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COMMUNICATIONS

CHRONIC ENDOPHTHALMITIS DUE TO *TOXOCARA**

BY

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NEMATODE infestations of the eye evoked little or no interest until the middle of the 20th century when Wilder (1950), whilst carrying out a histological survey of 46 cases of pseudogliomata, found nematode larvae or their hyaline capsules in 24, and tissue reactions characteristic of nematode endophthalmitis in the remaining 22. At that time, the larvae found in Wilder's series were believed to be those of the hookworm, and it was not until 6 years later that Nichols (1956), when reviewing this series, ascertained that the larvae present in five eyes were in fact those of *Toxocara canis*.

More recently, Irvine and Irvine (1959) reported one case in which a retinoblastoma had been diagnosed clinically but histological examination of the enucleated eye revealed only chronic endophthalmitis due to a larva of the genus *Toxocara* at the site of the clinical tumour.

No ocular lesions due to *Toxocara* had been identified in Britain until Ashton (1960) described four cases of retinal granuloma in which the larvae of this genus were actually demonstrated, and thereby established not only that the larva existed as an entity in human disease in Western Europe, but also that it was capable of producing a granulomatous ocular lesion which previously had sometimes been labelled as exudative choroiditis and which had certainly not formerly been associated with *Toxocara canis*. The importance of this discovery lies not only in the finding of a new lesion attributed to the *Toxocara*, but more especially in the fact that all four eyes reported by Ashton had been enucleated because the lesion strongly resembled a retinoblastoma.

Outside the field of ophthalmology, Beaver, Snyder, Carrena, Dent, and Lafferty (1952), during the investigation of eosinophilic granulomatous lesions of the liver, discovered portions of a larval nematode belonging to the genus *Toxocara* and, since this discovery, the larva has been located in human tissues by numerous workers, thus confirming the importance of *Toxocara* infestation as an aetiological agent in some diseases. No such case, however, has yet been reported in the United Kingdom, although the larva found by Beautyman and Woolf (1951) in the brain of a child and described as that of *Ascaris lumbricoides* may have been of this nature.

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As stated above, the granulomatous lesion described by Ashton was the only evident form of ocular *Toxocara* in Great Britain, but during the past year at the Institute of Ophthalmology, a chronic endophthalmitis due to *Toxocara* has been discovered in six eyes. It might be mentioned in passing that *Toxocara* infestation was suspected only after examination of the initial histological sections and that in only one case was its presence believed to have been considered in the clinical differential diagnosis.

Case Reports

Case 1, a boy aged 4½ years, attended hospital because his mother had noticed something white in his right eye. This had been present for the previous 3 or 4 months but not longer. On examination under general anaesthesia, a white retrolental mass suggestive of a neoplasm was found and the eye was subsequently enucleated.

Pathology

MACROSCOPICAL EXAMINATION.—The eye was opened horizontally to show a funnel-shaped retinal detachment with an abundant subretinal exudate containing cholesterol crystals. No intra-ocular new growth was seen (Fig. 1).

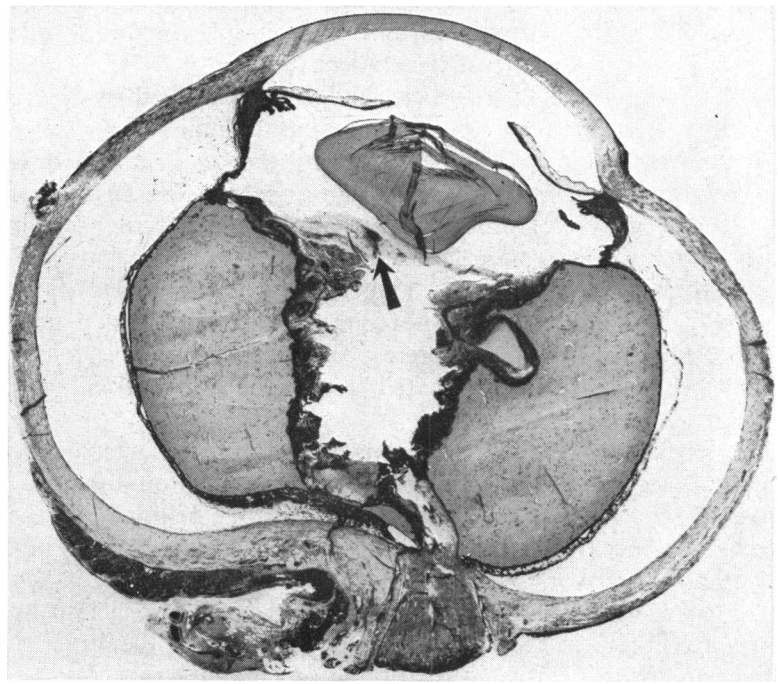

FIG. 1.—Case 1, section of eye, showing funnel-shaped retinal detachment and cyclitic membrane which contained larva (arrow). Celloidin section. Haematoxylin and eosin. ×6.

