
Drontal®

Nematocide and Cestocide for cats

Product information

International Edition

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Important note

This product information on Drontal is based on the available results of controlled international studies. User information is to be found in the instructions for use contained in the Drontal package inserts which have been approved by the regulatory authority.

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General observations

Worm infections continue to be a major problem in farm livestock and companion animals worldwide, as well as in man. A number of worms have adapted to particular species of farm or companion animals. Worm infestation is determined by factors such as geographic location, climatic conditions, the season and – equally importantly – the animals' living conditions. In most countries, farm livestock are dewormed regularly in order to avoid shortfalls in performance and the resulting economic losses.

In companion animals such as dogs or cats, on the other hand, control measures are often inadequate. The main reasons are a lack of awareness of the problem, a poor selection of products, and infrequent use. This is highly regrettable because hygiene is particularly important in this area in view of the often very close relationship between man and companion animals. Worm-infested dogs and cats constitute a major hygiene and health hazard, especially for children.

In the industrialised countries alone there are 100 million dogs and over 110 million cats – a considerable reservoir of potential worm infections.

The worm problem in cats

Roundworms (Nematodes)

Nematodes (Greek: nema = thread) are thread-shaped worms. Their body is tapered at both ends. The length of the adult worms ranges from 1 millimetre to 12 cm, depending on the species. All nematodes possess a stable, elastic cuticle and a complete digestive system. This begins with a buccal capsule which serves both for feeding and in some species also for attachment to the intestinal wall. Nematodes feed on chyme or intestinal contents of the host and on the host's body substance such as epithelial cells, mucosa or blood. The sexes are separate. The males are usually distinguishable from the females by their smaller size. The accessory organs (such as the copulatory bursa) of the reproductive system, and especially the buccal capsule and the form of the oesophagus are important features in species identification.

The number of eggs passed from each female worm can be very high, up to 200,000 eggs daily. The duration of the prepatent period (Period from infection of the animal to the appearance of the parasite's eggs.) also varies considerably.

The eggs pass to the exterior in the faeces of the host. There the larvae hatch and become infective after several moults. In some species larval development takes place inside the egg, i.e. embryonated eggs constitute the invasive stage. After infection of the host and further moults the adult worm stage is reached. At this time the larvae often migrate through various tissues

and organs of the host, and therefore cause severe damage during their development. A special phenomenon in some nematodes is hypobiosis – a state of arrested development of the final larval stage. It is initiated by external stimuli acting upon the infective larvae (e.g. low temperatures, drought) or by immunological and hormonal processes in the body of the host, although the nature of this phenomenon is not yet completely understood (multifactorial). These dormant larvae play a major role in the transmission of helminth infections from the queen to the kittens (transmammary infection).

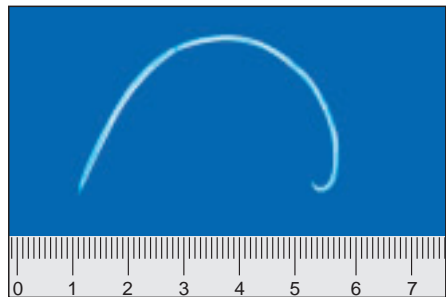


Fig. 1: *Toxocara cati*

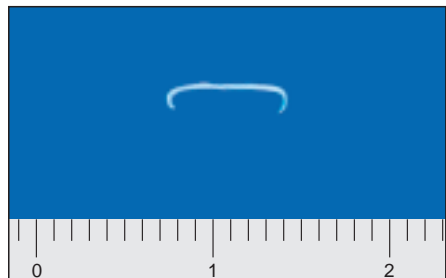


Fig. 2: *Ancylostoma tubaeforme*

Tapeworms (Cestodes)

Cestodes or tapeworms owe their name to the flat, tape-like body shape. These worms parasitise the small intestine of the definitive hosts. The body of the tapeworm consists of the head (scolex) which is designed as an attachment organ, an unsegmented neck and the segments (proglottids) which continually renew themselves. The entire chain of segments (strobila) can be up to several metres long, although some tapeworm species are only a few millimetres long. Each proglottid is an independently functioning unit. Feeding takes place through the body surface. Almost all tapeworm species are hermaphrodite. Each proglottid harbours a complete set of male and female reproductive organs. As the segment matures it is shed intact, packed with eggs. New segments are continuously formed from the neck to replace the mature proglottids that have been expelled.

Tapeworms are of importance in veterinary medicine as well as in human health, both as adult worms and in the larval form (cystic stage, metacestode). Their development proceeds indirectly via one or several intermediate hosts. In the Cyclophyllidea the hooked larva inside the egg (onchosphere) develops in the uterus of the tapeworm segment. The egg containing the hooked larva is ingested by an intermediate host. If the intermediate host is a mammal the hooked larva penetrates the gut wall and is distributed throughout the body via the blood and the lymphatic system. In certain organs (predilection sites) of the intermediate host it develops into an infective cysticercus. This cysticercus, which already contains the rudiments of the scolex, is ingested by the definitive host (dog, cat) when eating the raw flesh of the intermediate host. Inside the intestinal tract of the former, the scolex is evaginated. It attaches itself to the intestinal mucosa and the tapeworm develops to adulthood.

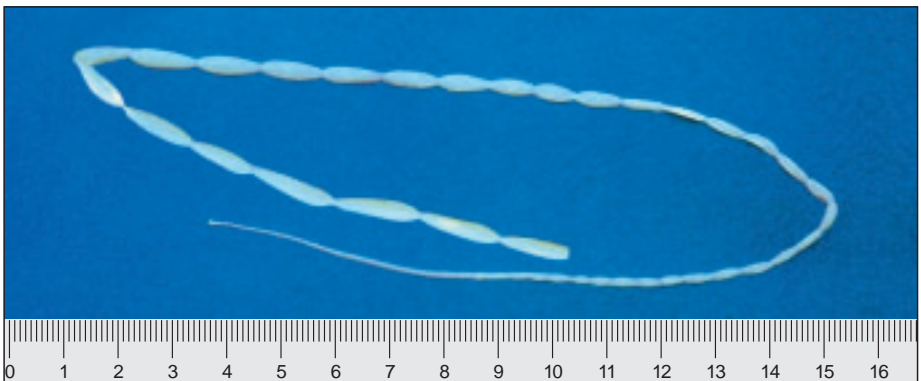
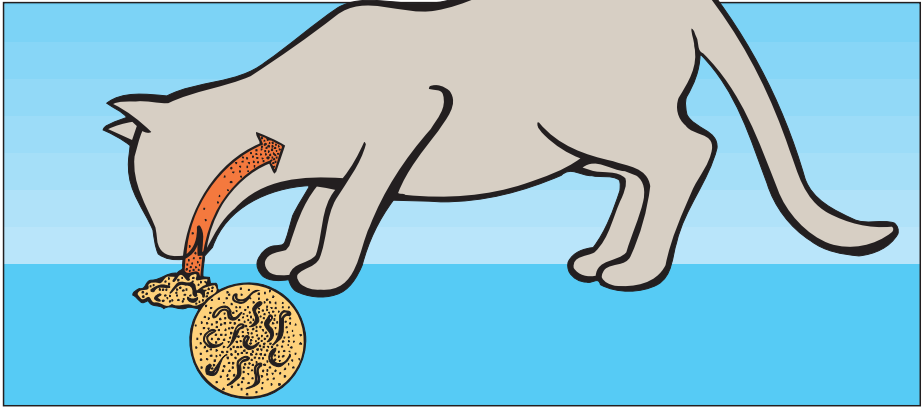


