Management and Treatment Options for Human Toxocariasis

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Introduction

Human toxocariasis is a zoonosis caused by infective larvae of Toxocara canis (Beaver, 1956) or Toxocara cati (Nagakura et al., 1990). These ascarids are commonly found in the tissues (larvae) and intestinal tract (adult worms) of dogs and cats, respectively. Infection results from ingestion of embryonated eggs in soil (Glickman and Schantz, 1981) or on contaminated fomites (Vázquez Tsuji et al., 1997). Live larvae can be ingested with raw or undercooked meat, giblets or offal (Nagakura et al., 1989; Stüurchler et al., 1990; Fan et al., 2004; Taira et al., 2004).

Toxocara infection results in a wide variety of syndromes in humans, although most infections are probably subclinical. Visceral larva migrans (VLM) was first described in 1952, in children with an enlarged liver and hypereosinophilia (Beaver et al., 1952). The typical VLM patient is a child between the ages of 2 and 7 years with a history of geophagia and exposure to puppies in the home. The clinical signs of VLM are usually associated with hepatic and pulmonary larval migration and include abdominal pain, decreased appetite, restlessness, fever, coughing, wheezing, asthma and hepatomegaly (Ehrard and Kernbaum, 1979). Significant laboratory findings included mild peripheral eosinophilia and increased total serum IgE. This syndrome was termed ‘common toxocariasis’ in adults (Magnaval et al., 1994a). In Ireland, the most frequent clinical findings in children infected with Toxocara larvae included fever, anorexia, headache, abdominal pain, nausea, vomiting, lethargy, sleep and behaviour disorders, pharyngitis, pneumonia, coughing, wheezing, limb pains, cervical adenitis and hepatomegaly. Twenty-seven per cent of patients had high anti-Toxocara antibody titres, but a normal eosinophil count. This form of the disease in children was coined ‘covert toxocariasis’ (Taylor et al., 1988).

Toxocariasis has also been associated with allergy-related syndromes including angioedema (Magnaval and Baixench, 1993), chronic urticaria (Wolfrom et al., 1996), prurigo (Humbert et al., 2000) and reactive arthritis (Bethel, 1981).
Ocular toxocariasis (see Chapter 9, this volume) typically occurs unilaterally in children and young adults. The most common symptom is visual loss with onset over a period of days to weeks. In some individuals these signs may wax and wane over a period of years, often related to migration of larvae in the retina and granuloma formation. Many ocular infections are subclinical and detected during a routine eye examination. Ocular toxocariasis apparently is an endemic disease in some areas of the USA (Maetz et al., 1987), and the prevalence was estimated at 6.6 cases per 100,000 persons in Ireland (Good et al., 2004).

Toxocara larvae readily migrate to the brain of experimentally infected laboratory animals (see Chapter 5, this volume). However, a review of the literature in English from 1950 to the present, found only 29 cases of neurological toxocariasis in humans (Moreira-Silva et al., 2004). Toxocara infection of the central nervous system (CNS) elicits nonspecific neurological signs such as seizures and headache, thus leading to an underdiagnosis of this condition (Magnaval et al., 1997).

**Diagnostic Methods for Toxocariasis**

A definitive diagnosis of toxocariasis is often a significant challenge for the clinician, since the clinical picture of this helminthiasis is quite nonspecific (see Chapter 7, this volume). For example, the symptoms can mimic those found with haematological malignancies, infections with other helminthic parasites and non-infectious conditions, including allergies and asthma. At this stage in the diagnostic process, a careful history regarding occupational and household chemical exposures, drug exposures, asthma, eczema or rhinitis, travel to tropical areas and country of origin, contact with domestic animals particularly puppies, consumption of raw or undercooked meats, and pica, specifically geophagia, should be obtained.