MICROSCOPICAL EXAMINATION.—Section showed a mild chronic inflammatory reaction in the uvea and posterior synechiae to the lens. There were cholesterol crystals in a massive subretinal exudate, and the totally detached retina contained replacement gliosis besides being adherent anteriorly to a cyclitic membrane in which there were numerous plasma cells, lymphocytes, and some polymorphonuclear leucocytes. In four of the serial sections examined, a small focus of fibrinoid necrosis was found within the cyclitic membrane. Fragments of a nematode larva probably that of *Toxacara* (Figs 2 and 3) were present within the fibrinoid necrosis, which was surrounded by endothelioid cells and numerous eosinophils. In addition, a large fibrous mass was found at the macula, and it is suggested that this indicated the point of entry of the larva before it eventually passed into the vitreous.

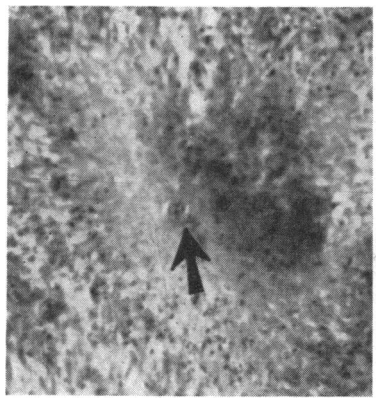

FIG. 2.—Higher-power view, showing fragment of nematode (arrow) amidst fibrinoid necrosis. ×120.

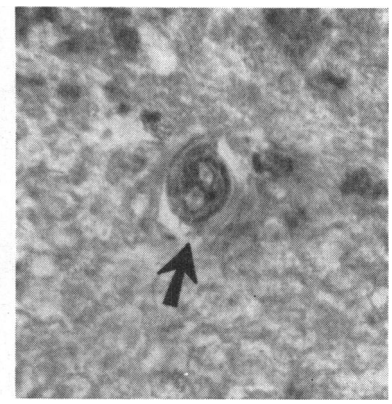

FIG. 3.—Transverse section of larva in which excretory columns and lateral alae are discernible. ×575.

In view of these findings, subsequent investigations revealed that the boy had always been in good health, and that he had always been frightened of animals and avoided them whenever possible.

Case 2, a boy aged 4½ years, was brought for ophthalmic examination because the mother thought the right eye started to diverge at about the age of 2½ years. The vision in this eye was poor and in addition to a low-grade iritis and posterior synechiae, a white mass was observed in the anterior vitreous. After a short period of observation, not only had the mass grown larger, but at the same time it had become yellowish in colour; enucleation was therefore performed. The other eye was healthy in all respects.

Pathology

MACROSCOPICAL EXAMINATION.—The globe was opened horizontally, revealing a total retinal detachment with extensive subretinal exudation. A retrolental membrane was present but there was no evidence of tumour (Fig. 4, overleaf).

MICROSCOPICAL EXAMINATION.—The cornea showed early stromal vascularization and the iris and angle structures were mildly infiltrated with chronic inflammatory cells, while an eosinophilic exudate occupied the anterior chamber. A subretinal exudate was present and the oedematous and totally detached retina was adherent anteriorly to a retrolental mass of granulation tissue consisting of endothelial cells, lymphocytes, and numerous eosinophils; in some serial sections, this mass was seen to contain foci of fibrinoid necrosis and occasional foreign body giant cells. In Sections 173–175, fragments