Fig. 3: *Dipylidium caninum* is the most common tapeworm in cats

Routes of infection

Oral infection

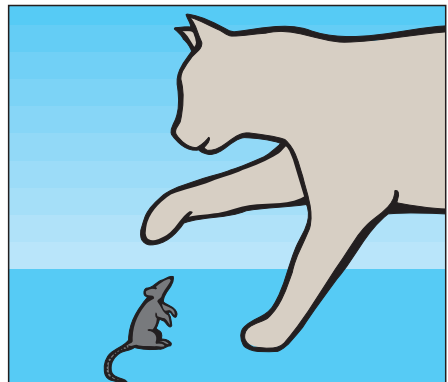
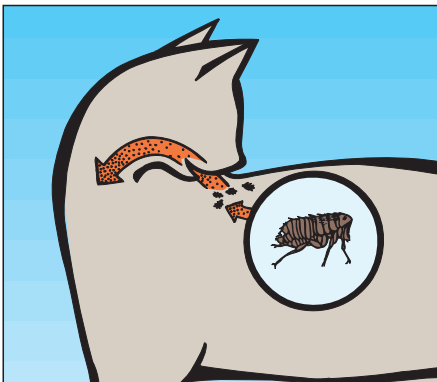
1. By direct ingestion of infectious eggs (ascarids) or infective larvae (hookworms).



2. By eating infested hosts.

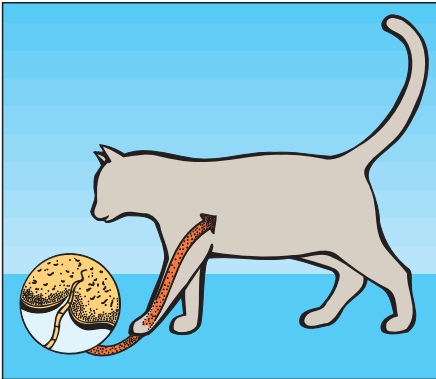
Ingestion of infested fleas is the common route of infection in cats with *D. caninum* (tapeworm). Ingestion of infested paratenic or intermediate hosts (mice, birds ...) is an

important route of infection in cats with roundworms (ascarids, hookworms) and also with the majority of tapeworms.



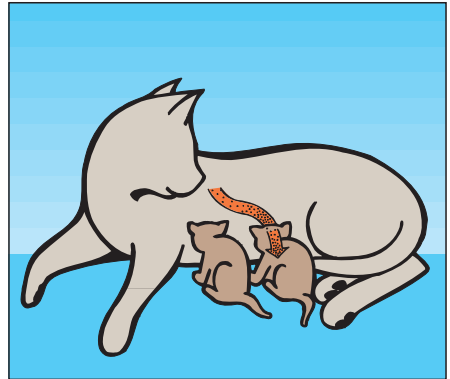
Percutaneous infection

3. By active larval invasion through the healthy skin of the definitive host (hook-worms)



Transmammary infection (post partum)

4. By remobilisation of dormant larvae from the tissues of the queen, which migrate via the bloodstream into the mammary gland. The kittens become infected during sucking. (ascarids)



Damage to health in cats

The damaging effects of the worms in their host are extremely variable. The pathogenic alterations, either singly or in combination, can give rise to organic disorders with a wide variety of clinical symptoms.

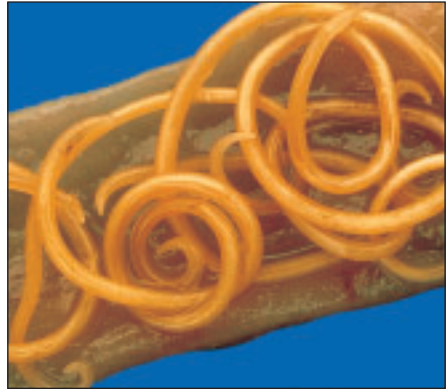


Fig. 4: *Toxocara cati* in the intestine

Main damage observed in infested cats	Causes
1. Mechanical damage to tissues	Due to the migration of the larvae through the organism (for example: skin lesions after percutaneous infection with <i>Ancylostoma tubaeforme</i>)
2. Obstruction of the gut and the bile ducts	Caused by massive roundworm infestation (for example: <i>Toxocara cati</i>)
3. Blood loss resulting in anaemia in cases of severe infection (particularly in young infested kittens)	Caused by blood-sucking worms (hookworms)
4. Deprivation of vitamins and other vital substances	Can occur in cases of infection with tapeworms or roundworms
5. Interference with the immune system (compromises the protection afforded by vaccinations)	Can occur in cases of infection with tapeworms or roundworms
6. Loss of condition in the host	Due to release of such substances as enzymes, toxins, hormones.

Clinical manifestations

Depending on their state of health, their resistance and the degree of parasite infestation, infected animals exhibit a wide variety of symptoms:

Dull, rough coat, emaciation, anaemia, distension of the abdomen (pot-belly), impaired fertility, reduced fitness and generally lower resistance and vitality.

Ascarids (roundworms) and other nematodes may cause vomiting in the affected animal.

Hookworms can produce anaemia. The blood loss is greatest 10 – 15 days after onset of the infection. *Ancylostoma tubaeforme* may cause fatal disease in heavily infested kittens.



*Fig. 5: In case of massive infestation, *Ancylostoma tubaeforme* can give rise to an haemorrhagic enteritis*

Routes of infection in man (false host)

Oral infection

In the vast majority of cases humans become infected by ingesting worm eggs. Infected dogs, cats and other companion animals are the most common vectors. They often pass large numbers of worm eggs in their faeces, thus constituting a permanent source of infection.

Potential modes of infection

1. During close physical contact with cats, worm eggs can pass from the animal's fur into the person's mouth (especially tapeworms). The accidental ingestion of a flea harbouring the larvae of *Dipilydium caninum* (tapeworm) can also infect man, and particularly children.



2. Dogs and cats tend to lick people's hands and face, or food intended for humans. They also come into close contact with towels, bedlinen and similar items used by their human owners.
3. Children are at risk from playing in sandpits contaminated with dog or cat faeces.
4. Eating unwashed wild berries can also cause worm infection. Here the fox is involved as a vector of Echinococcosis.



Percutaneous

Hookworm larvae can actively penetrate human skin if there is direct exposure to contaminated sandpits, moist, warm bathing beaches or lawns for sunbathing.



