Human *Toxocara* infection of the central nervous system and neurological disorders: a case-control study

J.-F. MAGNAVAL[1]*, V. GALINDO[1], L. T. GLICKMAN[2] *and* M. CLANET[3]

[1] *Service de Parasitologie, CHU Purpan, 31059 Toulouse, France*
[2] *Department of Pathobiology, School of Veterinary Medicine, West Lafayette, IN 47907, USA*
[3] *Service de Neurologie, CHU Purpan, 31059 Toulouse, France*

(*Received 5 March 1997; revised 6 May 1997; accepted 6 May 1997*)

SUMMARY

Infection with *Toxocara canis* is a common world-wide human helminthiasis, which rarely elicits central nervous system (CNS) impairment. A case-control study to investigate this discrepancy was carried out, in which the cases were 27 adult neurological inpatients for whom a definite aetiological diagnosis was lacking, and for whom positive immunodiagnosis of toxocariasis had been obtained, both in cerebrospinal fluid (CSF) and in serum. Two control groups were used. Controls were adult inpatients with other neurological diseases who had no evidence of *T. canis* infection of the CNS. Multivariate logistic regression analysis did not reveal any positive relation between case status and clinical signs. A significant association was observed between case status and an elevated CSF cell count. Rural residence, ownership of dogs, and dementia were shown to be risk factors for toxocaral infection of CNS. These results suggest that migration of *T. canis* larvae in the human brain does not frequently induce a recognizable neurological syndrome but is correlated with the association of several risk factors including exposure to dogs, a status possibly responsible for repeated low-dose infections.

Key words: toxocariasis, neurological disorders, case-control study.

INTRODUCTION

Toxocariasis is a parasitic zoonosis due to the infection of human beings by L_2 larvae of *Toxocara canis*, the common round worm of dogs (Soulsby, 1987). In northern industrialized countries, epidemiological surveys have revealed that the seroprevalence of this helminthiasis ranges from 2·5 to 5% in urban adults (Glickman & Schantz, 1981; Glickman, Magnaval & Brochier, 1985; Cauchie *et al*. 1990). In Europe, a higher rate has been reported in rural people, ranging between 17% among Swedish farmers (Ljungström & Van Knapen, 1989), 37% in French rural dwellers (Magnaval & Baixench, 1993), and over 40% in Irish children (Holland *et al*. 1995). Other studies in animal models demonstrated that *T. canis* larvae enter the CNS (Sprent, 1952; Dunsmore, Thompson & Bates, 1983; Glickman & Summers, 1983). In small rodents, larvae preferably accumulate in the brain (Sprent, 1952; Kayes & Oaks, 1976; Dunsmore, Thompson & Bates, 1983), thus producing a variety of CNS disorders (Epe *et al*. 1994) and behavioural changes (Hay *et al*. 1986). Given these observations, neurological disorders in humans, if due to the presence of *T. canis* larvae in the CNS, might not be an uncommon event. In fact, a review of the English literature, from the early 50's to the present, found only 12 cases of neurological toxocariasis, as determined by the finding of *Toxocara* larvae in the CSF or inside the brain or the meninges, and/or by immunodiagnosis on CSF (Beautyman & Woolf, 1951; Dent *et al*. 1956; Van Thiel, 1960; Moore, 1962; Beautyman *et al*. 1966; Schochet, 1967; Mikhael *et al*. 1974; Wang *et al*. 1983; Hill, Denham & Scholtz, 1985; Russegger & Schmutzhard, 1989; Ruttinger & Hadidi, 1991; Villano *et al*. 1992; Kumar & Kimm, 1994). Those patients had various neurological sequelae, including behavioural changes (1 patient), dementia (1 patient), encephalitis (5 patients), epilepsy (1 patient), meningitis (1 patient), myelitis (1 patient) or paresia/tetraparesia (2 patients). Moreover, toxocariasis has been suggested as a co-factor for epilepsy (Arpino *et al*. 1990) but a case-control study in children found similar rates of *Toxocara* seropositivity in epileptic patients with a known etiology (other than toxocariasis) and in patients with idiopathic epilepsy (Glickman *et al*. 1979).