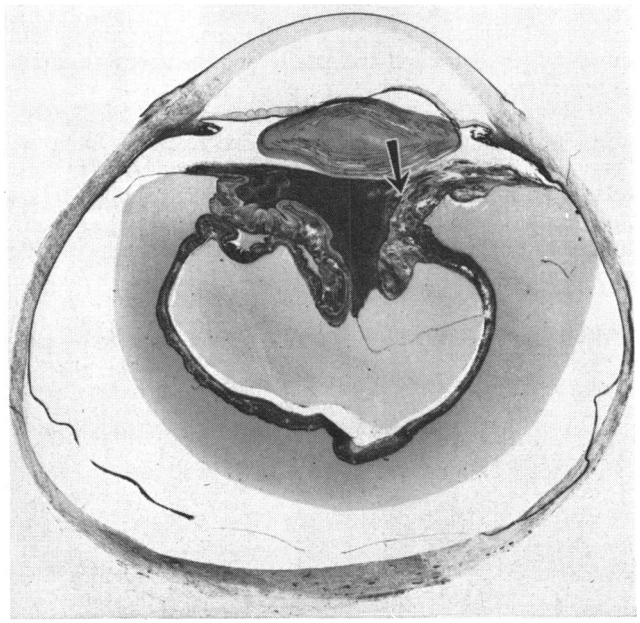

FIG. 4.—Case 2, section of right eye, showing totally detached retina adherent to retrolental granulation tissue, which contained the larva (arrow). Celloidin section. Haematoxylin and eosin. ×4.

of a nematode larva (Figs 5 and 6) measuring 20μ in cross section and, therefore, very probably that of the second stage larva of *Toxocara canis*, were found in these necrotic areas.

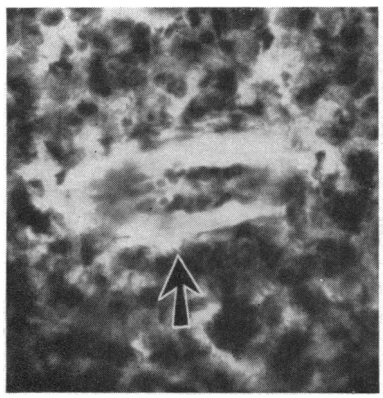

FIG. 5.—Longitudinal section of larval fragment surrounded by chronic inflammatory infiltration. ×575.

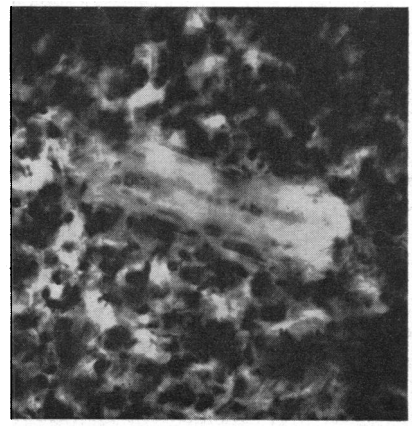

FIG. 6.—Another longitudinal section of larval fragment. ×385.

The child had been in close contact with a dog until the time of enucleation and apart from his ocular condition had always enjoyed excellent health.

Case 3, a girl aged 7 years, attended hospital with a right convergent strabismus. The right eye was blind and besides having a shallow anterior chamber and cataract it also exhibited an iritis. Transillumination was suggestive of neoplasm and enucleation was therefore performed. The other eye was clinically normal with visual acuity 6/6.

Pathology

MACROSCOPICAL EXAMINATION.—The eye was opened horizontally and no intraocular neoplasm was found, but a total retinal detachment with a green subretinal exudate was observed (Fig. 7).

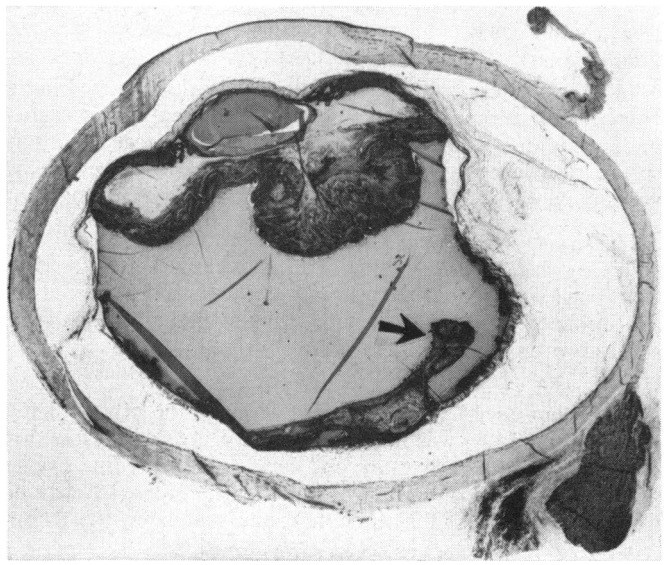

FIG. 7.—Case 3, section of right eye, showing total retinal detachment and chronic granuloma (arrow). Celloidin section. Haematoxylin and eosin. ×3·75.