Damage to human health (man as false host)

1. Damage due to *Toxocara* species

The human disease known as Visceral Larva Migrans is caused by larval forms of the dog or cat roundworm.

When infection has occurred the larvae hatch in the upper portion of the small intestine, penetrate the gut wall and migrate to the lungs by the lympho-haematogenic route. Thereafter they enter the arterial blood stream and are spread throughout the body. In the capillary regions the larvae actively leave the vascular system and migrate into the surrounding tissue. Preferred sites for somatic larvae of *Toxocara* spp. in man are the liver, the CNS and the eye, which considerably increases the dangerous nature of such an infection. At the Hospital for Tropical Diseases in London, 20 – 30 cases of eye lesions caused by *Toxocara* spp. are treated every year.

In the USA approximately 10,000 new cases of visceral larva migrans and 700 cases of ocular larva migrans are diagnosed

annually (STEHR-GREEN and Schantz, 1987). According to a survey of ophthalmologists in Alabama, USA, at least one case of ocular larva migrans is encountered in every 1,000 patients (Maetz et al., 1987).

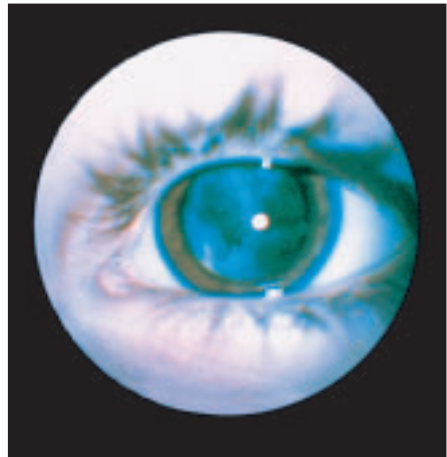


Fig. 6: Leukocoria (white appearance of the pupil) due to retinopathy caused by Toxocara larvae (eight-year-old boy)

Hygienic importance of helminth infections in man		
Worm species	Infective agent	Developmental stage in man
1. <i>Toxocara</i> spp.	Infective eggs	Larvae
2. <i>Ancylostoma</i> , <i>Uncinaria</i>	Infective larvae	Larvae
3. <i>Dipylidium caninum</i>	Cysticercoid in fleas	Adult worm
4. <i>Taenia</i> spp.	Infective eggs.	Cysticercus
5. <i>Echinococcus</i> spp.	Infective eggs	Cysticercus

2. Damage due to hookworms

Cutaneous Larva Migrans is a dermatitis caused by migrating nematode larvae. Mostly this disease is caused by larvae of *Ancylostoma* or *Uncinaria* genus.

Infection of humans occurs through skin contact with larvae. The most common sources of infection are shady, moist and warm sand or soil, contaminated either directly by faeces of infected dogs and cats or indirectly via sewage or effluent containing developmental stages or the causal agents of Cutaneous Larva Migrans. Children are especially at risk of catching the disease in sandpits, on playgrounds and in public parks. Bathing beaches can also be a source of infection.



Fig. 7: Cutaneous Larva Migrans (sole of foot)
(Prof. Seitz)

At the site of penetration reddish, severely itching skin lesions, similar to insect bites appear 2 – 4 days after the infection. A common complication is a secondary bacterial invasion of the affected skin areas which can give rise to purulent eczema.

Larval migration in the skin can be interrupted for many weeks and months only to resume suddenly for some as yet unknown reasons. Small papules form at the resting sites of the larvae.

The diagnosis of Cutaneous Larva Migrans is straightforward because of the pathognomonic symptoms.

3. Damage due to *Dipylidium caninum*

Infection can occur as a result of being licked by a cat which has chewed recently infected fleas or biting lice. When the infective cysticercoids have been swallowed the tapeworm develops in the small intestine to a length of approximately 50 cm. Clinical symptoms in heavy infestation can be abdominal pains, blood-stained mucoid diarrhoea and weight loss. The active emigration of the mature proglottids can cause considerable anal irritation and pruritus.

4. Damage due to *Taenia* species

The larval stages of *Taenia* species have thus far been encountered only occasionally in man. Little is known about the lesions they cause.

5. Damage due to *Echinococcus multilocularis*

Alveolar Echinococcosis is caused by the development of the larvae (hydatids) of *E. multilocularis*.

The hydatid, due to its uninhibited invasive growth, behaves like a malignant tumour which in approximately 98 % of cases affects primarily the liver, but can form secondary “metastases”, especially in the lungs and the CNS. The clinical symptoms resemble those of cirrhosis or carcinoma of the liver.

Improved diagnosis, the possibility of chemotherapy, and advances in surgical techniques have reduced the mortality of Alveolar Echinococcosis from about 95 % within 10 years in the 1960s to about 10 % at present. However, this has not altered the fact that Alveolar Echinococcosis continues to be one of the most dangerous zoonoses for man.

In man the diagnosis is confirmed by serological tests: immunofluorescence, ELISA, indirect haemagglutination and radioimmunoassay.

