THE CANADIAN MEDICAL ASSOCIATION

LE JOURNAL DE

L'ASSOCIATION MÉDICALE CANADIENNE

FEBRUARY 18, 1967 • VOL. 96, NO. 7

Uveitis in Children

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Endogenous uveitis in 117 children aged 15 years or under was investigated at The Hospital for Sick Children, Toronto, in a 12-year period from 1953 to 1964. This group included 55 children with anterior uveitis, 59 with posterior uveitis, and three with diffuse uveitis. An etiologic diagnosis could be made or the uveitis recognized as part of a definite clinical syndrome in approximately 47% of the 117 children. The commonest cause of posterior uveitis was toxoplasmosis and the commonest associated finding in anterior uveitis was juvenile rheumatoid arthritis. Chronic cyclitis of unknown etiology was a relatively common disease.

Au Hospital for Sick Children de Toronto, au cours d'une période de 12 ans allant de 1953 à 1964, on a étudié des cas d'uvéite endogène chez 117 enfants âgés de 15 ans au plus. Parmi ce groupe, figuraient 55 cas d'uvéite antérieure, 59 d'uvéite postérieure et trois cas d'uvéite diffuse. Il a été possible de porter un diagnostic étiologique dans près de 47% des 117 enfants ou de préciser que l'uvéite faisait partie d'un syndrome clinique précis. La toxoplasmose a été la cause la plus courante de l'uvéite postérieure, l'arthrite rhumatoïde juvénile était la constatation la plus fréquemment associée à l'uvéite antérieure. La cyclite chronique d'étiologie inconnue s'est révélée une maladie relativement courante.

UVEITIS is a relatively uncommon disease in children. It is, however, important to detect the disease early, for it tends to become chronic and develop complications which are often resistant to therapy.[1, 3]

In general terms, endogenous uveitis might be described as an inflammation of the uveal tract, secondary to some systemic infection or immune reaction. The specific cause of the inflammation remains undetermined in many cases. For this reason a study was undertaken to detect and tabulate specific associated disease in a large number of children in whom a diagnosis of uveitis had been recorded.

A study was made of 117 cases of endogenous uveitis in children 15 years of age or under that have been investigated at The Hospital for Sick Children, Toronto, during a 12-year period extending from 1953 to 1964. During this period there were 279,345 hospital admissions. Thus the incidence of clinically manifest uveitis in this age group was approximately 43 per 100,000.

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The hospital records contained a medical history and a complete physical examination in all cases. A detailed ocular examination was done in almost all cases, including slit-lamp examination and ophthalmoscopy with pupils dilated. Laboratory examinations and skin tests varied somewhat with the nature of the case being studied and the year of study. The cases were divided into anterior, posterior and diffuse uveitis according to the predominant site of inflammation.

Analysis of Cases

I. *Anterior Uveitis*

There were 55 cases of anterior uveitis (Table I). Most were characterized by an insidious onset and a prolonged course.

Juvenile Rheumatoid Arthritis

This was the commonest associated disease, being present in 14 (25.4%) of the cases of anterior uveitis (Table I). It is noteworthy that of the 300 patients admitted to the hospital with this condition, 4.7% were found to have ocular involvement. In 12 of the 14 cases there was active uveitis on the initial examination. The ocular

Canad. Med. Ass. J.
Feb. 18, 1967, vol. 96

TABLE I.—TYPE OF ANTERIOR UVEITIS IN CHILDREN (55 CASES)

	Total cases	*Ocular involvement*
Iridocyclitis		
1. Juvenile rheumatoid arthritis.	30	14
2. Herpes zoster		1
3. Idiopathic		15
Kerato-uveitis		
1. Congenital syphilis	26	4
Chronic cyclitis		21

findings in these 14 cases are shown in Table II. The visual acuities shown in the table represent the final results of tests taken at the end of the period of observation in the worst eye. Four of the cases were seen during the course of only one admission, and 10 cases were followed up from six months to seven years. These cases tended to be refractory to treatment. Nine had persistent disease in spite of various forms of therapy.

