

COMMUNICATIONS

PATTERN OF UVEITIS IN CHILDREN*

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THE comparatively few accounts of uveitis in children all agree that it is uncommon (Table I). This report concerns 150 cases of uveitis starting before the age of 16 years. Most of the children were below this age when first seen; although 5 were aged between 16 and 20 and 3 were over 20, there was good documentary evidence that the uveitis had started before the age of 16. The 150 cases represent 5 per cent. of the total of 2,890 referred to the Uveitis Clinic of the Institute of Ophthalmology in the period from 1956 to 1964.

The proportion of children under 15 years of age in the population of England and Wales in 1951 was over 20 per cent., so that there are fewer cases of uveitis in children than would be expected from the age structure of the population. It is interesting that Davis (1953) found a similar proportion of cases of uveitis in children—21 out of a total of 400—and Kimura, Hogan, and Thygeson (1954) 5·8 per cent. of 810 cases of uveitis.

TABLE I
INCIDENCE OF UVEITIS IN CHILDREN

Author	Total in Series	No. of Children	Age Group (years)	Percentage of Total
Blegvad (1941)	896	20	Under 15	2·2
Guyton and Woods (1941)	562	7	Under 10	1·3
		59	10-19	8·8
Marchesani (1949)	451	17	Under 15	3·7
Davis (1953)	400	21	Under 16	5·0
Kimura, Hogan, and Thygeson (1954)	810	47	Under 16	5·8
Bennett (1955)	332	7	Under 15	2·1
Perkins (1961)	1,718	40	Under 11	2·3
		169	11-20	9·8

The cases inevitably represent a selected group, as only those which were more severe and chronic are likely to have been referred for investigation. The methods of investigation used in the clinic have been described previously (Perkins, 1961).

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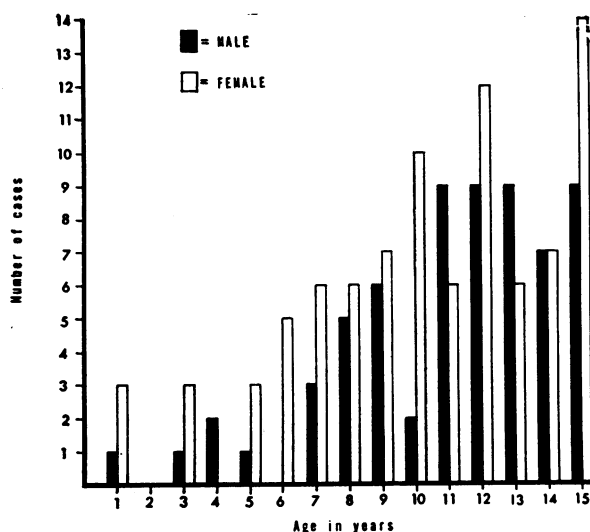


FIGURE.—Sex and age incidence in 150 cases of uveitis in children.

TABLE II
TYPE OF UVEITIS IN A SERIES OF 150 CHILDREN

Type of Uveitis	No. of Cases	Percentage of all Cases
Anterior acute	34	22.6
Anterior chronic	40	26.6
Posterior acute	29	19.3
Posterior chronic	30	20.0
Generalized acute	2	1.3
Generalized chronic	15	10.0
Total	150	

The sex and age distribution of the series is shown in the histogram (see Figure). Girls predominate in a ratio of 86 to 64, and in both sexes the prevalence increases with age. The incidence of the clinical types of uveitis (Table II) shows that chronic uveitis is more common than acute uveitis in this series. This distribution is the reverse of that found in uveitis in the adult. In a series of 1,718 cases of uveitis of all ages (which includes some of the children reported on here), acute cases accounted for three-quarters of the total (Perkins, 1961). This difference is highly significant in statistical terms (Table III). Other authors have also found that uveitis in children tends to be chronic rather than acute, and although it is possible that mild acute attacks of short duration are likely to be overlooked or diagnosed as conjunctivitis in children, the difference may well be real.

If the clinical categories are considered with the sex of the patients (Table IV), a marked excess of girls with chronic anterior uveitis is apparent. The difference between the sex distribution in this group and the chronic posterior and generalized groups together is statistically significant ($\chi^2 = 14$; $P < 0.01$).

TABLE III
COMPARISON OF INCIDENCE OF
ACUTE AND CHRONIC UVEITIS

Uveitis	Children	All Ages
Acute cases	65	1,305
Chronic cases	85	413
Total	150	1,718

$\chi^2 = > 50; P < 0.01$

TABLE IV
SEX DISTRIBUTION OF UVEITIS IN CHILDREN

Type of Uveitis	Male	Female	Female per cent.
Anterior acute	19	15	44.1
Anterior chronic	5	35	87.5
Posterior acute	15	14	48.3
Posterior chronic	14	16	53.3
Generalized acute	—	2	(100.0)
Generalized chronic	11	4	26.6

Anterior chronic versus other chronic cases: $\chi^2 = 14; P < 0.01$

This series of cases of uveitis in children shows a higher proportion (39.3 per cent.) of cases of posterior uveitis than that found in a series of all ages (19.2 per cent.; Perkins, 1961). This is partly due to the comparatively high incidence (20 per cent.) of chronic posterior uveitis in the children, compared with only 4 per cent. in a series of all age-groups.

Acute Anterior Uveitis

Thirty-four children, 19 boys and 15 girls, were diagnosed as having acute anterior uveitis, and this group of cases accounted for 22.6 per cent. of the total of 150. This is a smaller proportion than is found in adults with uveitis, but otherwise the pattern resembled the condition as seen in adults, including the failure to find any definite aetiology in the majority of cases.

