

## **Intra-ocular tuberculosis / by E. Treacher Collins.**

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# INTRA-OCULAR TUBERCULOSIS.

BY

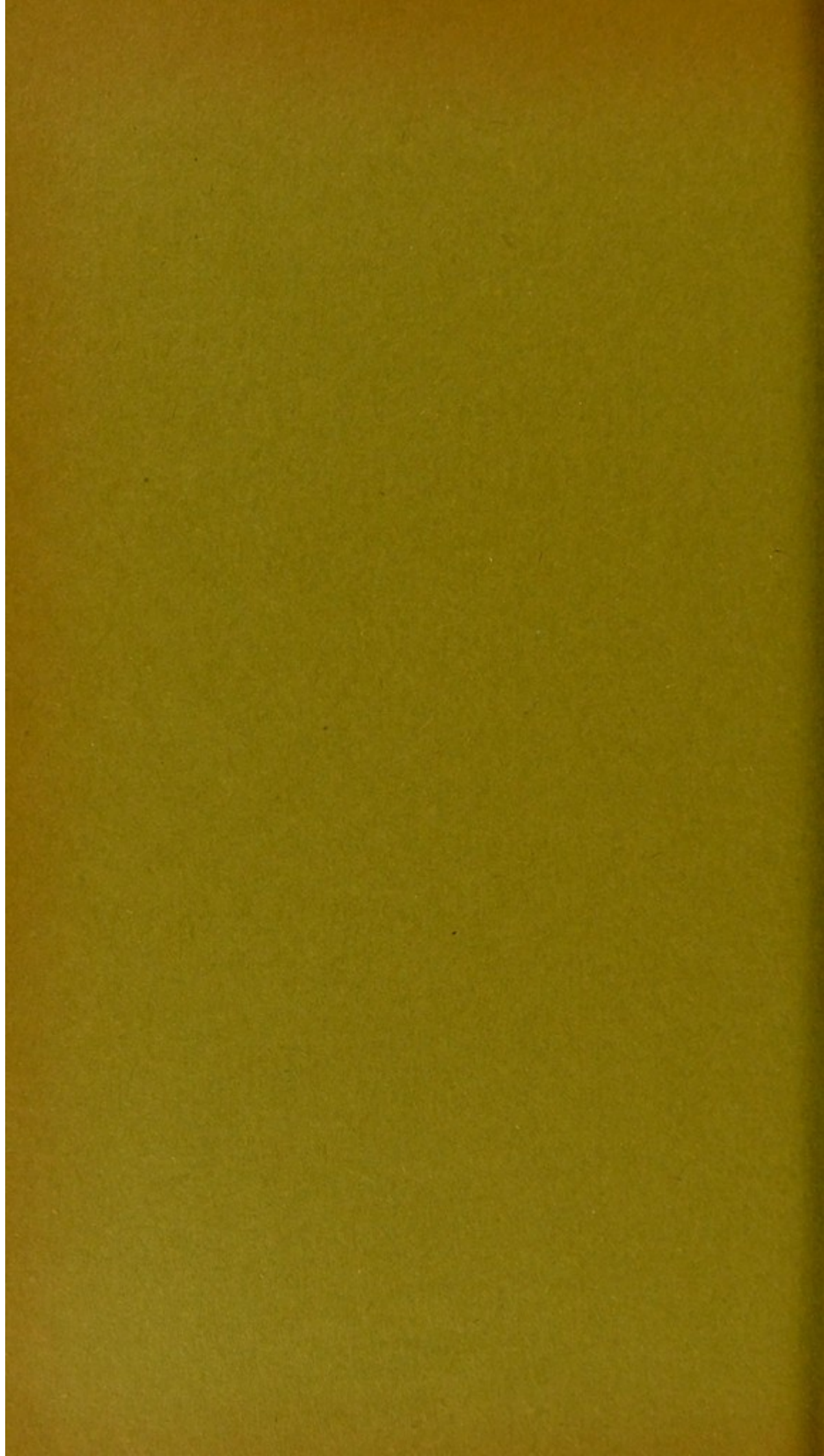
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# INTRA-OCULAR TUBERCULOSIS,\*

BY

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## Historical.

Affections of the eye which we now know to be tuberculous were during the first part of last century included under the heading of *fungoid growths of a non-malignant character*.

As far back as 1711 Maître-Jan<sup>(1)</sup> recorded a growth of this description, starting from the iris, implicating the cornea and projecting between the lids; after treatment with caustics it permanently shrivelled and cicatrised.

In the posthumous work of J. C. Saunders<sup>(2)</sup> published in 1811, two cases of a similar character are described. W. Lawrence<sup>(3)</sup> in 1833, and C. G. Lincke<sup>(4)</sup> in 1834, wrote excellent accounts of the disease.

It will be well here to quote that given by Lawrence, as it pictures stages in tuberculosis of the eye which now, owing to early enucleation, are not very frequently seen. He says:

Sometimes innocent fungous excrescences arise from inflammation affecting the anterior part of the globe. After severe external ophthalmia, with considerable redness, and often violent pain in the organ, a fleshy vascular substance may spring up from the surface of the sclerotic coat, from the orbiculus ciliaris, or from the cornea; or such a production may proceed from the iris, and cause ulceration of the cornea. Vascular or fungous growths, arising in this way, may assume a formidable appearance for some time and then gradually subside, the eye going into a state of atrophy. After the existence of severe inflammation a bluish prominence may arise in the seat of the orbiculus ciliaris, apparently proceeding from within outwards, so as to induce the suspicion that it may be a fungus arising from the interior of the globe. This swelling may become yellow, break and discharge matter; after which the globe shrinks, without further injury to the patient.

Lincke introduced the term "granuloma of the iris," which was afterwards employed by von Graefe, De Wecker, Hirschberg, Steinheim<sup>(5)</sup> and many others. It is now generally accepted that cases so spoken of are really tuberculous.

Mackenzie<sup>(6)</sup> in 1854 mentions a non-malignant solid tumour of the iris "which appears to be in general a scrofulous tubercle," and the same affection as that described by Delarue<sup>(7)</sup> under the head: *Des Excroissances charnues de l'iris*. In this affection he says:

\* A communication read at the XV International Congress of Medicine, Lisbon, 1906.

(1) *Traité des maladies d'œil*. (Troyes.)

(2) *Treatise on some Practical Points relating to Diseases of the Eye*. (London.)

(3) *A Treatise on Disease of the Eye*. (London.)

(4) *De fungo medalluri oculi*. (Leipzig.)

(5) *Archives of Ophthalmology*. Vol. I, 1870, p. 647.

(6) *Treatise on Diseases of the Eye*. 4th Ed., London, p. 705.

(7) *Cours Complet des Maladies des Yeux*, p. 206, Paris, 1820.

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The iris generally becomes first of all whitish at some particular part of its extent, and then rises into a tumour, which assumes a yellowish colour, with red vessels ramifying over it. Sometimes such a tumour suppurates, and bursts through the sclerotica, after which the eye becomes atrophic.

He further mentions that :

The posterior part of the choroid is sometimes the seat of a tumour, which is probably of the nature of scrofulous tubercle, or a fibro-plastic tumour. It separates the membrane into two laminae, between which it is deposited. Much more frequently have non-malignant growths been observed in the anterior part of the choroid.

The first description of tubercle of the choroid appears to have been given by G. de Mussy in 1837. He noted little yellow granules on the choroid at a *post-mortem* examination on a young girl who died of phthisis.

Jaeger recognized tubercle ophthalmoscopically in the living eye in 1855 and the diagnosis was verified some years subsequently by *post-mortem* examination.

Manz <sup>(1)</sup> was however the first to make a microscopical examination of tubercle of the choroid in 1858.

The first microscopical examination of tubercle of the iris was in a case published by Gradenigo <sup>(2)</sup> in 1869. The patient died of general miliary tuberculosis, and the histological examination of the iris tumour was made by Richetti. Berthold <sup>(3)</sup> followed in 1871 with the description of the histological appearances of the eye of a child, aged two, who had what was termed clinically "granuloma of the iris." It was enucleated and microscopical examination revealed the tuberculous character of the affection.

Having given the names of these pioneers, it is needless to refer to the many who have followed in their steps.

The inoculability of rabbits with tuberculous material injected subcutaneously having been demonstrated by Villemin in 1865, it occurred to Cohnheim in 1877 to introduce it into the anterior chamber of the eye, and by so doing he found he was able to set up a tuberculosis of the iris.

The experimental tuberculosis was shortly afterwards carefully investigated by Haensell <sup>(4)</sup>, Samelsohn <sup>(5)</sup>, Baumgarten <sup>(6)</sup> Leber, and others.

In 1882 Koch demonstrated that a specific organism could be separated from tuberculous tissue and cultivated outside the body, which would reproduce tuberculosis when inoculated.

The first observer to detect the bacillus tuberculosis in the

<sup>(1)</sup> *Archiv für Ophth.*, IV, 2, p. 120.

<sup>(2)</sup> *Annales d'oculistique.*, LXIV, p. 177.

<sup>(3)</sup> *Annales d'oculistique.*, LXVI, p. 88.

<sup>(4)</sup> *Archiv für Ophth.*, XXV, 1879, 4, p. 1.