TABLE II.—JUVENILE RHEUMATOID ARTHRITIS (14 CASES)

Age of onset	3 to 10 years, mean 6.1 years
Sex	Male 4, female 10
Ocular findings	*No. of cases*
1. Chronic anterior uveitis—all bilateral	12
2. Posterior synechiae—in one eye	2
Follow-up findings—10 cases followed up 6 mos. to 7 yrs.	
1. Visual acuity 20/20 - 20/40	3
20/40 - 20/100	2
Less than 20/200	5
2. Persistent activity	9
3. Complications	
a. Cataracts	6
b. Glaucoma	1
c. Hypotony	1
d. Posterior synechiae	10
e. Band keratopathy	6

The uveitis observed was somewhat variable in its appearance. Twelve cases showed a chronic, low-grade inflammation in both eyes, manifested by cells and flare in the anterior chamber, fine cellular precipitates of the endothelium, and band keratopathy. In two cases posterior synechiae were seen in one eye only.

The arthritis in all but one of the cases with ocular involvement was mild, and the severity of changes in the joints could not be correlated with ocular complications. In all but one of these cases joint involvement preceded the ocular involvement (i.e. the detection of ocular involvement).

This latter case was a 13-year-old girl who developed bilateral anterior uveitis at the age of 6, and at the age of 10 developed arthritis of the knees and wrists. Her arthritis has been well controlled on systemically administered steroids.

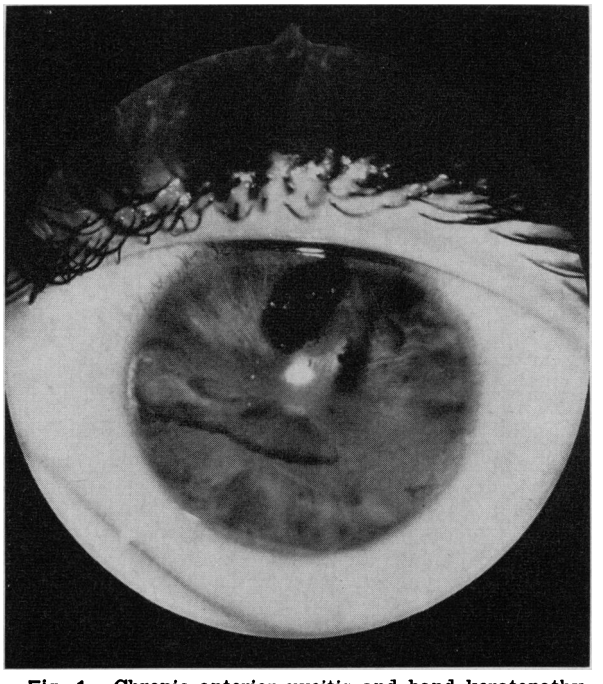

Fig. 1.—Chronic anterior uveitis and band keratopathy in juvenile rheumatoid arthritis.

The left eye developed an iris bombé (forward "ballooning" of the iris) from posterior synechiae and an iridectomy was done. There was a small bound-down pupil at the time of examination and band keratopathy was present (Fig. 1).

Herpes Zoster

A 4-year-old boy with a three-day history of severe headache, and a rash on the forehead and nose developed a transient unilateral acute iridocyclitis. Corneal involvement was not noted.

Idiopathic Iridocyclitis

Some cases in this category were of particular interest because of associated findings.

One 7-year-old boy with the Pierre-Robin syndrome[13] (micrognathia, cleft palate, glossoptosis) developed a chronic unilateral iridocyclitis and secondary cataract. Examination at the age of 3 had revealed no ocular abnormality. His teeth were extremely carious.

Bilateral chronic iridocyclitis and band keratopathy were present in an 8-year-old girl with a diagnosis of cerebral agenesis (Fig. 2). The teeth were severely carious, as in the patient with Pierre-Robin syndrome.