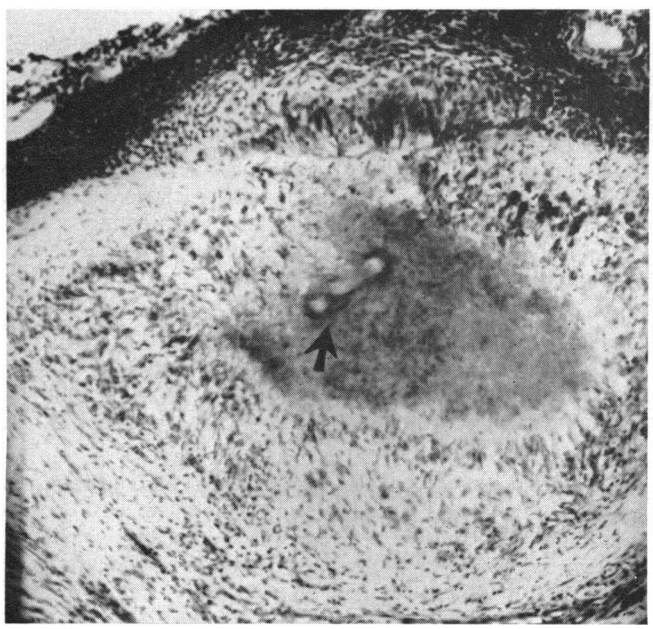

FIG. 8.—Higher-power view of granuloma showing hyaline capsule (arrow) amidst eosinophilic necrosis. ×72.

MICROSCOPICAL EXAMINATION.—Sections of the whole eye showed early pannus degenerativus, round-celled infiltration of the iris, and posterior synechiae to the lens, behind which lay an extensive cyclitic membrane heavily infiltrated by chronic inflammatory cells. There was advanced replacement gliosis of a totally detached retina, and the subretinal exudate was not only invaded by macrophages, lymphocytes, and polymorphonuclear leucocytes, but also contained cholesterol crystals. Scattered chronic granulomatous foci projected from the choroid into the subretinal exudate and in one of these there were giant cells, endothelioid cells, and eosinophils, together with extensive fibrosis around a central area of necrosis. Within this necrotic tissue there was a tube-like hyaline capsule (Fig. 8, previous page), which had almost certainly contained a *Toxocara* larva although it could not be found in the 426 serial sections examined.

In view of these findings, further investigations carried out revealed that this child had been subject to repeated attacks of "flu" and on one occasion at the age of 7 months had had pneumonia. Furthermore, the child's general condition seemed to improve after enucleation whereas before enucleation her health had been indifferent. For about 2 years previously she had been in close contact with a dog.

Haematological Examination.—This was carried out after enucleation. A differential count showed an eosinophilia of 13 per cent. The Wassermann reaction and Kahn test were negative. The toxoplasmosis dye test was positive at 1:256, and the complement-fixation test at 1:8. It was interesting to find a positive toxoplasmosis result—the only one known in the series.

Case 4, a boy aged 7 years, with poor vision in the left eye, first attended hospital at the age of 5 years when he was found to have a white mass below the left macula. Malignancy was not suspected at that time and during the succeeding 2 years a total retinal detachment gradually developed. The eye was then considered functionally useless so enucleation was performed. At that time, and one year later, the fellow eye was healthy in every respect.

Pathology

MACROSCOPICAL EXAMINATION.—The eye was opened horizontally to reveal a funnel-shaped retinal detachment with extensive subretinal albuminous exudation (Fig. 9, opposite).

MICROSCOPICAL EXAMINATION.—Sections showed both anterior and posterior chambers to contain a scanty granular exudate and posterior synechiae between the lens and iris which was infiltrated by round cells. There was a small suprachoroidal exudate anteriorly, while some haemorrhage and chronic inflammatory cells were present in a large subretinal exudate. The totally detached retina had undergone replacement gliosis, and part of its surface was lined by an inflammatory membrane containing round cells, giant cells, and numerous eosinophils, together with several eosinophilic abscesses.

Over 350 serial sections were examined and in sections numbered 298, 299, and 300 fragments of a larva were visible. In one section (Fig. 10, opposite), there was a typical cross-section of the larva measuring 20 μ and which showed lateral alae, excretory columns, and intestines, and was therefore probably a second-stage larva of the *Toxocara canis*.

Case 5, a boy aged 2 years, was brought to hospital because his mother had noticed a left convergent strabismus and a white reflex in the left eye during the previous year. Because of some delay in having the boy admitted to hospital locally the mother brought him to London where he was seen by several surgeons who unanimously agreed the lesion was suggestive of a retinoblastoma. This eye was therefore enucleated.