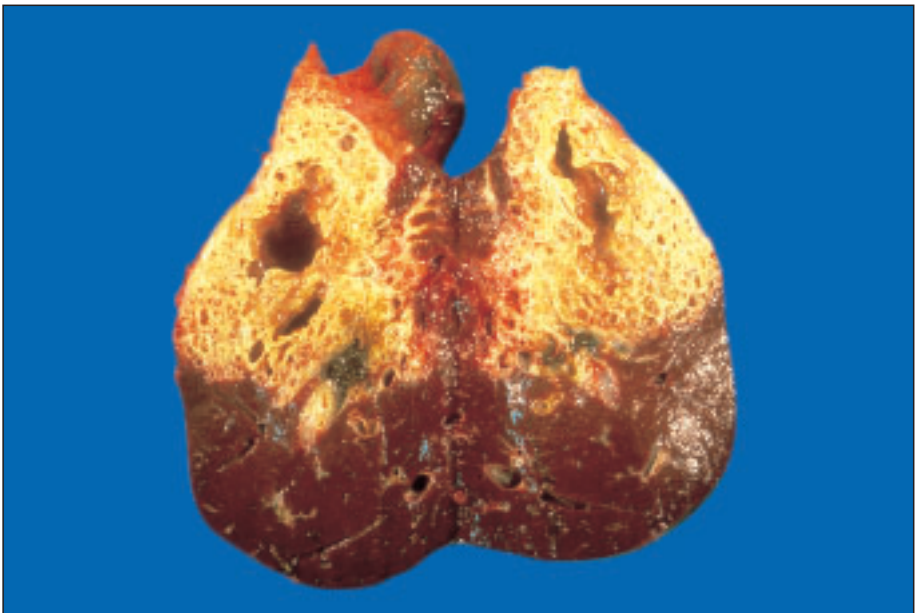
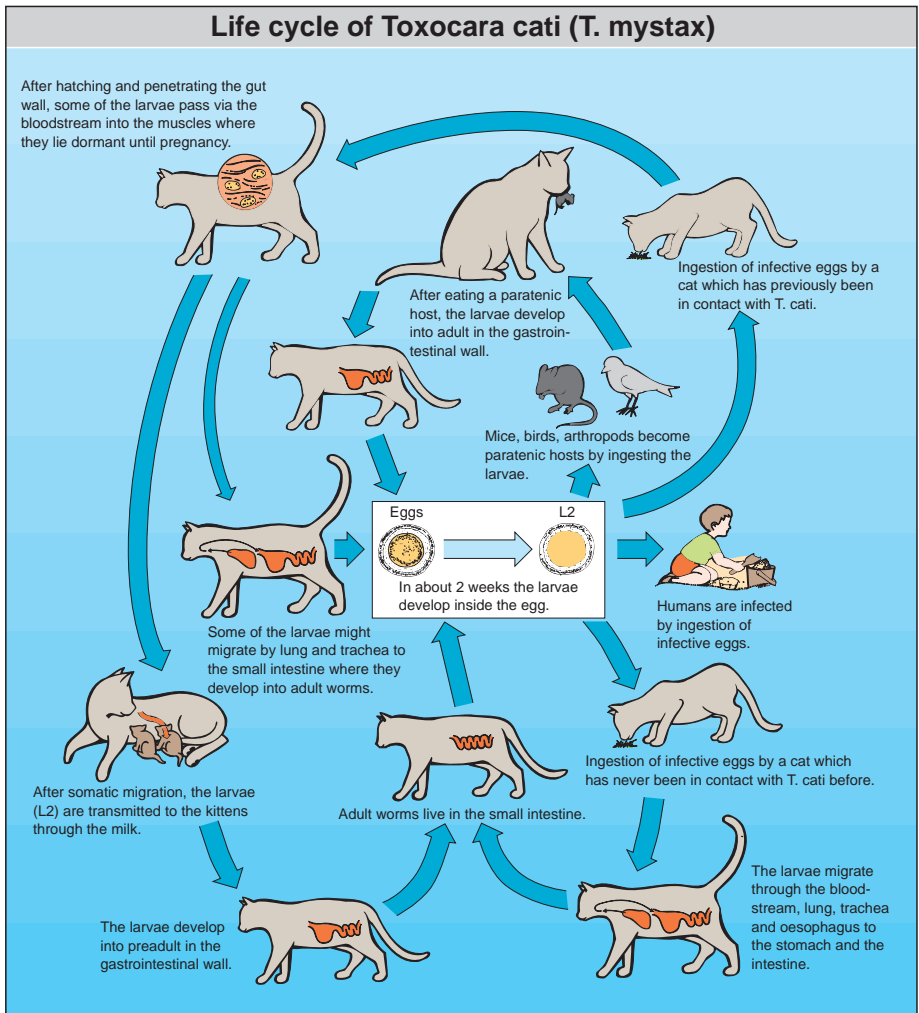


Fig. 8: Appearance of Alveolar Echinococcosis in a human's liver, cut open after hepatectomy. Note the yellowish, fibrous and multilocular aspect of the lesions. (Prof. Vuitton)

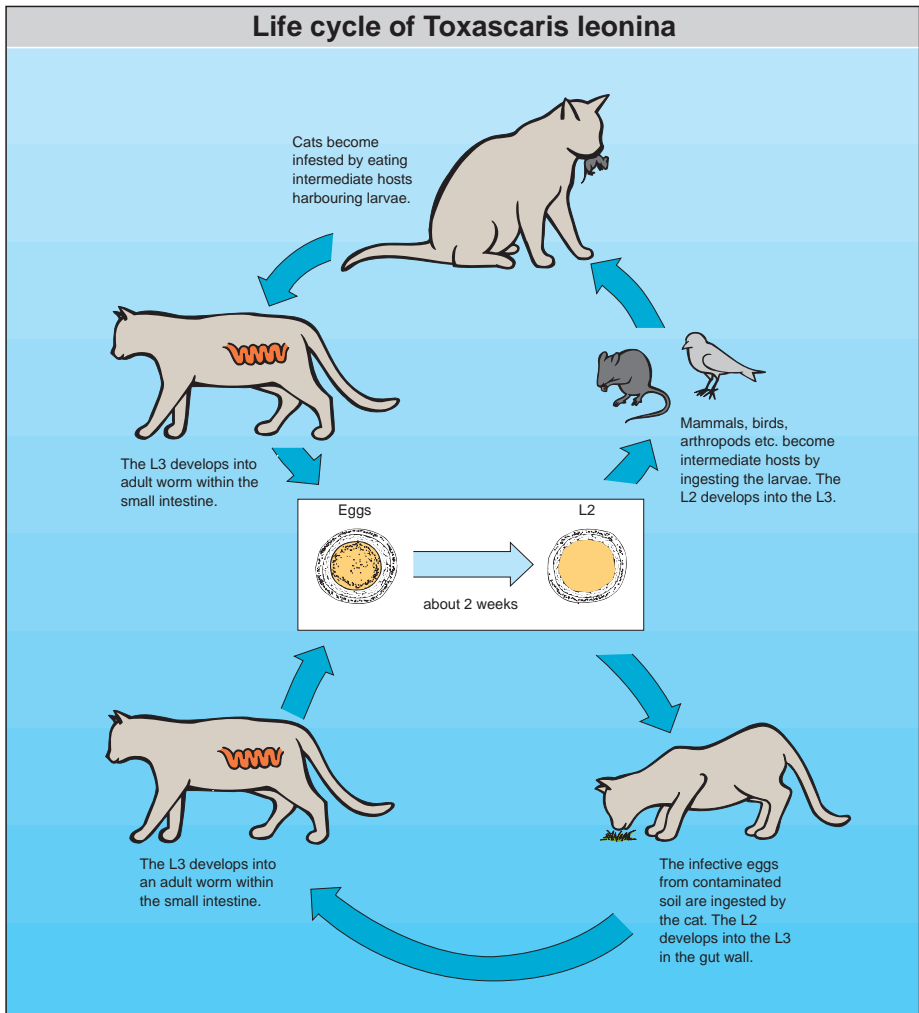
Life cycle of the most important intestinal worms of the cat