A diagnosis of cat-scratch disease was considered in a 10-year-old girl with a unilateral chronic iridocyclitis. She had a history of close association with cats, and the dermal antigen test was positive on two occasions. A few anterior cervical lymph nodes were moderately enlarged.

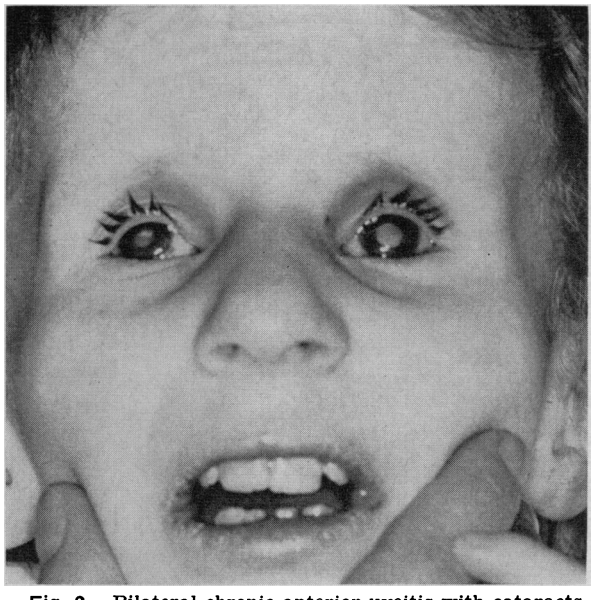

Fig. 2.—Bilateral chronic anterior uveitis with cataracts and band keratopathy seen in a case of cerebral agenesis.

There was no history of conjunctivitis.

One case of acute leukemia had a transient acute iridocyclitis. This case was not included in the series because of the likelihood of malignant infiltration as a cause of the inflammation.

Syphilis

These four cases were characterized by bilateral acute kerato-uveitis, with associated ocular pain and intense photophobia. There were three girls and one boy, between the ages of 7 and 12. Corneal edema developed in all cases, with stromal vascularization in two. The serological findings were of interest. The Wassermann test was positive in the three previously untreated cases; but it was negative in the one case treated with penicillin at age 2 months, at which time the Wassermann was positive. All cases were given a full course of penicillin. In two of the four, there were further relapses of acute kerato-uveitis during one year of follow-up.

Chronic Cyclitis

The largest group under this classification of anterior uveitis consisted of 21 cases of chronic cyclitis (Table III). In these, chronic cyclitis appeared to be a disease of otherwise healthy young children. Ten were bilateral. It appeared to affect the ciliary body primarily. Involvement of the anterior segment was usually minimal with mild flare, a few cells, and small precipitates on the back of the cornea. The vitreous opacities varied from fine, dust-like matter in an early case to coarse clumps and strands in more severe cases. In children the pars plana

TABLE III.—CHRONIC CYCLITIS—21 CASES

Age at onset: 5 to 15 yrs., mean 9.7 yrs.
Sex—male 13, female 8.

Ocular findings:

1. Anterior uveitis (active)	19
2. Hazy vitreous	21
3. Scattered focal chorioretinitis	9
4. Edema of the posterior fundus	3

Follow-up findings—(14 cases followed over one year)

1. Final visual acuity 10/20 - 20/40	7
20/40 - 20/100	5
20/100 - 20/200	1
less than 20/200	8
2. Persistent activity in cases followed over one year.	5
3. Complications	
a. Band keratopathy	4
b. Posterior synechiae	6
c. Cataract	9
d. Macular changes	5

region is not easily examined. However, scattered areas of focal chorioretinitis were seen in nine cases, and in some these may have represented the primary site of inflammation. Edema of the optic disc and macula were noted, but in many instances the vitreous was too hazy to obtain a good view of the posterior part of the eye. These cases were chronic, responding poorly to treatment and frequently showing significant loss of vision.