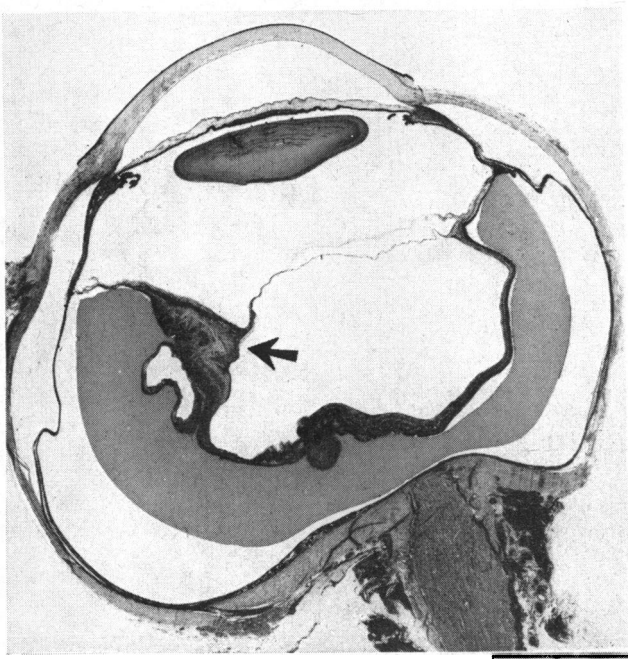

FIG. 9.—Case 4, section of left eye, showing totally detached retina with part of its surface lined by an inflammatory membrane in which larval fragments were located (arrow). Celloidin section. Haematoxylin and eosin. ×4.

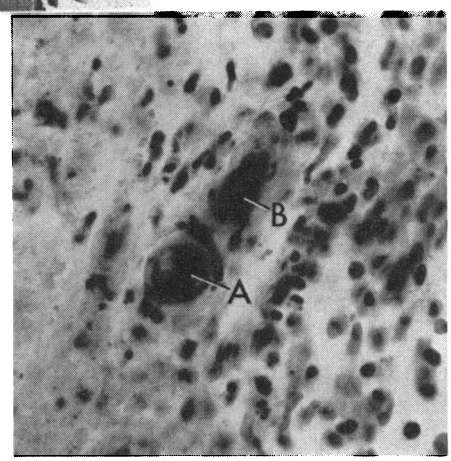

FIG. 10.—Transverse (A) and oblique (B) sections of the larval fragments found in the inflammatory membrane indicated in Fig. 9. ×405.

Pathology

MACROSCOPICAL EXAMINATION.—The globe was opened horizontally to reveal a funnel-shaped retinal detachment, extensive subretinal exudation, and a dense cyclitic membrane. No evidence of a neoplasm was found (Fig. 11, overleaf).

MICROSCOPICAL EXAMINATION.—Section of the whole eye showed a round-celled infiltration of the iris with posterior synechiae to the lens. The totally-detached retina contained scattered areas of intraretinal exudation and haemorrhage, whilst an eosinophilic granuloma was adherent not only to the surface of the retina, but also to a thick inflammatory cyclitic membrane. In this granuloma there were numerous giant cells, eosinophils, and chronic inflammatory cells. Section 123 (Fig. 12, overleaf) showed a longitudinal portion of a *Toxocara* larva lying in an eosinophilic zone of necrosis in the centre of the granuloma.