Human toxocariasis is most often a benign, asymptomatic and self-limiting disease, as long as re-infection does not occur. Residual anti-Toxocara antibodies have no pathological significance but can persist for years. Anti-Toxocara antibodies measured by ELISA were found to persist for up to 2.8 years in infected adults in Switzerland (Jeanneret, 1991), while anti-Toxocara antibodies detected by Western blot (WB) can persist for over 5 years (Rubinsky-Elefant, 2004). Seroprevalence surveys in Western countries found that 2–5% of apparently healthy adults from urban areas had a positive anti-Toxocara antibody titre compared with 14.2–37% of adults in rural areas (Magnaval et al., 1994a). In tropical countries, the seroprevalence of toxocarial infection was much higher, namely 63.2% in children and teenagers in Bali (Chomel et al., 1993), 86% in Saint Lucia, West Indies, among children (Thompson et al., 1986) and 92.8% in adults in La Réunion Island (Magnaval et al., 1994b). Since the presence of anti-Toxocara antibodies alone does not distinguish between current and past infections, it should be accompanied by other laboratory tests for blood eosinophil count and total serum IgE.

Chronic eosinophilia is generally considered a reliable indicator of active helminthiasis. However, the differential diagnosis of this sign is consistent with (in decreasing frequency): common allergies, hypersensitivity to drugs and chemicals (especially β-lactam antibiotics and cholesterol-lowering agents), helminthiases, non-allergic conditions including neoplasia (e.g. hepatic and pulmonary carcinomas, Hodgkin’s disease), dermatologic diseases (e.g. bullous pemphigoid), digestive diseases (e.g. Crohn’s and Whipple’s disease), vasculitis (e.g. Churg–Strauss syndrome, polyarteritis nodosa) and hyper eosinophilic syndrome (HES).

Following a history and clinical examination, biological investigations should include non-specific tests for erythrocyte sedimentation rate and C-reactive protein, and measurement of serum immunoglobulins IgG and IgE. Since the first report in 1968 (Johansson et al., 1968) of elevated total serum IgE in Ethiopian preschool children with ascariasis, elevated total serum IgE concentrations have also been found in patients with anisakiasis, cystic echinococcosis, filariasis, schistosomiasis, strongyloidiasis and toxocariasis. The finding of a substantial (≥fourfold the upper normal value) increase of serum IgE is therefore a valuable indication of helminth infection, especially when associated with blood eosinophilia. Non-allergic causes of eosinophilia, such as carcinomas and vasculitis, are usually not associated with an elevated level of total IgE, except in one form of HES (Roufosse et al., 2004).

Repeated stool examinations, including the Baermann method for detection of Strongyloides stercoralis larvae, should be performed to rule out other parasitic infections. Negative stool exams in
the presence of eosinophilia and an elevated serum IgE are indications for specific immunodiagnostic tests for parasites including anisakiasis, ascariasis, strongyloidiasis, trichinellosis and toxocariasis. Serological tests for cystic or alveolar echinococcosis may be indicated in endemic areas for this parasite, as are tests for tropical helminthic diseases including filariases and schistosomiasis for immigrants from endemic areas (Dupas et al., 1986; Ishibashi et al., 2000). Using computed tomography (CT), hepatic lesions may appear as low-density areas (Dupas et al., 1986; Ishibashi et al., 1992; Hartleb and Januszezewski, 2001).

The diagnosis of ocular toxocariasis is particularly challenging, since unlike the signs associated with the peripheral forms of toxocaral disease, eosinophilia is uncommon or mild even in patients with severe ocular manifestations (Glickman and Schantz, 1981; Altcheh et al., 2003). Furthermore, serum anti-Toxocara antibodies may not be detected either by ELISA (Glickman et al., 1986) or by the more sensitive WB (Magnaval et al., 2002). Anti-Toxocara antibodies when found in the aqueous or vitreous fluid of patients with clinical signs of ocular toxocariasis, however, should be considered diagnostic for ocular toxocariasis. The anti-Toxocara antibody titre in these fluids has been found to be higher than that found in serum obtained from patients with ocular toxocariasis (Brasseur et al., 1984; Bertelmann et al., 2003). Imaging techniques are especially helpful and, when they reveal an ocular granuloma, argue against the need for puncture of the anterior chamber to obtain aqueous fluid for immunodiagnosis. Ultrasound of 11 patients with ocular toxocariasis revealed a highly reflective peripheral mass, vitreous band or membrane and traction retinal detachment (Wan et al., 1991). These results are consistent with those found by CT or magnetic resonance imaging (MRI) (Templeton and Rao, 1987; Mahee et al., 1989).