<sup>(5)</sup> *Berl. klin. Woch.*, 1879.

<sup>(6)</sup> *Archiv für Ophth.*, XXIV, 1878, 3, p. 183.

tissues of the eye was Haab <sup>(1)</sup> in 1884. He was followed by Reissman <sup>(2)</sup>, Wadsworth <sup>(3)</sup>, and Lawford <sup>(4)</sup>.

### Tests for tuberculosis of the eye.

The foregoing brief historical note serves to show that we have three tests which can be applied for determining the tuberculous character of a growth in the eye. (1) The histological test, (2) The experimental test, and (3) The bacteriological test. The respective value of each of these tests will now be discussed.

(1) *The histological test.*—The essential histological features of tubercles have formed a fertile subject of discussion since the days of Laennec.

There is now, however, a consensus of opinion that the reaction of the tissues to the tubercle bacillus consists in an aggregation of cells consisting of a central giant cell of the type first described by Langhans and now known by his name, epithelioid cells, and marginal lymphocytes. Central degeneration, called caseation due to anæmic or toxic necrosis is a common termination of such aggregations; they may, however, undergo a fibrosis and become converted into a mass of cicatricial tissue.

A new growth in the eye showing histologically the aggregations of cells above mentioned, the so-called "giant cell systems," and also areas of caseation may almost certainly be pronounced tuberculous apart from any other evidence.

The presence of caseation alone, of giant cells alone, or even of giant cell systems, is not, however, sufficient proof.

The tissues may react to other stimuli, besides that of the tubercle bacilli, so as to produce these appearances.

As is well known, the injection of lycopodium spores or cinnabar granules into rabbits excites the formation around them of giant cells with epithelioid cells and lymphocytes.

Around foreign bodies implanted in the eye, such as a piece of an eyelash, or a caterpillar's hair in the affection termed ophthalmia nodosa, accumulations of cells take place similar in appearance to the giant cell systems of tubercle.

The giant cells, moreover, may be of the so-called Langhans' type, *i. e.*, having their nuclei arranged peripherally.

The writer has also met with giant cells of this type, epithelioid cells, and lymphocytes surrounding pieces of lens capsule which have become entangled in the wound after extraction of cataract.

At the Ophthalmological Society at Heidelberg in 1897,

<sup>(1)</sup> *Klin. Monats. für Augen.*, XXII, 1884, p. 391.

<sup>(2)</sup> *Arch. für Ophth.*, XXX, 1884, 3, p. 251.

<sup>(3)</sup> *Trans. Ophth. Soc.* III, p. 474.

<sup>(4)</sup> *Trans. Ophth. Soc. of U. K.* VI, 1886, p. 348.

Axenfeld showed specimens from eyes suffering from a uveitis which had caused sympathetic ophthalmitis, in which areas with epithelioid cells and giant cells like those met with in tuberculosis were present in the choroid. There was no caseation and bacilli were not present, and in spite of the histological appearance, Axenfeld did not regard them as tuberculous. He argued that, if they were, tuberculosis would be oftener met with in cases of sympathetic ophthalmitis. As Axenfeld says, in order to decide the question, it is desirable that pieces of the choroid from the freshly excised eye should be transplanted into the peritoneum of the guinea pig.

The writer has also met with the histological appearance of giant cell systems in the choroid of an eye which excited sympathetic ophthalmitis. The case was remarkable in another way, for three months after the injury the eyelashes and eyebrows of both eyes commenced to turn white, and ultimately became quite white. The clinical details of the case, on this account, were recorded by Tay in the *Transactions of the Ophthalmological Society of the United Kingdom* in 1892, Vol. XII.

(2) *The experimental test.*—Inoculation of tuberculous material has been made into various parts of the eyes of rabbits and guinea pigs; into the cornea by Haensell <sup>(1)</sup>, Panas and Vassaux <sup>(2)</sup>; into the vitreous humour by Deutschmann; and by numerous observers into the anterior chamber. The latter is the most suitable situation for these experiments, the aqueous humour forming an excellent medium for the growth of the tubercle bacillus.

Tuberculous material from different structures of the body, from its various organs, and from their secretions have been inoculated with positive results.

From eyes affected with tubercle, pieces of the iris, or of the choroid, and the aqueous humour have been inoculated. It is essential that the inoculated material should be free from pyogenic organisms, as otherwise a severe iridocyclitis and sometimes panophthalmitis is set up.

So uniform are the results of the inoculation of tuberculous material into the anterior chamber that the experimental test must be regarded as the most certain we possess. Examples of failures where the other evidence of tubercle of the eye was fairly conclusive have however been recorded by Samuelsohn, Haensell and Leber.

The immediate reaction after the implantation of a piece of tuberculous material into the anterior chamber is very slight.

(1) *Archiv für Ophth.*, Vol. XXVII, 3, 1881, p. 93.

(2) *Archives d'Ophthal.*, V, 1885, p. 193.

By the fifth to the eighth day the piece of implanted tissue becomes absorbed and the eye looks normal. After an incubation period of about 20 days in the rabbit or 12 days in the guinea pig the iris becomes inflamed and at the seat of the inoculated tissue some little grey nodules appear. Later, nodules of a similar character are seen scattered about all over the iris. They increase in size, become confluent, often filling the anterior chamber and invading the cornea. Sometimes they cause perforation, undergo caseous degeneration and then subside. General infection, from which the animal usually succumbs, follows after about 2 to 3 months.

(3) *Bacteriological test.*—Tuberculosis is well defined as “an infective disease due to the growth in the tissues of a parasitic micro-organism, tubercle bacillus.” (Watson Cheyne).

The demonstration of the bacillus in the tissue is therefore the most conclusive proof of its tuberculous character. Failure to find the bacillus even after skilled and prolonged search cannot, however, by itself be taken as disproving the tuberculous nature of a growth.

Failure to find the bacilli in what was undoubted tuberculosis of the eye has been a common experience of a large number of excellent observers and skilled microscopists. The bacilli in some cases, especially chronic ones, are very limited in number and they might easily escape detection in sections, unless one of them happened to have included a bacillus cut across in its long axis. It is also probable that some of the hardening re-agents used for the eye may interfere with the staining properties of the bacilli.

Haab <sup>(1)</sup> detected the bacillus in a number of specimens, though they were seven years old and had been immersed in Müller's fluid during that time.

Wadsworth <sup>(2)</sup> also discovered bacilli in a specimen of tubercle of the iris which had been hardened by Müller's fluid.

Lawford <sup>(3)</sup> found bacilli in only two out of six cases of tubercle of the choroid, though he examined many sections of each specimen and employed for each three different methods of staining, *viz.*, those of Weigart, Ehrlich, Gram, and Ziehl. In one case, though the bacilli could be easily discovered and were plentiful in preparations of the meninges, none could be discovered in the nodule in the choroid, though it presented every other characteristic of a tuberculous growth.

Hill Griffith <sup>(4)</sup> says that out of ten cases of tubercle of the

<sup>(1)</sup> *Klinisch. Monatsbl. für Augenheilk.*, XXII, 1884, p. 391.

<sup>(2)</sup> *Trans. Am. Ophth. Soc.*, III, 1883, p. 474.

<sup>(3)</sup> *Trans. Ophth. Soc. of U.K.*, VI., 1886, p. 348.

<sup>(4)</sup> *Trans. Ophth. Soc. of U.K.*, X., 1890, p. 84.

iris in which bacilli were looked for by different observers they were only demonstrated in four.

Lagrange <sup>(1)</sup> states that in three cases of tubercle of the iris he easily found the bacillus and in one case of the inflammatory type they were in great abundance.

### Mode of origin of intra-ocular tuberculosis.

Several cases of exogenous infection of the conjunctiva with tubercle as the result of wounds have been recorded.

Greeff has described a case of auto-infection of the cornea with the finger nail by a patient suffering from tuberculosis.

Fuchs in his *Text Book on Ophthalmology* mentions that he has seen a case of tuberculosis of the iris develop in consequence of a perforating wound, and the following case of a similar sort is recorded by Louis Dor <sup>(2)</sup> :

A little boy, aged 4 years, lived in the same house as two phthisical persons. These persons were in the habit of spitting on the floor of the shop where the child played. One day he fell and struck his eye against the ear of a wooden horse which he had been dragging about the floor of the shop. A month later when Dor first saw the child, the eye was quite blind. In the cornea at the seat of injury there was a thickened, yellow, non-vascular scar with a prolongation uniting it to the bound-down iris. An iridectomy was with difficulty performed three days later ; as the consequent exudation became absorbed, some small yellowish elevations were noticed. These were taken to be tuberculous and one was excised and inoculated into a guinea pig. The nodules in the patient's eye then increased in number and the whole iris became involved. The child then developed a cough and began to fall off in its general condition. Ultimately the eye was excised. Both ciliary body and choroid were, besides the iris, found to be invaded by tubercles. The guinea pig which was inoculated also developed tuberculosis.

It might have been thought that the dense fibrous tissue of the cornea and sclerotic would offer an insurmountable barrier to the infection of the interior of the eye by tubercle bacilli from the conjunctival sac. It has, however, been suggested <sup>(3)</sup> that tubercle of the iris may result by local inoculation in a healthy subject by way of an abrasion of the conjunctiva, or that the initial lesion may be a tuberculous ulcer of the conjunctiva. Mitvalsky, of Prague, suggests that if the respiratory mucous membrane can be infected by the tubercle bacillus after a simple

<sup>(1)</sup> *Tumeurs de l'œil*, 1901, Vol. I, p. 786.