The aim of the present study was therefore to assess the potential existence of an expanded spectrum of neurological toxocariasis, originating from non-specific features which together would make a characteristic syndrome, so far unrecognized.

PATIENTS AND METHODS

Subjects

Cases were 27 adult patients referred between January 1990 and August 1993 to the Department of

* Corresponding author: Service de Parasitologie, CHU Purpan, 31059 Toulouse, France. Tel: 33 05 61 77 20 12. Fax: 33 05 61 77 23 78. E-mail: magnaval@cict.fr

https://doi.org/10.1017/S0031182097001558 Published online by Cambridge University Press

Table 1. Variables used for matching or found to be significant at $P < 0{\cdot}1$ by univariate analysis

	Cases ($n = 27$)	Control group 1 ($n = 26$)	Control group 2 ($n = 41$)	Comparison*	
				Cases *vs.* 1	Cases *vs.* 2
Age (arithmetic mean)	52·0	54·3	51·2	$P = 0{\cdot}669$†	$P = 0{\cdot}935$†
S.E.	3·19	2·92	3·15		
Range	(18, 74)	(26, 80)	(19, 82)		
Sex-ratio (F/M)	14/13	13/13	23/18	$P = 0{\cdot}556$	$P = 0{\cdot}462$
Ethnicity (caucasian/other)	24/3	25/1	39/2	$P = 0{\cdot}319$	$P = 0{\cdot}307$
Travel outside EC‡ (yes/no)	7/20	4/22	11/30	$P = 0{\cdot}273$	$P = 0{\cdot}582$
Residence in a town < 5000 people (yes/no)	12/15	2/24	2/39	$P = 0{\cdot}003$	$P = 0{\cdot}001$
Ownership of dogs (yes/no)	13/14	6/20	6/35	$P = 0{\cdot}052$	$P = 0{\cdot}003$
Dementia (yes/no)	5/22	1/25	1/40	$P = 0{\cdot}104$	$P = 0{\cdot}032$
EEG abnormalities (yes/no)	5/12§	8/13§	20/10§	$P = 0{\cdot}416$	$P = 0{\cdot}015$
CSF cell count $\geqslant 4$ cells/mm^3 (yes/no)	14/13	4/22	7/34	$P = 0{\cdot}054$	$P = 0{\cdot}003$
CSF eosinophil count $\geqslant 1$ cell/mm^3 (yes/no)	4/23	2/24	1/40	$P = 0{\cdot}353$	$P = 0{\cdot}076$
CSF protein concentration $\geqslant 0{\cdot}5$ g/l (yes/no)	17/10	12/14	12/29	$P = 0{\cdot}170$	$P = 0{\cdot}006$

* Fisher's exact test, except otherwise indicated.
† Mann–Whitney test.
‡ European Community.
§ Missing data.

Neurology from the University Hospital (CHU) Toulouse-Purpan. Criteria for inclusion were a lack of a definite aetiological diagnosis at hospital discharge, together with a positive immunodiagnosis of toxocariasis by Western blot analysis both on serum and CSF. Moreover, cases had to exhibit negative results on a parasitological assessment comprising direct examination of blood, stools, and urine for ova and parasites, and immunodiagnostic tests for autochthonous (ascaridiasis, cystic hydatidosis, fascioliasis, strongyloidiasis, trichinosis) and tropical (filariasis, schistosomiasis) helminthiases. Laboratory investigations for Lyme borreliosis, bacterial, fungal, and viral infections also had to be negative.

Two control groups were assembled by identifying patients from the Department of Neurology using the same criteria as those cited for cases above, except the controls had a negative Western blot result for *T. canis* on CSF. Control group 1 included 26 subjects with a history of exposure to *T. canis* based upon a positive Western blot on serum. Control group 2 comprised 41 patients who had a negative blot for *T. canis* both in serum and CSF.

Direct examination of CSF was negative for *Toxocara* larvae in all cases and in control patients.