A related imaging method, ultrasound biomicroscopy (USB), appeared to be more accurate. In the absence of 15 patients with clinical and laboratory diagnosis of peripheral vitreoretinal toxocariasis, the following abnormalities were observed using USB: vitreal membranes (13 cases), Toxocara granuloma (11 cases), pseudocysts (eight cases), thickening of the ciliary body (six cases), cystic formation (two cases), peripheral retinal detachment (two cases), rectification of the iris root (one case) and posterior synechiae (one case) (Cella et al., 2004).

Neurological syndromes observed during Toxocara infection of the CNS are generally non-specific and peripheral eosinophilia is often lacking. Medical imaging is especially helpful to investigate these patients further. MRI can detect granulomas located cortically or subcortically, and these may appear as hyper-intense foci on proton-density and T2-weighted images (Ruttinger and Hadidi, 1991; Ota et al., 1994; Xinou et al., 2003). When associated with eosinophilia in the cerebrospinal fluid (CSF), such images are consistent with a toxocaral infection. The finding of Toxocara larvae in CSF, in brain tissue or in the meninges and/or a positive anti-Toxocara antibody titre in CSF represents a further decisive argument (reviewed by Moreira-Siva et al., 2004).
Rationale for Treatment with Anthelmintic Drugs

Limitations of experimental studies

There is scarce information about the drug susceptibility of Toxocara larvae in paratenic hosts. Most experiments have been done with experimentally infected T. canis mice and no drug susceptibility tests have been conducted with live larvae in vitro.

When comparing the results of experimental drug efficacy studies, there is always a concern about the relative size of the inoculum used. For example, in one study, rodents whose weight was about 35 g were given from 500 to 2000 embryo-nated eggs, corresponding to a dose of about 1–4 million eggs for a human adult. An analogous situation would only be encountered with children having a history of geophagia or pica that results in repeated infections with large numbers of Toxocara larvae. In most other clinical forms of toxocarial disease, such as covert or ocular toxocariasis, the larval inoculum is likely to be much smaller. In one experiment done in 1959, a human volunteer was given about 100 T. canis embryonated eggs per os. His blood eosinophil count increased to 13.5 × 10^9 cells/l on day 30 post-infection; 4.5 months post-infection it was 6.15 × 10^9 cells/l, and was accompanied by a persistent cough (Chaudhuri and Saha, 1959). This syndrome is similar to that observed in people with common or covert toxocariasis.

Testing anthelmintic activity in Toxocara canis-infected animals

Most anthelmintic drug studies were conducted during the 1970s to the mid-1980s (Dafalla, 1972; Nicholas and Stewart, 1979; Holt et al., 1981; Abo-Shebada and Herbert, 1984; Abdel-Hameed, 1984; Delgado et al., 1989; Fok and Kassai, 1998), and there have been very few studies conducted since then (Hrčková and Velebny, 2001) (see Chapter 12, this volume). The efficacy of drugs has been generally assessed following infection and treatment of mice using larval recovery from artificially digested tissues as the outcome measure, and by comparing the findings with untreated and infected control animals. Some drugs including thiabendazole (TBZ) had a negligible larvicidal effect, but produced marked inhibition of larval migration through the tissues (Abdel-Hameed, 1984). Levamisole, ivermectin, albendazole (ABZ) and fenbendazole (FBZ) have been associated with larval retention in the liver followed by migration of very few larvae to muscles and brain of treated mice (Abo-Shebada and Herbert, 1984). Most larvae retained in the liver subsequently died and were notrecoverable by day 35 post-treatment. However, these findings are likely to have minimal application to the treatment of humans, since treatment of patients with VLM or ocular toxocariasis would typically be instituted long after most larval migration ceases.

Interesting results were obtained in a study conducted by Fok and Kassai (1998) in which mice infected once with T. canis larvae were treated on days 2, 14, 81, 87 or 123 post-infection using several drug regimens. The larvicidal potential of ABZ, FBZ, flubendazole (FUBZ), oxibendazole (OBZ) and ivermectin was assessed. Reductions of 98.8 or 100% in group mean larval counts were recorded after a 30-day course of FBZ at 750 mg/kg b/w daily, or ABZ at 220 mg/kg b/w daily, respectively. Efficacy rates of 88.2 or 81.1% were achieved by a 20-day course of FUBZ at 700 mg/kg b/w daily or OBZ at 750 mg/kg b/w daily, respectively. Ivermectin, when given at various doses, showed only moderate larvicidal potential. The blood–brain barrier was found to be permeable to most drugs evaluated, but the daily doses used in this study were far greater than those currently recommended for human therapy.

