*Efficacy of anthelmintics against the adult stage of Toxocara*
Lower efficacy values of anthelmintics were found in puppies and kittens suffering diarrhoea which is often caused by the stresses of weaning, change of diet and moving to a new environment.

The rate of passage of ingesta through such very small animals may influence the efficacy of the anthelmintic and therefore repeat dosing is advised as a single dose may not always give the desired effect (51, 67, 102).

Even daily treatment of young dogs, in combination with weekly application of infective *T. canis* eggs to simulate natural continuing exposure, could not prevent egg output in all animals (69). Monthly (ivermectin, milbemycin) or daily administration (DEC/oxibendazole) of anthelmintics in lower dosage in a heartworm prevention schedule were found to provide optimal suppression of *T. canis* egg counts (86).

Despite voluntary anthelmintic treatment of dogs by owners, patent infections of varying incidence are found in every survey among dogs and cats; it can be concluded that this has only a limited practical efficacy in the control of toxocarosis in dogs, cats and humans (7). Experimental treatment of patent *Toxocara* infections in dogs revealed high efficacy rates (17, 51), but the same treatment in practice often showed lower efficacy. It is not known whether the treatment itself is inefficacious or re-infections are more frequent (8). Anthelmintic resistance of *Toxocara* has not been reported to date, in contrast to some parasites in ruminants and horses (20).

More trials with anthelmintics under field conditions are therefore required to provide a comparison with experimental results, although it would be difficult to find a reliable source of animals with patent infections. Puppies can be used more easily for this purpose since all are born infected with *T. canis*; much more still needs to be elaborated regarding the efficacy of anthelmintics in unweaned puppies (46). Guidelines have been designed for studies for the assessment of the efficacy of drugs against helminth parasites of dogs and cats (52).

**Efficacy of anthelmintics against somatic larvae**

Elimination of the larvae from the tissues and therefore prevention of vertical intrauterine and transmammary transmission would have a significant effect on the parasite population (56). Deworming of bitches during pregnancy is sometimes advised in anthelmintic schedules (40), but this advice is questionable. Efficacy of anthelmintics against somatic larvae in experimental animals (mice) and bitches (not in queens) has been intensively investigated.

In a report about the efficacy of anthelmintics in experimentally infected mice (2), it was mentioned that small laboratory animals present difficulties when used for screening of
anthelmintics targeted at domestic animals and human beings, e.g. a certain disproportion in the dose volume related to the digestive tract. In other aspects such as monitoring larval migration, studying histopathological changes and enumerating larvae in the body, small laboratory animals have obvious advantages.

Nicholas and Stewart (70) showed that a four week treatment of mice infected with *T. canis* with fenbendazole at a dose of 20-30 mg/kg per day (starting 10 days after infection) killed almost all larvae, but the same dose over two weeks did not. Furthermore, neither oxfendazole nor fenbendazole were effective against larvae 8 to 12 weeks after infection.

Holt et al. (44) did not demonstrate any significant reduction in larvae in the brains of infected mice when treated for 4 days with high doses of 6 different anthelmintics (piperazine 4 g/kg, mebendazole 0.15-0.3 g/kg, oxfendazole 2 g/kg, albendazole 1 g/kg, fenbendazole 2.5 g/kg and diethylcarbamazine 0.2 g/kg) starting directly after infection or at 19 days later.

To investigate if the blood-brain barrier may be preventing anthelmintics from reaching the CNS in effective concentrations, mice were treated with fenbendazole and flubendazole at various intervals after experimental infection. The larvae in brain and muscles were equally vulnerable to the drugs and it was concluded that the brain of mice does not seem to provide a site facilitating survival of larvae during anthelmintic treatment (56).

A deworming schedule of the pregnant bitch with fenbendazole (50 mg/kg/day), starting at the 40th day of pregnancy until the 14th day postpartum resulted in an 89% decrease of *T. canis* in puppies (15, 59). If the treatment schedule was stopped on the day of parturition, only a 64% reduction of *T. canis* could be established (15).