Cases were frequency matched with controls on the basis of age, sex, ethnicity and travel history outside the European Community. Data were collected by investigating medical files and by interviewing patients, their family, and/or their personal physician. A questionnaire was used which inquired about: place of residence, consumption of raw or undercooked liver, geophagia, consumption of salads of dandelions gathered in the countryside, ownerships of dogs and their medical care status (e.g. worming). Twenty-three clinical items were evaluated based on a general and neurological examination, (weakness, loss of appetite, loss of weight $\geqslant 2$ kg, fever $\geqslant 38$ °C, agnosia, aphasia, apraxia, ataxia, cerebellar syndrome, coma, dementia, encephalitis, epilepsy, meningitis, myalgias, cranial nerve impairment, polyneuropathy, Guillain-Barré syndrome, pyramidal syndrome, cutaneous and deep sensibility impairment), electroencephalogram (EEG), and computerized tomography (CT scan

https://doi.org/10.1017/S0031182097001558 Published online by Cambridge University Press

Table 2. Logistic regression analysis of clinical and laboratory findings associated with toxocaral CNS disease (cases) compared with controls*

Variable	Coefficient	*P*†	Odds ratio‡	95% CI
Overall model A, using controls from group 1				
CSF cell count $\geqslant 4$ cells/mm^3				
	1·631	0·014	5·107	(1·384, 18·85)
Likelihood ratio statistic on 2 D.F. = 6·809, $P = 0·033$				
Overall model B, using controls from group 2				
CSF cell count $\geqslant 4$ cells/mm^3				
	1·655	0·003	5·231	(1·724, 15·87)
Likelihood ratio statistic on 2 D.F. = 12·10, $P = 0·02$				

* Fully tabulated data, including non-adjusted odds-ratio values, concerning the variables tested in these models are available on request.
† Wald test based.
‡ Estimates adjusted for the other variables by logistic regression analysis.

showing low density areas) and/or magnetic resonance imaging (MRI showing T2 weighted images). Seven laboratory items were considered, including total white blood cell count, blood eosinophil count, CSF cell count, CSF eosinophil count, CSF protein concentration, and results from toxocariasis immunodiagnosis by Western blot analysis both in serum and in CSF. For all patients, clinical, radiological and laboratory investigations were performed in the Departments of Neurology and Neuroradiology, and in the Laboratories of Parasitology, Clinical Chemistry, Hematology and Microbiology, from CHU Toulouse-Purpan. The collection of interview data was carried out by the same investigator (V.G.).

Toxocara *immunodiagnosis*

Immunodiagnosis of toxocariasis was based upon the results of a Western blotting procedure that detected IgG specific for *T. canis* excretory–secretory larval antigens (TES–Ag).

Production of TES–Ag was by cultivation of *T. canis* larvae according to De Savigny's method (De Savigny, 1975). The Western blot procedure has been previously described by Magnaval *et al.* (1991). Assessment of Western blot specificity had been undertaken using sera from laboratory animals infected by various helminths including *T. canis*, from French toxocariasis cases, from French people exhibiting chronic eosinophilia and a positive *Toxocara* ELISA test, and from patients with other helminthic diseases. By Western blotting, animal and human reference sera from toxocariasis cases showed a typical pattern in which 7 bands were split into 2 groups, the first group including 4 low molecular weight bands, the other group 3 high molecular weight bands. Statistical analysis of the results from all sera demonstrated that these 7-band patterns were significantly correlated with toxocariasis cases. Banding patterns showing only the high molecular weight bands were evocative of cross-reactions, since they were significantly more often yielded by sera from various helminthiasis. In the present work, all cases (in CSF and serum) and controls from group 1 (in serum) exhibited blotting profiles with a typical 7-band pattern.