<sup>(2)</sup> *Revue Gén. d'ophtalmol.*, XXII, 1903, p. 252.

<sup>(3)</sup> A. Pechin.—*Gaz. hebdom. de Med. et de Chir.*, Jan. 28, 1900.

catarrh and a mere *derangement* of epithelium, so may the conjunctiva, though it had not previously suffered a loss of substance.

The following is a case recorded by Allen T. Haight <sup>(1)</sup>: A girl, aged 4 years, had a contused wound of the outer canthus and upper lid, perfect recovery was made. Fourteen months afterwards the vision in the eye of the same side failed and several whitish tumours were seen in the choroid involving the macular region. Tubercle of the choroid was diagnosed and the eye enucleated. Four months later iritis developed in the other eye, and shortly afterwards the child died of tuberculous meningitis.

In this case it may have been that tubercle bacilli were inoculated at the outer canthus at the time of injury, that they were carried to the choroid of the eye on the side injured, and 14 months later developed the tuberculous deposits there, which gave rise to a general infection before the eye was removed.

On the other hand, it must be admitted that 14 months is a long interval to have elapsed between the receipt of the injury and the manifestation of the primary lesion, and that there is no proof that there were not some foci of tubercle in a lymphatic gland which may have been a common origin of the disease in the eye and meninges.

Endogenous infection of the eye with tubercle in acute disseminated tuberculosis was first pointed out as occurring in the choroid by Cohnheim; it also occurs, though less frequently, in the iris. In association with chronic tubercle, intra-ocular tubercle is also met with, and numerous cases are recorded of eye affection secondary to a tuberculous lesion situated in a bone, a joint, a lymphatic gland, or the skin.

Besides these cases, however, there are others in which tuberculosis appears in the eye without any previous sign of the disease being detected in any other part of the body. In some of these cases tuberculous lesions have later made their appearance elsewhere, but so far as can be made out from clinical examination, there has been nothing to show that the patient was suffering from tuberculosis previous to the affection of the eye.

It will be well here to quote a classification of recorded cases given by Denning <sup>(2)</sup>:

(1) Thirty-eight cases in which there was no tuberculosis before, and in which the patients were otherwise absolutely healthy at the time of the ocular affection.

(2) Fourteen cases with a tuberculous history, but healthy before and during the attack.

<sup>(1)</sup> *American Medicine*, Feb. 8th, 1902.

<sup>(2)</sup> *Archiv f. Augenheilk.*, XXXI, 1895, p. 359

(3) Three cases with earlier signs of tubercle, healthy at the time of the attack.

(4) Seventeen cases of ocular tuberculosis coinciding with tuberculosis in other organs.

(5) Nine cases which succumbed to general infection.

(6) Ten cases in which the patients remained healthy after the disappearance of the ocular affection.

In the cases where no other tuberculous lesion is discoverable previous to the eye affection, many writers have described the disease in the eye as primary. Fuchs, Leber, and De Wecker, have, however, dissented from this view, holding that a primary tuberculous focus (*e.g.*, caseous bronchial glands) although not demonstrable clinically, must be assumed to exist.

The fact that in more than one-half of all autopsies made upon children, evidences of tuberculous adenitis are to be found, shows that tuberculous lesions of which there is no evidence clinically are often present.

In connection with this matter, case 5, recorded at the end of this report, is of some importance. The child, aged 9 years, came with well-marked tuberculous nodules in the iris of the right eye. No other evidence of any tuberculous affection could be detected in any other part of the body after the most careful clinical examination. The case was treated with injections of Koch's tuberculin. In the course of one month ten injections were made, after each of which there was reaction with rise of temperature. Notwithstanding the injections the affection in the eye progressed, and it was ultimately excised. Five days after the excision an experimental injection of Koch's tuberculin was made. A reaction was produced, the temperature rising to 101.5° F., eighteen hours after it. This seemed to show that, though the eye had been removed and no other tuberculous lesion could be detected clinically, some tuberculous foci was still present. Five years after the removal of the eye a tuberculous gland was removed from the child's neck.

Except through a perforating lesion bacilli could only gain entrance to the eye by being conveyed there in the lymphatic or blood streams.

Deutschmann demonstrated how, after the meninges had been inoculated with tubercle, the optic nerve sheath became involved not by direct spread of infection, but by metastasis. The bacilli carried along in the lymph stream were arrested in their progress and gave rise to nodules of growth. At the lamina cribrosa, where their arrest was especially likely to occur, nodules were frequently met with.

Lagrange <sup>(1)</sup> produced infection of the eye with tubercle in

<sup>(1)</sup> *Tumeurs de l'œil*, 1901. Vol I, p. 779.

rabbits by injecting into the carotid a virulent bouillon-culture of the bacillus.

It has been shown that tubercle bacilli may gain entrance to the blood stream of the foetus from that of the mother through the placenta.

Baumgarten holds, and his view is supported by some clinical and experimental evidence, that tubercle bacilli may lie latent in an organ until something happens which renders the surrounding structures less resistant, when they produce active changes constituting tuberculosis.

It is possible, therefore, that tubercle bacilli having gained entrance to the blood stream of the foetus through the placenta may be carried to the eye, lodge there and remain for a time latent. When subsequently aroused into activity by some change in their surroundings they would give rise to a tuberculosis which would be primarily of the eye. Such an origin of intra-ocular tuberculosis must, however, be regarded as of exceedingly rare occurrence.

There is no definite evidence of the possibility of tubercle bacilli entering the blood stream, apart from direct inoculation, in any other way than by the involvement of the blood vessel in some nodule of the disease. So that involvement of the eye through the blood stream is probably nearly always secondary to some foci of tuberculosis elsewhere.

There is a good deal of evidence to show that tubercle bacilli may pass through the mucous membrane of the respiratory tract or alimentary canal and be taken up by the lymphatics without leaving any trace or lesion behind them. Their further progress then becomes arrested by the lymphatic glands which they infect.

It would seem unlikely that bacilli can pass through a mucous membrane into the lymphatic stream and be carried by it to the eye without any involvement of the lymphatic glands.

### **The predisposing causes of intra-ocular tuberculosis.**

In discussing the predisposing causes of intra-ocular tuberculosis there are three sets of influences which it is necessary to differentiate :—

- (1) Those which predispose the individual to the disease.
- (2) Those which predispose to the localization of the disease in the eye.
- (3) Those which predispose certain parts of the eye to be the starting points of the affection.

(1) Of the causes which predispose the individual to tuberculosis it is not necessary to enter much here in dealing with the disease as it affects a particular organ. It will suffice to point

out that when tubercle affects the eye, as when it affects other parts, there is frequently a history of tuberculosis in the family. This is well brought out in the table of cases at the end of this paper in which it will be seen that there is some family history of tubercle recorded in nearly every case in which details were obtained.

A family history of tubercle may imply one or both of two things: (a) a want of resistance power on the part of the individual to the specific organism or (b) increased risk of exposure to infection.

(2) In considering the predisposing causes to the localization of the disease in the eye, it may be pointed out that, as in other forms of what is often spoken of as "surgical tuberculosis," the intra-ocular form of the disease is most frequently met with in childhood, though all periods of life are liable to it.

Wojtasiewicz <sup>(1)</sup> says: "Ocular tuberculosis is most common in the first half of life. It has, however, been met with at all ages, in very young infants, in adults and in the aged (case of Costa-Pruneda in a child of 38 weeks; Ulrich, 10 months; Leber, 15 months; Herter, 39 years; Manfredi and Cofler, 43 years; Cohnheim, 42 to 58 years; Weiss, 51 years; Hock, 62 years). Nevertheless, it is most frequent after 2 years and above all between 10 and 25 years. We have notes, however, of several cases between 30 and 34 years (Leber, Nettleship, Poncet, Gérin-Roye, Haab, Ulrich)."

Hill Griffith <sup>(2)</sup> found in 32 collected cases of tubercle of the iris the average age of the patient was 12 years, the youngest being 4 months and the oldest 52 years.

Pechin <sup>(3)</sup> states that tubercle of the iris is most frequently met with between the ages of 5 and 25 years.

Of the 18 cases recorded at the end of this paper the youngest was 8 months and the oldest 56 years:

|                          |   |   |        |
|--------------------------|---|---|--------|
| 2 were under 1 year.     |   |   |        |
| 4 between 1 and 2 years. |   |   |        |
| 3                        | " | 2 | " 3 "  |
| 1                        | " | 3 | " 4 "  |
| 1                        | " | 4 | " 5 "  |
| 1                        | " | 5 | " 6 "  |
| 1                        | " | 8 | " 9 "  |
| 2                        | " | 9 | " 10 " |
| 1 aged 14                |   |   |        |
| 1 " 18                   |   |   |        |
| 1 " 56                   |   |   |        |

So that 15 of the 18 cases were under what Hill Griffith gives as the average age and only 3 over.