Uveitis secondary to herpetic keratitis occurred in 5 cases, in 3 tuberculosis was suspected, 2 were probably traumatic in origin, and some evidence of recent infection in teeth and tonsils, for instance, was noted in 6 cases. Case 58 in Table V had signs and symptoms suggesting juvenile rheumatoid arthritis.

On the whole, the condition responded well to treatment, although systemic steroids were required in a few cases, and recurrences have been observed in at least six.

The clinical features are summarized in Table V. It will be noted that most of the cases occurred in children over the age of 7, the mean age of onset in the girls being 10.5 and in the boys 11.8 years. It is unlikely that acute anterior uveitis in children differs greatly, except in overall incidence, from that seen in adults.

Chronic Anterior Uveitis

There were 40 children in this diagnostic category and the cases are summarized in Table VI. The aetiology in 2 patients, one boy and one girl, was thought to be tuberculosis, in 2 sarcoidosis, and 4 had heterochromic uveitis. Two patients (Cases 128 and 82 in Table VI) had marked anterior vitreous opacities and may have had peripheral choroiditis, although no note was made of fundus changes. Case 119 was a baby with microphthalmos and a chronic uveitis which may have been present since birth. The remaining 29 exhibited a syndrome possibly confined to children:

TABLE V
ACUTE ANTERIOR UVEITIS

Cases	Age at Onset (years)	Sex	Clinical Features	Eye	Aetiology and Remarks
6	13	F	Non-specific	Both	
8	9	F	Nodule in iris	L	
11	12	M	Non-specific	Both	
12	8	F	Non-specific	R	Urinary infection
13	7	F	Non-specific	Both	
17	13	M	Non-specific	R	Traumatic
18	1	F	Non-specific	L	? Tuberculosis
24	14	M	Non-specific	Both	Dental abscess
25	6	M	Non-specific	Both	
26	15	F	Non-specific	Both	
28	7	M	Corneal lesions	R	Herpes simplex
30	12	F	Non-specific	R	Tonsillitis
31	10	F	Non-specific	R	
47	15	F	Non-specific	Both	Arthritis of elbow
48	11	M	Non-specific	R	
58	15	M	Non-specific	Both	Still's disease
60	11	M	Non-specific	Both	? Tuberculosis. Tuberculous glands in neck
61	15	M	Non-specific	R	
63	10	F	Non-specific	L	Appendicitis
67	14	F	Corneal lesions	L	Herpes simplex
74	13	M	Non-specific	R	Nephritis
76	12	M	Corneal lesions	L	Herpes simplex
84	12	F	Corneal lesions. Iris atrophy	L	Herpes simplex
87	12	F	Corneal lesions. Secondary glaucoma	L	Herpes simplex
90	15	M	Non-specific	L	
93	9	M	Non-specific	R	? Tuberculosis. Family history and glands in neck
94	8	M	Hypopyon	R	Raised eosinophil count
100	11	F	Non-specific	R	
116	8	M	Non-specific	L	
120	12	M	Non-specific	L	Traumatic
123	15	M	Non-specific	R	Dental abscess
129	15	M	Non-specific	L	Sacro-iliitis
132	13	M	Non-specific	Both	
138	9	F	Non-specific	L	

a chronic iridocyclitis with posterior synechiae, band-shaped degeneration of the cornea, and secondary lens changes. Six out of the total of 40 cases of chronic anterior uveitis had all these features, a further 10 had a chronic iridocyclitis with corneal changes but no secondary cataract, and 13 presented with similar uveal changes but no abnormality of the cornea or lens.

This type of uveitis has been described in association with Still's disease, but that it can occur without evidence of rheumatic disease seems certain (Davis, 1953; Unger and Schomerus, 1954; Smiley, May, and Bywaters, 1957), and in this series only two of the patients had physical signs of joint disease, a further five giving a history of pain in one or more joints. Only two of those in whom there was any evidence of rheumatism had band degeneration and lens changes. In the four others with the complete syndrome and the ten with corneal changes and iridocyclitis there was no history of joint disease.

It is possible, of course, that the joint manifestations may occur at a later date, but two of the patients were free from joint disease many years (twenty-nine in one

TABLE VI
CHRONIC ANTERIOR UVEITIS

Cases	Age at Onset (years)	Sex	Clinical Features	Eye	Remarks
75	14	M	Nodules in iris	L	? Tuberculosis
39	7	F	Severe iritis	Both	? Tuberculosis
78	10	M	Typical heterochromic uveitis	R	
83	12	F	Typical heterochromic uveitis	R	
15	15	F	Typical heterochromic uveitis	R	
51	15	F	Typical heterochromic uveitis	?	
145	13	F	Kerato-uveitis	Both	? Sarcoidosis
144	8	M	Non-specific	Both	? Sarcoidosis
128	15	F	Vitreous opacities +	L	? Peripheral choroiditis
119	1	F	Microphthalmos	L	Congenital uveitis
32	9	F	Band opacity. Lens changes	Both	Rheumatic history
117	14	F	Band opacity. Lens changes	R	Rheumatic history
133	5	F	Band opacity. Lens changes	R	
20	4	F	Band opacity. Lens changes	Both	
66	6	F	Band opacity. Lens changes	Both	
37	6	F	Band opacity. Lens changes	Both	
7	14	F	Band opacity	Both	
147	9	F	Band opacity	Both	
111	6	F	Band opacity	Both	
40	4	F	Band opacity	Both	
86	6	F	Band opacity	Both	
105	6	F	Band opacity	Both	
23	8	F	Band opacity	Both	
106	7	F	Band opacity	Both	
50	11	F	Band opacity	Both	
118	10	F	Band opacity	Both	
71	15	F	Non-specific	Both	
1	14	F	Non-specific	Both	
9	11	F	Non-specific	Both	
82	13	F	Vitreous opacities	R	Eosinophils 2,000/c. mm. ? <i>Toxocara canis</i>
109	5	F	Non-specific	Both	
148	3	F	Non-specific	Both	
114	12	M	Non-specific	Both	Developed polyarthritis later
41	3	F	Non-specific	Both	
96	12	F	Non-specific	R	
121	15	F	Non-specific	Both	
98	10	F	Non-specific	L	History of pain in knees
110	6	F	Non-specific	Both	History of pain in knees
34	7	M	Non-specific	Both	History of pain in ankle
33	15	F	Non-specific	Both	History of muscular rheumatism