The cases were followed up for various periods of time. Fourteen cases have been observed for one to seven years. In nine of these the uveitis had subsided, but in five it was still active. In eight of these children visual acuity was 20/200 or less. Complications that have been noted include band keratopathy, posterior synechiae, cataracts (mainly posterior subcapsular) and macular changes.

In 12 of the cases eosinophils were 4 to 9% of the total leukocyte count. In 10 cases of this group a focus of infection could be pinpointed, the diagnoses including sinusitis, tonsillitis, marked dental decay, urinary tract infection, and pinworms or whipworms in the intestine.

The fundus photograph in Fig. 3 is of an 8-year-old boy with bilateral cyclitis who had been followed up for one year. By this time there were macular changes in both eyes with a vision of O.D. 20/60 and O.S. 20/50.

II. *Posterior Uveitis*

Posterior uveitis including chorioretinitis was present in 59 cases (Table IV).

Toxoplasmosis

Of the 28 cases of toxoplasmosis, organisms were isolated at autopsy from the brain and eyes in three instances. In the other cases the diagnosis was presumptive; it was made on the

Canad. Med. Ass. J.
Feb. 18, 1967, vol. 96

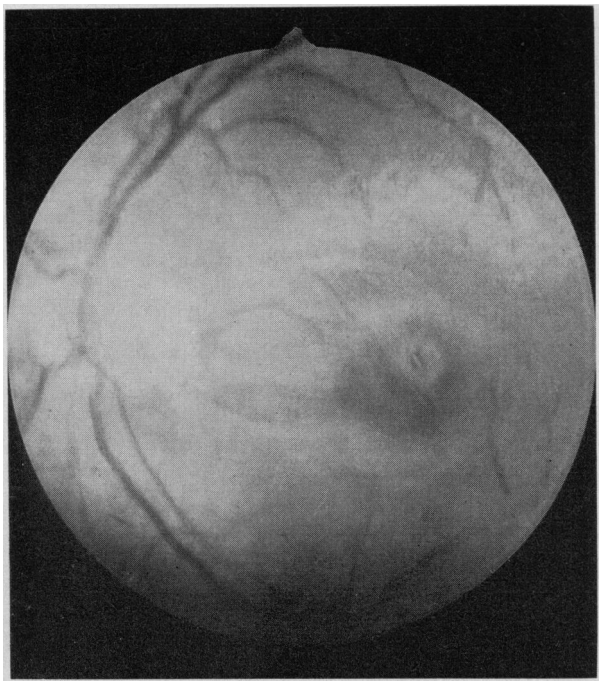

Fig. 3.—Macular degenerative changes in chronic cyclitis.

basis of the clinical picture supported by positive toxoplasmosis dye tests, complement-fixation tests, and skin tests. In the 13 cases in which the dye test was done, the titres were all 1:64 or greater. For the purpose of discussion, these cases of toxoplasmosis have been divided into three groups.

TABLE IV.—POSTERIOR UVEITIS—ETIOLOGICAL FACTORS
59 CASES

	Total cases	*Ocular involvement*
1. Toxoplasmosis	28	27
2. Tuberculosis (including three miliary and 17 meningeal cases)	250	2
3. Histoplasmosis (presumptive diagnosis)	2	2
4. Cytomegalic inclusion disease	12	1
5. Rubella syndrome		1
6. Idiopathic		26

The first group consists of seven congenital cases that had active systemic and ocular disease with changes noted at birth (Table V). Five were males and two were females. The systemic signs included hepatosplenomegaly, jaundice, petechiae, hydrocephalus, cerebral calcification, and convulsions. The ocular findings were bilateral in all cases. All had acute uveitis, predominantly posterior. In most cases the haze in the vitreous prevented visualization of the fundus. Several of these eyes were microphthalmic. Five of the children died within three months. Of the three groups of toxoplasmosis

TABLE V.—CONGENITAL TOXOPLASMOSIS

Group 1—*Active systemic and ocular disease*..... 7 cases
Age at onset: birth
Sex—male five, female two

Systemic signs	*Bilateral ocular signs*
1. Hepatosplenomegaly	1. Uveitis, predominantly posterior
2. Jaundice	2. Microphthalmos
3. Petechiae	
4. Hydrocephalus	
5. Cerebral calcification	
6. Convulsions	

Course: Five died within three months.

cases the dye-test titres were highest in this group. The toxoplasmin skin test was positive in all but one case. Three of the mothers of the children had dye-test titres of 1:1024. Tests were not done in the other mothers.