When mebendazole (MBZ) was tested in experimentally infected mice, a 3-day regimen of 100 mg/kg b/w daily, given from days 1 to 3 post-infection, resulted in a 43% decrease in whole-body larval recovery (Bardon et al., 1995). Diethylcarbamazine (DEC) given intraperitoneally at 25 μg/kg b/w for 3 days post-infection elicited a 84.7% reduction in larval recovery (Dafalla, 1972).

Anthelmintic therapy in humans

Though numerous anthelmintic drugs have been tested for efficacy against T. canis in animals, few have been licensed for use in humans, and randomized studies have rarely been conducted.
Benzimidazole derivatives

These compounds bind selectively to parasite β-tubulin and prevent microtubule formation (Martin et al., 1997).

Albendazole

ABZ (methyl-5-propylthio-1H-benzimidazol-2-ylcarbamate) is poorly absorbed from the gastrointestinal tract, and should be taken with fat (Dayan, 2003). A controlled randomized study in which ABZ was given at 10 mg/kg b/w daily for 5 days found a clinical success rate of 47% (Stürchler et al., 1989). Sixty per cent of patients complained about minor side effects. Despite these mixed results, a review of the literature found numerous anecdotal reports (Bhatia and Sarin, 1994; Varga and Auer, 1998; Abe et al., 2002; Inoue et al., 2002; Bachmeyer et al., 2003) indicating that ABZ was a commonly used drug for the treatment of toxocariasis. This is probably related to the fact that its use is associated with few significant adverse reactions and it is widely available in most countries.

A large, randomized, controlled study of ABZ using DEC as reference drug was conducted from 1998 to 2004 in the Department of Parasitology of Toulouse University Hospital. The ABZ treatment arm comprised 42 patients and the DEC arm 44 patients, all diagnosed by WB using T. canis excretory–secretory antigens (Magnaval et al., 1991). The design of the study was similar to that previously described for the assessment of the efficacy of DEC and MBZ (Magnaval, 1995). The treatment groups were not statistically different with respect to demographic characteristics (age and sex ratio) and epidemiological features (type of residence, risk factors for toxocariasis), body weight, duration of the disease prior to first consultation, clinical impact of the disease (using a scoring system; Magnaval, 1995) and presence of atopy as determined by the detection of specific IgE against common inhalant allergens and laboratory parameters (blood eosinophil count, serum total IgE titre and specific anti-Toxocara IgE).

A longer course of ABZ was used than in a study by Stürchler et al. (1989). In the treatment of neurocysticercosis with ABZ, good results were obtained with regimens of 15 mg/kg b/w daily for 15 days (Garcia et al., 1997). Moreover, in 1998, two large outbreaks of trichinellosis involving 448 persons occurred in the Toulouse area of France. According to the instructions from the French Ministry of Health, these patients were treated with a combination of ABZ (13 mg/kg b/w daily for 10 days) and corticosteroids. This regimen was found to be safe and efficient (Leclerc et al., 1999). As a consequence, ABZ was given in the toxocariasis study at 10–13 mg/kg b/w in two divided doses daily for 15 days, but no corticosteroids were added. For the DEC arm, the therapy started at 25 mg daily (1/4 tablet) and the dose progressively increased in an attempt to avoid adverse reactions due to parasite lysis. The full dosage was 3–4 mg/kg b/w in three divided doses daily for 21 days. No anti-histamine drugs were used.

Preliminary results at 4–6 weeks post-treatment showed that both DEC and ABZ elicited a significant decrease in the clinical score and blood eosinophil count, but these differences were not statistically different between the two treatments. More information on changes in specific anti-Toxocara IgE is described below. The rate of side effects was similar in both groups: 15 patients (35.7%) in the ABZ group complained of mild asthenia and/or nausea, while 21 (47.7%) in the DEC group reported neurological disturbances (dizziness, headache), gastric pain, and/or an increase in allergic signs.

The rate of unsuccessful treatments consisting of patients who did not exhibit clinical improvement together with a ≤30% decrease in their eosinophil count, was significantly greater in the ABZ group (11 patients (26.2%) versus three (6.8%) in the DEC arm ($\chi^2$: 5.92; $P = 0.014$).