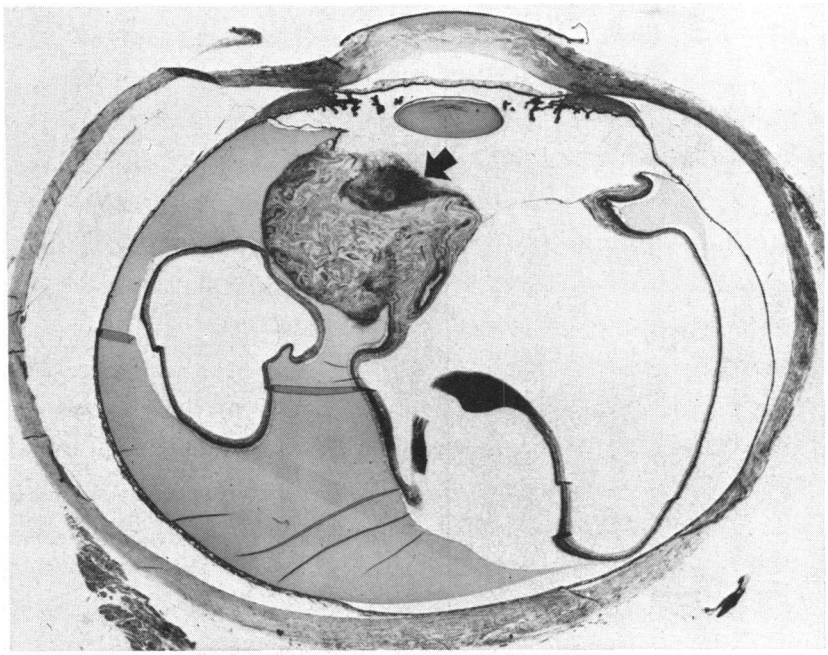

FIG. 11.—Case 5, section of left eye, showing totally detached retina with an eosinophilic granuloma, containing the larva (arrow), adherent to the retina. Celloidin section. Haematoxylin and eosin. ×4·7

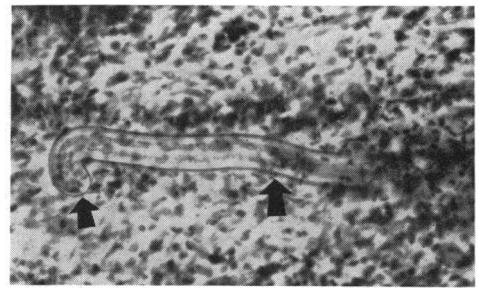

FIG. 12.—High-power view of granuloma, showing longitudinal section of larva (arrows) surrounded by chronic inflammatory cells. ×210.

Subsequent inquiries revealed that this child had been in contact with a dog for the past year and that he had an eosinophilia of 7 per cent. (Total 1,421 per cu.mm.) During the past year, he had been subject to bouts of coughing but otherwise was in good health. This case is particularly interesting not only because of the differences in clinical and pathological diagnosis, but also because the initial sections of the eye showed little evidence of inflammatory reaction and eosinophilic infiltration. If no further sections had been cut, an erroneous diagnosis of Coats's disease might well have been made.

Case 6.—The clinical history of this case has already been published by Waldron Harris (1961) and will be only briefly summarized here with a more detailed account of the pathological findings.

A child aged 2 years and 9 months was brought to the hospital because the mother thought she was not seeing well. Examination under general anaesthesia at about the age of 4½ years, revealed features suggestive of neoplasm in the right eye and this was enucleated.

Pathology

MICROSCOPICAL EXAMINATION.—A section sent for opinion to Prof. Ashton at the Institute of Ophthalmology, showed a complete retinal detachment without evidence of a tumour (Fig. 13). The presence of a few pockets of eosinophils together with a mild chronic inflammatory reaction suggested parasitic infection. Dr. E. M. Ward, Pathologist, Leicester, kindly supplied the paraffin block containing the remainder of the eye and further serial sections were cut. About 680 sections from this block were examined and in four of them fragments of the nematode larva (Fig. 14) were discovered amidst fibrinoid necrosis in the centre of a choroidal granuloma, protruding into the subretinal exudate. This granuloma also contained a round celled infiltration, giant cells, and an intense eosinophilic reaction. The larval fragments measured 18 μ in width and therefore correspond to the second-stage larva of *Toxocara*.

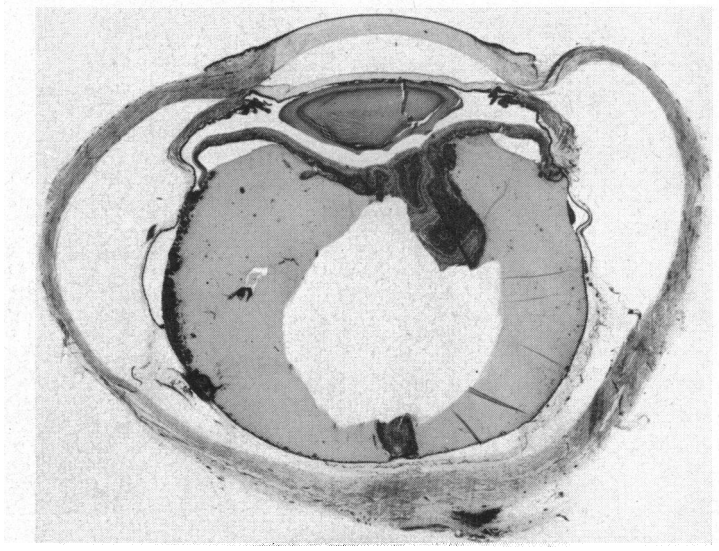

FIG. 13.—Case 6, section of right eye, showing retinal detachment and choroidal granuloma which contained the larva. Haematoxylin and eosin. ×3·75.