case and eighteen in the other) after the onset of the uveitis, and 18 replies to a questionnaire sent to the patients' doctors revealed that only one patient had subsequently developed arthritis. This was Case 114 (Table VI), one of the few boys in this group, who had had attacks of arthritis in an ankle eighteen months and two and a half years after the onset of uveitis and then, three years later, developed a polyarthritis. The mean period of follow-up for these 18 patients was over seven years (minimum three years, maximum thirteen years).

It is likely, therefore, that band degeneration is independent of a rheumatic aetiology and is associated only with the uveitis which may or may not be linked with joint disease. Band-shaped degeneration of the cornea was seen in one case of sympathetic ophthalmitis.

The figures suggest that the band degeneration occurs more frequently in the

younger children. The mean age of onset of the uveitis in the children with band-degeneration was 7.9 years and the mean age in those without band-degeneration was 10.4 years. In Vesterdal and Sury's (1950) series of cases of rheumatoid arthritis there were 21 with band-degeneration, the mean age at onset (excluding those where this was doubtful) being 5 years, and 10 cases without corneal changes with a mean age of 11 years. In the present series there was also some correlation with the period of activity, the corneal changes being more frequent in cases in which the uveitis was more prolonged.

Table VI also shows the marked preponderance of girls with chronic anterior uveitis. In the group with evidence of joint disease the sex ratio was 5 females to 2 males, which corresponds with Vesterdal and Sury's (1950) figures of 23 to 11 and the similar ratio of 22 females to 9 males which the same authors found in a review of the literature.

In the present series all but one of the 24 patients with chronic anterior uveitis without a history of rheumatism or other aetiology were girls. This is a surprising finding and can hardly be a chance association. In the series of children with uveitis described by Kimura, Hogan, and Thygeson (1954) there were 3 patients with chronic iridocyclitis, all of whom were girls, and 15 out of 19 with iridocyclitis with band-degeneration described by Unger and Schomerus (1954) were also girls.

I know of no aetiological factor likely to be involved in these children which shows such a marked difference in sex incidence. Urinary infections are more common in girls than in boys, but evidence of such infection was only found in one case (Case 133, Table VI). Investigations revealed no active systemic disease in the other cases, but a raised white blood cell count was reported in 7; in 3 cases this may have been the result of steroid therapy. One (Case 82) had an unexplained eosinophil count of 2,000/c. mm; examination of the stools for ova and parasites was negative. Only one eye was affected, and although no fundus lesions were seen these may have been obscured by the dense vitreous opacities. In retrospect, this could have been an infestation with *Toxocara canis*, and is included in the discussion of this condition later.

Cases 147 and 148 are of some interest, as they are sisters. One, aged 9, was referred from school because of defective vision; examination showed a bilateral chronic anterior uveitis with early band-shaped degeneration of the cornea. The other, aged 3, had no visual symptoms, but she also was found to have a mild anterior uveitis in both eyes, without band-shaped opacity of the cornea. The elder sister had been treated for epilepsy and the younger child was backward in talking. Medical examination was negative and the only abnormality found was in the blood counts, which were as follows:

Elder sister (Case 147, Table VI), aged 9: Total white blood count, 12,000/c. mm. Polymorphs: neutrophils, 4,800; eosinophils, 600; basophils, none; lymphocytes, 6,000; monocytes, 600.

Younger sister (Case 148, Table VI), aged 3: Total white blood count, 11,000/c. mm. Polymorphs: neutrophils, 3,300; eosinophils, 110; basophils, none; lymphocytes, 6,600; monocytes, 990.

A familial incidence of uveitis is very rare in my experience and suggests either a common infective agent or some hereditary condition. The toxoplasma dye test

was negative in both children and there was no history of recent infective disease or febrile illness. The fundi were normal and the electro-oculogram was normal in both children and in the mother. The elder sister had had "fluid on the knee" during the previous year, which was thought to have followed a fall. The condition of both children was essentially the same three months later in spite of treatment with local steroids.

Acute Posterior Uveitis

This group comprised 29 children, 15 boys and 14 girls, representing 19.3 per cent. of the whole series. The condition was characterized by discrete focal chorio-retinal lesions, some inactive and discovered accidentally, others showing a recurrence of activity near an old lesion and a few showing an active chorio-retinal lesion but without scars of previous lesions. As so many of the patients had evidence of previous lesions but gave no definite history of symptoms, it is not possible to assess the age of onset of the condition accurately. The mean ages when first seen were: boys 11.4 years and girls 11.3 years.

The most striking feature of this group of cases is the fact that all of them had positive toxoplasma dye tests, compared with only 44 per cent. of the remaining 103 children in whom this test was done (Table VII).

Table VIII compares the dye test results in acute posterior cases with those of the cases of anterior uveitis (acute and chronic), in which toxoplasmosis is unlikely to be an aetiological factor.