The typical manifestation of fundus disease consisted of an acute retinochoroiditis with severe inflammation and necrosis, as well as exudation into the vitreous. When seen in the tissues, the *Toxoplasma gondii* were both extracellular and intracellular. The extracellular form was crescent-shaped while the intracellular form was more rounded. Fig. 4 shows a Toxoplasma cyst located in the necrotic retina of an autopsy eye.

The second form of ocular toxoplasmosis listed as "active ocular disease" consisted of recurrent retinochoroiditis (Table VI). There were 11 cases in all, most of whom had an active focal chorioretinitis along with the old scars of previous activity. Three of the eight cases so involved had accompanying iridocyclitis. This appeared to be a particularly destructive form of the disease, and nine of the 11 cases so classified had a visual acuity of 20/200 or less.

In this series recurrent activity tended to reappear at puberty. Of the 11 patients, eight were 11-14 years of age. There were seven females 7-13 years old, and four males 8-14 years of age.

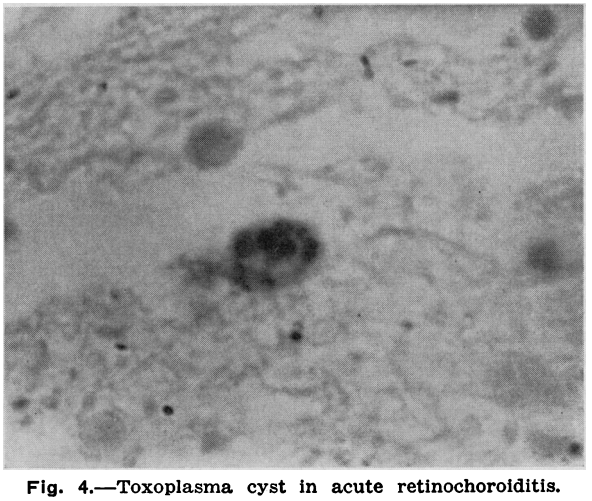

Fig. 4.—Toxoplasma cyst in acute retinochoroiditis.

TABLE VI.—CONGENITAL TOXOPLASMOSIS

Group 2—*Active ocular disease*..... 11 cases
Age at onset: 7 to 15 yrs., mean 11 yrs.
Sex—male 4, female 7

Ocular signs

1. Active focal chorioretinitis and old scars. Three of these patients had iridocyclitis.	8 (including 3 with iridocyclitis)
2. Active focal chorioretinitis only	1
3. Inflammatory retinal detachment	2

Course: Macular involvement occurred in nine cases with a visual acuity of 20/200 or less. Three cases had bilateral involvement.

The third form of ocular toxoplasmosis was classed as "inactive ocular disease" and consisted of nine cases, seven bilateral (Table VII). These essentially took the form of focal chorioretinal scarring, usually with macular involvement.

TABLE VII.—CONGENITAL TOXOPLASMOSIS

Group 3—*Inactive ocular disease*..... 9 cases
Age noted: 1 to 12 yrs., mean 4.5 yrs.
Sex—male 2, female 7.

Ocular signs

1. Focal chorioretinal scarring.....	9 cases
(Macular involvement).....	(6 cases)
2. Bilateral—7 cases	

Tuberculosis

In the two cases with a presumptive diagnosis of tuberculous uveitis, the uveitis was inactive. One case had the appearance of an isolated miliary tubercle in the posterior fundus, and the other had a juxtapapillary chorioretinitis.