<sup>(1)</sup> *Thèse pour le Doctorat en Médecine, Paris, 1886.*

<sup>(2)</sup> *Trans. Ophth. Soc. of U. K., X, 1890, p. 84.*

<sup>(3)</sup> *Gaz. hebdomad. de Méd. et de Chir., Jan., 1900.*

With regard to the influence of sex in connection with tuberculosis of the eye, Wojtasiewicz <sup>(1)</sup> says speaking of all classes of cases that "Sex apparently has no influence in the etiology, the two are equally liable, there being if anything a slight predominance in favour of the female sex." He mentions that out of 20 cases of tuberculosis of the conjunctiva 13 occurred in females.

Bossis <sup>(2)</sup> in reference to tuberculosis of the iris says: "The sex has not a great influence from the etiological point of view, it is, however, slightly more frequent in the female sex."

Of the 18 cases of intra-ocular tuberculosis recorded in this paper the greater tendency of the female sex is shown by 12 having been females and 6 males.

Hill Griffith <sup>(3)</sup> in an analysis of a series of cases of tubercle of the iris found the disease was confined to one eye in 20 cases and that in three both eyes were affected. Of the 20 cases in which one eye was involved the left was affected 14 times and the right 6 times.

In the writer's 18 cases of intra-ocular tuberculosis, the preponderance in favour of the left side, found by Hill Griffith, is not borne out. In one case both eyes were affected, in 11 the right eye and in 6 the left.

Localization of tuberculous disease in a bone or joint frequently seems to be determined by some slight injury or blow, it being probable that the delayed or obstructed circulation resulting from the injury has allowed of the lodgement of bacilli in the locality.

It might reasonably be expected that some injury to the eye would often be the precursor of intra-ocular tuberculosis, and it was so in the cases quoted below. It must, however, be admitted that in cases of intra-ocular tuberculosis a history of local injury was not often been recorded. Possibly it might have been more frequently elicited if special inquiry had been made.

In a case of tubercle of the iris in a boy, aged 8, recorded by Volfe <sup>(4)</sup> in 1882, there was a history of affected eye having been struck and subsequently swollen a month previous to a white swelling being noted on the iris. The eye was excised and examined by Hirschberg, who pronounced the disease to be tuberculous.

W. J. Collins <sup>(5)</sup> in 1889, recorded the case of a boy, aged 9, who a week after being struck on his left eye by his

<sup>(1)</sup> *Thèse pour le Doctorat en Médecine, Paris, 1886.*

<sup>(2)</sup> *La Tuberculose de l'iris, Paris, 1893.*

<sup>(3)</sup> *Loc cit.*

<sup>(4)</sup> *British Med. Journal, 1882, I, p. 299.*

<sup>(5)</sup> *Trans. Ophth. Soc. of U. K., IX, 1889, p. 110.*

brother developed several small pinkish-grey nodules on the iris. He had been seen the day after the injury and there was no perforating wound. Apart from deafness, dating from birth, his health was in other respects good.

Allan T. Haight <sup>(1)</sup> of Chicago, who is a strong believer in the influence of injuries of the eye as a cause of tuberculosis, recorded in 1902 the case already referred to, in which there had been a contused wound at the outer canthus preceding tubercle of the choroid; and also the two following. It will be seen that the interval in all these three cases between the receipt of injury and the appearance of the disease in the eye is considerably longer than in Wolfe and W. J. Collins' cases. His first case is that of a girl, aged eight, who had tubercle of the iris, the diagnosis being confirmed by microscopical examination and the finding of bacilli after the eye had been removed. Two years previous to the commencement of the affection, the eye had been struck with a rattan whip, there was considerable ecchymosis and swelling which took several weeks to subside. The other case was that of a boy, aged 14, who in his left eye had optic neuritis, and eight or ten circular nodules, yellowish white in the centre, situated in the choroid around the disc which were diagnosed as tuberculous. A year previously he had been struck between the eyes by a stone, the septum of his nose being broken and the eyes bloodshot and inflamed. The eye was enucleated, and eight months later there had been no other manifestations of tubercle.

Case 15 recorded in the table at the end of this paper; a child aged two years and nine months with tuberculosis of the iris and ciliary body, 18 months previous to the appearance of the affection was struck on the eye by a cricket ball which caused considerable subsequent discoloration.

(3) There can be little doubt that the most frequent way in which the eye becomes infected with tubercle is by the blood stream. Tubercle bacilli carried by the blood would most likely be arrested and so capable of starting foci of disease in the eye, where anastomosis of vessels occur, where its capillary plexuses are finest, and where abrupt bends take place in the vessels.

Hence it is not surprising to find that in tubercle of the iris the nodules characteristic of the disease generally appear first near its pupillary or ciliary margins, *i.e.*, in the regions of the anastomosis of its blood vessels known as the larger and lesser circle of the iris.

In the ciliary body the copious vascular plexus of the ciliary processes situated between their epithelial covering and

<sup>(1)</sup> *American Medicine*, Feb. 8, 1902.

the ciliary muscle is the site at which the affection most frequently starts. In the choroid the close capillary plexus forming its inner layer is the usual seat of primary election.

Intra-ocular tubercle commencing in the retina is of rare occurrence, but when it is met with, the starting point is generally in the nerve head just inside the lamina cribrosa, where the retinal vessels make an abrupt bend in passing into the interior of the eye.

### The frequency of Intra-ocular tuberculosis.

As to the frequency with which intra-ocular tuberculosis occurs there is much diversity of opinion. Most writers speak of it as a very rare disease. Michel has strongly urged that tuberculosis is a much commoner etiological factor in eye affections than is generally supposed, and Ludwig Bach<sup>(1)</sup> asserts that tuberculosis of the eye is by no means a rare affection.

There can be no doubt that of recent years the number of cases of affections of the eye recognised as due to tuberculosis has largely increased.

All writers agree that the uveal tract is the intra-ocular structure most frequently involved, and that of the three divisions of the uveal tract the choroid is more often affected than the ciliary body or iris.

All writers further seem to be agreed that it is in acute miliary tuberculosis that the choroid mostly becomes attacked. As to what percentage of cases of acute miliary tuberculosis have tubercle of the choroid, and as to whether choroidal tubercle is more frequently met with in general tuberculosis without meningitis, or where meningitis is present, we find widely different statements.

Cohnheim laid it down that choroidal tubercle is more commonly met with in cases of general tuberculosis than in tubercular meningitis. Gowers<sup>(2)</sup> agrees with this statement, quoting Heinzel who never saw tubercle of the choroid in 41 cases of tuberculous meningitis which he examined with the ophthalmoscope, and, Garlick, who at the Hospital for Sick Children, found tubercle in the choroid in only one case out of 26 which he repeatedly examined.

De Wecker, on the other hand, says: "If in miliary tuberculosis the meninges are attacked, there will generally be a corresponding deposition in the choroid."

A discussion on this subject arose at the Ophthalmological Society of the United Kingdom in 1883, at which Coupland<sup>(3)</sup>

<sup>(1)</sup> *Archives of Ophth.*, XXIV, p. 43.

<sup>(2)</sup> *Medical Ophthalmoscopy*, 4th Ed., p. 65.

<sup>(3)</sup> *Trans. Ophth. Soc. of U.K.*, III, 1883, p. 131.

said: "I should prefer to say that there is no necessary connection between the choroidal and meningeal condition, either may be present (or absent) as part of the general infection, and their association in any case is purely accidental."

Sir Thomas Barlow summed up the matter very excellently as follows:—

(1) Cohnheim's generalisation that tubercle of the choroid exists more commonly in cases of general tuberculosis than in tubercular meningitis, ought not to be taken as final, for (a) tubercular meningitis is often only a part of general tuberculosis, and the distinction, therefore, is not a good one, and (b) of the cases which I have given, in 13 out of 16 tubercle of the choroid co-existed with tubercular meningitis.

(2) No statistics on the absence of choroidal tubercle in cases, of tubercular meningitis should be accepted without a post-mortem examination of the backs of the eyes, because (a) of the general difficulty of accurate ophthalmoscopy in such patients, and (b) the special difficulty of excluding very minute tubercular dust of Barthoz and Rilliet, and which certainly sometimes co-exist with unquestionable choroidal tubercular nodules.

(3) That in the choroid we ought to be prepared for considerable variety of tubercles, viz., (a) minute nodules in which we may see changes from day to day, (b) semi-confluent nodules, (c) diffuse massive deposits caseating in the centre, quite comparable with scrofulous tumours of the brain, and, perhaps, comparable with (a) and (b) in the same way as some caseous lobular pneumonia is with miliary tubercles of the lung.

Bouchut<sup>(1)</sup> found tubercles of the choroid 10 times in 100 cases of tubercular meningitis.

Carpenter and Stephenson<sup>(2)</sup> say that out of 42 unselected cases of acute miliary tuberculosis and tuberculous meningitis which they examined with the ophthalmoscope, they found 21 with tubercles of the choroid, or exactly 50 per cent. In 13 of these cases tubercle was recognised in one eye only, and in both eyes in the remaining 8 cases. This gives a total of 29 eyes (13 single and 8 bilateral) in which the changes of tuberculosis were detected. In 18 of the eyes the lesion was solitary in the sense that it consisted of a single tuberculous deposit. In the remaining 11 eyes the number of separate lesions ranged from as few as 2 to as many as 12.

