Ocular Toxocariasis in Schoolchildren

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Ocular toxocariasis in humans is typically a unilateral disease caused by second-stage larvae of the *Toxocara* species. Serological evidence of widespread infection in humans provides little information on clinical disease. There is only a single previous estimate of the prevalence of ocular toxocariasis (from Alabama). The present survey examined the extent of consultant-diagnosed toxocaral eye disease among a population of schoolchildren. More than 120,000 participants were surveyed by questionnaire and follow-up. Two sets of control subjects from the same school and from the same county were compared with persons who had ocular toxocariasis. The prevalence of consultant-diagnosed toxocaral eye disease was 6.6 cases per 100,000 persons when only cases regarded as definite by the consultant ophthalmologist were included. This increased to 9.7 cases per 100,000 persons when both definite and strongly suspected cases were included. Geophagia and a history of convulsion were associated with toxocaral eye disease in both of the case-control studies.

Toxocariasis is a zoonotic disease caused by the infection of humans with second-stage larvae of *Toxocara* species. Three clinical entities have been recognized in humans: visceral larval migrans, ocular larval migrans, and covert toxocariasis. In children, the seroprevalence of *Toxocara* infection has been estimated to be 4%–31% in developed countries and may increase to 86% in tropical regions, where environmental conditions favor the transmission of geohelminths [1].

Ocular toxocariasis may cause blindness [2]. Most reports of ocular toxocariasis have consisted of isolated case reports and selected case studies with documentation of clinical features [3–5]. The single documented estimate of the prevalence of ocular toxocariasis was published as an abstract recording the number of cases seen in eye clinics in Alabama over a 6-month period [6]. An estimate of 1 case per 1000 persons (increasing to 11 cases per 1000 persons when ophthalmoscopy was performed) was reported [6].

Results from earlier studies performed in Ireland established a high seroprevalence figure (31% at a cutoff

titer of 1:50), compared with reports from Europe, the United States, Japan, and Jordan, but no cases of ocular toxocariasis were found in >2000 children [7]. The aim of the present study was to assess the prevalence of ocular toxocariasis from a population-based sample in the Republic of Ireland and to identify factors associated with ocular toxocariasis through a matched case-control study.

PATIENTS AND METHODS

All primary and secondary school principals (with the exception of the special disability schools and 15 schools that had participated in an earlier seroprevalence study [7]) were sent a copy of the questionnaire for parents and a covering letter describing the background and aims of the survey. A total of 979 (24.2%) of 4043 schools agreed to participate. One copy of the questionnaire was sent to the parents of each child attending that school. A good geographical spread of participation was achieved, with schools from all 26 counties being represented. Boys and girls of all school years aged 3-19 years are represented in the sample. The response rate from parents who received a questionnaire was 56.2%. The response rate was higher among primary school pupils (71%) than among secondary school pupils (35%). Demographic details, in-

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cluding the age, sex, and location (urban or rural) of the child, were requested. Questions concerning risk factors included geophagia and pet ownership. Information was sought regarding lifetime asthma, eczema, hayfever, convulsion, and wheeze in the previous 12 months. The questionnaire was designed to identify ophthalmologist-diagnosed ocular toxocariasis. The questionnaire stated the following: "These questions are about eye disease caused by *Toxocara canis* (toxocariasis), a worm spread by dog droppings. Almost all children with this uncommon eye disease will have been told the name and the cause by a specialist." This was followed by the questions, "Has your child ever had *Toxocara* eye disease?" and "If 'yes' what year was it first noticed that there was something wrong with the eye?"

A case patient was defined as any child who received a diagnosis or for whom there was strong suspicion (confirmed by a consultant ophthalmologist) of having ocular toxocariasis. Positive responses to the question on toxocaral eye disease were followed up, first with the parents and then with the ophthalmologists concerned. In Ireland, consultant ophthalmologists hold hospital consultant posts. Both the direct and indirect ophthalmoscope is used in the examination of the eye for toxocaral lesions. The indirect ophthalmoscope is generally preferred because of the wider view obtained and its advantage when dealing with less cooperative patients. For each case patient, 4 control subjects from the same school and 4 control subjects from the same county but from different schools were

matched for age (to the nearest birth date), sex, and urban/rural status in the case-control study. Because control subjects were individually matched to case patients, a conditional logistic regression with exact significance (to account for low sample size) was used for the analysis of the relationship between host factors and risk factors between the case patients and the controls (LogXact for Windows; Cytel Software).

