Section of Ophthalmology

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Uveitis in Childhood

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UVEITIS is one of the commonest conditions met with in ophthalmic practice. It is responsible for much loss of time in industry and in business, and it results in a considerable degree of blindness. It is caused by many different factors, some definite and some speculative, and among all the cases which are seen a large proportion are of undiagnosed ætiology.

Uveitis is less common in children than in adults and it seems possible to establish the ætiology in a larger proportion of juvenile than of adult cases, or at least to classify them into clearly defined groups. In the young, a more pure strain of the disease would appear to be produced, and so it may be worth while studying the types found in children in order to help solve the overwhelming basic problem of the ætiology of uveitis. This communication is based on a series of patients in whom the onset of uveitis was before the age of 16 years.

Uveitis is a suitable name for this clinical entity because, in the large proportion of cases, the condition is not confined either to the iris, the ciliary body, or to the choroid. Most parts of the uveal tract are affected to some extent in every case. In anterior uveitis the iris and ciliary body are predominantly attacked, while it is the choroid which is mostly inflamed in cases of posterior uveitis.

In cases of pan-uveitis there is an equal reaction throughout the uveal tract. The terms iritis, iridocyclitis, and choroiditis are now obsolete.

ANTERIOR UVEITIS

Causes and Groups: Syphilis—Interstitial keratitis. Acute specific fevers. Tuberculosis. Sarcoidosis. Still's disease. Brucellosis. Vogt-Koyanagi syndrome.

Syphilis of the congenital type causing interstitial keratitis has always been one of the most usual causes of anterior uveitis in children. It is becoming far less common as a result of the introduction of antibiotic drugs. The efficient treatment of syphilis in pregnant women with penicillin has reduced greatly the incidence of interstitial keratitis in the children, while the cases which do occur as a result of the use of cortisone are not nearly so likely to suffer permanent visual disability as in the past. Indeed, it is possible that this condition may become a rarity within our generation.

Acute specific fevers may occasionally cause uveitis whether they be due to bacterial or virus agents. Most of these conditions seem to have a septicæmic phase before the disease becomes more localized, and transient uveitis has been seen in children both in meningococcal meningitis and in rubella; it has been described in others of the exanthemata. It is possible that the condition occurs not infrequently in mild form, and proceeds to spontaneous and complete cure.

Tuberculosis is undoubtedly a cause of anterior uveitis in children. An infection of the iris and ciliary body by the tubercle bacillus occurs rarely, but when it happens it seems that it progresses to cause serious damage of the eyeball and often its loss. I have not had the opportunity to treat such a case with streptomycin, PAS, or isoniazid, but a few cases seen previously to the introduction of these drugs, deteriorated steadily until the eyeball had to be removed. The affection of the eyeball by a sensitivity to the products of toxins produced by the tubercle bacillus is a different problem. This is an acknowledged cause of uveitis in adults and in children throughout the world, though the incidence in children has never been clearly defined. The incidence in adults varies greatly in the statistics of different writers, possibly due to the difficulties of diagnosis, which tends to be made on inadequate evidence and by a process of exclusion. The points which are helpful in diagnosing tuberculous anterior uveitis of the sensitivity type are a history of present or past tuberculosis either in the patient or in his family, or of other contact with tuberculous patients; the presence of a positive Mantoux reaction (though it must be realized that this only indicates a skin sensitivity and not a uveal sensitivity to tuberculin); and the clinical attributes of large "mutton fat" K.P., iris nodules and an associated sclerokeratitis. To this can be added the therapeutic test which suggests that four to six months under a sanatorium regime of rest, graduated exercise and adequate nourishment, should cure any lesion of a tuberculous type. No serological test is available, similar to the Wassermann reaction in syphilis, to indicate the presence of active tuberculosis. A series of tests with the Middlebrook Dubos test which Dr. N. Ashton and Dr. R. W. Riddell have carried out in patients from the Eye Sanatorium at Swanley, has been quite inconclusive both in adults and in children.

It is interesting to note that phlyctenular keratoconjunctivitis, usually regarded as a tuberculosis sensitivity reaction, used to be a common condition but that any associated uveitis was rare.