Statistical analysis

Data were analysed using Statpak™ statistical software (Northwest Analytical, Portland, USA) and Epi-Info™ (Center for Disease control, Atlanta, USA). Continuous laboratory variables were split in 2 classes (elevated or not) according to the upper limits used in the laboratories from CHU Toulouse-Purpan. All epidemiological, clinical and laboratory variables were tested one at a time (univariate analysis) for their association with neurotoxocariasis. This was performed by comparing the distribution of these variables between the cases and each of the 2 control groups separately, by the Mann–Whitney or Fisher's exact tests as appropriate. In this screening procedure, a $P < 0·1$ was used to identify variables for inclusion in the multivariate logistic regression models. The rationale for using $P < 0·1$ in the univariate analysis was to avoid premature dismissal of potentially important symptoms or risk factors for neurotoxocariasis. Two multiple logistic models, A and B, implemented with Egret™ (Statistics and Epidemiology Corporation, Seattle, USA) were used to further evaluate questionnaire items that were significant in univariate analysis at $P < 0·1$. Model A compared cases with control group 1; model B compared cases with control group 2. Odds ratio estimates were adjusted for the other variables by logistic regression analysis; approximate 95% confidence limits were based on maximum likelihood

https://doi.org/10.1017/S0031182097001558 Published online by Cambridge University Press

Table 3. Logistic regression analysis of risk factors for toxocaral CNS disease (cases) compared with controls*

Risk factor	Coefficient	P†	Odds ratio‡	95% CI
Overall model A, using controls from group 1				
Residence in a town < 500 people				
	2·262	0·007	9·6	(1·881, 49·0)
Likelihood ratio statistic on 2 D.F. = 10·02, $P = 0·007$				
Overall model B, using controls from group B				
Residence in a town < 5000 people				
	2·86	0·001	17·46	(3·063, 99·48)
Ownership of dogs				
	1·848	0·007	6·345	(1·643, 24·51)
Dementia	2·578	0·038	13·17	(1·152, 150·6)

* Fully tabulated data, including non-adjusted odds-ratio values, concerning the variables tested in these models are available on request.
† Wald test based.
‡ Estimates adjusted for the other variables by logistic regression analysis.

estimates of logistic parameters. Assessment of the best fit model was realized by forward and backward stepwise regressions (Statistics and Epidemiology Research Corporation, 1993).

RESULTS

Epidemiological, clinical and laboratory findings

Table 1 compares the cases with the 2 control groups for variables used for matching, or found to be significantly ($P < 0·1$) different between the cases, and at least 1 control group.

In models A and B, an unconditional regression analysis of significant clinical and laboratory results was conducted. EEG abnormalities were not included in the models, since complete data were not available. Table 2 shows that, in model A, case status (positive Western blot result in CSF) positively correlated with a CSF cell count greater than 4 cells/mm^3. In model B, a significant association was found only with an elevated CSF cell count; an independent association was demonstrated between case status, and a CSF protein concentration $\geqslant 0·5$ g/l.

Risk factor analysis

The risk factors are shown in Table 3. In both models, regression analysis showed that residence in a town with less than 5000 inhabitants was significant. In model B, dog ownership and dementia were also significantly associated with toxocaral CNS infection.

DISCUSSION

Whether the specific IgG detected in CSF by Western blotting was intrathecally synthesized, or due to a leakage from blood was not determined in the study. Since Western blotting is not a quantitative method, it was not possible to use the standard ratio of specific anti-*T. canis* IgG levels in CSF and in serum divided by their respective albumin levels to evaluate antibody production in CSF (Reiber, 1986). Due to ethical and funding reasons which limited the number of lumbar punctures and the cost of CSF investigations, more accurate assays, including protein profiles of CSF, were not performed. However, intra-CNS production of *Toxocara* antibodies in cases who had a positive Western blot with both CSF and blood is suggested by a lack of evidence for blood leakage into the CNS. That is, the mean CSF protein level and the percentage of patients with an elevated CSF protein concentration were similar in cases and patients in control group 1 who had a negative Western blot with CSF, but a positive blot with blood.