1. Nematodes

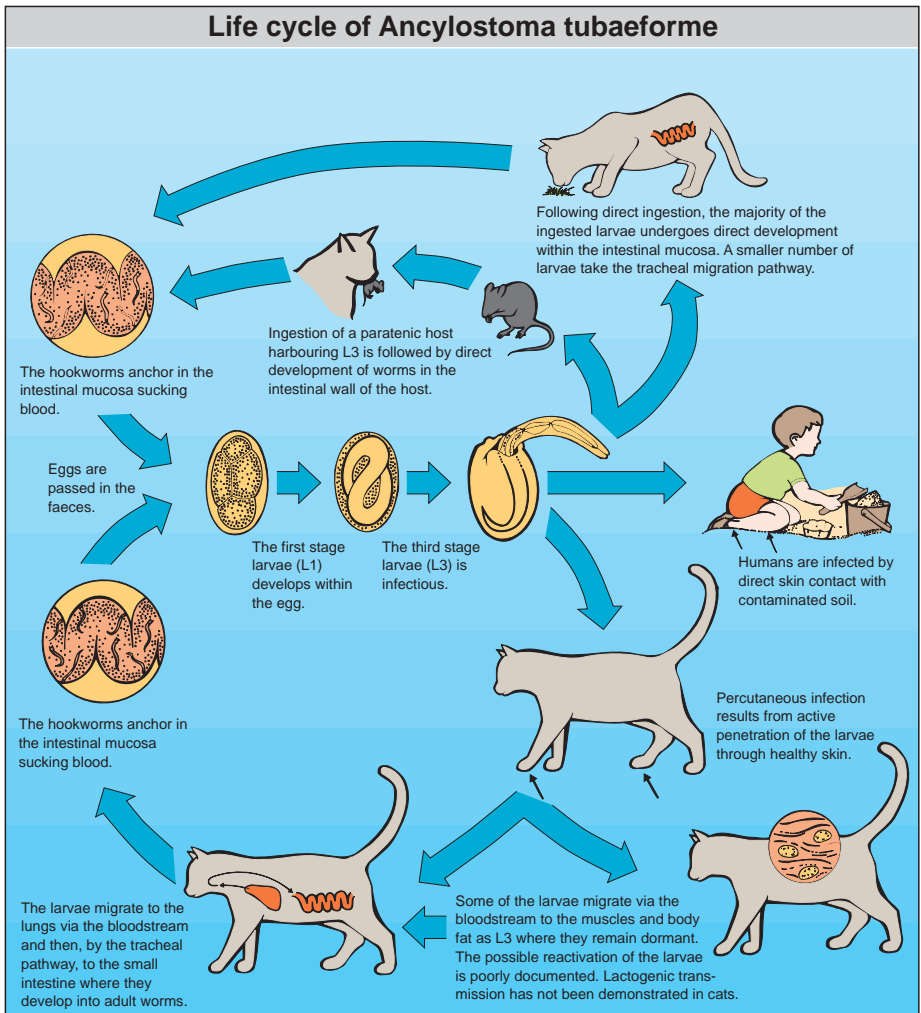
1.1 Ascarids



Ascarids

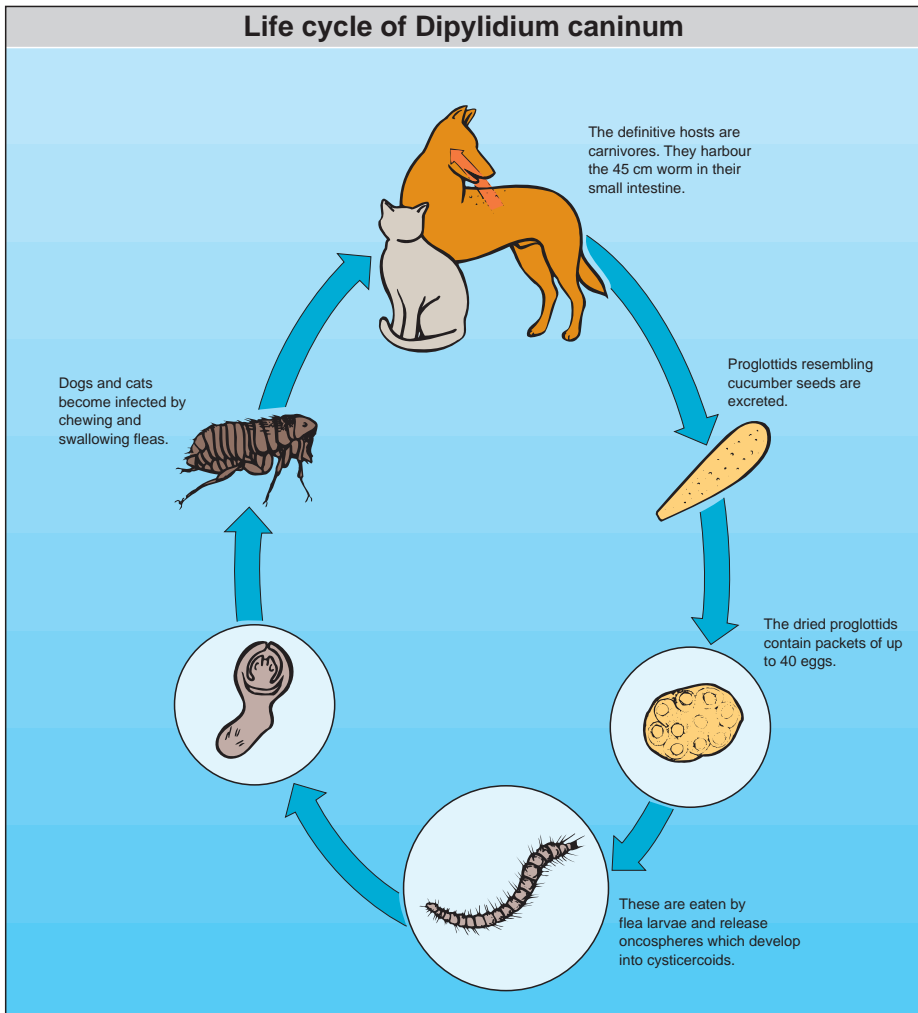


1.2 Ancylostomes (hookworms)

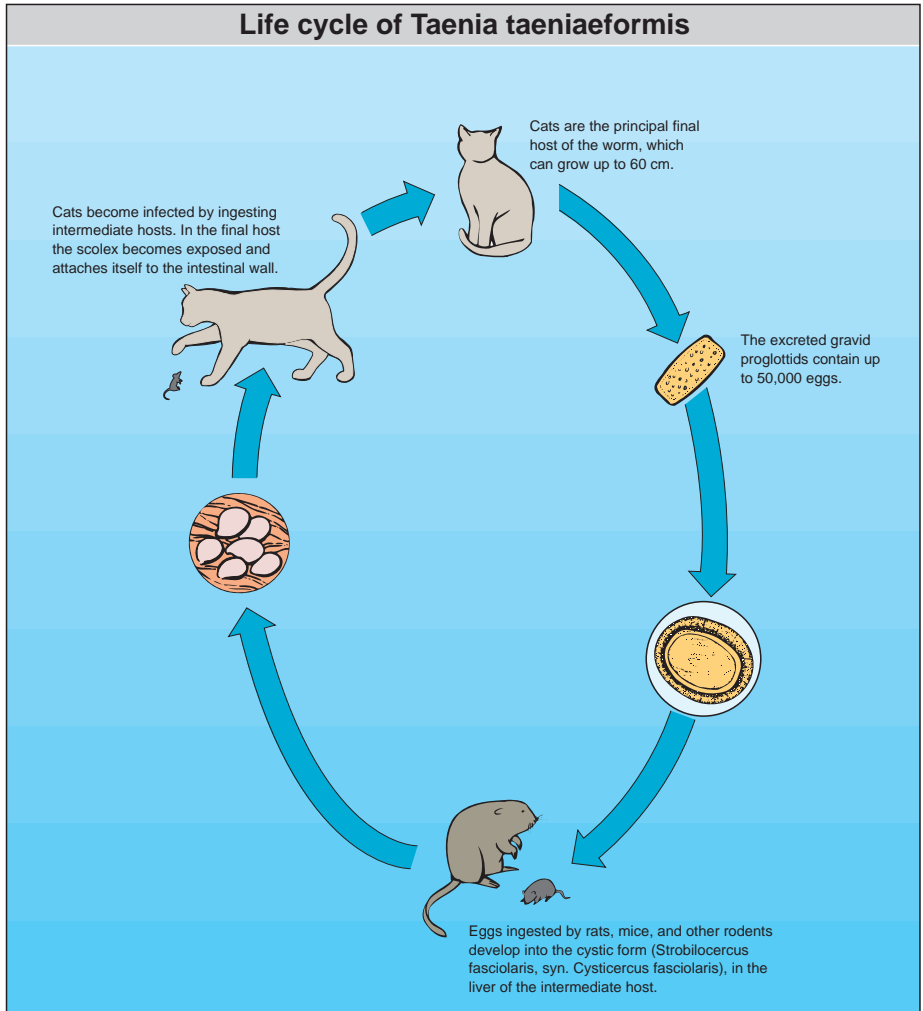


2. Cestodes

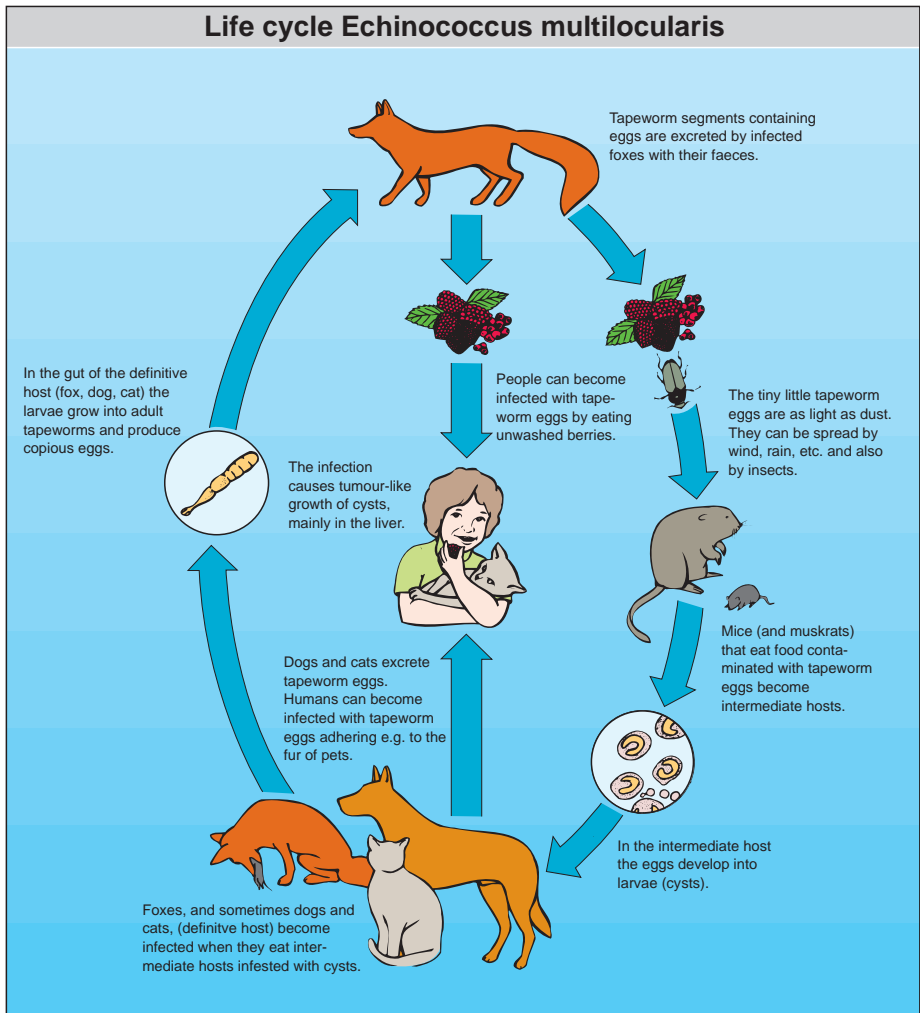
2.1 Dipylidium caninum



2.2 Taenia species



2.3 Echinococcus



Control of worm infections in cats

Diagnosis and prepatent periods

The most commonly practised laboratory method for the diagnosis of helminth infection is the microscopic examination of the faeces. This can only serve as an aid in establishing a diagnosis, however, some inherent weaknesses do exist

- If faecal findings are positive:
The morphological similarity of tapeworm eggs permits no reliable differentiation between extremely dangerous species such as *Echinococcus multilocularis* and species that are less significant in man like *Taenia* spp. and *Multiceps* spp.
- If faecal findings are negative:
Helminth infections during the prepatent period and dormant larvae in the muscles (e.g. of nursing queens) are not detected by routine laboratory tests.

Treatment programmes

The worldwide danger posed by worm infections can only be reduced by appropriate education campaigns and deworming programmes.

In view of the wide variability of the prepatent periods of individual helminth species encountered in the cat (from 2 weeks to 3 months), the unreliability of faecal examinations, and the constant threat of reinfection from the environment (eggs and infective larvae), a policy of routine deworming treatments seems advisable. Cats should therefore be wormed regularly at least 4 times a year.