Bosse and Stoye (13) obtained larvae-free puppies when bitches, experimentally infected with 20,000 *T. canis* at D0 of pregnancy, were treated with albendazole, fenbendazole and oxfendazole at a dose of 100 mg/kg per day from the 30th day of pregnancy until parturition. Fenbendazole or albendazole at a dose of 150 mg/kg/day for 3 days, showed a reduction of somatic larvae from the tissues other than the brain (see also Holt, 1981) of non-pregnant bitches by more than 95% (64). The dogs in this trial were between 7 to 9 months of age, treated 5 weeks after experimental infection with *T. canis*, and examined at post mortem 4 weeks after treatment. It was concluded that administration of these benzimidazoles before pregnancy might be helpful in the prevention of prenatal transmission of *T. canis* to future litters, but it will not prevent transmission of infection if the bitch acquires a new infection during pregnancy or early lactation. This finding is remarkable and in contrast with the opinion that only larvae activated during pregnancy are susceptible to the action of anthelmintic drugs, particularly during migration from the granuloma (56, 81). As in several
other studies, the dogs were treated at a stage relatively early after infection which cannot be considered to be comparable with naturally infected dogs.

The influence of the time of experimental infection in relation to the efficacy of the treatment was also indicated by the results from a three day treatment of mice with benzimidazoles at a dose of 100 mg/kg per day (101). Treatment at 90 days after experimental infection showed a reduction of one third of the larvae, while at D120 no significant reduction could be established.

Early (at D25 and D35) and late (at D45 and D55) treatment of pregnant bitches, also experimentally infected at D0 with *T. canis* eggs, with 0.3 – 1.0 mg/kg ivermectin (not approved for this use) resulted in 34% and 94% reduction of adult *Toxocara* worms in the intestine of the puppies respectively (59). In both treatment groups the egg output was still high in the offspring. In another study bitches, experimentally infected at D0 of pregnancy, were treated with 2 injections of doramectin (not approved for this use) at a dose of 1 mg/kg at D40 and D55 of pregnancy. The treatment did not eliminate somatic larvae in the bitch and did not completely prevent perinatal infections with *T. canis* (92). In all puppies egg output started at D28 after birth, but the puppies from treated bitches had lower egg counts. Four of the 5 treated litters and the control litter showed intestinal stages post mortem.

Only complete prevention of intra-uterine and lactogenic infections can be regarded as effective, because even puppies with a low infection rate will contribute considerably to the contamination of their environment with *T. canis* eggs (92). Anthelmintics at the recommended doses are not effective against inhibited somatic larvae (26) and treatment of bitches before mating and two weeks before the anticipated whelping date has no useful effect on prenatal transmission (30). Therefore it is not advised to deworm pregnant dogs and cats, but repeat dosing during puppyhood is a necessity (10, 30, 64). Furthermore, long and precise treatment schedules during pregnancy are not compatible with practical use because of considerations such as expense (7) and the risk of toxic side effects on the foetuses. After treatment of bitches during pregnancy (100 mg/kg albendazole, fenbendazole and oxfendazole from D30 of the pregnancy until birth) low birth rates and palatoschisis (albendazole and oxfendazole) were reported (13).

In relation to the reported efficacy of anthelmintics against somatic larvae, an important restriction should be considered. Swerczek (1971) investigated the transmammary passage of *T. cati* in the cat and found a marked difference between the yield of larvae from tissues in queens killed with sodium pentobarbital (low yield of nonviable larvae) and ether (high yield and viability). He concluded that sodium pentobarbital or similar drugs kill or immobilise the
larvae and should not be used when Baermannized tissues are examined quantitatively for larvae. In studies, published after 1971, in which larvae were recovered to determine influences on somatic larvae, the way of euthanasia of the experimental animals is seldom described (2) and in the majority of the reports omitted (13, 64, 70, 92, 101). This can therefore be ultimately a confounding factor for the results.

**Immunisation**

Any method of effective control should destroy *T. canis* in the reservoir provided by the tissues of adult hosts. As described before, the dormant hypobiotic larvae are highly resistant to anthelmintics. Therefore an anti-parasitic activity is required that can destroy activated *T. canis* larvae as well as newly acquired infections. Ongoing administration of anthelmintics is neither a practical nor a reliable solution. Immunisation on the other hand, is inherently long-lasting and more potent (7).

Immunisation of mice with *Toxocara* larval extracts or metabolic excretion/secretion products showed a certain level of immunoprotection and it was concluded by Barriga (7) that an effective anti-*T. canis* vaccine could be expected in the future.

Vaccination of mice using ultraviolet irradiated embryonated *T. canis* eggs showed the best protection after re-infection, while ES-antigen afforded less protection and whole adult worm vaccine and whole L2 culture vaccine gave no protection (3).

Oral or parenteral immunisation of mice on three or more occasions with *T. vitulorum* eggs induced significant protection against challenge doses of eggs. The most effective were three or more injections with peri-enteric fluids from adult worms, inducing 100% protection (4). Differences in the immunogenicity of the parasite species might account for differences between results as well as the immunisation regimes and adjuvants used.