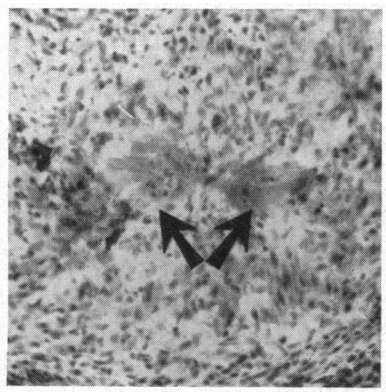

FIG. 14.—Higher-power view of granuloma showing round celled infiltration and eosinophilic necrosis around larval fragments (arrow). ×125.

Subsequent inquiry revealed that the child had been in fairly close contact with a puppy and a cat. She had suffered frequent nightmares, waking up and shaking, and she had an eosinophilia of 6 per cent. The fellow eye was healthy in all respects.

Discussion

The nematode *Toxocara* is one of the commonest intestinal parasites of dogs and cats, and is particularly prevalent in puppies during the first 2 months of life. Adult worms (Fig. 15) present in the stomach or small intestine may either be vomited by the puppy or remain in its gut, the ova (Fig. 16) being excreted in the faeces. Garden soil therefore may become heavily contaminated by a single infested animal. According to prevailing conditions the ova may die, but they are remarkably resistant and may actually remain dormant or develop to a limited extent.

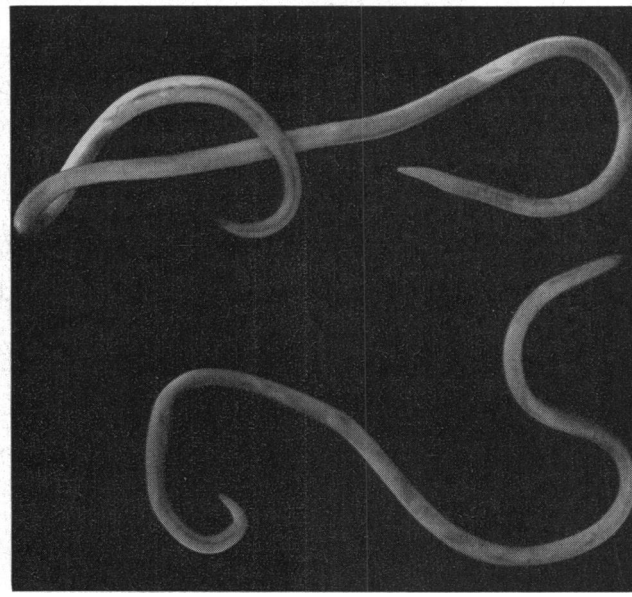

FIG. 15.—Adult male and female *Toxocara canis* worms. ×2.

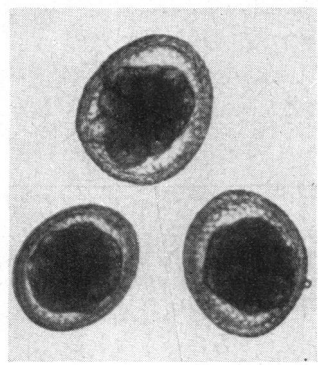

FIG. 16.—*Toxocara* ova isolated from faeces of an infested dog. ×210.

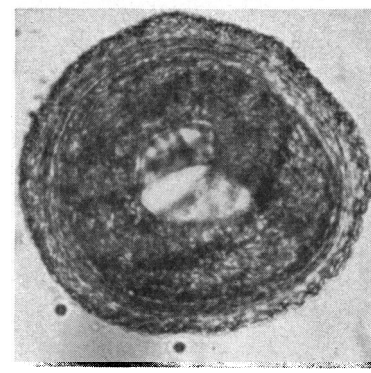

FIG. 17.—First-stage larva of *Toxocara canis*. The larva is curled up within its protective shell. ×525.

A child of dirt-eating age may accidentally come into contact with and swallow *Toxocara* ova, which develop further in the child's intestine, producing first-stage larvae within a protective shell (Fig. 17). Under favourable conditions or through intestinal activity, the shell ruptures (Figs 18, 19, 20), liberating the second-stage* larva (Fig. 21), which migrates from the gut into the tissues or blood stream (hence the name visceral *Larva migrans*). According to Sprent (1958), *Toxocara* larvae are active borers and it is conceivable that they might lodge in any organ or tissue. *Toxocara* lesions are found usually in the liver, lung, and brain where respectively jaundice, pneumonitis, and encephalitis may result. A larva may migrate further, by chance reaching the eye where it gives rise to a chronic inflammatory reaction. Figs 16 to 21 show actual photomicrographs of developing ova and larvae which the author has cultivated under suitable conditions in the laboratory.