In contrast with this high percentage of cases in which choroidal tubercle was met with, we have the statement of Jessop<sup>(3)</sup>, who, having examined large numbers of cases of acute miliary tuber-

(1) *Gaz. des Hôp.*, 1876.

(2) *Report of the Soc. for the Study of Dis. of Children*, Vol. I.

(3) *Trans. Ophth. Soc. of U.K.*, XXIII, p. 58.

ulosis and tuberculous meningitis ophthalmoscopically, speaking roughly, says he has only met with choroidal tubercle in about 1 to 5 per cent. and then only a few hours or days before death.

In determining the frequency with which tubercle of the choroid occurs in association with chronic tuberculous lesions, or in cases where other manifestations of tubercle cannot be detected clinically, we encounter the difficulty which there is in determining from ophthalmoscopic examination alone whether an inflammatory affection of the choroid is really tuberculous. And, further, there is some uncertainty as to what are the ophthalmoscopic appearances left by a tuberculous lesion of the choroid after the active changes have subsided.

Until there is uniformity of opinion on these points it must be expected that widely different estimates as to the frequency of the occurrence of the affection will be arrived at.

Denig<sup>(1)</sup> examined for ocular metastasis 60 cases of tuberculosis of the lung, 90 of the bones, 20 of the lymphatic glands, and 20 of various other organs; in only 5 of these did he find tuberculous disease in the eyes.

The observations of Maurice Perrin and of König are in keeping with those of Denig.

Carpenter and Stephenson<sup>(2)</sup> state that they have examined with the ophthalmoscope 119 cases of chronic tuberculosis in children whose ages ranged from 8 months to 16 years. They suffered from such various affections as tuberculous joints, chronic tubercular adenitis, spinal caries, chronic tuberculous cerebral tumour (2 cases), and lupus. Amongst these they found choroidal changes in no fewer than 11 or 9·24 per cent., of which 3 were verified post-mortem.

These choroidal changes were not those described in text books as typical of tubercle of that membrane, nor such as are generally accepted as of tuberculous origin. They were mostly solitary, fairly large, more or less circular patches of atrophy with pigmentation around them, situated in the central part of the fundus. Carpenter and Stephenson regarded them, however, as cases of obsolescent tuberculosis of the choroid.

Jessop says that he has only observed 2 cases of choroidal change of a tuberculous nature in cases other than acute miliary tubercle or tubercular meningitis.

Tubercle of the choroid, forming a large conglomerate mass which leads to enucleation or destruction of the eyeball, is apparently rarer than conglomerate tubercle of the iris and ciliary

(1) *Arch. für Augenheilk.*, XXXI, 1895, p. 359.

(2) *Loc. cit.*

body of a similar character. The number of such cases on record is comparatively small. Out of the 18 cases of intra-ocular tuberculosis which necessitated excision of eye recorded in this report, 11 commenced in the iris or ciliary body, and 6 in the choroid; in one case all parts of the uveal tract were equally involved, so that it was impossible to say which was first attacked.

Horner estimated tubercle of the iris to occur once in 4,000 patients, and Hirschberg as 6 times in 60,000 patients. Pechin regards these figures as under-estimating its frequency.

At the Royal London Ophthalmic Hospital, during six years the writer was pathologist, 1,523 eyes were removed, and only 7 of these for intra-ocular tuberculosis, 6 of the iris and ciliary body, 1 of the choroid.

### **Intra-ocular tuberculosis as it affects different structures of the eye.**

It will be convenient, in discussing the different appearances presented by intra-ocular tuberculosis, to speak of the clinical characters and pathological changes produced by it in each of the different anatomical divisions of the eye separately. As a matter of fact, however, tuberculosis occurring in the eye has not much regard for anatomical divisions. When it starts in one part it frequently involves others.

The uveal tract being the part most frequently affected, the appearances presented by tuberculosis in each of its three divisions, iris, ciliary body and choroid, will first be dealt with.

#### **Tubercle of the iris.**

Most writers divide cases of tuberculosis of the iris into two classes :

- (a) Cases in which there are miliary disseminated nodules.
- (b) Cases where there is a circumscribed mass made up of conglomerate or confluent nodules.

To these <sup>(1)</sup> Woijtasiwicz adds a third class, consisting of

- (c) Cases where there is a tuberculous iritis, microscopically showing considerable thickening of the iris with inflammatory cells, in the middle of which are ill-defined tuberculous nodules, which later, however, undergo caseous degeneration.

Besides these three divisions, reference will also be made here to iritis occurring where some other part of the eye is affected with tubercle, and where, though there is cellular exudation and a formation of posterior synechiæ, none of the typical histological changes of tubercle are found in the iris.

<sup>(1)</sup> *Essai sur les rapports de la tuberculose oculaire avec la tuberculose générale*, 1886.

It may at once be pointed out that these different classes often merge into one another. Thus, in cases beginning with disseminated nodules, a conglomerate mass sometimes results as the affection progresses. A case which, when first seen, has one large mass springing from the iris, often subsequently develops several small satellites around it. An iritis of variable amount is frequently met with in association with miliary disseminated nodules, or a conglomerate mass.

(a) The miliary disseminated nodules appear first, usually, as previously stated, at the ciliary margin of the iris and extreme periphery of the anterior chamber, or at its pupillary border. It has been pointed out that the lower part of the iris is more often involved than the upper; this is borne out by the cases recorded in this report. In 5 of these when the starting point of the affection is noted in the iris, in 4 it was in the lower half, and in the upper.

The nodules measure usually from 2-3 mm. in diameter. They are of a greyish colour and semi-transparent, or of a yellowish hue and more opaque. The yellowness and opacity is probably accounted for by necrotic change commencing in the nodule. Some difference in the appearance of the nodules may also be due to difference of depth in the iris at which they are situated. In microscopical sections of an affected iris nodules are sometimes seen situated right at its anterior surface, projecting some considerable distance forwards into the anterior chamber; the deep layers of the iris including the pigment epithelium passing beneath them and showing scarcely any sign of disturbance. In other cases the nodules are met with deep in the stroma of the iris, often breaking up and destroying the pigment epithelium on its posterior surface, so that no continuous line of pigment can any longer be traced and only scattered particles of pigment are seen. Evidence of the depth of a nodule in the iris tissue is sometimes afforded clinically, apart from its colour, by the presence of blood vessels on its anterior surface.

In association with the nodules in the iris there is usually some, not very intense, ciliary injection, but very little photophobia or pain. Very frequently deposits of a grey colour are seen on the back of the cornea; these may be of various sizes, some of them large and constituting what has been termed the "mutton fat" variety of "keratitis punctata." Microscopical examination of these deposits show them to consist of collections of polynuclear and mononuclear leucocytes on the inner surface of the endothelium of Descemet's membrane.

Disseminated miliary tuberculous nodules may be met with in the iris without marked signs of iritis and with the formation of few, if any, posterior synechiæ. Microscopically, the lines of

demarcation of the nodules may be seen to be very sharply defined with but little cell infiltration of the surrounding tissue.

The mode of termination of a case of disseminated miliary tuberculosis of the iris varies. The nodules may disappear and leave but little permanent damage behind them, constituting what Leber has termed attenuated tubercle. The disease may spread backwards, involving the ciliary body, and by destroying the source of supply of the intra-ocular fluid bring about an atrophic or shrunken condition of the globe. The miliary nodules may run into one another, form a conglomerate mass which invades the cornea and terminate in the way to be described later under the heading of conglomerate tubercle of the iris.

In some cases the affection remains localized in one eye, in others both become affected. A general diffusion of tubercle nodules throughout the body may precede or succeed a miliary tuberculosis of the iris.

These different modes of termination may be accounted for by the varying powers of attack on the part of the invading organisms or by the varying powers of resistance of the host. On the one hand, the attacking organisms may vary in number or in the virulence of their type; on the other, invaded individuals may vary in their phagocytic power or in their capability of generating anti-toxins.

(b) A circumscribed conglomerate mass of tubercle in the iris presents the appearances of a yellowish neoplasm of that membrane, often commencing without any sign of iritis. The mass continues to enlarge, secondary nodules sometimes forming around it until the anterior chamber becomes partly or completely filled by the growth.

The cornea usually becomes first invaded in the region of the ligamentum pectinatum, for it is there that the protuberant mass most frequently first comes into contact with it. As destruction of the fibrous tissue of the cornea takes place, the tuberculous mass with the iris from which it springs protrudes forward into the gap left, and a staphylomatous condition is seen clinically in that situation. Perforation then follows and a fungating, ulcerated vascular mass forms, which ultimately undergoing caseation disappears, leaving a shrunken globe, as described in the passage quoted from Lawrence at the commencement of this report.

(c) As already stated, the amount of iritis occurring in connection with tubercle of the iris is of variable amount and may in cases of circumscribed conglomerate tubercle be absent altogether. In some cases, however, it may be the most conspicuous feature of the affection. It is questionable whether it is desirable to form a distinct class for such cases which can

usually be well grouped under one of the other two. The cases referred to by Lagrange <sup>(1)</sup> as belonging to this class are those recorded by Edmunds and Brailey, Costa-Pruneda, Knaggs, and Kalt.