When 27 adult in-patients from the Department of Neurology exhibiting a positive *Toxocara* immunodiagnosis in CSF and serum, together with various unexplained neurological signs or syndromes at hospital discharge were compared with 26 controls previously exposed to *T. canis* infection and 41 non-exposed controls, both having a negative Western blot in CSF, a previous CNS infection with *T. canis* larvae was not positively correlated with any specific clinical signs or clinical syndrome.

Light or transient infection of CNS by *T. canis* larvae could be a partial explanation for this negative finding since larvae were not found by microscopical examination of CSF. In mice, a larval inoculum *per os* as large as 2500 embryonated eggs (Sprent, 1952) resulted in a relatively small percentage (6·6%) of larval recovery from the brain. Moreover, the larval density in mouse brain has been correlated with the size of inoculum (Kayes & Oaks, 1976). In 16 monkeys (*Macaca fascicularis*) given a dose of 45000 *Toxocara* embryonated eggs *per os*, a visceral *larva*

https://doi.org/10.1017/S0031182097001558 Published online by Cambridge University Press

migrans (VLM) syndrome (Beaver, 1956) was produced. Three of these animals also developed neurological signs characterized by ataxia and nystagmus, and larvae were observed within granulomas in frontal and occipital cortex and the cerebellum (Glickman & Summers, 1983). In humans, among the recognized risk factors for toxocariasis (Glickman & Schantz, 1981; Glickman, 1993), only contact with puppies and geophagia are implicated in the swallowing of large *T. canis* inoculums by children. None of the cases or controls in the present study had a history of contact with puppies, and geophagia was reported in only 1 case. Therefore the 27 cases were likely to harbour only a few larvae in their CNS. These light infections were sufficient, however, to produce positive Western blot results, despite the fact they did not elicit a specific clinical CNS syndrome.

A genetic susceptibility factor may also be involved. When mice of 5 different strains were inoculated with 1000 *Toxocara* embryonated eggs, BALB mice exhibited less CNS signs and a better survival rate than the other strains (Epe *et al*. 1994). Histological examination showed that demyelinization and mixed-cell infiltration occurred later and to a lesser extent in brains of BALB mice.

Medical imaging abnormalities, namely low density areas by CT scan and/or T2-weighted images by MRI, have been reported from histologically established cases of *T. canis* infection of the CNS (Ruttinger & Hadidi, 1991) and liver (Dupas, Barrier & Barre, 1986; Ishibashi *et al*. 1992), and were due to parasitic granulomas. In this study, imaging abnormalities did not significantly differ between the cases and the controls. However, the borderline value of $P = 0{\cdot}13$ and the relatively small size of the groups, suggest a trend that should be further investigated.

Surprisingly, a low rate of elevated blood eosinophil count was found in cases, and the univariate analysis of laboratory results indicated that this abnormality did not significantly differ between cases and controls. Blood eosinophilia has been frequently observed in patients with visceral *larva migrans* syndrome (Ehrard & Kernbaum, 1979) and in French adults with immunoblot-confirmed *T. canis* infection (Glickman *et al*. 1987), but was noted in only 5 from 9 patients with neurological toxocariasis for whom this information was available, which is consistent with the results from the present study. Light and/or transient, or conversely long-standing *T. canis* infection in cases could explain this discrepancy. In mice experimentally infected with *T. canis* larvae, peripheral eosinophilia gradually decreased and returned to the baseline level at 21 weeks post-infection (Epe *et al*. 1994). Moreover, the pathogenesis of neurological toxocariasis might be similar to that of the ocular form of the disease, since both eye and CNS are closed environments. In ocular toxocariasis, only 3 patients out of 16 in one study had a blood eosinophilia of $\geqslant 0{\cdot}5 \times 10^9$ cells/l ($\geqslant 500$ cells/mm^3) (Gillespie *et al*. 1993). This may reflect the presence of only a few larvae in the eye or CNS, which is sufficient to cause local lesions but is insufficient to provoke blood eosinophilia.

