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OCULAR TUBERCULOSIS*

BY

A. L. WHITEHEAD

LEEDS

It is with great diffidence that I address you to-night from this distinguished position.

In the first instance I desire to offer you my thanks for the honour you have conferred upon me in electing me your President. I regard it as a compliment to provincial ophthalmology and a tribute to the great school of medicine at Leeds, of which I am a member. Although the honour is great, the responsibility and the obligations involved in the occupancy of this chair are even greater, when I consider the roll of previous distinguished occupants.

It will be my earnest endeavour to maintain the high reputation of the section during my term of office.

In the past year ophthalmology has received important recognition at the hands of the King.

Two members of the Council of this section have been honoured with knighthoods—Sir John Parsons and Sir Richard Cruise. The valuable work which they have carried out is worthy of the highest public acknowledgment.

We have to deplore the loss by death of two distinguished

* Presidential address delivered on October 13, 1922, in the Section of Ophthalmology of the Royal Society of Medicine.

members of the section. Edward Stack, of Bristol, a member of the Council, will be much missed. With an engaging personality he combined a keen and observant mind, a mature judgment and a wide ophthalmic experience.

Charles Wray, of Croydon, an energetic ophthalmologist, has enriched our literature by many contributions.

Epoch-making discoveries are rare in the history of medicine, and rarer in our speciality. I cannot indicate any such discoveries in the past year and I have none to bring before you to-night.

Opportunities for research are few in a very busy clinical and teaching practice, but I may detain you for a few minutes with some observations on a common aspect of eye disease.

The tubercle bacillus is so widely distributed and lesions due to it are so common elsewhere in the body that it is only natural that much should have been written about tuberculous diseases of the eye.

I do not propose to occupy your time with a digest of the extensive literature of the subject, but to give you some of my own impressions of ocular tuberculosis in comparison with the experience of other observers.

Tuberculosis is more frequent in Leeds and less frequent in the West Riding of Yorkshire than in England and Wales as a whole. The official figures supplied to me by the Ministry of Health and the Medical Officer's annual reports are as follows for 1920 :—

England and Wales, with a population of 37,524,000, had a tuberculosis case rate of 2.07, incidentally, I may mention, the lowest since 1914.

The West Riding of Yorkshire, with a population of 1,498,453, had a case rate of 1.61, also the lowest since 1914.

Leeds, with a population of 448,913, had a case rate of 2.61, the lowest since 1914.

A large percentage of our cases in hospital and private practice reside outside Leeds, so it is very probable that on the average the general case rate will not be very dissimilar from that of England and Wales as a whole.

Every ophthalmologist must have been struck by the comparative rarity of tuberculous lesions of the eye in pulmonary tuberculosis, and in serious cases of surgical tuberculosis, but if cases of ocular tuberculosis are followed up, there is good evidence that in after years other manifestations are frequently present.

A very valuable paper bearing upon this point was contributed in 1921 by Igersheimer and Prinz⁽¹⁾, dealing with the after history of 92 scrofulous eye cases followed up for 10 to 30 years. They found that in 13.9 per cent. there were changes in the lungs, and in 13 per cent. there were symptoms of active tuberculosis.

In discussing the various forms of ocular tuberculosis, I shall refer again to this question.

There seems to be a very important difference between the severe spreading invasions of the eye, leading to more or less complete destruction of the eyeball, and the more chronic and benign forms of tuberculous infiltration. In the former, typical giant cells are common, and the tubercle bacilli are frequently found; in the latter, careful search and inoculation tests usually fail to demonstrate the bacillus.

There is a general consensus of opinion that in the latter group of cases the infection is due to a tuberculo-toxin acting on a specially prepared area. This view has been supported by experimental evidence by Guillery⁽²⁾ and others.

Of conglomerate tubercle of the uveal tract, leading to destruction of the eyeball, either by perforation of the outer coats of the eye or by caseation and subsequent shrinking of the globe, I do not propose to say anything.

The standard text-books deal very fully with these cases and my experience coincides with the usual description.

Tuberculous choroiditis.—Miliary tubercles of the choroid in acute tuberculosis of infants are frequently present. In nearly all of the many cases of fatal tuberculous meningitis in which I have had the opportunity of examining the fundus, I have found miliary tubercles.

Isolated tubercles, usually single, are not infrequent, and unless at or near the macula, attract little attention. They occur in the same class of individuals in whom the less severe forms of tuberculous infection of the eye are usually found. They are small, $1/3$ to $1/2$ of the size of the optic disc, greyish yellow with a soft indefinite margin. In the later stages the circular clean-cut edges of the atrophic patch are very characteristic. Occurring in early infancy, they are not usually recognized until, as the child grows up, the interference with vision attracts attention. I do not think I have seen them in individuals over the age of 30.