The accounts given of them are briefly as follows: Brailey and Edmunds' <sup>(2)</sup> case was that of a child, aged 3, the early stages of the affection in whose eye are not recorded. The description given is that, at the time of excision, the eye was in a state of atrophy from suppurative panophthalmitis. Scarcely any iris tissue could be recognised previous to excision or with the microscope afterwards.

Costa-Pruneda's <sup>(3)</sup> case, a child, aged 38 weeks, is said to have had purulent iridocyclitis and a peripheral ectasia of the cornea. Shortly after enucleation it died of tuberculous meningitis.

Knaggs' <sup>(4)</sup> case was that of a boy, aged 9 months, in whose right eye the aqueous was turbid, the iris cloudy and discoloured being of a greyish pink tint, whilst projecting from its anterior surface were from 14 to 20 white nodules as big as pins' heads. Microscopically the iris was found to have numerous tuberculous nodules in it and one large caseating mass. The pupil was filled by a false membrane adherent to the lens capsule. The fibrous tissue at the sclerocorneal margin was invaded and also the ciliary body, and there were tuberculous masses in the circumlental space.

Kalt's <sup>(5)</sup> case was that of a girl, aged 12 years, who, 15 months previous to the eye affection had disease of the right hip joint with periarticular abscesses.

The eye affection came on rapidly with failure of vision and pain, the latter only lasting three days.

When seen on the tenth day the iris presented a greenish yellow colour and had scattered over its surface a number of little whitish points—the size of a pin's head. Some of them were becoming confluent, whilst between them was a network of capillaries looking like hæmorrhages. The pupil was blocked and there was a violet coloured prominence in the ciliary region up and in. Perforation of sclera occurred in this position and the eye was enucleated. Microscopically the iris and ciliary body were found to be diffusely infiltrated with limphoid cells. Accumulations of epithelial cells with giant cells in their centre were also seen, no bacilli were found. There was no caseation.

<sup>(1)</sup> *Tumeurs de l'œil*, Vol. I, 1901, p. 785.

<sup>(2)</sup> *Trans. Ophth. Soc. of U.K.*, II, 1882, p. 269.

<sup>(3)</sup> *Arch. für Ophth.*, XXVI, 1880, 3, p. 174.

<sup>(4)</sup> *Trans. Ophth. Soc. of U.K.*, XII, 1892, p. 79.

<sup>(5)</sup> *Société de Biologie*, V, 1893, p. 233.

Inoculation of a portion of the subconjunctival mass into the anterior chamber of a rabbit did not produce any tuberculosis in the animal.

In case 7, in the table at the end of this report, clinically the appearances were those of iritis, with secondary glaucoma and cataract. The patient was 56 years of age, and a large iridectomy and extraction of cataract was performed, the coloboma rapidly became filled with dense lymph and the other eye also developed iritis. It was not until a histological examination was made after excision of the eye that the case was recognised to be one of tuberculosis. The choroid, ciliary body and iris were all much thickened and numerous typical giant cell systems were found scattered throughout those structures.

Three of the cases recorded by the writer in this report with conglomerate tubercle of the choroid had also iritis resulting in the formation of posterior synechiæ and a pupillary membrane, but in none of the eyes examined were there any tuberculous nodules in the iris. Cases of a similar character have been observed by others. The probable explanation is that toxins were generated by the bacilli in the tuberculous tissue at the posterior part of the globe and passed forwards to the iris exciting a simple, non-specific, inflammation of that structure. It has, however, been asserted that in these cases small nodules are really always present in the iris but are overlooked in clinical examination; or microscopically when only some sections of an eye are examined. In a case recently recorded of tuberculosis of the nerve head by Coats, iritis was present, and the eye was examined in serial sections, but no tuberculous nodules were found in the iris.

### **Tubercle of the ciliary body.**

Tubercle involving the ciliary body begins most frequently in the ciliary processes on the inner surface of the ciliary muscle where its capillary plexus of blood vessels is finest. It may, however, also occur in the lymphatic spaces external to the ciliary muscle between that structure and the sclerotic.

The affection appears to have started in this position in cases 8 and 9 recorded in this report. In a specimen where the iris and ciliary body are both involved, it is often very difficult to determine which was primarily the seat of the affection. In both the above-mentioned cases, however, the lymph spaces external to the ciliary muscle were extensively affected, the growth having extended outwards into the sclerotic and produced episcleral nodules which were seen clinically. It is not usual for tubercle of the iris to spread back through the ligamentum pectinatum to the lymph spaces external to the ciliary muscle.

If it affects the ligamentum pectinatum it generally spreads forwards into the cornea. If it spreads to the ciliary body it usually invades the ciliary processes.

In case 8 a failure of sight preceded the onset of inflammation in the affected eye, which can be accounted for by interference with the ciliary muscle.

Tubercle involving the tissue of the inner surface of the ciliary muscle may be in the form of small scattered miliary nodules or of a large conglomerate mass. The latter rapidly spreads inwards destroying the pigment epithelium and filling up completely the circumlental space in its vicinity. There seems a much greater tendency for tuberculous growth starting in this position to extend forwards and inwards than backwards. It is remarkable how completely the space bounded by the back of the iris, side of the lens and anterior hyaloid of the vitreous, may be found filled with tuberculous tissue, without the vitreous being involved, the fibres of the suspensory ligament being entirely destroyed, but the anterior limiting membrane of the vitreous remaining quite intact.

Where the ciliary body is affected with tubercle, the vitreous generally contains fibrinous exudate and excess of cells, but is not invaded by the tuberculous nodules. If, however, in association with tubercle of the ciliary body there is much cyclitis, as is sometimes the case, there will be a more plastic exudate into the vitreous humour which goes on to the formation of fibrous tissue.

In conglomerate tubercle of the choroid, the ciliary body, like the iris, may be affected by plastic inflammation without being the seat of tuberculous nodules, in which case the vitreous generally becomes shrunken and fibrous.

### **Tubercle of the choroid.**

There are two forms which tubercle of the choroid is definitely known to assume :

(a) Scattered miliary nodules which are seen ophthalmoscopically as grey patches.

(b) A conglomerate mass which gives rise to symptoms of an intra-ocular tumour.

(a) The scattered miliary nodules are met with in cases of acute miliary tuberculosis, and as they generally develop shortly before death, frequent opportunities are afforded of comparing the ophthalmoscopic appearances with the histological alterations in the acute stage of the affection.

The patches are mostly met with in the posterior part of the globe in the vicinity of the optic disc and yellow spot. They are circular and vary in size, seldom exceeding that of one-third of the optic disc. Their actual measurement has been estimated

at 0.5 to 2.5 mm. They have a greyish or greyish-yellow colour with a soft ill-defined edge which shades off gradually into the surrounding fundus. There is no pigmentation about them ; a slight arching forwards of the overlying retinal vessels show the larger ones to be raised a little above the level of the surrounding choroid.

Many writers have commented on the rapidity with which the patches may make their appearance. Carpenter and Stephenson<sup>(1)</sup> have made the definite statement that they saw three small tubercles near the optic disc in an eye in which nine days previously they had not detected any changes.

Histologically the patches are seen to be composed of one or more typical giant cell systems situated in the vascular layers ; in an early stage or when small, not extending into the lamina suprachoroidea or up to the sclerotic. The effusion, however, nearly always reaches up to the lamina vitrea which is usually arched slightly inwards together with the pigment epithelium lining it.

In the largest patches, in which necrotic changes are seen, the lamina vitrea will sometimes be found to have disappeared, the pigment epithelium cells to have been destroyed and the granules of pigment widely scattered.

(b) In a conglomerate mass of tubercle of the choroid a large area, if not the whole of that membrane, is involved in the affection. The confluence of the nodules causes it to become considerably thickened, large caseating patches forming in the centre of it. The membrane of Bruch with the pigment epithelium lining it soon becomes destroyed. The retina becomes detached. Sometimes owing to invasion of the retina with tuberculous tissue where the nerve fibres and retinal vessels enter the eye, that structure undergoes extensive necrosis so that hardly any of its elements can be recognised in sections microscopically. Where the retina is detached the sub-retinal fluid is of an opaque grumous consistency and is seen microscopically to contain a quantity of fatty globules in suspension.

Secondary foci of the disease may appear in the anterior portion of the uveal tract, more frequently a plastic iridocyclitis is excited by the toxins liberated from the disease in the choroid. Often the root of the iris is found in contact with the periphery of the cornea, a glaucoma having been set up. As the choroid becomes thickened the sclerotic is invaded, later becoming perforated.

The symptoms which a conglomerate mass of tubercle in the choroid gives rise to are very similar to those of a gliomatous

(1) *Report of the Society for the Study of Disease in Children*, Vol. I, 1901, p. 169.

growth of the retina. The detached retina with the tuberculous mass behind gives rise to a light coloured reflex seen behind the lens by focal illumination with the retinal vessels on its surface. The tension of the eye is frequently increased. Posterior synechiæ are often present, sometimes small satallitic nodules may be detected in a part of the choroid where the retina is not displaced, or in the iris.

Besides the two above well-defined classes of tubercle of the choroid, there are other cases, where patches of choroiditis are seen ophthalmoscopically in the acute stage, or where the atrophic changes resulting from such patches are met with, in which no other constitutional cause to which the affection can be attributed, other than tubercle, can be detected. Whether or not the changes seen in these cases are really due to tubercle, as has been suggested by some writers, is as yet uncertain.