Informed consent was obtained from the parents or guardians of all subjects. The study was approved by the research ethics committee of the Federated Dublin Voluntary Hospital and St James's Hospital.

RESULTS

Replies for 121,156 pupils were received. A total of 184 positive replies to the question on toxocaral eye disease were obtained. Subsequent clarification of the questionnaire replies with the parents resulted in the rejection of 149 cases, 10 nonresponses, and 25 suspected ocular toxocariasis cases with details of their eye specialists. After this, clinical aspects of the suspected ocular toxocariasis cases were clarified with their consultant ophthalmologists. Because confirmation of the diagnosis could not be obtained for the 10 nonresponders (of whom 2 had emigrated), they were classified as having tested negative for ocular toxocariasis.

Eleven ocular toxocariasis cases were identified from the 25 suspected cases after receiving details from the patients' oph-

Table 1. Epidemiological description of toxocaral eye disease cases divided by urban and rural place of residence.

		Age, years					
Location, county	Sex	At time of survey	At onset of eye symptoms ^a	Eye affected	Geophagia ^b	Ocular toxocariasis ^c	Toxocara ELISA titer ^d
Urban							
Kerry	F	10	6	Left	No	Suspected	NA
Tipperary	М	16	5	Left	"No idea"	Yes	NA
Cork	F	16	4	Right	Yes	Yes	NA
Cork	М	12	10	Right	No	Yes	0.05
Dublin	М	13	5	Right	No	Yes	0.5
Rural							
Cork	F	17	14	Left	Yes	Yes	NA
Tipperary	М	12	4	Right	Yes	Suspected	0.11
Limerick	F	6	2	Right	No	Yes	1.29
Galway	М	12	8	Left	Yes	Yes	NA
Offaly	Μ	16	11	Left	"Don't know"	Suspected	NA
Dublin	F	16	3	Left	Yes	Suspected	NA

NOTE. NA, not available.

^a Age at which it was first noted that there was something wrong with the eye.

b "No idea" and "don't know" are recorded as nonresponses.

^c Ocular toxocariasis records the consultant ophthalmologist's opinion as to the diagnosis. "Yes" indicates a definite diagnosis, and "suspected" indicates a strongly suspected diagnosis.

d The titer is that obtained from the case notes expressed as optical densities. NA, not available

Table 2. Potential risk factors and their association with ocular toxocariasis using county-matched control subjects.

Factor	Case patients, n/N (%) ^a	Control subjects, n/N (%) ^a	OR (95% CI)	Р
Dog ownership ever	10/11 (90.9)	24/44 (54.5)	7.6 (0.97–349.4)	.0552
Cat ownership ever	4/9 (44.4)	22/44 (50)	0.55 (0.05-4.2)	.8214
Bird ownership ever	3/9 (33.3)	8/44 (18.2)	2.2 (0.31-12.7)	.5248
Dog ownership in the past 2 years	9/11 (81.8)	18/44 (40.9)	5.5 (1.04-56.1)	.0422
Cat ownership in the past 2 years	4/8 (50)	20/44 (45.5)	0.82 (0.08-6.7)	1
Bird ownership in the past 2 years	3/8 (37.5)	4/44 (9.1)	4.1 (0.54-28.1)	.1884
Wheeze in the past 12 months	4/11 (36.4)	8/44 (18.2)	2.5 (0.43-13.3)	.3687
Asthma	3/11 (27.3)	3/44 (6.8)	8.9 (0.62-498.4)	.1312
Eczema	1/11 (9.1)	4/44 (9.1)	1 (0.02-14.1)	1
Hayfever	3/11 (27.3)	7/44 (15.9)	2.3 (0.25-20.0)	.6149
Convulsion	4/10 (40)	1/44 (2.3)	16 (1.58–788)	.0134
Geophagia	5/9 (55.6)	4/44 (9.1)	8.2 (1.4–62.2)	.0183

NOTE. Additional matching factors were age, sex, and urban/rural residence (case patients, 11; control subjects, 44)

thalmologists (table 1). The estimated prevalence of ocular toxocariasis was 6.6 cases per 100,000 persons when only cases regarded as definite by the consultant ophthalmologist were included. This increased to 9.7 cases per 100,000 persons when both definite and strongly suspected cases were included. Of the 11 patients, 8 received a diagnosis of ocular toxocariasis, and for 3, the diagnosis was strongly suspected. Six patients were boys and 5 were girls. Five were urban and 6 were rural dwellers. Ocular toxocariasis cases were identified in 7 counties (table 1), 4 of which were in the south of the country. The mean age $(\pm SD)$ at which the eye was first noted to be abnormal was 6.5 ± 3.6 years (range, 2–14 years). Eye disease was reported in the left eye in 6 patients and in the right eye in 5 patients. No bilateral cases were reported. Eye symptoms were first noticed at an earlier age among girls (mean age, 5.8 years) than among boys (mean age, 7.2 years), but this difference was not statistically significant.