These failures in ABZ therapy might have been due to slow and erratic drug dissolution and absorption in vivo, a problem previously noted in the treatment of neurocysticercosis (Jung et al., 1998). In healthy volunteers, it was demonstrated that the blood concentration of the metabolite ABZ sulphoxide varied sixfold 1 h after a 600 mg ABZ dose, and this variability was still observed from 1 to 4.5 at 24 h post-treatment (Sarin et al., 2004).

Mebendazole

MBZ (methyl-5-benzoyl-1H-benzimidazol-2-ylcarbamate) is practically insoluble in water and therefore should be taken with a fatty meal.
Large variations however, in the plasma concentrations of the active metabolites of MBZ have been observed in patients treated for hydatid disease or for toxocariasis (Luder et al., 1986; Magnaval et al., 1989).

Various drug regimens were used in three different controlled randomized trials. MBZ was given at either 25 mg/kg b.w daily for 7 days (Magnaval and Charlet, 1987) or at 20–25 mg/kg b.w daily for 3 weeks (Magnaval, 1995). A discontinuous regimen, namely 10–15 mg/kg b.w daily for 3 consecutive days in a week for 6 weeks, was compared with a placebo, to assess efficacy against dormant Toxocara larvae in tissues (Magnaval and Charlet, 1992). In this study, MBZ efficacy was found to be similar to that of placebo. The use of MBZ continuously at a higher daily dosage yielded better results, namely a 57% cure rate for clinical manifestations (Magnaval and Charlet, 1987) or a 70% reduction in the clinical score (Magnaval, 1995). Side effects including weakness, dizziness, nausea and abdominal and gastric pain were mild. The incidence of adverse effects ranged from 9.6% (Magnaval and Charlet, 1987) to 17% (Magnaval, 1995).

Thiabendazole

TBZ (2-thiazol-yl-IH benzimidazole) has poor solubility and should be given with a fatty meal.

The efficacy of TBZ was assessed in three controlled, randomized trials. TBZ was given per os daily from 25 mg/kg b/w (Magnaval and Charlet, 1987) to 50 mg/kg b/w (Bass et al., 1987; Stürchler et al., 1989) for 3 days (Bass et al., 1987), 4 days (Bass et al., 1987), 5 days (Stürchler et al., 1989) or 7 days (Magnaval and Charlet, 1987). The cure rate for clinical manifestations ranged from 50% (Magnaval and Charlet, 1987) to 53% (Stürchler et al., 1989). Moderate side effects were observed in 50% (Magnaval and Charlet, 1987) to 60% (Stürchler et al., 1989) of patients and included dizziness, nausea or vomiting. Such side effects have been previously reported with the use of TBZ (Parfit and The RPSGB, 1997). However, more severe adverse reactions, including cholestasis (Rex et al., 1983), cholestatic hepatitis (Eland et al., 1998) or ductopenia (Manivel et al., 1987; Skandrani et al., 1997), have been reported with a 2 or 3 day course of TBZ at 25 mg/kg b/w daily for treatment of strongyloidiasis. Due to only moderate efficacy together with a relatively high rate of side effects, some of which may be serious, the use of TBZ for treating toxocariasis cannot be recommended.

Diethylcarbamazine

DEC (diethyl-4-methylpiperazine-1-carboxamide) is a highly water-soluble compound and has been the mainstay for filariases chemotherapy since 1949. In the presence of specific antibodies, it enhances both the adherence and cytotoxicity of neutrophils and eosinophils to microfilariae after altering their surface layer (Piessens and Beldekas, 1979). DEC also activates platelets that release free radicals; this action is antibody independent and triggered by a filarial excretory antigen (Cesbron et al., 1987). Moreover, DEC interferes with arachidonic acid metabolism resulting in the production of prostaglandin E2 (PGE2), PGE12 and thromboxane in both the filarial parasites and the host (Martin et al., 1997). A direct anthelmintic effect has also been demonstrated in vitro on Wuchereria bancrofti microfilariae characterized by morphological alterations such as loss of the microfilarial sheath and lysis of the cytoplasm together with the destruction of organelles and the formation of vacuoles (Peixoto et al., 2004).