The group of generalized chronic cases had the next highest proportion of positive dye tests, and it is probable that two of these cases were toxoplasmic. The height of the dye test titres in the diagnostic groups is shown in Table IX.

TABLE VII
DYE TEST RESULTS IN ACUTE POSTERIOR UVEITIS IN CHILDREN

Type of Uveitis	No. with Positive Dye Test	No. with Negative Dye Test	Total
Acute posterior	29	—	29
All other cases	46	57	103

$\chi^2=23$; $P<0.01$

TABLE VIII
DYE TEST RESULTS IN ACUTE POSTERIOR UVEITIS AND ACUTE ANTERIOR UVEITIS

Type of Uveitis	No. with Positive Dye Test	No. with Negative Dye Test	Total
Acute posterior	29	—	29
Acute anterior	28	38	66

$\chi^2=19$; $P<0.01$

TABLE IX
DYE TEST RESULTS IN ALL TYPES OF UVEITIS

Type of Uveitis	Negative	Positive 1 : 4-1 : 32	Positive >1 : 32	Total Positive	Mean Titre
Anterior acute	16	10	4	14	1 : 28
Anterior chronic	22	10	4	14	1 : 30.5
Posterior acute	—	19	10	29	1 : 55
Posterior chronic	15	7	4	11	1 : 16
Generalized acute	—	—	—	—	—
Generalized chronic	4	4	3	7	1 : 174

Two of the highest titres in the whole series of children (1 : 380 and 1 : 760) occurred in the generalized chronic group and account for the mean dye test titre being highest in these cases. The mean titre in the posterior acute cases is the next highest, but although toxoplasmosis was the most likely diagnosis in these cases two-thirds had dye test titres of 1 : 32 or less. Although *Toxoplasma* organisms have been recovered from patients with very low or even negative dye test titres (Hogan, Zweigart, and Lewis, 1958; Zscheile, 1964), many authorities are reluctant to diagnose a uveitis as toxoplasmic unless the dye test titre is 1 : 64 or more.

Certainly it would be surprising if an acquired infection with *Toxoplasma* severe enough to cause retinal lesions provoked such a low antibody response. However, a positive dye test is proof of previous infection and a low titre is most easily explained by postulating that the acute phase of the disease occurred some years—perhaps many years—previously. The problem is to decide when the initial infection did take place. Very few patients with typical ocular lesions of toxoplasmosis give a history of recent systemic disease suggesting toxoplasmosis, although a few cases (Hogan, 1958; Perkins, 1961; Remky, 1962) have been reported. Similarly, systemic toxoplasmosis in the adult rarely gives rise to ocular lesions. If post-natally acquired toxoplasmosis is not associated with ocular lesions, it is surprising that such an infection should be followed years later by ocular disease without other evidence of systemic recurrence.

The one circumstance in which ocular lesions commonly occur in the course of a systemic infection is in the congenital disease, in which the infection is transmitted to the child *in utero* by the mother, who herself shows no overt evidence of infection. It seems likely, therefore, that the toxoplasmic lesions of children and young adults are recurrences of a congenitally acquired infection which was not sufficiently severe to arouse comment in the newborn infant.

Three patients (Cases 38, 54, and 113) in the present series (Table X) were found accidentally to have choroidal scars in the fundus without any activity and with no history of symptoms. Two children (Cases 49 and 108) were seen during the first three years of life, and in both of these the lesions were inactive, but attention had been drawn to the eyes because the lesions were at the macula and had therefore resulted in gross visual defect. If the lesion does not involve the macula and remains inactive no symptoms arise and the scar is discovered only during routine examination.

Those patients comprising the bulk of the remaining cases with active lesions were found on examination to have scars of previous lesions, usually adjacent to the active area. In only four (Cases 16, 57, 62, and 68) was there any doubt as to the presence of a previous lesion, and it is possible that in these children the infection had been acquired recently. One of these (Case 16) had the highest dye test titre in the series of cases with acute posterior uveitis, 1 : 290 when seen. In three others (Cases 5, 36, and 81) there was a history of activity within the previous two years, and although the clinical signs suggested that some of the old scars seen had been present for much longer periods the possibility of an acquired infection in childhood remains.

In the remaining 22 cases all the evidence suggests that the old scars might have been present since birth. Four of these children had squints, and in an additional child the vision in the affected eye had always been poor. The scars in all these

TABLE X
ACUTE POSTERIOR UVEITIS

Cases	Age when Seen (years)	Sex	Clinical Features	Eye	Dye Test Titre	Remarks
3	10	M	Old scar with recurrence	R	1 : 24	Squint
4	9	M	Old scars. Inactive	Both	1 : 24	
5	15	F	Recurrence R. Old scar L.	Both	1 : 8	Squint
10	12	F	Recurrence R. Old scar L.	Both	1 : 7	
14	9	M	Old scars at macula	L	1 : 160	Squint
16	12	F	Active lesion. No old scar seen	R	1 : 290	
22	15	M	Old scar upper nasal vessels	L	1 : 32	
36	13	F	L. active. Old scar R.	Both	1 : 13	
38	11	F	Old scar. Inactive	R	1 : 14	
42	14	F	Old scar with recurrence	L	1 : 11	
43	15	M	Old scar with recurrence	L	1 : 19	
49	3	F	Old scar with recurrence	R	1 : 32	Squint
52	13	F	Old scar. Inactive	R	1 : 32	Nystagmus since age of 3 mths
53	8	M	Old scars at maculae	Both	1 : 50	
54	10	M	Old scar near disc	L	1 : 4	
56	9	F	Old scar R. Active L.	Both	1 : 280	
57	14	F	Vitreous opacities. Scar seen later	L	1 : 8	
62	10	F	Active lesion L.	L	1 : 84	
64	13	M	Old scar with recurrence	R	1 : 8	
65	13	M	Active lesions	L	1 : 16	
68	14	M	Macular lesions, active	R	1 : 50	
81	13	F	Old scar both. Active L.	Both	1 : 26	
88	12	M	Recurrence R. Microphthalmos L.	Both	1 : 28	
108	1	M	Old scars. Cerebral calcification	Both	1 : 36	
113	8	F	Old scar. Inactive	L	1 : 54	
122	12	M	Old scars with recurrence	R	1 : 200	
139	13	M	Recurrence R. Old scar L.	Both	1 : 8	
141	14	M	Old scars with recurrence	L	1 : 8	
143	14	F	Old scar. Detached retina	R	1 : 4	