Treatment programme for kittens:		Treatment programme for adult cats:
Worming	At age of	Worming
1st	2 weeks	● Every 3 months or, if risk of infection is high, at intervals equal to prepatency
2nd	4 weeks	● Queens before mating and 10 days before whelping.
3rd	8 weeks	All subsequent worming treatment at same time as the kittens.
4th	12 weeks	
5th	4 months	
6th	5 months	
7th	6 months	

The most important tapeworms (cestodes) of the cat					
Name	Length (appr. cm)	Host	Intermediate host	Larval stage (metacest.)	Special features
Taeniidae					
Taenia taeniaeformis	15 – 60	cat, dog	Mouse, rat	Cysticercus fasciolaris (Strobilocercus)	Typical cat tapeworm. Metacestode usually in the liver of the intermediate host
Echinococcus multilocularis	0.14 – 0.34	fox, dog, cat	Field mouse, small rodents (man)	Echinococcus alveolaris	Man: Alveolar Echinococcosis cancer-like infiltrative growth; 98 % of the cases in the liver, often fatal
Dilepididae					
Dipylidium caninum	20 – 45	cat, dog	Flea	Cysticercoid	Most common tapeworm species of carnivores, human infection possible
Mesocestoididae					
Mesocestoides lineatus	30 – 250	fox, cat, dog	1. Oribatid mites (suspected but not confirmed yet) 2. Amphibia, reptiles, birds, mammals	1. Cysticercoid 2. Tetra-thyridium	Some of the metacestodes burrow through the intestinal wall of the definitive host, invading the peritoneal cavity or other organs