In a controlled, randomized study versus MBZ, DEC, when given according to the regimen described above, resulted in a 70% decrease in the clinical score (Magnaval, 1995). Twenty-eight per cent of patients reported minor side effects including increased weakness, dizziness, nausea, vomiting or abdominal pain. These disturbances were dose dependent and waned when the daily dosage was tapered. In 10% of subjects, a Mazzotti-like reaction (itching, urticaria and/or oedema) was observed, suggestive of accelerated larval lysis. One patient experienced a major adverse reaction (severe gastric pain) and had to stop treatment. A consideration in the use of DEC is antagonism by corticosteroids that partially inhibit DEC's mechanism of action (Maizels and Denham, 1992). Therefore, DEC and corticosteroids must be given sequentially.

Ivermectin

Ivermectin is primarily a veterinary drug that became available in the 1980s for the chemotherapy of some human helminthiases. This macrocyclic lactone compound has dramatically
improved the outcome for patients with oncho-
cerciasis (Boussinesq et al., 1997), the cause of river
blindness (Addiss et al., 1997; Shenoy et al., 1998).
Ivermectin has also been registered in the
European Union and in the USA for treating
strongyloidiasis (Marti et al., 1996). Physicians
may therefore be tempted to use ivermectin for
the treatment of toxocariasis, particularly because
it can be given in a single 12 mg dose and does not
usually elicit side effects. However, no controlled
study has been conducted to evaluate its efficacy
for toxocariasis. Ivermectin was tested on 17 con-
secutive patients with common toxocariasis
and resulted in a 40% reduction in clinical mani-
festations, but no significant decrease in blood
eosinophil count (Magnaval, 1998a). Thus, iver-
mectin should not be used for the treatment of
ocular toxocariasis until the question of its efficacy
is answered by a controlled study.

Patients Eligible for Therapy

Whether a patient with toxocariasis should be
treated depends on the clinical presentation or
syndrome. All children and adults with acute
VLM should be treated. Patients presenting with
common toxocariasis (Glickman et al., 1987;
Magnaval 1994a) or covert toxocariasis (Taylor
et al., 1988) that have blood eosinophilia should
not necessarily be treated, since persons with these
forms of the disease typically recover spontan-
eously. Anthelmintic treatment need not be
started immediately and need only be considered
for patients who remain symptomatic following
measures to prevent re-infection (see below).
Asymptomatic subjects presenting with chronic
eosinophilia do not require any specific therapy,
but rather prophylaxis.

Since ocular toxocariasis is an uncommon
and often severe disease, no controlled therapeutic
trials have been published. Based on results of
anecdotal case reports or cases series (Dinning
et al., 1988; Gillespie et al., 1993; Saint-Blancat
et al., 1997) and our own experience (Glickman
and Magnaval, 1993), corticosteroids are recom-
manded for initial therapy of ocular toxocariasis.
These drugs reduce the inflammatory process
caused by local release of excretory-secretory
antigens from larvae. If use of oral and/or topical
corticosteroids is ineffective, the addition of a
specific anthelminthic drug should be considered.
It is not known, however, whether the benzimidia-
zo derivatives or their active metabolites pene-
trate into the human eye. However, ABZ given
with corticosteroids was found to be ef-
fective (Dietrich et al., 1998; Barisani-Asenbauer
et al., 2001).

In mice infected with T. canis, DEC accumu-
lated in the brain and in the aqueous fluid (Hawk-
ing, 1979). Further circumstantial evidence of the
efficacy of DEC for toxocariasis is based on
experience gained with treatment of human
onchocerciasis (Dadzie et al., 1987). Most data
suggest that DEC could be used for treating ocu-
lar toxocariasis. However, DEC should not be
given concomitantly with corticosteroids. In
a collaborative multi-centre study including
19 subjects, eight patients with ocular toxocariasis
were treated with corticosteroids followed by
DEC (3–4 mg/kg b/w daily for 21 days), with
good to excellent results. In contrast, when both
drugs were given simultaneously to three patients,
two did not exhibit any improvement after 2 months. An important deterioration occurred
in the third subject who presented with chorioreti-
nitis and hyalitis, leading to enucleation of the eye
(Glickman and Magnaval, 1993; Magnaval, un-
published data).