A notable feature of the results was the distribution of the positive cases between primary schools (children under ~13 years of age) and secondary schools (children aged ~13 years and older). When the children were divided by age into <13 years (n=90,486) and ≥ 13 years (n=28,397), on the basis of the 11 cases, the prevalence rates were 5.53 cases per 100,000 persons for those aged <13 years (n=90,486) and 21.13 cases per 100,000 persons for those aged ≥ 13 years (n=28,397). This difference was statistically significant (P<.03, by Fisher's exact test). Adjustment of the results for the age distribution of children in the country according to the National Census gives an overall prevalence of ocular toxocariasis of 12.10 cases per 100,000 persons in the 3–19-year-old age groups. This gives an estimate of 135 cases of ocular toxocariasis in school-aged children in the Republic of Ireland.

The prevalence of host factors and exposure to potential risk factors are shown in tables 2–4. Geophagia and having had a convulsion were 2 factors that were strongly associated with ocular toxocariasis in the analysis of both case-control studies. Irrespective of which set of control subjects was used, cat and bird ownership showed no evidence of an association with ocular toxocariasis. Dog ownership showed an association with ocular toxocariasis when the county control subjects were used. In contrast, when the school control subjects were used, no association was evident between dog ownership and ocular toxocariasis, but there was an association that approached statistical significance between a history of wheeze and ocular toxocariasis.

DISCUSSION

To our knowledge, no previous European study has established a prevalence estimate for ocular toxocariasis. Ophthalmic examination of the fundus of 102 hydatid officers in Wales, 28.4% of who were seropositive for Toxocara species, did not reveal any evidence of ocular disease [8]. Holland et al. [7] found no cases of toxocaral eye disease among 2129 Irish schoolchildren, 31% of whom were seropositive. M. Rogers (personal communication, 1998) stated that, in discussions with 5-6 ophthalmologists on Merseyside (Liverpool, United Kingdom), whose hospital practices served a population of about 200,000 children, they could only recall 3 cases of ocular toxocariasis between them in the previous 20 years. In contrast to this, Irish ophthalmologists would expect see 1-2 cases per year (including review cases). The findings of the present population-based, case-control study are useful in providing us with an appreciation of the public health significance of this zoonotic infec-

^a No. positive for the factor/no. replying to the question.

Table 3. Potential risk factors and their association with ocular toxocariasis using school-matched controls.

Factor	Case patients, n/N (%) ^a	Control subjects, n/N (%) ^a	OR (95% CI)	Р
Dog ownership ever	10/11 (90.9)	32/44 (72.7)	3.7 (0.43–177.3)	.3893
Cat ownership ever	4/9 (44.4)	26/43 (60.5)	0.16 (0.003-1.9)	.215
Bird ownership ever	3/9 (33.3)	14/38 (36.8)	0.88 (0.12-5.6)	1
Dog ownership in the past 2 years	9/11 (81.9)	26/44 (59.1)	3.5 (0.54-42.0)	.2581
Cat ownership in the past 2 years	4/8 (50)	20/42 (47.6)	0.53 (0.09-3.1)	.6234
Bird ownership in the past 2 years	3/8 (37.5)	9/39 (23.1)	1.3 (0.18-8.6)	.9939
Wheeze in the past 12 months	4/11 (36.4)	3/44 (6.8)	5.3 (0.90-36.4)	.0667
Asthma	3/11 (27.3)	3/43 (7.0)	3.8 (0.51-28.5)	.2182
Eczema	1/11 (9.1)	6/43 (14.0)	0.63 (0.012-6.8)	1
Hayfever	3/11 (27.3)	3/44 (6.8)	4.7 (0.52-58.4)	.1984
Convulsion	4/10 (40)	2/44 (4.5)	16.4 (1.9–∞)	.0096
Geophagia	5/9 (55.6)	3/44 (6.8)	22.2 (2.8-∞)	.0019

NOTE. Additional matching factors were age, sex, and urban/rural residence (case patients, 11; control subjects, 44).

tion among a defined population and suggests that ocular toxocariasis is an uncommon condition among children between the ages of 3 and 19 years living in Ireland. Maetz et al. [6] were concerned that the prevalence rates in Alabama of 1 case per 1000 persons increasing to 11 cases per 1000 persons (where ophthalmoscopy was performed) might be an underestimation. The higher prevalence reported from Alabama, the low rate for the present study, and the very low rate for the Liverpool (Merseyside) area suggest that the prevalence varies from region to region. Climate, soil humidity, and urbanization may be important factors in ocular toxocariasis.