Sarcoidosis is a cause of uveitis in children though this condition is rare in the young. The ocular inflammation may be an isolated, or almost an isolated, manifestation of the condition, or it may be associated with a generalized state of sarcoidosis affecting many tissues of the body. The clinical manifestations are so characteristic as to allow a provisional diagnosis of the condition to be made, and it is possible that it is a more common cause of uveitis than is generally appreciated. The predominant features are the large profuse K.P. which have a ground-glass appearance, in contrast to the more yellow appearance of the K.P. which is characteristic of tuberculosis. The Mantoux test is usually negative, not always a significant point in children where this is a common finding. BCG inoculation will, however, usually produce a positive Mantoux reaction in children, in the absence of sarcoidosis. Other manifestations of the condition are sometimes found, especially in the lymph glands of the mediastinum. When affected lymph glands exist near the skin surface, they may be excised so that histological examination can confirm the diagnosis. The albumin-globulin ratio of the plasma proteins is often disturbed, showing an elevation of the globulin fraction, and the erythrocyte sedimentation rate may be raised. Nodules in the iris may occur, but these are not always present. The treatment of generalised sarcoidosis by systemic cortisone and by ACTH may be prolonged and require a large dosage, but the treatment of anterior uveitis due to sarcoidosis by local application of cortisone drops gives very satisfactory results. It is important to remember that uveitis occurring in a child may be an indication that sarcoidosis is present in the body, and that it may spread to other tissues.

Still's disease.—This condition in which rheumatoid arthritis accompanies anterior uveitis in children is a well-recognized syndrome. The uveitis is chronic in type, and is not associated with large or profuse K.P. It is, however, associated with a plastic type of exudate, with band degeneration of the cornea, and with complicated cataract. The uveitis may precede the arthritis or it may develop after the joint changes are manifest. It may be uniocular or binocular and the inflammation may settle down at any stage of its development. A very characterististic complication of the condition is the cataract which tends to come on steadily at a fairly early stage in the disease. It appears that both this and the band degeneration of the cornea must be regarded as due to a change in the constitution of the aqueous humour, as a result of the effects of inflammation upon the ciliary body, with resulting changes in the nutrition of the lens and cornea. The surgical treatment of these cataract cases is a matter of extreme difficulty because frequently the active uveitis persists for a long period, and there is a tendency to shrinking of the eyeball. There is a considerable risk that attempts to remove the lens while the active uveitis persists may result in phthisis bulbi. It is worthy of emphasis that it seems that cases occur of "Still's disease without arthritis". Certainly, cases of uveitis occur in children which show the characteristic plastic uveitis, band degeneration of the cornea, and complicated cataract, and in which arthritic changes never develop. Some of these cases are regarded as of tuberculous ætiology, but often they show none of the characteristics of that condition which have previously been enumerated. It is certain that these cases tend to have a uniformly bad prognosis. Local cortisone therapy and a sanatorium regime appear to do little to help, while the whole battery of antibiotics may be employed without avail. It may be that, with ACTH and cortisone becoming more easily available, these preparations may be used systemically. This is certainly justified as a sight-saving treatment since it would appear that the causative agent is transient, even if sometimes of long duration. Cataract extraction in these children is fraught with the same dangers as in those with arthritis, and even with a "cortisone umbrella", success is questionable.

Brucellosis may be a cause of uveitis in children. The diagnosis can be determined clearly from skin tests, and from brucella agglutinin and complement-fixation tests. Usually a chronic uveitis is associated with nummular keratitis.

Vogt-Koyanagi syndrome.—This syndrome which, when complete, comprises bilateral uveitis, poliosis, vitiligo, alopecia, and dysacousis has occurred in my experience in two children. The cause of this condition is uncertain but it is thought to indicate an inflammation of the meninges, and possibly of the hypothalamic region of the brain. It has been suggested that this inflammation is either due to a specific virus or as the result of tuberculosis, but it might equally well be due to a sensitivity factor which is also responsible for the uveitis.

Posterior Uveitis

Causes and Groups: Toxoplasmosis. Syphilis. Tuberculosis. Exudative choroiditis.

This condition can occur in children, but like anterior uveitis it is not common. In some of the patients, anterior uveitis may also be present, but in these cases the posterior uveal tract is predominantly affected.

Toxoplasmosis.—This is, possibly, the commonest cause of posterior uveitis in childhood. It is the result of a maternal infection with the toxoplasma parasite and was fully considered by the Section of Ophthalmology on February 11, 1954 (*Proceedings*, **47**, 481). Evidence is accumulating in the United States of America that toxoplasmosis may cause not only posterior uveitis but also

perivasculitis retinæ and anterior uveitis. The various tests for toxoplasmosis are therefore essential in the routine investigation of all cases of uveitis in children.

Syphilitic posterior uveitis.—This has been a frequent cause of uveitis in children, usually causing the well-known picture of disseminated choroidoretinitis. This condition, like interstitial keratitis, is often the result of congenital syphilis and it has become very much less common on account of the more efficient treatment of syphilis in expectant mothers.