The most important round- and hookworms (nematodes)						
General name	Scientific name	Length (app. cm)		Host	False or paratenic hosts	Special features
		Male	fem.			
Roundworms	<i>Toxocara cati</i> (<i>T. mystax</i>)	3 – 7	4 – 12	cat	Mice, birds, anthropods (man)	Transmammary and oral route of infection
	<i>Toxascaris leonina</i>	2 – 7	2 – 10	cat, dog	“reservoir” small mammals, birds	
Hookworms	<i>Ancylostoma tubaeforme</i>	0,9 – 1,1	1,2 – 1,5	cat	“reservoir” mouse (man)	Oral and percutaneous route of infection
	<i>Ancylostoma braziliense</i>	0,6 – 0,75	0,7 – 1,0	cat	“reservoir” mouse (man)	Oral and percutaneous route of infection

Prepatent period of the most important intestinal worms of the cat	
Worm species	Prepatent period
Roundworms <i>Toxocara cati</i> (<i>T. mystax</i>) <i>Toxascaris leonina</i>	6 – 8 weeks 3 weeks for galactogenic infection approx. 10 weeks
Hookworms <i>Ancylostoma tubaeformae</i> <i>Ancylostoma braziliense</i> <i>Uncinaria stenocephala</i>	2.5 – 3 weeks 2 – 3 weeks 2 – 2.5 weeks
Tapeworms <i>Taenia taeniaformis</i> <i>Echinococcus multilocularis</i> <i>Dipylidium caninum</i> <i>Mesocestoides lineatus</i>	5 – 11 weeks 4 – 6 weeks 3 weeks 2 – 3 weeks

Drontal Product Profile

1. Active ingredients

Drontal for cats is a broad-spectrum anthelmintic containing a combination of the active ingredients praziquantel and pyrantel embonate.

This combined formulation has the following advantages:

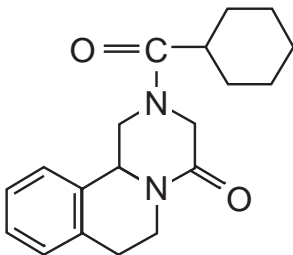
- Comprehensive spectrum of activity (roundworms and tapeworms)
- One administration per worming is sufficient
- Convenient handling facilitates regular use
- Excellent tolerance

Presentation and composition:

1 Drontal tablet for cats contains
20 mg praziquantel
230 mg pyrantel embonate

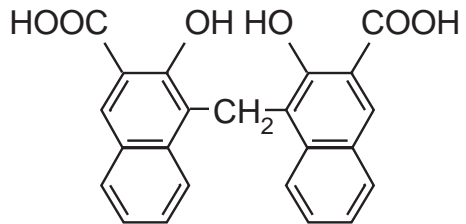
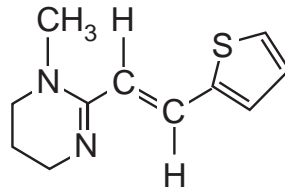
Praziquantel (INN)

2-Cyclohexylcarbonyl-1,2,3,6,7,11 b-hexahydro-4H-pyrazino-[2,1-a]-isoquinoline-4-on (IUPAC)



Pyrantel embonate (INN)

Pyrantel (USAN) (E)-1, 4, 5, 6-tetrahydro-1-methyl-2-[2-(2-thienyl) vinyl]-pyrimidine 4,4'-methylene bis [3-hydroxy-2-naphthoate] 1:1 (IUPAC)



2. Mode of action

Praziquantel

Praziquantel kills mature and immature stages of tapeworms in the intestine after a single treatment.

Within a few seconds of the tapeworm coming into contact with praziquantel its interaction with phospholipids and proteins causes damage to the tegument. The inflow of Ca^{2+} -ions results in an immediate contraction of the entire strobila. Moreover, these changes lead to a reduction of glucose intake and an accelerated depletion of energy reserves.

Pyrantel embonate

Pyrantel, an anthelmintic of the tetrahydropyrimidine group acts by inducing a depolarising neuromuscular blockade. Pyrantel, being a cholinergic agonist, acts as an excitatory neurotransmitter at the nicotinic receptor causing spastic paralysis of the parasite.

3. Spectrum of activity/ Indications

Drontal possesses an extremely wide spectrum of activity which covers infestation with the following cat nematodes and cestodes:

Nematodes

Ascarids

- *Toxocara cati* (T. mystax)
- *Toxascaris leonina*

Hookworms

- *Ancylostoma tubaeforme*
- *Ancylostoma braziliense*

Cestodes

- *Dipylidium caninum*
- *Echinococcus multilocularis*
- *Taenia* spp.
- *Mesocestoides* spp.
- *Joyeuxiella pasqualei*

4. Dosage

1 tablet per 4 kg bodyweight

The tablets are given orally to the animal, preferably concealed in a piece of meat, cheese, or titbit.

No special dietary measures are required either in adult cats or in kittens.

The product is given as a single dose. (administration over several days is not necessary.)

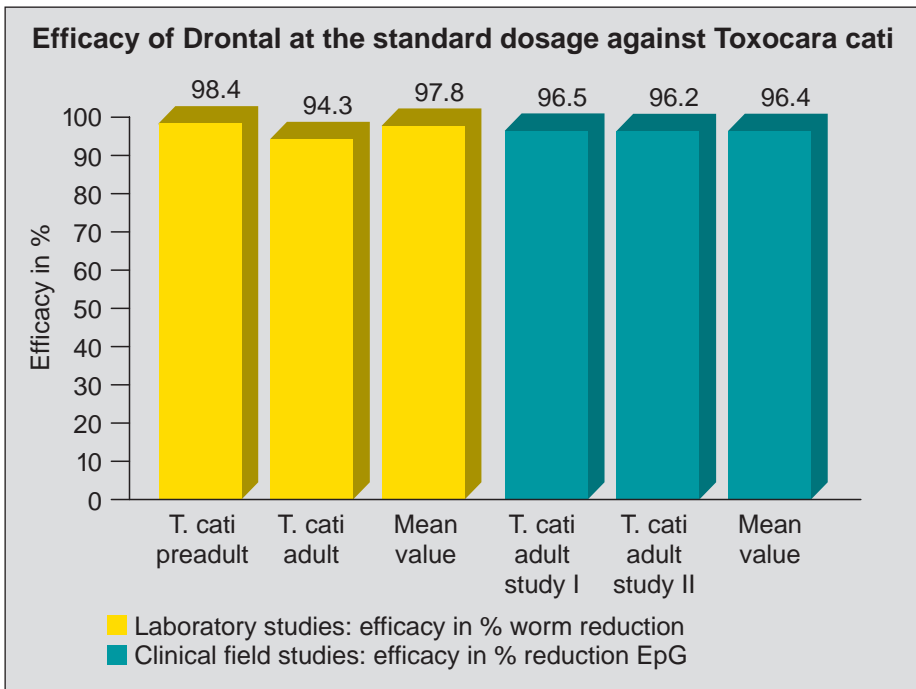
5. Efficacy

Drontal has been tested on a large number of cats of various ages, sexes and breeds. Efficacy was demonstrated on the basis of laboratory studies and field studies (coprological tests: EpG).