In his text book on *Diseases of the Eye* Nettleship says :

It is also probable that certain cases of localised choroidal exudation, not accompanied by serious general symptoms or by inflammatory symptoms in the eye may be of tubercular nature.

And in another place, in discussing anomalous forms of choroidal disease, he says :

Single large patches of atrophy, with pigmentation, and not located in any particular part, are occasionally met with. Probably some of these have followed the absorption of tubercular growths in the choroid.

It is not often that the late stages of choroidal effusion in which there is definite evidences that it was due to tubercle are seen ophthalmoscopically ; the following case recorded by Jessop<sup>(1)</sup> is therefore of considerable interest. It was that of a girl aged 9, who had tuberculous lymphatic glands and tuberculous bone disease. In her right eye a yellowish-white swelling formed adherent to the lower and outer part of the sclerotic beneath the ocular conjunctiva. An attempt was made to dissect this mass as a whole from the sclerotic, but it was only removed down to it, that structure being much thinned but not perforated. The central portion of the mass consisted of thick caseating yellowish pus. A guinea pig was inoculated with the caseating material, and an abscess formed at the seat of inoculation which contained tubercle bacilli. The neighbouring glands became caseous, and also contained tubercle bacilli.

An ophthalmoscopic examination of the affected eye showed at first two separate, non-vascular, spherical, steep detachments of the retina. The one on the temporal side of a darkish grey colour covered the optic disc. That on the nasal side was shallower, and of a greyish-white colour.

The course of these swellings seen in the fundus was watched,

(1) *Trans. Ophth. Soc. of the U. K.*, XXIII, 1903, p. 58.

and the changes in them noted over a period of 18 months. The masses became of a lighter colour, some yellowish (lichen coloured) spots making their appearance on the nasal one. They seemed to sink down and move towards the periphery of the fundus so that the optic disc, which was at one time hidden from view, became visible. Some whitish effusion was seen around the optic disc, which at first increased on the temporal side and became less on the nasal. It gradually absorbed, leaving soft small patches with some cholesterin. Around the choroidal atrophy which ultimately resulted there was very little pigmentation. At no time was there any vitreous opacities.

In another case which Jessop watched over a course of three years, and which in all probability was tuberculous, there was a similar absence of pathological pigmentation and vitreous opacities. On these two points, together with the absence of new vessels to be seen ophthalmoscopically, Jessop lays considerable emphasis as characteristics of tuberculous choroiditis.

Carpenter and Stephenson, in their estimation of the frequency of tuberculous choroiditis in connection with chronic tubercle, accepted as what they termed "obsolescent tuberculosis" choroidal lesions which, as a rule, were solitary, fairly large, and situated in the central part of the fundus. They were for the most part circular, containing one or more pigment rings, and very seldom indeed were associated with outlying patches of peripheral choroiditis.

### Tubercle of the cornea.

Tuberculosis of the cornea has been produced experimentally by inoculation in rabbits and guinea pigs by Haensell <sup>(1)</sup> in 1879, and by Panas and Vassaux <sup>(2)</sup> in 1885.

The latter found a nodule to form at the seat of inoculation on the 8th day, which was at first surrounded by an area of opalescent haze. Some other small white nodules afterwards appeared around the first one, these nodules became confluent, and an irregular cratiform ulcer formed which became vascular and healed by the 76th day, a small nebula being all that was ultimately left.

The cornea does not, however, appear to be a very good culture media for the tubercle bacillus. Parsons <sup>(3)</sup> failed to get any result in rabbits from the inoculation with virulent culture unless the anterior chamber was opened.

A case has been recorded by Greef of auto-inoculation of the

<sup>(1)</sup> *Archiv. für Ophth.*, XXV, 4, p. 1.

<sup>(2)</sup> *Archives d'Ophthal.*, V, 1885, p. 193.

<sup>(3)</sup> *The Pathology of the Eye*, Vol. I, p. 200.

cornea with the finger nail by a patient suffering from tuberculosis. A vascular ulcer formed which showed very little tendency to heal.

The evidence as to the possibility of endogenous tuberculosis of the eye starting in the cornea is not very conclusive. Bach<sup>(1)</sup> writing on this point says :

As to whether tuberculosis of the cornea may be an independent disease or is always secondary to a similar affection of the uveal tract (including, of course, the ligamentum pectinatum) my answer, made upon the basis of my own observation, is that tubercular disease of the cornea is usually secondary to similar disease in the ligamentum pectinatum, but that the marginal zone of the cornea may be primarily the seat of tuberculous nodules, which later on make their appearance on the cornea itself.

When the uveal tract is the seat of tuberculosis, the cornea may be affected in two different ways :—

- (a) It may be invaded by typical tuberculous nodules.
- (b) It may be the seat of a diffuse inflammatory infiltration, interstitial or parenchymatous keratitis.

(a) Wechsberg showed that in tubercle of the lung destruction of the elastic fibres very readily occurs, whether due to the action of the tubercle bacilli or to other factors is as yet undetermined. In tubercle of the eye a marked capacity of the disease for the destruction of the elastic membranes is also to be observed. When in tubercle of the iris the protuberant mass of growth comes into contact with the membrane of Descemet, or the fibres of the ligamentum pectinatum, those structures seem to melt away before it. When a gap is formed in the elastic membrane of Descemet in this way, the substantia propria rapidly becomes invaded by the tuberculous tissue, typical giant cell systems form in it. The invasion proceeds until perforation takes place and the tuberculous mass fungates out through the opening, ultimately breaking down and undergoing caseous degeneration.

As one of the commonest starting points of tubercle of the iris is its extreme periphery, and as this is the part of the iris in closest proximity to the posterior surface of the cornea, the position in which invasion of it most frequently occurs is the region of the ligamentum pectinatum. When the ligamentum pectinatum becomes involved, the tuberculous growth extends straight outwards towards the surface of the eye.

- (b) It has been already pointed out that there is a good deal of evidence to show that simple iritis may be excited by toxins generated by a tuberculous mass situated at the posterior part of the globe. Likewise it seems probable that a simple interstitial or parenchymatous keratitis may be caused by toxins generated in tuberculous nodules of the iris diffusing into the cornea.

<sup>(1)</sup> *Archives of Ophth.*, Vol. XXIV, p. 49.

In sections from several eyes examined by the writer, in which a portion of the cornea has been invaded by tuberculous growth from the iris, he has found the uninvaded parts, at a considerable distance from the seat of perforation, swollen with its lymph spaces filled with inflammatory cells as in parenchymatous keratitis.

In cases also where the ligamentum pectinatum has been alone involved in a tuberculous nodule starting from the iris, he has found all the characteristic histological appearances of parenchymatous keratitis. There has been a distention of lymph spaces, an invasion of them by leucocytes, and a new formation of blood vessels. In some cases the cell infiltration has been very marked immediately beneath the anterior limiting membrane.

The writer has not met with any specimen showing parenchymatous keratitis in which the ligamentum pectinatum was not affected, or in which a perforation of Descemet's membrane had not occurred.

### Tubercle of the sclerotic.

The sclerotic not infrequently becomes invaded by tubercle of the uveal tract ; it is doubtful if it is ever the starting point of tubercle of the eye.

Wojtasiewicz <sup>(1)</sup> says : "Tuberculosis entirely limited to the sclerotic has not been observed ; in the eye the fibrous tissue is an unfavourable soil for tubercle."

In tubercle of the choroid, when nodules become confluent and form a conglomerate mass, it extends into the lymph spaces constituting the boundary between the choroid and sclerotic, and invades the latter. The sclerotic then bulges outwards and presents a dull grey appearance externally, instead of its usual whiteness ; this was so in Case 3. Gradually it becomes more infiltrated and thinned, until ultimately perforation takes place, and there is an extension of the tuberculous tissue into Tenon's capsule, which gives rise to symptoms clinically of orbital cellulitis, as in Case 17.

As has been already mentioned, some cases of tubercle of the ciliary body seem to start in the lymph spaces external to the ciliary muscle ; when this takes place as in Cases 8 and 9 there is early involvement of the sclerotic. A nodule on the external surface of the eye in the ciliary region simulating a patch of episcleritis is an early clinical feature in such cases. A tuberculous nodule situated in this locality may undergo caseation and ulceration. The case of Jessop's already referred to is an example of a caseating tuberculous mass in the sclerotic.

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(1) *Loc. cit.*

Tubercle of the iris which invades the ligamentum pectinatum, when it extends forwards and leads to perforation of the eye, makes its appearance on the surface in the sclerotic just outside the corneal margin.

### Changes in the lens in intra-ocular tuberculosis.

An avascular structure enclosed in capsule like the crystalline lens cannot be the primary seat of an intra-ocular tuberculosis; it may, however, become affected in intra-ocular tuberculosis arising in other parts, resulting in opacity of it to a greater or less extent.

In tuberculosis of the ciliary body the masses of tuberculous tissue which sometimes fill the circumlental space come into contact with the elastic capsule, and may cause destruction of it. A gap having been formed in the capsule the lens substance becomes invaded with inflammatory cells, and becomes absorbed.