cases consisted of atrophic areas with marked pigment accumulation. In only one patient (Case 143) were the appearances less typical; this was a child of 14 with degenerative myopia and a detachment of the retina in the right eye. There was a deeply pigmented lesion in the eye with the detachment which did not show the usual punched-out area of chorio-retinal atrophy, and may not have been toxoplasmic in origin. The dye test was positive only in a titre of 1 : 4.

Remky (1962) considers that the clinical appearances of the fundus lesions in acquired toxoplasmosis differ from those in the congenital disease. However, he includes cases of central serous retinopathy in his toxoplasmic cases on the grounds of a raised antibody level in the aqueous. No one has, to my knowledge, demonstrated *Toxoplasma* organisms in such cases. It is certainly true that the cases which are first recognized in adult life do not show the bilateral macular "rosettes" commonly seen in the congenital disease, the lesions usually being associated with the main retinal vessels or adjacent to the disc. The fact that the macula is not involved is the reason why the lesion is not noticed until a recurrence causes symptoms. A mild congenital infection may therefore result in atypical lesions away from the macula, cause no symptoms in the infant, and be recognized only when a recurrence occurs at a later age.

Why the *Toxoplasma* organisms lie dormant for many years and then suddenly become active again is not known. The peak incidence of such recurrences occurs in the years of adolescence and early adult life and may be linked with the changes in hormonal balance which are occurring at this period. Trauma to the eye may occasionally play a part, and stress may be a factor. Pregnancy may be associated with reactivation of a lesion and I have seen several patients in whom this has happened. Fears for the child have been expressed in this situation, but none of the infants has been affected. This supports the view that invasion of the foetus takes place only during the initial infection of the mother, before circulating antibodies appear. Once such antibodies are present in the circulation the risk of transplacental infection is negligible.

If the view that most cases of ocular toxoplasmosis in the child and young adult are recurrences of congenital infection is correct, it would account for much of the difficulty in determining the source of the infection. These patients do not give any particular history of contact with animal sources of infection and they do not show a greater incidence of contact with animals than patients with uveitis of other aetiology (Perkins, 1961). This anomaly is resolved if the infection occurred prenatally, and what is required is a careful study of the environment of the mother during pregnancy. Such information, however, is very difficult to obtain many years after the event.

It would also be interesting to know whether all the mothers of patients with toxoplasmic chorio-retinitis had positive dye tests. In the few cases in which, to my knowledge, this has been done the mother has also given a positive result. If the ocular lesions in children and young adults follow a post-natally acquired infection, there is little reason to suppose that the mothers of such patients would show an incidence of positive dye tests greater than that in the normal population. A positive result in the mother would not, of course, mean that the patient had acquired the disease pre-natally, but a negative result in the mother would be strongly suggestive of a post-natal infection. If the patient and the mother were living together it could be argued that the fact that both had a positive dye test might result from infection from a common source. A negative dye test in the mother would therefore be much more significant.

Four of the patients considered to have toxoplasmosis are known to have had further recurrences of activity since they were first seen in the Uveitis Clinic. One (Case 81, Table X) had received treatment with Daraprim, and one (Case 57) with spiramycin. Specific therapy therefore does not prevent recurrences, presumably because the encysted forms are resistant to these drugs.

Chronic Posterior Uveitis

Thirty cases, 14 male and 16 female, were included in this diagnostic category (Table XI). Eighteen of them presented with exudative lesions in the periphery of the fundus or protruding into the vitreous at the posterior pole, accompanied in the active stage of the disease by gross vitreous opacities. These eighteen cases show some clinical resemblance to two of those diagnosed as having chronic anterior uveitis and to five diagnosed as having chronic generalized uveitis. All twenty-five have therefore been grouped together and will be discussed later.

TABLE XI
CHRONIC POSTERIOR UVEITIS

Cases	Age at Onset (years)	Sex	Clinical Features	Eye	Remarks
2	11	M	Vitreous opacities and macular oedema	L	
19	4	M	Peripheral uveitis	R	
21	6	F	Peripheral mass	L	
27	12	F	Uveitis and papillitis	Both	? Sarcoidosis
29	11	F	Peripheral uveitis	L	
35	15	M	Uveitis with perivasculitis	L	
44	12	M	Squint and choroiditis	R	? Toxoplasmosis
45	7	F	Mass at disc with vitreous bands	R	
46	5	M	Vitreous opacities ++	L	
55	10	F	Organized vitreous bands	L	? Endophthalmitis
59	15	F	Perivasculitis	Both	? Eales's disease
69	12	F	Peripheral uveitis	Both	
70	10	F	Peripheral uveitis	L	
73	11	M	Disseminated choroiditis	Both	Congenital syphilis
79	9	M	Peripheral mass with vitreous bands	R	
80	11	F	Uveitis and papillitis	Both	Urinary infection
89	7	F	Secondary cataract. Vitreous opacities	Both	
92	14	M	Retinal haemorrhages	L	
95	14	M	Perivasculitis	Both	? Eales's disease
97	8	M	Vitreous opacities	Both	
101	6	F	Peripheral uveitis	Both	Severe facial herpes
104	15	M	Perivasculitis	R	
115	10	F	Perivasculitis	L	
126	10	F	Raised lesion at macula	R	Toxocara skin test weakly positive
130	10	F	Raised lesion at macula	R	Toxocara skin test positive
131	9	M	Vitreous opacities. Mass in periphery	L	Toxocara skin test positive
134	9	F	Vitreous opacities. Mass in periphery	L	Toxocara skin test positive
135	3	M	Granulomatous mass	L	Toxocara skin test positive
136	9	M	Retinal fold, peripheral mass	L	Toxocara skin test positive
142	8	F	Vitreous opacities. Mass in periphery	L	Toxocara skin test positive