Tuberculous posterior uveitis.—This condition like tuberculous anterior uveitis is not always easy to diagnose. The typical tuberculoma presents a characterististic appearance, but this is not commonly seen. The multiple tuberculous nodules associated with miliary tuberculosis and with tuberculous meningitis are well known in these days when streptomycin and allied drugs cause life to be prolonged in these cases. More doubtful in origin are those patches of solitary choroiditis, believed by some authorities to be tuberculous in origin. These patches are often quiescent when seen and the diagnosis of the cause has to rest upon the same indeterminate factors which have to be considered when considering the diagnosis of tuberculous anterior uveitis.

Exudative posterior uveitis of solitary type is seen in children fairly frequently. The appearance of a fluffy exudate in the fundus, with vitreous opacities, and sometimes with K.P. is characteristic. Some of these cases may be due to toxoplasmosis and some may be tuberculous in origin, but the ætiology in the majority is obscure. Some of the children are prone to hay fever and asthma. The condition tends to run a course and to settle, leaving choroidoretinal scars, and this is often helped by the use of cortisone or of ACTH and though there is some tendency to recurrence the condition does not usually cause serious visual disturbance unless the macula or its immediate area is affected.

Pan-uveitis

Causes: Sympathetic ophthalmitis. Non-specific pan-uveitis.

This type of inflammation affects the whole uveal tract in like amount and frequently it causes severe visual disturbance. It often tends to be bilateral.

Sympathetic ophthalmitis is the most common example of this type of ocular inflammation and little need be said about it here. It is not common but it occurs sufficiently frequently, and more often in children, to keep it constantly in our minds in casualty departments and in the wards, when perforating injuries have occurred. The true malignant type of sympathetic ophthalmitis remains a therapeutic problem. In spite of the use of cortisone and ACTH it still seems that there is little that can be done to halt this condition once it has developed. In almost all cases the result is total and complete loss of vision, both in the exciting and sympathizing eye.

Non-specific pan-uveitis.—These children sometimes appear in the neurological departments of hospitals, because though there is often a complaint of defective vision, the main finding on examination of the eye is a blurring of the optic disc which may suggest plero-cephalic œdema. Careful examination of the eye always shows fine K.P. with flare and with cells in the aqueous humour. The whole uveal tract is inflamed and patches of choroidal scarring may appear. It seems that the inflammatory condition spreads to the optic nerve, and these cases may suffer rapid and often complete loss of vision in both eyes, the end-result being an optic atrophy of secondary type. If they are recognized and it is essential that all cases of optic neuritis should be examined for the presence of uveitis, these cases can be controlled and the sight can be preserved by the adrenocortical hormones.

Ætiology.

Having discussed the main types of uveitis which are found in children, it is possible to consider the extent to which they help us in deciding the ætiology of the whole condition. It is agreed that some cases of uveitis are due to protozoal or bacterial infection, that some are due to viruses, and that, in all probability, the remainder are due to sensitivity reactions. Toxoplasmosis uveitis is an example of a protozoal infection, while tuberculous uveitis, brucellosis uveitis, and syphilitic uveitis are of bacterial nature.

The sensitivity theory seems to satisfy the cases due to tuberculosis where no bacteria are present within the eye, and sarcoidosis, which, though there are many theories for its cause, may be regarded as a state of generalized sensitivity to some antigen. Even Still's disease might fall into this category, and it is possible that interstitial keratitis is essentially a sensitivity reaction of the cornea and uveal tissues to the presence of the *Treponema pallidum*. The cases of uveitis in which other manifestations appear, like the Vogt-Koyanagi syndrome, might also be due to a sensitivity reaction of tissues outside the eyeball, as well as to tissues of the uveal tract.

The virus theory would appear to fit more satisfactorily our knowledge of sympathetic ophthalmitis, and Still's disease could, of course, have a virus origin. The Vogt-Koyanagi syndrome also could be due to the spreading effects of a virus infection.

The problem remains unsolved. Continuous efforts must be made to isolate a virus from cases of uveitis, and, at the same time, the immunologists should seek to demonstrate in animals a variety of sensitivity reactions similar to those which appear in the condition of uveitis in humans. The work which is being carried out in the United States on the sensitivity reaction of the many strains of

streptococcus appears to be of great importance. The immunity reactions of children appear, in general, to be less complex than those of adults and it may be that, in this field, the sensitivity reactions of uveitis can be solved.

The President said that Mr. Cross had referred to tuberculosis forming massive exudates. He presumed the lesion was of a similar character to the so-called tuberculoma sometimes seen in the eyes of human beings and also of animals. The appearance had been reported in the eye of a cat and he was able to examine one such case in which there was a large single tuberculoma of the choroid.