Primary tubercle of the retina I have not seen, but I have notes of one case in which I regarded a nodule in the papilla as probably tuberculous. Degenerative changes in the blood vessels, usually the veins, followed by haemorrhages, either small and confined to the retina, or large and bursting into the vitreous, have been described by Jackson and Finnoff and by de Schweinitz.

In my own experience, in two instances, vitreous haemorrhages have preceded any other manifestations of general tuberculous infection. In both these cases, pulmonary tuberculosis became manifest in 12 to 18 months after the appearance of the haemorrhages; in one a typical tuberculous iritis with nodules came

on after the pulmonary signs were defined, but cleared up under treatment.

Chatterton⁽³⁾, at a meeting of this Section in 1913, reported a case of tuberculous iritis with vitreous haemorrhages treated by tuberculin. It is possible that some of the unexplained cases of recurrent vitreous haemorrhage may be due to toxin infection from a tuberculous focus elsewhere in the body. Several observers, notably Schieck⁽⁴⁾, have reported favourably on the use of tuberculin in recurrent retinal haemorrhages.

Tuberculous iritis.—I have nothing to add to the text-book descriptions of the various forms of tuberculous nodules in the iris. We have all seen many examples of the recognized varieties. Again, however, I would point out that in many of the milder cases the nodules are small, disappear early and leave little, if any, permanent change in the iris structure. They occur usually in young and apparently robust adults, frequently females, and with no other evidence of tuberculosis, but often with the family history of susceptibility to infection. In these cases the value of tuberculin treatment by proper dosage has been repeatedly demonstrated.

Hessberg⁽⁵⁾ considers that more than 50 per cent. of all cases of iritis are attributable to tuberculosis; he states that the nodules are frequently very small, lasting often only a few hours, and may disappear without leaving any scar. Phthisis and joint tuberculosis are rarely present, but the lymphatic glands of the mediastinum and mesentery are frequently affected. I do not think many ophthalmologists will agree with this extraordinarily high percentage.

Tuberculous disease of the lacrimal sac is not common in my experience. I have seen it secondary to lupus of the nose and as a forward extension of tuberculous disease of the ethmoid.

The possibility of an epiphora and dilatation of the sac secondary to nasal tuberculosis should always be remembered in young adults. In one case under my care, such a chronic dacryocystitis followed a tuberculous ulceration of the inferior turbinate and septum. Tuberculous ulceration of the vulva occurred in this case, a young girl of 12, and was entirely cured by local and general treatment; about a year later a toe had to be amputated for tuberculous "dactylitis"; then the nose and lacrimal sac became affected. Later on the pharynx and larynx were involved. The whole process has continued for 5 years, during which the child has looked the picture of health, and is of the most robust physical development. What her ultimate fate will be I cannot say.

Tuberculous conjunctivitis.—The severe forms with large sub-epithelial nodules leading to ulceration and formation of large

granulations and the so-called coxcomb excrescences are, in my experience, rare. Lupus of the conjunctiva spreading by direct infection from the face is quite characteristic and calls for no comment.

Many papers have been written in many languages discussing the possible tuberculous origin of the common phlyctenular conjunctivitis of children. Veeder and Hempelmann⁽⁶⁾, in the *New York Medical Journal* of 1920, reported 196 cases of phlyctenular disease. There was a positive von Pirquet skin reaction in 93. Tuberculous lesions involving other organs were found in half the cases, and in children kept under observation for one year or longer, four-fifths gave evidence of other tuberculous processes.

For some time past I have frequently noticed a type of phlyctenular conjunctivitis which I have come to regard as definitely tuberculous. It occurs in young adults, rarely in small children, is very chronic in type and resistant to the ordinary treatment. The phlyctenules are small, closely set, aggregated together near the corneo-scleral junction, and there is frequently infiltration of the cornea, with rather large invading vessels; ulceration is very rare. In some instances iritis is also present. I have water-colour drawings of two typical cases of this variety of conjunctivitis with slight corneal invasions and iritis.

In all the cases there are either evidences of tuberculous processes elsewhere or a clear family history of susceptibility to tubercle invasion.

The von Pirquet reaction is frequently positive, but not invariably so, although a definite but slight reaction occurring between 24 and 48 hours after inoculation, and, regarded by some observers as positive, is almost always present.