**Hygiene.**

For dogs and cats hygiene can be achieved by removing the faeces (89, 100) and thorough cleaning of kennels (95). *Toxocara* eggs are highly resistant to a wide range of chemicals, but are killed by ultraviolet light, aqueous iodine and high temperatures. It is advisable to start cleaning kennels with a 20% solution of commercial bleach (1% sodium hypochlorite). This does not kill the eggs, but removes their sticky outer protein coat. These decorticated eggs are then easier to remove from inaccessible areas (32, 81). On the other hand, the infectivity of eggs treated in this manner will rise significantly and higher recovery rates are found in infected animals compared with situations in which the outer layer is left intact (74). Finally,
expulsed worms should be destroyed and predation and scavenging on carcasses by dogs and cats should be prevented.

**Education.**

Dog and cat owners can help to avoid contamination of the environment with *Toxocara* eggs and the exposure of other persons to unnecessary risks of *Toxocara* infections. Proper information about this zoonosis and the social concept of responsible pet ownership is required. Pet owners should be advised about deworming schemes, effective anthelmintics and to prevent their animals from defecating on children’s playgrounds (53).

The important role that the veterinarian can play in this education process was described in 1980, when the American Veterinary Medical Association adopted the following resolution concerning *Toxocara* infection: ‘The AVMA recommends that veterinary practitioners conduct appropriate client information programs with the goal of reducing the prevalence of infection in pet dogs and minimising the potential of transmission to human beings’ (6). It is recommended that information disseminated to pet owners should include the following:

- A description of *T. canis* and *T. cati* and how they affect their hosts;
- A description of prenatal and transmammary transmission;
- An explanation of how *Toxocara* can be transmitted to and produce damage in humans;
- An explanation of how prevention can most effectively be achieved;
- Information on how pet owners should routinely collect and safely dispose of their pets’ faeces, especially from children’s play areas;
- Advise children not to play in potentially contaminated environments (5).

Although veterinarians should be the most appropriate sources of information for their clients regarding the dangers and the control of toxocarosis, several surveys (41, 57, 78) have demonstrated that client education on this issue is lacking.

**Treatment of patients**

When a patent *Toxocara* infection is diagnosed in dogs and cats, worms should be removed by treatment with an effective and larvicidal anthelmintic with a low toxicity. In the Netherlands, benzimidazoles (fenbendazole, flubendazole, mebendazole, oxfendazole and oxibendazole), probenzimidazoles (febantel), pyrantel, levamisole and (only for dogs) nitroscanate are registered for this indication. Benzimidazoles have in general significant larvicidal effects (2, 46) and are virtually without toxicity at therapeutic dose rates (11, 29, 107). Piperazine, nitroscanate, levamisole and pyrantel are not efficacious against immature
worms and should be used routinely in adult animals only (14, 29, 46, 67). Levamisole is fairly toxic, especially in cats and an injectable formulation should never be used (11). Most anthelmintics for dogs and cats are evaluated in adolescent or adult dogs (50), but the most important treatments are those administrated to suckling puppies and young kittens. Due to concomitant physiological changes and the complexity of the host-parasite relationship, it is important that anthelmintics intended for control of *T. canis* and *T. cati* should be evaluated by means mimicking as nearly as possible conditions of field usage (51). If the efficacy of anthelmintics is evaluated by post mortem worm counts after treatment, high efficacy values can be obtained even when less potent compounds are used. This can give a false sense of security as they provide no information about the ante mortem faecal egg-output (46). It can result in marked differences, e.g. in one study the worm burden had been reduced by 86.2% following treatment with piperazine, but the egg-output, when compared with that of untreated controls, was hardly suppressed at all (30). In addition to the population dynamics of *Toxocara* (somatic migration of larvae at the moment of deworming and re-infection throughout the suckling period), there are other considerations that must be taken into account which necessitate repeated administration after 10 to 14 days on at least one occasion in adult animals and several times in juveniles (46, 64, 81). These considerations include: the different intestinal physiology of the unweaned puppy, the influences on the efficacy of anthelmintics such as diarrhoea (increased intestinal passage) and the fat contents of the bitches’ milk.

**Acknowledgements**

I thank prof. dr. A.W.C.A. Cornelissen, prof. dr. F. van Knapen and dr. J.H. Boersema at the Faculty of Veterinary Medicine, Utrecht University; prof. dr. L. Glickman at the School of Veterinary Medicine, Purdue University, West Lafayette, Indiana, U.S.A. and dr. C.W. Taylor of Virbac U.K for their helpful comments on this manuscript.

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