5.1 Efficacy against ascarids

Several laboratory and clinical field trials were performed with Drontal, in order to assess the efficacy against ascarids.

The following results were obtained:

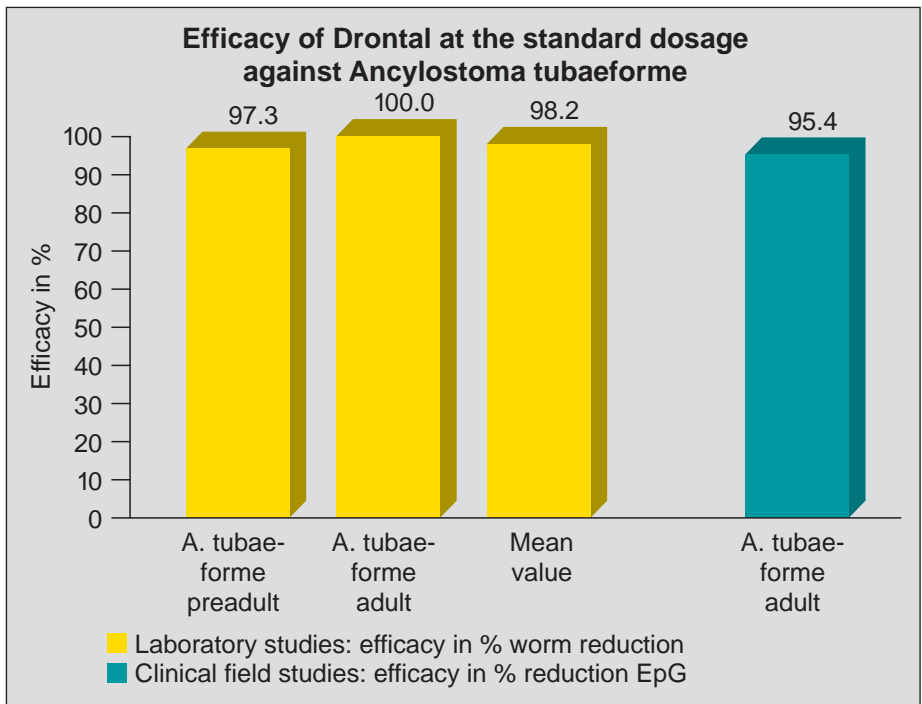


5.2 Efficacy against hookworms

Several laboratory and clinical field trials were performed with Drontal, and con-

firmed the very high efficacy against hookworms.

The following results were obtained:

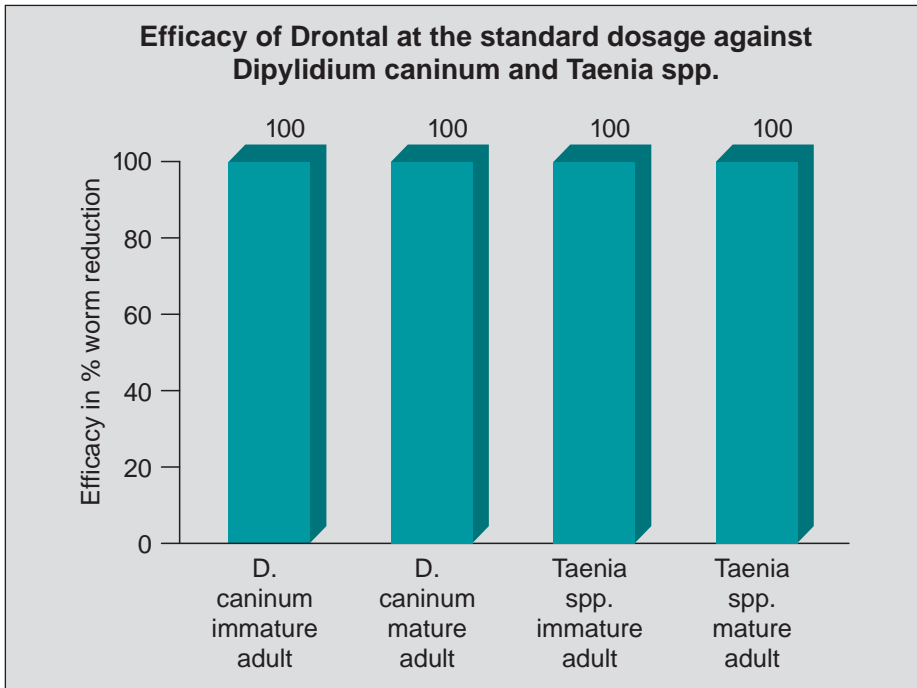


5.3 Efficacy against tapeworms

Several laboratory and clinical field trials were performed with Drontal again confirming the excellent efficacy of Prazi-

quantel against tapeworms, which has already been proven against *Echinococcus multilocularis*, *Mesocestoides* spp. and *joyeuxiella* spp.

The following results were obtained:



5.4 Mixed infections

Field studies were performed in domestic cats aged between 2 months and 5 years. 62.6 % of the tested cats were infected with one or more species. The following mixed infections were identified (worm egg examination):

- Toxocara cati and Ancylostoma tubaeforme
- Toxocara cati and Taenia spp.
- Toxocara cati, Ancylostoma tubaeforme and Taenia spp.

After treatment with Drontal, mixed infections were controlled on average at similar levels to monoinfections.

Interactions with other drugs:

Due to negative impact on efficacy, Piperazine should not be administered at the same time.

6. Tolerability

The tolerability of the Praziquantel/Pyrantel embonate combination was tested in 373 cats of various breeds and both sexes, aged 3 weeks to 15 years. Both single-dose and multiple-dose treatment were carried out. The doses were up to 5,3 times the therapeutic dose of Praziquantel/Pyrantel embonate tablets. The tolerability was evaluated on the basis of clinical parameters (appearance, general behaviour, reflexes and posture), body weight gain, and haematological as well as biochemical parameters.

Drontal was confirmed to be without side effects up to a 5 fold overdosage in young and adult cats.

Safety trials with very young kittens (3 – 5 weeks) have also shown that Drontal is well tolerated using up to 3 times overdosage.

The good tolerability of the product under veterinary practice conditions was confirmed within the framework of the clinical field trials, in which 232 cats were treated with the recommended clinical dose.

The tolerability of Drontal administered concomitantly with a number of other veterinary drugs (among which: antibiotics, eye and ear preparations, gastrointestinal drugs, hormones, ectoparasiticides, topical drugs) at the recommended clinical dose was tested in a further study. No incompatibilities were observed.

Contra-indications:

Until sufficient studies have been performed with the combination Praziquantel/Pyrantel, Drontal should not be used during pregnancy.

Warning:

Keep out of the reach of children. For animal treatment only.

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