Examination of the tissue removed does not show typical giant cells or the presence of tubercle bacilli, and inoculation of guinea pigs has given negative results.

Although this group of cases is very resistant to ordinary treatment, immediate and striking improvement follows tuberculin injections. It is most important to give in each case the appropriate dose.

Tuberculin B.E. is used and the initial dose is $1/5,000$ mg. to $1/10,000$ mg., according to the age of the patient; four-hourly temperature records are taken for 24 hours with the patient in bed; if there is no temperature or general reaction, an increasing dose is given three days later.

Our usual scale is $1/5,000$, $1/2,500$, $1/1,000$, $1/750$, $1/500$, $1/250$, $1/100$, $1/50$ mg.

When the reaction is obtained the dose is repeated, and if there is again a reaction the dose short of this is given and repeated at weekly or fortnightly intervals according to the case. I have

dealt with this in detail, since I am quite satisfied that only the dose suitable for the individual will give good results. The efficient dose has varied from 1/50 mg. to 1/500 mg. even in cases of about the same age, showing the uselessness of a uniform dose. A severe general reaction is very unusual, an elevation of temperature of 1° to 2° being the usual indication; in a very few cases local reaction at the site of injection with suppuration is the only indication.

Of the method of treatment suggested by Ellis and Gay⁽⁷⁾, of tuberculous eyes by the direct local application of various dilutions of tuberculin P.T.O. (bovine) I have no experience, and I do not know whether the authors have found a more prolonged trial of this treatment to justify its use. Appropriate constitutional treatment is of the greatest importance; if possible an entirely open-air life on sanatorium principles should be insisted upon.

Since it is almost established that these minor lesions of ocular tuberculosis are due to toxin infection from a focus elsewhere, it is of the greatest importance to search for such a focus and, when found, to employ suitable treatment. Infected tonsils and adenoids should, of course, be dealt with by operation.

The question of treatment of enlarged glands by operation or otherwise is of great importance.

Wolff⁽⁸⁾, of Amsterdam, has strongly urged the value of the treatment of the tuberculous lymphatic glands by X-rays in cases of tuberculous conjunctivitis and keratitis. I have no experience of this, neither have I tried injections of milk in these cases.

Siegrist⁽⁹⁾, after an X-ray examination of the thorax in cases of chronic uveitis, came to the conclusion that the intra-thoracic bronchial glands were probably the primary focus.

Directly bearing upon the question of the possibility of the mediastinal glands being the primary focus in cases of toxin infection of the eye, Prof. Stewart has supplied me with some very important observations.

In post-mortems on 100 cases of death from rapidly fatal war injuries on men of the best physique from the front lines, the following striking facts were elicited. In 42 per cent. there were undoubted evidences of tuberculous disease, in 11 per cent. scarring at the apices of the lungs, and in 1 per cent. extensive old pleuritic adhesions, making 54 per cent. probable tuberculous lesions.

In 32 per cent. of the total there were definite signs of glandular infection, 15 per cent. being bronchial, 15 per cent. mesenteric, 1 per cent. pre-pancreatic, and 1 per cent. cervical.

In view of these facts indicating the frequency of latent tuberculosis in the glands, it seems very probable that the primary focus in these cases of tuberculo-toxin infection may be in the bronchial or other glands.

Kleinschmidt⁽¹⁰⁾ believes that a small portion of phlyctenular cases only are free from tubercle and many others have a quiescent lesion only.

Ordinary local treatment is also employed, atropin ointment and boric acid lotion irrigations in the early stages, yellow oxide of mercury ointment and powdered calomel insufflations, as the more acute symptoms subside.

Operative treatment in some of the cases is of the greatest value. I have tried excision of the affected conjunctiva in some cases, but without especially satisfactory results. In cases where there is a vascular invasion of the cornea, a form of peritomy is of the greatest service. The most satisfactory results seem to be obtained if a strip of conjunctiva, 2 or 3 mm. in width, is excised all round the corneo-scleral junction and the larger superficial vessels involving the cornea are carefully scarified by the point of a Graefe's knife; six or seven cuts are made across each vessel.

The value of peritomy has been emphasized by several ophthalmic surgeons; my revered colleague, Mr. Pridgin Teale, possibly the doyen of ophthalmologists, now in his 91st year, has advocated the operation repeatedly, and in later years Sir Anderson Critchett and Sir Richard Cruise have urged its performance in suitable cases.