Multivariate logistic regression analysis showed a significant association of a positive Western blot result in CSF with an elevated CSF cell count. This finding is consistent with published reports. For example, among neurological toxocariasis cases for whom the information was available, the CSF cell count was found elevated in 6 out of 7 patients (Beautyman & Woolf, 1951; Schochet, 1967; Wang *et al*. 1983; Russegger & Schmutzhard, 1989; Ruttinger & Hadadi, 1991; Kumar & Kimm, 1994).

Rural residence, ownership of dogs, and dementia were found to be risk factors for CNS toxocariasis. Presence of dementia was associated with case status while controlling for other significant risk factors. Toxocariasis is primarily a soil-borne zoonosis (Glickman, 1993) in which humans are infected by ingesting embryonated eggs from contaminated soils. In the United States (Herrmann *et al*. 1985) and in France (Glickman *et al*. 1987) controlled studies found that living in a rural area was a risk factor for toxocariasis. Rural environments favour the persistence of *T. canis* eggs, and increase human exposures. People suffering from dementia problems might be at a greater risk of repeated *T. canis* infection due to behavioural troubles and/or poor personal hygiene. A survey carried out among mentally retarded adults indeed showed that mental retardation was a significant risk factor for toxocariasis when associated with contact with dogs and pica (Huminer *et al*. 1992). Demented patients' activity should therefore be closely supervised in potentially *T. canis* contaminated environments, e.g. around dogs.

In conclusion, the results of this study suggest that, following low dose and repeated infections by *T. canis*, some larvae migrate to the CNS and induce local antibody production as evidence by a positive Western blot result with CSF. These light parasitic burdens do not appear to elicit a specific clinical syndrome, but longer term follow-up is needed to fully evaluate this significance. Moreover, since all subjects included in the present study were adults, possible differences could be observed in children, given their greater exposure potential.

Since commercial test kits for the immunodiagnosis of toxocariasis by ELISA are currently available, this assay can be easily performed on CSF and serum. Neurologists and other medical practitioners could require *T. canis* antibody tests for neurological patients in whom a definite aetiological diagnosis is difficult to establish. Surely a positive result is always important, but particularly so if consistent with epidemiological findings of a rural

dwelling, ownership of dogs and dementia, laboratory results such as elevated CSF cell count and protein concentration, and possibly imaging abnormalities such as low-density areas by CT scan and/or T2-weighted images by MRI.

The authors thank Dr Charlet (CHU Purpan, Toulouse, France), Professeur Dumas (CHU Limoges, France), Dr Espagno (Clinique des Cèdres, Toulouse, France), Dr Vigier (Grenoble, France) for their kind help and G. Carrière, D. Darties, M. Dorion, E. Dubly, A. Galasso, R. M. Gueux and M.-J. Touchard for technical assistance.

REFERENCES

ARPINO, C., GATTINARA, G. C., PIERGILI, D. & CURATOLO, P. (1990). *Toxocara* infection and epilepsy in children. A case-control study. *Epilepsia* **31**, 33–36.

BEAUTYMAN, W. & WOOLF, A. (1951). An *Ascaris* larva in the brain in association with acute anterior poliomyelitis. *Journal of Pathology and Bacteriology* **63**, 635–647.

BEAUTYMAN, W., BEAVER, P. C., BUCKLEY, J. J. C. & WOOLF, A. L. (1966). Review of a case previously reported as showing an ascarid larva in the brain. *Journal of Pathology and Bacteriology* **91**, 271–273.

BEAVER, P. C. (1956). Larva migrans. *Experimental Parasitology* **5**, 587–621.

CAUCHIE, V., CHAILLET, P., BIGAIGNON, G., TOMASI, J. P. & VERVOORT, T. (1990). Etude comparative des infections à *Toxocara* en Belgique et dans les autres pays. *Acta Clinica Belgica* **45**, 227–239.

DE SAVIGNY, D. H. (1975). *In vitro* maintenance of *Toxocara canis* larvae and a simple method for the production of *Toxocara* ES antigens for use in serodiagnostic tests for visceral larva migrans. *Journal of Parasitology* **61**, 781–782.