The difference in the response rates between the primary and secondary schools was not unexpected. Irish primary schools are little involved with academic examinations. Irish secondary schools are deeply involved with examinations, which play a large part determining a child's future education and employment. Primary school teachers and parents are therefore much more willing to become involved in surveys that secondary school teachers and parents regard as a distraction from the main objective for their pupils.

In contrast to visceral larval migrans, earlier studies have concluded that ocular toxocariasis occurs mainly in children aged 7–8 years [9]. Ocular toxocariasis has been noted within the age range of 1–17 years (Memphis, TN), 4–17 years (Atlanta, GA), and 2–27 years (England) [5, 9, 10]. In the present study, an eye abnormality was first noticed at a mean age of 6.5 years. This lower mean age may be influenced by a higher response rate among primary schools. The difference between the prevalence of ocular toxocariasis in children younger and older than 13 years should be interpreted with caution. Because age at the time of survey is used in this analysis, this mea-

surement actually represents cumulative incidence; and because ocular toxocariasis is not reversible, it is not surprising that the figure is higher in older children. However, in contrast, the age at identification of an eye abnormality in this study was under 12 years in all but one case.

According to earlier studies, boys were twice as likely to have ocular toxocariasis than girls [5, 10, 11]. In the present study, this difference was not found. A slightly higher proportion of ocular toxocariasis cases occurred among children who came from a rural background, which is agreement with the higher seroprevalence found in rural children [7].

Schantz et al. [11] highlighted the importance of dog ownership as a risk factor for developing eye disease. Although very high rates of dog and cat ownership was evident in this study (table 4), a statistically significant association between pet exposure and ocular toxocariasis was only found in the countymatched control study. The clustering of cases in this study (to 7 counties with 4 in the south of the country) could not be explained by higher regional rates of dog and cat ownership specific to these 7 counties (table 4). These counties are exposed to the dominant South Westerly air stream and so are warmer and wetter than other parts of the country, which may be an important factor for the survival of embryonated eggs. When the schools that the patients attended were examined in the same way as the counties, it was seen that the rate of dog ownership was higher among these 11 schools than in the entire survey population (table 4).

Whether the clustering of cases evident in this study is a result of a higher prevalence of *Toxocara* infection in dogs from the southern counties cannot be verified. The only estimates of the prevalence of *T. canis* infection in dogs in Ireland are

^a No. positive for the factor/no. replying to the question.

Table 4. Comparative summary of the frequencies of geophagia, pet ownership, and clinical features between patients with ocular toxocariasis and a survey population without ocular toxocariasis.

Characteristic	Ocular toxocariasis cases (n = 11)	School responses ^a	County responses ^b	Survey population $(n = 121,156)$
Pet ownership				
Dog ownership ever	10/11 (90.9)	1160/1584 (73.2)	40,672/64,434 (63.1)	76,423/113,896 (67.1)
Cat ownership ever	4/9 (44.4)	774/1378 (56.2)	25,250/56,668 (44.6)	51,057/100,800 (50.7)
Bird ownership ever	3/9 (33.3)	308/1171 (26.3)	14,447/51,655 (28)	24,293/87,944 (27.6)
Dog ownership in the past 2 years	9/11 (81.8)	984/1515 (65)	34,147/61,875 (55.2)	65,304/109,445 (59.7)
Cat ownership in the past 2 years	4/8 (50)	614/1300 (47.2)	20,989/53,979 (38.9)	42,837/95,611 (44.8)
Bird ownership in the past 2 years	3/8 (37.5)	164/1099 (14.9)	9096/48,313 (18.8)	15,601/82,112 (19)
Clinical features				
Geophagia	5/9 (55.6)	111/1594 (7)	5632/66,460 (8.5)	9221/117,754 (7.8)
Asthma	3/11 (27.3)	211/1572 (13.4)	8796/65,311 (13.5)	14,897/115,502 (12.9)
Eczema	1/11 (9.1)	136/1525 (8.9)	6166/63,623 (9.7)	10,468/112,254 (9.3)
Hayfever	3/11 (27.3)	200/1549 (12.9)	6308/63,623 (9.9)	10,610/112,502 (9.4)
Wheeze in the past 12 months	4/11 (36.4)	230/1564 (14.7)	9184/64,918 (14.1)	16,496/114,863 (14.4)
Convulsion	4/10 (40)	65/1591 (4.1)	2373/65,635 (3.6)	3997/115,961 (3.4)

NOTE. Data are no. of patients positive for the factor/no. who replied to the question (%).

from Counties Dublin (83%) and Cork (25% and 45%, respectively), but a direct comparison cannot be made because of the different methodology used [12, 13].