Histoplasmosis

Two children with posterior fundus lesions had positive histoplasmin skin tests. Serological tests done in one showed positive complement fixation and fluorescent antibody tests for histoplasmosis at a titre of 1:8. Radiographs of the chest did not show characteristic lesions in either case.

One child had a punched-out macular lesion without visible peripheral lesions, and the other had a raised whitish lesion near the macula and dense chorioretinal scarring in the equatorial region. Neither case had the usual clinical picture associated with histoplasmosis, and for this reason the diagnosis of histoplasmosis is only presumptive.

Cytomegalic Inclusion Disease

Cytomegalic inclusion disease is an acute and often fatal viral disease of infants and young children.

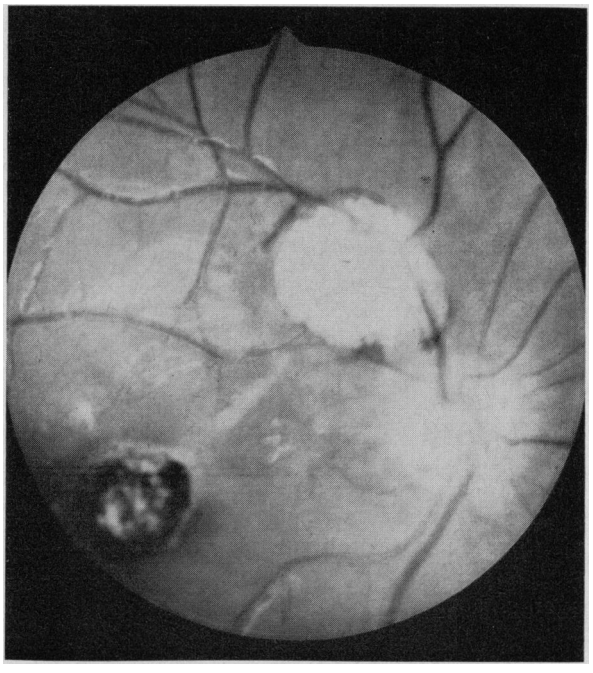

Fig. 5.—Focal chorioretinal scarring with macular involvement in probable toxoplasmosis.

One baby who died from disseminated infection was admitted at the age of 2 months, severely ill and dehydrated. Fundus examination showed bilateral inactive focal chorioretinitis together with patches of fresh inflammation and superficial hemorrhages. The urine showed epithelial cells with large basophilic inclusion bodies in the nuclei and cytoplasm.

Subsequent pathological examination of the brain showed necrotizing encephalitis, calcification, and the presence of inclusion-containing cells. An acute chorioretinitis was present. The histologic picture is shown in Figs. 6 and 7. Illustrated is a cell with a large basophilic inclusion body surrounded by a clear halo within the nucleus and a few smaller inclusion bodies in the cytoplasm.

Rubella

A 1-year-old child with multiple congenital anomalies, whose mother had rubella during the first trimester, was noted to have a "salt-and-pepper" type of chronic chorioretinitis in the left fundus. There was a mature cataract in the right eye.

Idiopathic

Twenty-six cases were undiagnosed. In seven cases with suspected tumours (pseudogliomas) the diseased eye was removed. Non-specific inflammatory changes were noted.

Canad. Med. Ass. J.
Feb. 18, 1967, vol. 96

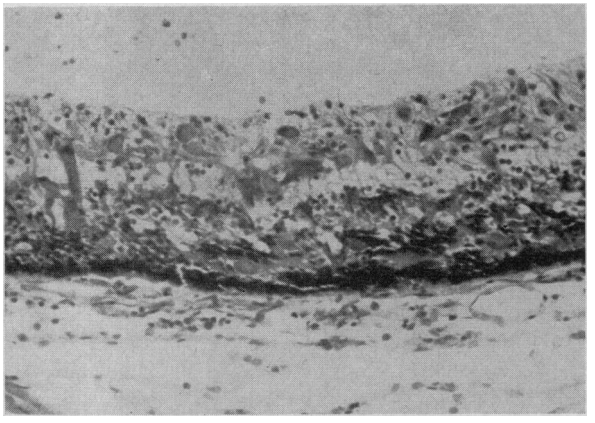

Fig. 6.—Retinochoroiditis in cytomegalic inclusion disease.