DENT, D. H., NICHOLS, R. L., BEAVER, P. C., CARRERA, G. M. & STAGGERS, R. M. (1956). Visceral *larva migrans* with case report. *American Journal of Pathology* **32**, 777–803.

DUNSMORE, J. D., THOMPSON, R. C. A. & BATES, I. A. (1983). The accumulation of *Toxocara canis* larvae in the brains of mice. *International Journal for Parasitology* **13**, 517–521.

DUPAS, B., BARRIER, J. & BARRE, P. (1986). Detection of *Toxocara* by computed tomography. *British Journal of Radiology* **59**, 518–519.

EHRARD, T. & KERNBAUM, S. (1979). *Toxocara canis* et toxocarose humaine. *Bulletin de l'Institut Pasteur* **77**, 225–287.

EPE, C., SABEL, T., SCHNIEDER, T. & STOYE, M. (1994). The behavior and pathogenicity of *Toxocara canis* larvae in mice of different strains. *Parasitology Research* **80**, 691–695.

GILLESPIE, S. H., DINNING, W. J., VOLLER, A. & CROWCROFT, N. S. (1993). The spectrum of ocular toxocariasis. *Eye* **7**, 415–418.

GLICKMAN, L. T. (1993). The epidemiology of human toxocariasis. In *Toxocara and Toxocariasis. Clinical, Epidemiology and Molecular Perspectives* (ed. Lewis, J. W. & Maizels, R. D.), pp. 3–10. Institute of Biology and British Society for Parasitology, London.

GLICKMAN, L. T., CYPRESS, R., CRUMRINE, P. K. & GITLIN, D. A. (1979). *Toxocara* infection and epilepsy in children. *Journal of Pediatrics* **94**, 75–78.

GLICKMAN, L. T., MAGNAVAL, J.-F. & BROCHIER, B. (1985). Séroprévalence des *larva migrans* viscérales dans la Région Midi-Pyrénés. *Presse Médicale* 14, 1094.

GLICKMAN, L. T., MAGNAVAL, J.-F., DOMANSKI, L. M., SHOFER, F. S., LAURIA, S. S., GOTTSTEIN, B. & BROCHIER, B. (1987). Visceral *larva migrans* in French adults. A new disease syndrome? *American Journal of Epidemiology* **125**, 1019–1033.

GLICKMAN, L. T. & SCHANTZ, P. M. (1981). Epidemiology and pathogenesis of zoonotic toxocariasis. *Epidemiologic Reviews* **3**, 230–250.

GLICKMAN, L. T. & SUMMERS, B. A. (1983). Experimental *Toxocara canis* infection in cynomolgus macaques (*Macaca fascicularis*). *American Journal of Veterinary Research* **44**, 2347–2354.

HAY, J., ARNOTT, M. A., AITKEN, P. P. & KENDALL, A. T. (1986). Experimental toxocariasis and hyperactivity in mice. *Zeitschrift für Parasitenkunde* **72**, 115–120.

HERRMANN, N., GLICKMAN, L. T., SCHANTZ, P. M., WESTON, M. G. & DOMANSKI, L. M. (1985). Seroprevalence of zoonotic toxocariasis in the United States: 1971–1973. *American Journal of Epidemiology* **122**, 890–896.

HILL, I. R., DENHAM, D. A. & SCHOLTZ, C. L. (1985). *Toxocara canis* larvae in the brain of a British child. *Transactions of the Royal Society of Tropical Medicine and Hygiene* **79**, 351–354.

HOLLAND, C. V., O'LORCAIN, P., TAYLOR, M. R. H. & KELLY, A. (1995). Seroepidemiology of toxocariasis in school children. *Parasitology* **110**, 535–545.

HUMINER, D., SYMON, K., GROSKOPF, I., PIETRUSHKA, D., KREMER, I., SCHANTZ, P. M. & PITLIK, S. D. (1992). Seroepidemiologic study of toxocariasis and strongyloïdiasis in institutionalized mentally retarded adults. *American Journal of Tropical Medicine and Hygiene* **46**, 278–281.