The significantly higher level of geophagia reported in the ocular toxocariasis group (55.5%) than in either of the control groups (6.8% and 9.1%) or the entire survey population (7.8%) is clear (tables 2-4). The percentage of geophagia observed among the ocular toxocariasis cases is higher (55.5%) than that reported by previous US studies (41% [9] and 38% [10]). A statistical association between seropositivity and geophagia has been established [7, 14, 15]. The absent or weak association between ocular toxocariasis and exposure to dogs, but a significant association between ocular toxocariasis and geophagia recorded in the present study implies that the problem lies more with the type of human behavior that increases exposure than with the level of dog ownership. Previous studies in Ireland have shown that the percentage of soil samples that were positive for Toxocara ova varied from 8.3% in adventure playgrounds to 22% in neighborhood parks and 38% in domestic gardens [16, 17]. A geophagic child may therefore be particularly vulnerable to ingestion of Toxocara eggs under conditions in Ireland.

The only clinical feature associated with ocular toxocariasis in both case-control studies was convulsion. *Toxocara* larvae in the human brain at autopsy have been reported [18]. Meningitis, encephalitis, optic neuritis, and epilepsy are among the conditions reported after a cerebral infection of *Toxocara* larvae in humans [19–22]. Glickman et al. [23] investigated the re-

lationship between toxocaral infection and epilepsy but were unable to conclude whether the increased seroprevalence was associated with geophagia or epilepsy. Magnaval et al. [24] have concluded that *T. canis* larvae in the human brain do not frequently induce a recognizable neurological syndrome. However, Watzke et al. [25] found that intraperitoneal injection of 2000 larvae in primates subsequently gave rise to numerous granulomata in the brainstem, cerebellum, and regions of the midbrain adjacent to the entry of the optic tracts.

Convulsions are relatively common in children. Febrile convulsions form the bulk of these convulsions and occur in ~3.6% of children, in whom two-thirds will have a single convulsion and one-third will have multiple convulsions. They occur between 6 months and 6 years of age and are thought to reflect the immaturity of the developing brain. Seven of the 11 patients were within the febrile-convulsion age range at the onset of eye symptoms. There is no information available from these data to indicate whether cerebral migration of larvae had occurred and caused a convulsion or whether the convulsions were due to some systemic upset associated with the toxocaral infection, which in turn caused a febrile convulsion, or whether children who have convulsions are more susceptible to ocular toxocariasis. Specific information regarding these points was not sought in the questionnaire and would require a further study.

In the school-matched control subjects, wheeze approached but did not reach a statistically significant association with eye involvement. A number of previous studies have reported an

^a Summary of the responses from the schools in which the ocular toxocariasis cases were identified.

b Summary of the responses from the counties in which the ocular toxocariasis cases were identified.

association between Toxocara seropositivity and wheeze and asthma [26-28]. Wheeze in this study refers to wheeze in the previous 12 months, which, in all cases, would follow the date of initial eye abnormality. It does not, however, exclude the possibility that patients might have experienced earlier wheeze (about which no enquiry was made), which may have started before, during, or after eye involvement. If such an association existed, it would link eye invasion to lung invasion, thus adding further support to the hypothesis that ocular toxocariasis occurs as part of a generalized larval invasion, although it could be argued that wheeze could be the result of immune sensitization rather than direct lung invasion. No data are available from the study to distinguish whether direct invasion of the lung resulted in wheeze, whether this was part of a general response to systemic parasitic infection, or whether children who wheeze (and in most cases have asthma) are more susceptible to ocular toxocariasis.

This study provides evidence that, despite a relatively high level of exposure to toxocariasis among the study population, this does not translate into a high incidence of toxocaral eye disease among the same population. Furthermore, this study emphasizes the importance of geophagia as a risk factor for ocular toxocariasis and provides some support for the hypothesis that ocular toxocariasis may be part of a more widespread systemic invasion by larvae, giving rise, in some cases, to convulsion.

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