Personally I am firmly convinced that it is one of the most valuable aids to treatment which we possess of these otherwise very intractable cases. In ten recent cases of the type of phlyctenular conjunctivitis which I have described, the ages ranged from 10 to 27, the average being 15.3. In four cases there were enlarged cervical glands; in one a patch or lupus on the cheek, not in the neighbourhood of the eye; in one a tuberculous synovitis of the knee; in one the mother had suffered from tuberculous peritonitis, and in another a sister died of acute pulmonary tuberculosis. Many of the cases had been under the usual treatment for long periods without benefit; in one case for nearly three years, and in another for over 18 months. Peritomy was performed in five cases. In one case where vision had been less than 6/60 six months ago, it is now 6/9 in one eye and partial 6/6 in the other, and the corneal opacities have almost disappeared. In all the improvement was rapid and very marked, and there has been an entire freedom from relapses, which had been frequent before the special treatment was undertaken.

Tuberculous keratitis following infection after injury is, I think, rare, and secondary infection from the conjunctiva, the ciliary body or the iris is equally uncommon. A parenchymatous affection, to some extent simulating the keratitis of congenital syphilis is frequent and is worthy of greater attention. In tuberculous keratitis the surface of the cornea is more irregular, although actual

ulceration is rare, the patches of opacity are less regular in distribution and the vascular invasion of the cornea is much more superficial. The onset is not so rapid and the progress is much more erratic.

In congenital syphilis it is usual to find the keratitis steadily and progressively advancing, followed by steady and progressive resolution. Peritomy is, in my experience, of the greatest value in the treatment of the pannus of tuberculous keratitis and quite valueless in congenital syphilitic keratitis. The possibility of a mixed infection must always be borne in mind.

Tuberculous scleritis and episcleritis, often with involvement of the iris and cornea, are possibly in some instances due to direct tuberculous infection. One of the most serious and intractable cases I have ever seen, occurred in a gentleman whose wife was suffering from advanced pulmonary tuberculosis, although he himself had no evidence of infection elsewhere.

The conclusions to which my observations point, but for which I do not claim any originality, are:—

1. Ocular tuberculosis is much more frequent than is usually taught.

2. Two very well defined classes of these lesions exist.

- (a) The destructive, caseating or necrosing variety in which the infection is primary, or part of a generalized distribution of tubercle, progressive, and only slightly, or not at all, amenable to treatment. Tubercle bacilli are frequently discovered in these cases.

- (b) A much milder form of infection, often called attenuated tuberculosis, probably of a toxic nature, since bacilli and giant cells are rarely found. The primary focus is usually not in the eye, and in many cases cannot be discovered by a careful investigation. The bronchial or mediastinal glands may, in many instances, be the focus in question.

In the second class recovery is the rule, with more or less interference with vision according to the areas of the eye affected. In the treatment of this group, properly graduated tuberculin injections are of the greatest value. In tuberculous vascular keratitis, peritomy and scarification of the invading vessels is a most valuable aid to treatment. If the primary focus is in a situation where removal can be carried out by surgical means, operation should be carefully considered. If, as seems frequently the case, the focus is in the bronchial or mesenteric glands, constitutional treatment of the most thorough variety obtainable must be undertaken.

Finally, I wish to express my indebtedness to Prof. Stewart and Dr. McLeod, of the Pathological Department of the University of

Leeds, for valuable assistance in investigating the pathology and bacteriology of some of my cases; and to Mr. S. D. Lodge and the sisters of my wards in the General Infirmary at Leeds, and to various tuberculosis officers for the careful supervision and execution of the treatment.

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OCULAR SARCOMA WITH WIDE EXTENSION, INVOLVING BRAIN AND SPINAL CORD

BY

HUMPHREY NEAME

LONDON

(*Conclusion*)

**Report on the specimen submitted by Mr. H. Neame, F.R.C.S.,
to the Pathological Committee***

A PATHOLOGICAL Committee was formed at the meeting of the Ophthalmic Section of the Royal Society of Medicine, for the purpose of examining the sections of this specimen and of reporting thereon.

The Committee have examined the specimen submitted to them and are unanimously of opinion that it is impossible to arrive at a definite conclusion as to whether the growth was primarily intra- or extra-ocular.

The majority of the Committee are inclined to the view that the growth was primarily intra-ocular. The sight remaining good for some time after the appearance of an epibulbar growth is not inconsistent with flat sarcoma of the choroid, of which cases have been reported of long duration without serious symptoms.

Flat sarcomata starting in and spreading along the lymph spaces cause almost uniform thickening of the uveal tract, as in this case. They are also specially prone to extend outside the

* See *Proceedings of the Royal Society of Medicine*, 1922, XV (Sect. Ophth.), p. 22.