ISHIBASHI, H., SHINAMURA, R., HIRATA, Y., KUDO, J. & ONIZUKA, H. (1992). Hepatic granuloma in toxocaral infection. Role of ultrasonography in hypereosinophilia. *Journal of Clinical Ultrasound* **20**, 204–210.

KAYES, S. G. & OAKS, J. A. (1976). Effect of inoculum size and length of infection on the distribution of *Toxocara canis* larvae in the mouse. *American Journal of Tropical Medicine and Hygiene* **25**, 573–580.

KUMAR, J. & KIMM, J. (1994). MR in *Toxocara canis* myelopathy. *American Journal of Neuroradiology* **15**, 1918–1920.

LJUNGSTRÖM, I. & VAN KNAPEN, F. (1989). An epidemiological and serological study of *Toxocara* infection in Sweden. *Scandinavian Journal of Infectious Diseases* **21**, 87–93.

MAGNAVAL, J.-F. & BAIXENCH, M.-T. (1993). Toxocariasis in 'Région Midi-Pyrénées', France. In *Toxocara and Toxocariasis. Clinical, Epidemiological and Molecular Perspectives* (ed. Lewis, J. W. & Maizels, R. D.), pp. 83–87. Institute of Biology and British Society for Parasitology, London.

MAGNAVAL, J.-F., FABRE, R., MAURIERES, P., CHARLET, J.-P. & DE LARRARD, B. (1991). Application of the western-blotting procedure for the immunodiagnosis of human toxocariasis. *Parasitology Research* **77**, 697–702.

MIKHAEL, N. Z., MONPETIT, V. J. A., ORIZAGA, M., ROWSELL, H. C. & RICHARD, M. T. (1974). *Toxocara canis* infestation with encephalitis. *Canadian Journal of Neurological Sciences* **1**, 114–120.

MOORE, M. T. (1962). Human *Toxocara canis* encephalitis with lead encephalopathy. *Journal of Neuropathology and Experimental Neurology* **21**, 201–218.

REIBER, H. (1986). Evaluation of blood-cerebrospinal dysfunction in neurological diseases. In *The Blood-brain Barrier in Health and Disease* (ed. Suckling, A. G., Rumsby, M. G. & Bradbury, M. W. B.), pp. 132–146. Horwood, Chichester.

RUSSEGGER, L. & SCHMUTZHARD, E. (1989). Spinal toxocaral abscess. *Lancet* **ii**, 398.

RUTTINGER, P. & HADIDI, H. (1991). MRI in cerebral toxocaral disease. *Journal of Neurology, Neurosurgery and Psychiatry* **54**, 361–362.

SCHOCHET, S. S. (1967). Human *Toxocara canis* encephalopathy in a case of visceral *larva migrans*. *Neurology* **17**, 227–229.

SOULSBY, E. J. L. (1987). *Larva migrans* in perspective. In *Helminth Zoonoses* (ed. Geerts, S., Kumar, V. & Brandt, J.), pp. 137–148. Martinus Nijhoff, Dordrecht.

SPRENT, J. F. A. (1952). On migratory behavior of larvae of various *Ascaris* species in white mice. *Journal of Infectious Diseases* **90**, 163–176.

STATISTICS AND EPIDEMIOLOGY RESEARCH CORPORATION. (1993). *Egret Reference Manual*. 4th Edn. Seattle: SERC.

VAN THIEL, P. H. (1960). Comments on a case of *Toxocara* infection in the Netherlands. *Tropical and Geographical Medicine* **12**, 67–70.

VILLANO, M., CERILLO, A., NARCISO, N., VIZIOLI, L. & DEL BASSO DE CARO, M. (1992). A rare case of *Toxocara canis* arachnoïdea. *Journal of Neurosurgical Sciences* **36**, 67–69.

WANG, C., HUANG, C. Y., CHAN, P. H., PRESTON, P. & CHAU, P. Y. (1983). Transverse myelitis associated with *larva migrans*. Finding of a larva in cerebrospinal fluid. *Lancet* **i**, 423.