Mr. O. Gayer Morgan said that one sometimes saw youngish people of 16 or so, but also older persons, complaining of misty vision. They had a vitreous haze and in the fundus there was evidence of old choroido-retinitis and an active focus, very often a part of the old scar or in its neighbourhood. Sometimes one would find in a sector—curiously enough an area of the fundus which seemed to involve one retinal vessel—several of these scars and an active small new focus which had produced the vitreous haze. Could these be due to toxoplasmosis? In other words did toxoplasmosis have later periods of activity which one could see clinically? He did not think it did. But these cases of choroidoretinitis in a certain sector of the fundus were quite common and, if they were choroidal, it was curious that they should always be associated with one particular sector, which corresponded with the arrangement of the retinal vessels. Did Mr. Cross think that these cases were due to a local sensitivity of retinal tissue so that if the patients got run down or had some other illness they would develop a new active spot of choroido-retinitis?

Mr. F. G. Hibbert asked whether Mr. Cross felt that the degree of retinal reaction—retinal œdema—was really due to irritation. Were some of these cases primarily neuro-retinitis?

Mr. E. F. King asked whether Mr. Cross found it easy to differentiate cases of uveitis into granulomatous and non-granulomatous varieties as suggested by Professor Alan Woods.

Mr. R. W. Stephenson said that Mr. Cross had mentioned Still's disease and anterior uveitis. He would suggest that this might be in the nature of a total reaction. He recalled the case of a girl who had Still's disease and under cortisone the activity of the disease was reduced and cataract extraction was carried through smoothly. The pupillary area remained fairly clear. Unfortunately the vitreous was so full of deposit that there was no possibility of any good visual result.

Mr. W. K. Smiley said that he had been interested in Still's disease for about five years and during that time he had examined over 100 children with juvenile rheumatoid arthritis. Of this number about 5 or 6% showed ocular changes. This proportion was not nearly as high as was suggested in reports from Denmark where it was stated that 20% of children with Still's disease showed an anterior uveitis, very often with a band opacity. Of the few he had discovered in the last few years two were now in Blind Homes. One of them was interesting because the eye changes developed two-and-a-half years before any signs were shown in the joints and it was only by a strict follow-up of the case that one was able to prove that it was a case of Still's disease. He tried to remove the cataract from one eye in this case under local cortisone protection. He got rid of the cataract quite well but he found that the vitreous was so opaque that the child's vision was not better and indeed the eye did not seem able to withstand the surgery. Eventually it became soft and shrunken. The other eye also had a complicated cataract, but one would rather hesitate to operate on it except that one felt the child had nothing to lose.

Another case with a cataract did better, and again there was fairly rapid disappearance of the cataract by needling, but many vitreous opacities remained and vision was 6/36. The other eye was blind. This patient also had bilateral band opacity and one felt that a lamellar graft might be necessary. He thought that he might be able to get this patient out of the Blind School where he was at the moment. With Still's disease one could have an irreversible condition of post-cyclitic vitreous opacities which defeated all one's efforts even if the cataract was removed. One of his cases was a girl who had gross corneal band opacities and whose photograph he had shown at the meeting. Looking at her one would never imagine that she could see to read, but fortunately she had not got cataract and the band itself seemed to be a relatively insignificant factor in visual impairment. The vision was 6/9 in one eye and 6/18 in the other, and she could read and do quite fine needlework. He had two other children on treatment with cortisone which seemed, temporarily at least, to cure the uveitis, but, of course, the condition might well recur when treatment stopped.

Mr. F. J. Curtis asked whether Mr. Cross had found malignant change to be at all common in posterior uveitis. He had in mind a boy of about 7 who started with posterior uveitis and developed a single lesion of the choroid which was subsequently found to contain malignant cells and the eye had to be removed. He wondered whether that often happened.

Mr. Cross, in replying on the discussion, said that the cases which Mr. Morgan had described fell into his classification of patients with the exudative type of posterior uveitis. The observation of the segmental distribution was one of interest and he was unable to provide any explanation for its cause.

In what he had described as non-specific pan-uveitis, K.P. was visible on the back of the cornea. There was also a flare in the anterior chamber. In his opinion the majority of these cases did not show excessive retinal œdema in the region of the disc. If such retinal œdema were present, it was unlikely that these cases would be confused with cases of plero-cephalic œdema.

On the question of the differentiation of granulomatous and non-granulomatous types of uveitis, he had purposely refrained from considering that problem, but in his opinion this conception had not greatly clarified the ætiology. It might be true that the uveitis of Still's disease was a pan-uveitis. He had always thought that the main inflammatory reaction was in the ciliary body and that the exudate from that region was responsible for the vitreous opacity. The case which Mr. Curtis had mentioned would be recalled by several members of the Moorfields' Staff. This child with retinoblastoma of one eye had attended with apparent posterior uveitis, and had later developed what appeared to be a hypopyon. The diagnosis of retinoblastoma had been confirmed on histological examination, after removal of the eye.