Six cases diagnosed as having chronic posterior uveitis presented with peri-vascular retinal lesions, and probably fall into the category of Eales's disease. Two showed uveitis with swelling of the optic disc; one of these was thought to be due to sarcoidosis. One case of disseminated choroiditis occurred in a child with congenital syphilis and one case of focal choroiditis may have been toxoplasmic in origin.

Peripheral Choroiditis and *Toxocara canis* (Table XII)

Some of the patients with chronic uveitis, although this was diagnosed variously as chronic anterior, chronic posterior, and chronic generalized uveitis, seem in retrospect to form a relatively homogeneous group, characterized by dense vitreous opacities often completely obscuring the fundus but sometimes with visible lesions in the periphery. Although the aetiology is obscure in many cases, the lesions in some of them are characteristic of infestation with *Toxocara canis*, and it may be helpful to review these cases in more detail in an attempt to identify pathognomonic signs.

As none of the eyes was removed and examined pathologically, the evidence of *Toxocara* infestation is indirect. The best circumstantial evidence would be a history

TABLE XII
PERIPHERAL CHOROIDITIS AND TOXOCARA CANIS INFESTATION

Cases	Type of Uveitis	Age at Onset (years)	Sex	Clinical Features	Eye	Eosinophilia per cent.	Skin Test	History of Contact
<i>Probable Toxocara canis Infestation</i>								
107	Chronic generalized	13	M	Central raised lesion	R	7	Positive	Yes
126	Chronic posterior	?3	F	Central raised lesion	R	1	Weakly positive	Yes
130	Chronic posterior	10	F	Central raised lesion	R	Not done	Positive	Yes
131	Chronic posterior	9	M	White mass in periphery	L	3	Positive	Yes
134	Chronic posterior	9	F	White mass in periphery	L	5	Positive	Yes
135	Chronic posterior	3	M	White mass in periphery	L	1	Positive	Yes
136	Chronic posterior	9	M	White mass in periphery with retinal fold from disc	L	4.7	Positive	Yes
142	Chronic posterior	8	F	White mass in periphery	L	7	Positive	Yes
<i>Possible Toxocara canis Infestation</i>								
2	Chronic posterior	11	M	Vitreous opacities. Macular oedema	L	1	Not done	Yes
21	Chronic posterior	6	F	White mass in periphery	L	1	Not done	Yes
45	Chronic posterior	7	F	Mass near disc with vitreous bands extending to organized tissue in periphery	R	3	Not done	No
79	Chronic posterior	9	M	White mass in periphery with vitreous bands from disc	L	0	Not done	Yes
82	Chronic anterior	13	F	Vitreous opacities	R	25	Not done	Not known
97	Chronic posterior	8	M	Vitreous opacities	Both	6	Not done	Yes
137	Chronic generalized	11	M	Anterior vitreous opacities	Both	1	Positive	No (cat)
<i>Unknown Aetiology</i>								
19	Chronic posterior	4	M	Vitreous opacities. Peripheral lesion	R	3	Not done	No
29	Chronic posterior	11	F	Vitreous opacities and cyclitic membrane. Peripheral lesion	L	2	Not done	Not known
46	Chronic posterior	5	M	Vitreous opacities and cyclitic membrane. Convergent squint	L	3	Not done	Not known
69	Chronic posterior	12	F	Peripheral lesion R. Vitreous opacities L.	Both	0	Not done	No (cat)
70	Chronic posterior	10	F	Vitreous opacities. Peripheral lesion	L	0	Not done	No (cat)
85	Chronic generalized	11	M	Vitreous opacities	Both	0	Not done	No
101	Chronic posterior	6	F	Vitreous opacities. White masses in periphery in both eyes	Both	0	Negative	No
124	Chronic generalized	11	M	Vitreous opacities	Both	1	Not done	No
127	Chronic generalized	15	F	Exudates in vitreous with macular oedema	L	0	Not done	No
128	Chronic anterior	15	F	Vitreous opacities	L	4	Not done	Not known

of contact with a dog, a granulomatous mass in the eye, eosinophilia, and a positive skin test (or serological test) for *Toxocara*—a combination found in Cases 107, 134, 136, and 142 (Table XII). Similar evidence, except for a lesser degree of eosinophilia (3 per cent. or less), was present in Cases 126, 130, 131, and 135. It is highly probable that all these cases were caused by *Toxocara* infestation. Case 126 was aged 10 years at the time of examination, but the history suggested that the condition had been present for many years.