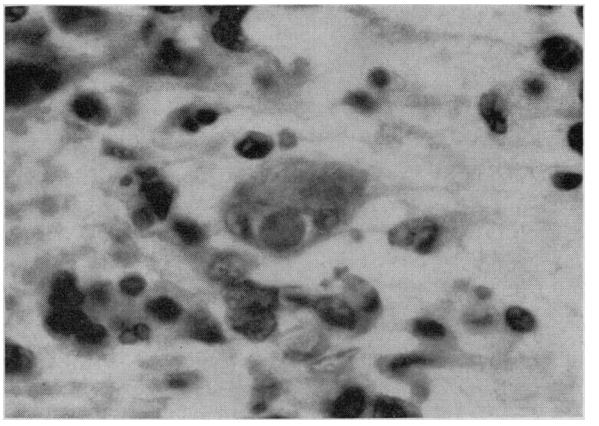

Fig. 7.—Nuclear and cytoplasmic inclusion bodies in cytomegalic inclusion disease.

Two cases of cystinosis with peripheral pigmentary degeneration resembling chorioretinitis were seen. These were not included as cases of uveitis.

III. DIFFUSE UVEITIS

There were three cases of diffuse uveitis, all presumed to be sympathetic ophthalmia.

Sympathetic Ophthalmia

Three children developed severe uveitis at an interval of three weeks to several months following penetrating injury to the opposite eye. All cases were complicated by the development of glaucoma. Predisposing factors to this included the development of dense posterior synechiae and, possibly, the prolonged use of systemic and topical corticosteroids. Iridectomies were required in two cases.

The long-term outcome was favourable in one case followed up for five years. Residual visual acuity was 20/40 and the uveitis was controlled on continuous therapy, corticosteroids given *per os*.

A second patient followed up for 10 years developed a cataract, and has vision less than 15/400 in the only eye.

The third case has been followed up for over one year, and the uveitis has been difficult to control.

COMMENT

In this series of childhood uveitis patients, anterior and posterior uveitis were of about equal incidence. Kimura and Hogan[2] in their series of 274 cases and Perkins[20] in a series of 150 cases found a preponderance of anterior uveitis. All these cases, including our series, represent a selected group, as only the more severe problems are likely to have been referred for investigation. Diffuse uveitis appears to be uncommon in all series.

The incidence of ocular complications of juvenile rheumatoid arthritis, as recorded in the literature varies from 5.5 to 21%.[6-8] The uveitis is usually insidious in onset and is frequently overlooked until complications develop. Chronic iridocyclitis is frequently severe, and before the introduction of corticosteroid therapy it often caused blindness. Ansell and Bywaters[9] reported that in some older children, particularly boys, a more superficial iritis is observed which disappears in a few weeks. Another eye complication recently recognized is the occurrence of posterior subcapsular cataracts in patients who have received systemic steroids for long periods.[10-12] This complication was noted in six of our patients, but could not be differentiated from cataracts secondary to uveitis.

The diagnosis of syphilis should be suspected in cases with acute bilateral anterior uveitis and intense photophobia. There is usually an associated interstitial keratitis.

In several of the cases of chronic cyclitis there was a significant focus of infection, and this may play a role in that disease, possibly as source of antigen. The presence of eosinophilia in several cases of chronic cyclitis may indicate an allergic mechanism. In this regard, however, it should be noted that moderate eosinophilia is common in children. Intestinal parasitism including relatively benign nematode infections such as whipworms or pinworms must be considered in the differential diagnosis of eosinophilia. The possibility of ocular nematodiasis should be considered in uniocular cases in the light of recent findings of Hogan, Kimura and O'Connor[4] and of Hogan, Kimura and Spencer[5] of a *Toxocara canis* larva in the peripheral retina of a child with monocular cyclitis.