Medical or surgical methods such as cryo-
pexy or vitrectomy may help to restore vision in
patients with ocular damage due to larval migra-
tion and granuloma formation, but these will not
be discussed further.

Drug therapy for neurological toxocariasis
has consisted primarily of corticosteroids (Robin-
son et al., 2002), or of the combination of cortico-
steroids and DEC (Komiyama et al., 1995), MBZ
(Duprez et al., 1996) or TBZ (Kumar and Kimm,
1994). In some patients with CNS signs, DEC
alone (Ruttinger and Hadidi, 1991) or TBZ
alone (Russegger and Schmutzhard, 1989) has
been used with equivocal results.

Post-treatment Follow-up

The evaluation of treatment efficacy relies primar-
ily on the clinical response, but some signs may
not resolve completely until many months follow-
ing cessation of treatment. The appropriate time
interval for evaluation of treatment efficacy is
critical. This was evident in a study of the use of ABZ (Sturchler et al., 1989) in which a twofold increase in clinical signs was noticed between follow-up exams performed at the 2nd and 6th week post-treatment. In contrast, a clinical improvement observed after a year or more could have been related to treatment or simply corresponded with the natural course of the disease (Wolfrom et al., 1996; Rubinsky-Elefant, 2004). Based on personal observations, we suggest for the follow-up of VLM or covert toxocariasis that clinical exams be performed between the 4th and the 6th week post-treatment.

The use of a scoring system to quantify the clinical severity as described elsewhere (Magnaval et al., 1992b; Magnaval, 1995) is helpful for assessing treatment efficacy. Abnormal patterns detected by medical imaging techniques including hypoechoic lesions on US, low-density areas on CT in the liver or T2-weighted images by MRI in the brain usually resolve within 1 to 2 months following treatment.

Among non-specific laboratory tests, a high rate of decrease of blood eosinophilia seems to have good prognostic value (Magnaval, 1995). The detection of specific anti-Toxocara IgG antibodies by ELISA appeared not to be useful for monitoring therapy. When ELISA IgG titres were compared between treated and untreated children with VLM, the kinetics of specific anti-Toxocara IgG did not differ (Bass et al., 1987). In another study, 23 Brazilian patients with VLM were treated with TBZ and a follow-up exam was performed 22–116 months later (Rubinsky-Elefant, 2004). Only ten subjects were found to have a significant decrease in ELISA anti-Toxocara IgG titres, and the decline in IgG titres was consistent with predicted normal clearance rate (Jeanneret, 1991). WB, when used to detect specific IgG, was no more useful. In the unpublished study comparing the efficacy of ABZ with DEC (see above), only one subject in each group was negative at the post-treatment consultation. In the Brazilian study, WB was evaluated at the same time as IgG ELISA, and a lower-intensity banding pattern was observed in 12 of 23 patients. Conversely, specific anti-Toxocara IgE antibody titres determined by ELISA (sIgE) seemed to correlate better with the clinical outcome. If elevated prior to therapy, the mean sIgE level significantly decreased (Magnaval et al., 1992), and in eight of nine Brazilian patients the sIgE decreased by two or more dilutions (Rubinsky-Elefant, 2004). DEC-treated atopic subjects had a significant reduction of IgE following treatment compared with non-atopic patients (Magnaval, unpublished data).

### Prophylaxis for Toxocariasis

Regardless of the clinical form of toxocariasis encountered or the chemotherapy regimen used, measures should be taken to prevent re-infection. The patient or surrogates should be questioned carefully to identify personal risk factors for Toxocara infection and to identify likely sources of Toxocara eggs in the environment. Risk factors for infection include behaviours such as geophagia and poor personal hygiene. Any roundworm-infected dogs or cats in the patient’s environment should be treated by a veterinarian (see Chapters 16 and 17, this volume), and any contaminated soil removed or the area closed so it is not accessible to small children. Household gardens should be fenced to eliminate contamination by dogs or cats. Similarly, smaller gardens and sand boxes should be covered by appropriate materials. Vegetables or fruits gathered in possibly contaminated gardens should be thoroughly washed before eating. Raw or undercooked meat that could harbour Toxocara larvae should be avoided. Parents and children should receive counselling for geophagia. Personal hygiene including hand-washing is important, especially when handling foods and dogs.