Typical fundus lesions and a history of contact with dogs were present in two patients (Cases 21 and 79); in neither of these were skin tests done, nor was the eosinophil count raised. Case 137 presented with marked vitreous opacities and gave a positive toxocara skin test, although there was no history of contact with dogs. Cases 2 and 97 both gave a history of contact with dogs. Case 2 showed marked vitreous opacities with macular oedema, but no granulomatous mass was seen in the fundus and the eosinophil count was only 1 per cent. of the total white blood count. Case 97 had marked vitreous opacities in both eyes but no focal lesions could be seen. The eosinophil count was 624, 6 per cent. of the total white blood count. Skin tests were not done in these cases.

Three further patients, Cases 45, 69, and 101, showed rather similar fundus changes. Case 45 had a granulomatous mass near the disc with vitreous bands extending to organized tissue at the periphery of one eye. There was no history of contact with dogs; the toxocara skin test was not done, but the eosinophil count was 3 per cent. (138) of the total white blood count. Case 69 had extensive peripheral lesions in the inferior temporal area of the right fundus and gross vitreous opacities with no observable fundus lesions in the left eye. The toxocara skin test was not done and there was no history of contact with dogs, but the family kept a cat. Case 101 had a severe bilateral uveitis and developed organized white masses in the periphery of both fundi. The toxocara skin test was negative, no eosinophils were present in the blood, and there was no history of contact with dogs.

One other patient (Case 82), presenting with a marked vitreous haze in one eye which obscured details of the fundus, had a high eosinophil count of 2,000, 25 per cent. of the total white blood count. No cause for the eosinophilia was discovered, but at the time of examination *Toxocara* infestation was not considered as a possible aetiological factor and there was no inquiry as to contact with animals.

The remaining cases listed in Table XII were characterized clinically by dense vitreous opacities, sometimes with peripheral areas of choroiditis. None of them gave a history of contact with dogs, eosinophil counts were within normal limits, and toxocara skin tests were not done.

In Table XII the cases are divided into three groups: those probably due to *Toxocara*, those possibly due to *Toxocara*, and those of unknown aetiology. Those probably or possibly due to *Toxocara* tended to be younger and to have higher eosinophil counts, and in all except two the uveitis was unilateral, compared with the group of unknown aetiology in which the mean age was higher and the eosinophil count lower, and in which 4 out of 10 cases were of bilateral uveitis.

The toxocara skin test used in this series was that described and developed by Duguid (1961). The results so far have correlated well with pathological and clinical findings, but whether the test is specific for *Toxocara canis* has not been

proved. A high eosinophil count is very suggestive of a parasitic infestation but may occur in other allergic conditions. A low count does not exclude *Toxocara*, as the primary infestation may have occurred some years previously or the infestation may be very light.

In summary, it may be said that *Toxocara* infestation should be suspected in any child with white or grey lesions in the fundus which protrude into the vitreous either at the posterior pole or in the periphery. Some of the cases described by Schepens (1950) as peripheral choroiditis and by Welch, Maumenee, and Wahlen (1960) as pars planitis may well have fallen into this category, and Hogan (1965) has reported one typical case in which the eye was excised and the nematode discovered in an eosinophilic granuloma lying in the periphery of the retina. Hogan also pointed out that in his series of cases the condition had never spread to the other eye if one eye only was affected when the patient was first seen. Invasion of both eyes with *Toxocara* larvae is much less likely than invasion of one eye only, and it is likely that most cases of bilateral uveitis are due to some other cause as yet undiscovered. It is interesting to note that many of the reported cases of peripheral choroiditis or pars planitis have occurred in children, although adults are by no means immune. Unfortunately, *Toxocara* infestation has not been considered in the aetiology of the published cases.

Reliable serological tests for *Toxocara* infestation are not yet available. Wood, Ellison, Kelley, and Kaufman (1965) have described a haemagglutination test, but although higher titres were obtained with serum containing *Toxocara* antibodies the test also gives positive results with *Ascaris*. These authors' results do suggest that antibodies to *Toxocara* are not uncommon in children in Florida.

Acute Generalized Uveitis

Only two cases were diagnosed as having an acute generalized uveitis. One of these was a 3-month-old girl with an endophthalmitis. The other was a girl of 9 years with a history of sudden onset of blurring of vision and a red eye; she was found to have an anterior uveitis, a small focus of choroido-retinitis peripherally, and swelling of the optic disc. Investigations revealed a mild normochromic normocytic anaemia, with a rather low white blood count (4,400/c. mm.) and a neutrophil count of 1,496. No cause was found for the uveitis and the condition improved spontaneously over the next two months.

Chronic Generalized Uveitis

Characterized by a chronic uveitis involving the anterior and posterior segments, this was a rather mixed group and overlapped to some extent with cases in the chronic posterior and anterior groups. As will be seen from Table XIII, one case of definite peripheral choroiditis, three cases of uveitis with marked vitreous opacities, and one with a macular lesion, were similar to some of the cases diagnosed as having chronic posterior uveitis and have been discussed with them.

Case 125 (Table XIII) was probably one of congenital toxoplasmosis and had the highest dye test titre of all the children studied. Case 107 had a lesion typical of *Toxocara canis* infestation and had a positive skin test and eosinophilia. This

TABLE XIII
CHRONIC GENERALIZED UVEITIS

Cases	Age at Onset (years)	Sex	Clinical Features	Eye	Remarks
72	12	M	Uveitis and papillitis	Both	? Sarcoidosis
77	9	M	Secondary cataract. Vitreous opacities	L	
85	11	M	Vitreous opacities	Both	See Table XII
91	15	F	Iris nodule. Secondary cataract	L	
99	6	M	Chronic uveitis with poliosis and vitiligo	Both	Vogt-Koyanagi syndrome
102	10	F	Bilateral uveitis following trauma	Both	Sympathetic ophthalmitis
103	15	F	Uveitis and papillitis	Both	Followed B.C.G. vaccination.
107	13	M	Central raised lesion	R	See Table XII
112	13	M	Band opacity of cornea	Both	Sympathetic ophthalmitis
124	11	M	Vitreous opacities	Both	See Table XII
125	?Birth	M	Large central scars L. Recurrence R.	Both	Congenital toxoplasmosis Dye test positive 1 : 760
127	15	F	Peripheral choroiditis with macular oedema	L	See Table XII
137	11	M	Vitreous opacities	Both	See Table XII
140	4	M	Chronic endophthalmitis	R	Confirmed pathologically
146	4	M	Uveitis and papillitis	Both	

patient also had a dye test titre of 1 : 380. In three cases the uveitis was accompanied by swelling of the disc.