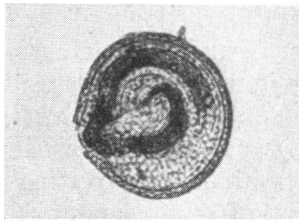

FIG. 18.—The shell has just ruptured and the larva approaches the opening. ×210.

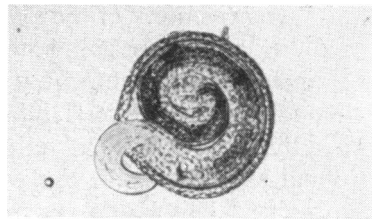

FIG. 19.—Larva protruding from shell. ×210.

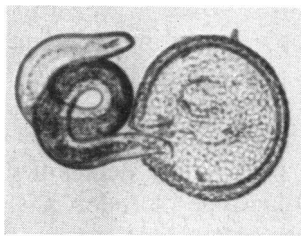

FIG. 20.—Larva almost liberated. ×210.

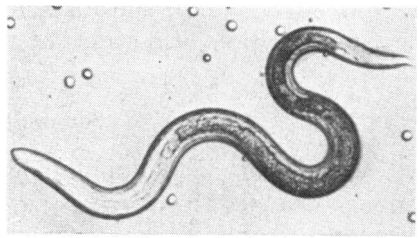

FIG. 21.—The migrating second-stage larva, now free, lies amidst erythrocytes. ×210.

At present, it is impossible to estimate the incidence of ocular *Toxocara* infestation, as time-consuming histological examinations, often of several hundred serial sections from each eye, have to be carried out, and even then, if found, the larval fragments may be present only in two or three sections. In the Department of Pathology at this Institute, there are sections from several eyes showing features of parasitic involvement in which no larvae have been demonstrated. These cases parallel 22 of the 46 cases from Wilder's series, but it is probably preferable to follow Ashton's advice—"to confine

* This larva measures about 20 μ in diameter and 350–450 μ in length.

any further reports to cases where the nematode larvae have actually been demonstrated".

It would appear that two types of ocular lesion may be produced by *Toxocara*: the first a granuloma and the second a chronic endophthalmitis with exudation. The granulomatous lesion resembles that found in some cases of tuberculosis in adults with a low tissue sensitivity and high resistance, resulting in little more than an intensified foreign body reaction with subsequent "healing" by fibrosis and encapsulation. This type of lesion might be simulated in children when several larvae have entered the tissues and have remained there sufficiently long for the host to acquire a high resistance to them. When this has occurred, it is possible that one of the larvae migrates further afield to become lodged in the eye where, in the circumstances, a granulomatous lesion is formed. In the second group with chronic endophthalmitis, it may be that the larva passes rapidly to the eye and, due to high toxicity and high sensitivity of the host, tissue destruction and exudation are present in addition to chronic inflammation. This results in chronic endophthalmitis and retinal detachment, well seen in the six cases described in this article. In addition, it is understandable that an ocular *Toxocara* lesion may commence in the more superficial retina as a granulomatous mass and following intraretinal exudation give rise to a parasitic mass projecting forwards into the vitreous. This lesion resembles a clinical case under observation and may represent an intermediate stage between the granulomatous lesion and that with chronic endophthalmitis and retinal detachment.

Toxocara canis infestation should be remembered as a cause of chronic endophthalmitis in children and certainly investigated or considered along with other known aetiological agents of chronic uveitis in the young.

Summary

(1) Six cases of chronic endophthalmitis with retinal detachment due to *Toxocara canis* are described. This particular type of lesion has not previously been described in Great Britain.

(2) The life cycle of the parasite is briefly described, with particular reference to ocular involvement.

(3) *Toxocara* larvae may present two differing ocular lesions, namely a granulomatosis and a chronic endophthalmitis with retinal detachment. The possible reason for this difference in presentation is discussed.

(4) Ocular *Toxocara* infestation should be borne in mind in the differential diagnosis of pseudoglioma and of chronic endophthalmitis in the young.

I am particularly indebted to Prof. Norman Ashton for his valuable criticism and encouragement, not only during the preparation of this paper but also while the work has been carried out. In addition I wish to thank Mr. A. McNeil, Mr. V. E. Elwood, and Mr. P. Aldred for their technical assistance, and Miss E. FitzGerald for secretarial help.

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