Puppies should be treated for roundworms starting about 3 weeks of age (Harvey et al., 1991) and the treatment repeated every 2 weeks until 12 weeks of age (Soulsby, 1987) in order to avoid environmental contamination with T. canis eggs. Adult dogs should be dewormed or have a faecal exam twice a year, except for bitches which should also be treated before and 1 month after whelping. Cats should be similarly treated or tested for roundworms in the first few weeks of life. Adult outdoor cats can be re-infected by preying upon paratenic hosts and should therefore be retreated or tested two or three times a year unless they are kept strictly indoors (see Chapters 16 and 17, this volume).
### Table 8.1. Recommended treatments for toxocariasis.

<table>
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<tr>
<th>Syndrome</th>
<th>Drug of choice</th>
<th>Recommended dose</th>
<th>Major side effects</th>
<th>Minor side effects</th>
<th>Availability</th>
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<th>Alternative therapy</th>
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<tbody>
<tr>
<td>VLM</td>
<td>DEC</td>
<td>3–4 mg/kg b/w daily for 21 days</td>
<td>Burst of allergy signs; gastric pain; vomiting</td>
<td>Dizziness; nausea</td>
<td>USA; Western Europe; filariasis-endemic countries</td>
<td>Very low</td>
<td>Weak</td>
<td>MBZ</td>
<td>Corticosteroids</td>
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<tr>
<td>Common/covert toxocariasis</td>
<td>DEC</td>
<td>See above</td>
<td>See above</td>
<td>See above</td>
<td>See above</td>
<td>Strong</td>
<td>ABZ</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MBZ(^a)</td>
<td>25 mg/kg b/w daily for 21 days</td>
<td>None</td>
<td>Dizziness; nausea; abdominal or gastric pain</td>
<td>Worldwide</td>
<td>Low</td>
<td>Strong</td>
<td>ABZ</td>
<td>None</td>
</tr>
<tr>
<td>Ocular toxocariasis</td>
<td>Corticosteroids (prednisone)</td>
<td>1 mg/kg b/w daily for 1 month</td>
<td>See <em>Martindale</em>(^{\text{c}}) (Parfitt and The RPSGB 1997)</td>
<td>See above</td>
<td>Worldwide</td>
<td>Moderate</td>
<td>Moderate</td>
<td>None</td>
<td>Surgery and other non-medical interventions(^{\text{b}})</td>
</tr>
<tr>
<td></td>
<td>DEC</td>
<td>See above 400 mg (children) 800 mg (adults) b.i.d. for 10–14 days</td>
<td>See above</td>
<td>Mild weakness; nausea</td>
<td>Worldwide</td>
<td>See above</td>
<td>Weak</td>
<td>ABZ</td>
<td>See above</td>
</tr>
</tbody>
</table>

DEC, diethyl-carbamazine; MBZ, mebendazole; ABZ, albendazole.

\(^{a}\)If DEC not available, or if occurrence of major side effects.

\(^{b}\)Cryopexy, photocoagulation.
Conclusion

Corticosteroids are indicated for the treatment of acute inflammatory manifestations of both VLM and ocular toxocariasis. There is currently no information available on the efficacy of the non-steroidal anti-inflammatory drugs for Toxocara. For many years, a commonly held belief was that anthelmintic therapy of toxocariasis was unsatisfactory, especially for VLM. This was based on the high larval inoculum size that causes this form of toxocariasis, the lack of effective prophylaxis for high-risk children with geophagia that results in repeated infections, as well as equivocal results of drug tests in rodent models. However, results from controlled and randomized human drug trials suggest effective therapy is possible for both the common and covert forms of toxocariasis.

The appropriate drug for treating toxocariasis depends on several factors including what is licensed and available for use in a physician's country as well as a physician's previous experience with treating toxocariasis (see Table 8.1). DEC, if available, is probably more effective than ABZ for the treatment of toxocariasis. However, the drug has been associated with a high rate of neurological side effects and should preferentially be used by well-experienced physicians. MBZ is available in many countries and would appear to be a good alternative to DEC, e.g. if the occurrence of major DEC-related side effects is feared. ABZ, in spite of a recent report supporting its efficacy (Despommier, 2003), should not be considered as the drug of choice for reasons discussed previously. However, ABZ is widely available, has proved to be safe and could therefore be used to treat lightly infected persons with toxocariasis.

References