In the newborn, uveitis is likely to be caused by toxoplasmosis or cytomegalic inclusion disease,[14] both of which cause acute necrotizing retinochoroiditis. The simultaneous existence of these two diseases has been described by Hemsath and Pinkerton.[15]

It is interesting to note that of the 250 children admitted to the hospital with tuberculosis (three with miliary tuberculosis and 17 with meningeal pathology) only two were noted to have ocular involvement. By comparison, 27 of 28 children admitted with a diagnosis of toxoplasmosis had ocular involvement.

Boyd[19] in 1956 reported a series of 134 treated cases of proved tuberculous meningitis in children seen during the preceding eight and one-half years at this hospital. Streptomycin therapy was available during this time. The eyes of all patients were carefully followed up by the ophthalmologists. Miliary tubercles in the fundus were seen only twice in meningeal cases, oftener in non-meningeal miliary disease. The commonest finding was optic atrophy.

The threat of sympathetic uveitis following penetrating ocular injury, particularly with injury to the uveal tract or iris prolapse, must be kept in mind. The three cases in this series benefited from the used of corticosteroids, but all were complicated by the development of glaucoma.

A definite pathological diagnosis of sympathetic uveitis could be made in only one case on the basis of histologic findings in the eye originally involved. In the eye with sympathetic ophthalmia, a phaco-anaphylactic reaction may co-exist.[16, 17] Easom and Zimmerman[17] have reported four cases of pure phaco-anaphylactic reaction in the so-called "sympathizing" eye. Thus the clinical diagnosis of sympathetic ophthalmia can only be presumptive.

Fuchs's syndrome of heterochromic cyclitis is not common in children. The diagnosis was not made in this series, although some of the idiopathic cases could fall in this category. Other causes of uveitis in children not diagnosed in this series include sarcoidosis and *Toxocara canis* infection. Neither Behçet's syndrome nor the Vogt-Koyanagi syndrome was seen. Cases of uveitis associated with herpetic keratitis were not included in this series.

A non-granulomatous uveitis may be associated with numerous febrile illnesses, such as measles, mumps, chickenpox, influenza and whooping cough.[18] The uveitis is usually bilateral, mild and self-limited. It is likely that a number of such cases were overlooked in this series.

A number of conditions must be included in the differential diagnosis of uveitis. These include retinoblastoma, juvenile xanthogranuloma, metastatic tumours, intraocular foreign bodies, retinal degenerations, retinal vasculitis, retinal detachment, Coats' disease and endophthalmitis.

SUMMARY AND CONCLUSION

One hundred and seventeen cases of endogenous uveitis in children aged 15 years and under have been studied. Among these were 55 cases of anterior uveitis, 59 cases of posterior uveitis and three cases of diffuse uveitis.

An etiologic diagnosis could be made in approximately 47% of these 117 cases or they could be recognized as part of a definite clinical syndrome.

Toxoplasmosis was the commonest cause of posterior uveitis, and juvenile rheumatoid arthritis was the commonest associated finding in anterior uveitis. Chronic cyclitis of unknown etiology was a relatively common disease.

The most helpful form of treatment in this series of cases was the use of corticosteroids by either systemic or topical administration. They seemed to play a significant role in the control of both iridocyclitis and chronic cyclitis. However, cataracts, a frequent complication, may be due in part to the effect of corticosteroids.[11, 12]

Uveitis was frequently diagnosed on routine examination in cases where no complaints were made by either the child or his family. It would seem that a thorough examination at an early age of all children is of value; in the presence of such diseases as toxoplasmosis and rheumatoid arthritis, a careful study of the eyes should be made.

We wish to thank the eye staff of The Hospital for Sick Children for supplying the follow-up data on their cases, as well as the Records Department, the Photography Department and the Pathology Department for their help.

Dr. Samuel J. Kimura, Dr. Phillips Thygeson and Dr. G. Richard O'Connor kindly reviewed the paper and supplied valuable suggestions as to the arrangement of the data.

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