The one case of Vogt-Koyanagi's syndrome occurred in an Egyptian boy and was characterized by a chronic uveitis with diffuse fundus changes, poliosis, and vitiligo.

Discussion

It is clear from this review that uveitis in children shows a different pattern from that in adults. The acute anterior uveitis of a non-specific character which preponderates among adult patients is much less common in children. However, there are some distinctive types of uveitis among the children which are seen less often among adults. Chief among these is the chronic uveitis which may involve mainly the anterior segment or the ciliary body and periphery of the choroid. Those cases in which the inflammation is mainly anterior include some of juvenile rheumatoid arthritis, and although the ocular signs may precede the joint symptoms it is probable that most of these children will not develop rheumatism. The aetiology of the uveitis in those without rheumatism may, of course, be the same as that in the rheumatic disease, but the great preponderance of girls in this group suggests a different though unknown aetiology.

As might be expected, the most important aetiological factor in uveitis in children is toxoplasmosis, and it was thought to be the cause in 20.6 per cent. of the 150 children. In only a few of these was there evidence that the lesions were of recent origin; the majority presented with inactive scars or an active area of chorio-retinitis adjacent to an old focus, and this may well have been a recurrence of congenital infection. A squint, nystagmus, or a history of defective vision from an early age, made a diagnosis of congenital toxoplasmosis almost certain in 7 cases. Although the dye test was positive in all cases there were few with high titres, again suggesting that the initial infection had taken place many years previously. None of the

patients gave a history of systemic disease consistent with toxoplasmosis except for one with definite congenital disease who had had fits as a child and showed cerebral calcification. Two other patients had a history of gastro-enteritis as babies and one was mentally retarded, although there was no definite evidence of cerebral toxoplasmosis.

If, as I believe, most cases of toxoplasmic chorio-retinitis in children and young adults are recurrences of congenital infections, it is likely that the infection had subsided by the time the child was born, leaving, however, small foci of encysted *Toxoplasma* organisms, some of which are in the retina and may become active at a later age.

Toxocara canis infestation probably or possibly accounted for 15 cases in this series, 10 per cent. of the total. The patients' ages ranged from 3 to 13 years. Twelve gave a history of contact with dogs, usually puppies, and in those tested the skin test for *Toxocara* was positive. *Toxocara* infestation should be suspected in any child with a granulomatous mass in the posterior segment. Eosinophilia is not necessarily present, as this will depend on the severity of the initial infestation and the length of time which has elapsed since it occurred.

Peripheral choroiditis was noted in 5 cases and a further 6 had dense vitreous opacities and possibly had similar peripheral lesions which could not be seen. No history of contact with dogs was elicited in these cases, and although clinically they resembled some of those thought to be due to *Toxocara* infestation there was no supporting evidence for this diagnosis. No other aetiological factor was discovered.

Four cases presented with a chronic uveitis accompanied by swelling of the optic disc and one of these was thought to be due to sarcoidosis. Sarcoidosis was also thought to be the cause of 2 cases of chronic anterior uveitis.

Six cases were found to have perivascular retinal lesions, but no definite aetiological factor was discovered. There were 4 patients with heterochromic uveitis in the series, and 2 were thought to have metastatic bacterial endophthalmitis, a condition known to occur more frequently in children than in adults.

A possible or probable aetiology or distinct disease entity could be assigned in 76 (50·2 per cent.) of the children (Table XIV).

TABLE XIV
PROBABLE AETIOLOGY OF UVEITIS IN 150 CHILDREN

Probable Aetiology	No. of Cases	Percentage of Total
Toxoplasmosis	31	20·6
<i>Toxocara canis</i>	15	10·0
Vasculitis	6	4·0
Herpes simplex	5	3·3
Tuberculosis	5	3·3
Heterochromic uveitis	4	2·6
Sarcoidosis	4	2·6
Sympathetic ophthalmitis	2	1·3
Endophthalmitis	2	1·3
Syphilis (congenital)	1	0·6
Vogt-Koyanagi syndrome	1	0·6
Total	76	50·2

Summary

The clinical features of uveitis in 150 children and the possible aetiological factors are reviewed.

Uveitis is less common in children than in adults and is more likely to be chronic in character. Chronic anterior uveitis with band-shaped opacities of the cornea and secondary cataract may be associated with juvenile rheumatoid arthritis, but in many cases there was no evidence of rheumatism. There was a marked preponderance of girls among the cases of chronic anterior uveitis.

Toxoplasmosis was thought to be responsible for the uveitis in 20 per cent. of all cases, and was typified by focal chorio-retinitis; in most cases the evidence suggested that the disease was congenital in origin.

Toxocara canis infestation was the probable or possible cause in 10 per cent. of cases. Herpes simplex, tuberculosis, sarcoidosis, and syphilis were each responsible for a few cases, and there were some cases of vasculitis retinae, heterochromic uveitis, and sympathetic ophthalmitis. In half the cases no definite aetiological factor could be found.

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