In tuberculosis of the iris the mass may press on the anterior capsule, and in that locality an area of shrunken lens fibres and proliferated capsule cells make their appearance without any perforation of the capsule.

In extensive tuberculosis of the choroid with detachment of the retina and shrinking of the vitreous humour, an alteration in the shape of the lens sometimes occurs. It becomes flattened laterally, and lengthened antero-posteriorly, a sort of lenticonus posterior being produced.

### Tubercle of the retina.

Intra-ocular tuberculosis starting in the retina is of exceedingly rare occurrence, and there are but few cases on record in which the retina was the only part of the eye involved.

Secondary implication of the retina in tubercle of the choroid is more frequent, but even that is rare. When the retina is affected the optic nerve head is the commonest seat of the disease.

The first case of this sort which was seen ophthalmoscopically, and where the diagnosis of tubercle was confirmed subsequently by microscopical examination, is recorded by O'Sullivan and Story<sup>(1)</sup>.

The appearances seen in this case were those of an extensive brilliant white swelling in the region of the optic disc, with tortuous and distended retinal vessels, and some small white spots in the macular region. The amount of swelling and whiteness was more intense than is seen in any simple case of papillitis. Pathological examination showed that the tuberculous tissue was

(1) *Trans. Royal Acad. of Med. Ireland*, XVII, 1899, p. 451.

entirely confined to the nerve head and retina. A very similar case to this has been described by Arnold Knapp <sup>(1)</sup>, in which the retina was completely detached, the solid white growth lying at its apex posteriorly. The condition was taken to be glioma clinically, microscopically its tuberculous character was demonstrated and tubercle bacilli were found. In a case recorded by Spalding <sup>(2)</sup> a yellowish tumour, found to be tubercular, sprang from the optic papilla and filled one-third of the vitreous chamber. The symptoms it gave rise to were inflammation of the eye, yellow reflex from the fundus, loss of sight and considerable general disturbance with increase of temperature. After excision of the eye the health of the child rapidly improved.

In a case recently recorded by Coats of tubercle of the nerve head, the tuberculous tissue extended backwards a little way into the optic nerve, and laterally for a short distance into the surrounding choroid.

Brailey <sup>(3)</sup> had previously described a case of tubercle of the nerve head forcing back the lamina cribrosa in which there was a similar mass in the adjacent choroid. Ophthalmoscopically a greyish vessel-bearing layer could be seen, made up apparently of two folds separated by a horizontal crease.

Emanuel <sup>(4)</sup> and Weiss <sup>(5)</sup> have described cases of tubercle of the retina secondary to the disease in the uveal tract; Sattler <sup>(6)</sup> a case secondary to tubercle of the optic nerve; and Perls and Manfredi cases of disseminated tuberculous nodules in the retina associated with tuberculous growths in almost all the structures of the eye.

Hancock <sup>(7)</sup> has recorded a case in which a yellowish-white patch was seen ophthalmoscopically on the temporal side of the optic disc, the sides of which were equal in length to the diameter of about two discs, and which was estimated to be raised  $1\frac{1}{2}$  mm. The history of the case and the histological examination of the patch, which was found to be entirely retinal, were in favour of its being tubercular, but no bacilli were demonstrated.

In Cases 4 and 13 recorded in this paper of tubercle of the choroid, the retina was involved. In Case 4 the retina was completely detached and it was the posterior part which was thickened with tuberculous growth. In Case 13 there was a

<sup>(1)</sup> *Archives of Ophth.*, XXXII, 1903, p. 22.

<sup>(2)</sup> *Trans. American Ophth. Soc.*, X, 1, 1903, p. 141.

<sup>(3)</sup> *Trans. Ophth. Soc. of U. K.*, III, 1883, p. 129.

<sup>(4)</sup> *Klin. Monat. für Augenheilk.*, XL, 2, 1902, p. 210.

<sup>(5)</sup> *Arch. für Ophth.*, XXIII, 1877, p. 4, 141.

<sup>(6)</sup> *Arch. für Ophth.*, XXIV, 1878, p. 3, 127.

<sup>(7)</sup> *Royal Lond. Ophth. Hosp. Rep.*, XVI, 1905, p. 150.

large tuberculous mass of the choroid in the vicinity of the entrance of the optic nerve and the optic nerve head was involved.

In Cases 12 and 17 of extensive conglomerate tubercle of the choroid the retina was exceedingly necrotic, the position it occupied could only with difficulty be made out, the nuclei of its cells staining so faintly with the hæmatoxylin. The probable reason of this necrotic condition of the retina is the plugging of its vessels through invasion of its tissue in the vicinity of the optic nerve where they enter. The terminal character of the retinal vessels would prevent its nutrition being carried on by collateral circulation after they had become plugged.

### Tubercle of the optic nerve.

Tubercle of the optic nerve most frequently starts in its pial sheath as scattered nodules, these may become confluent so that the nerve becomes completely ensheathed in tuberculous growth (Bach). Tubercle may also extend into the nerve itself, destroying the nerve fibres and forming conglomerate masses.

The sheath of the nerve may become affected in association with tuberculous meningitis or independently of meningitis. Extension of growth into the nerve may take place from tubercle of the sheath or from intra-ocular tubercle involving the choroid and retina.

Optic neuritis (choked disc) may occur without any tuberculosis of the nerve but in association with an intra-cranial tuberculous mass, in the same way as it occurs in association with other intra-cranial tumours.

All parts of the optic nerve and the chiasma may be the seat of tubercle. In Sattler's<sup>(1)</sup> case the whole nerve and its sheaths from the chiasma to its intra-ocular expansion were found to be involved in the tuberculous disease.

Cruveilhier<sup>(2)</sup> described a tuberculous nodule in the intra-cranial portion of the optic nerve in association with tuberculous basilar meningitis. Tubercle of the chiasma has been described by Hjort<sup>(3)</sup> and in association with affection of the orbital portion of the nerve by Bach.<sup>(4)</sup> A case of tubercle of the orbital portion of the nerve is also recorded by Cirincione. Tubercle of the optic nerve as an extension from tubercle of the choroid is described by Wageman<sup>(5)</sup>, and from the retina by

<sup>(1)</sup> *Arch. für Ophth.*, XXIV, 1878, 3, p. 127.

<sup>(2)</sup> *Traité d'anat. path. gén.*, IV, 1862, p. 793.

<sup>(3)</sup> *Kl. Monatsbl. für Augenheilk.*, V, 1867, p. 166.

<sup>(4)</sup> *Arch. of Ophth.*, Vol. XXIV, 1888, p. 53.

<sup>(5)</sup> *Arch. für Ophth.* XXXIV, 1888, 4, p. 178.

In two of the cases of conglomerate tubercle of the choroid included in the table in this report the optic nerve was found invaded. In Case 3 the nerve for some little distance behind the globe was enlarged and on section presented a greyish necrotic appearance especially in its central parts. It was here that microscopically caseating areas and typical giant cells were found, though the nerve throughout was much infiltrated with leucocytes.

Tubercle of the optic nerve may give rise to the symptoms of choked disc and proptosis. In Sattler's case there was proptosis distention of the eyelids, restricted ocular movements and chemosis together with the appearance of a white mass projecting into the vitreous with enlarged and tortuous retinal vessels on it. At the autopsy, besides the extensive affection of the nerve already alluded to, deposits were found in the orbital tissue. The patient died of tuberculous meningitis and Sattler locates the primary lesion in a bronchial gland.

In Bach's case there were symptoms of choked disc on both sides followed by atrophic discolouration of the optic papillæ, there was slight exophthalmos on one side. The primary seat of the disease was in the right temporal bone.

### Diagnosis.

The diagnosis of intra-ocular tuberculosis may be, and not infrequently is, beset with difficulties. There are a variety of conditions due to other causes which clinically give rise to symptoms closely simulating those produced by tuberculosis. Not infrequently eyes have been removed for what was taken to be a malignant growth, which subsequent microscopical examination proved to be a tuberculous mass.

The injection of tuberculin by the reaction which it excites has in several doubtful cases afforded considerable assistance in diagnosis.

There is, however, the risk in employing it that some fresh dissemination of the disease may result.

In Case 5 the injection of 1 milligram of Koch's tuberculin sufficed to produce a rise of temperature but no alteration in the appearance of the nodules in the iris. After an injection of 2 milligrams, besides the rise of temperature, the nodules seemed to enlarge slightly and tend to become more confluent.

Though a positive result as regards reaction from the injection of tuberculin is of definite value in the diagnosis of intra-ocular tubercle, a negative result cannot be considered as certainly excluding its presence.

Bongartz<sup>(1)</sup> has recorded a case in which he injected tuberculin three times and in which no reaction followed. After the eye

(1) *Inaug. Dissert. Würzburg*, 1891.

had been removed the typical histological appearances of tubercle were found, together with the tubercle bacillus.

The utilisation of the aqueous humour, obtained by a paracentesis of the anterior chamber, for inoculation into rabbits' eyes in doubtful cases of intra ocular tuberculosis was suggested by Gourfein<sup>(1)</sup>.

He has recorded 2 cases of tubercle of the iris in which he obtained definite results by this method. The rabbits developed a granular iritis in which tubercle bacilli were found. The employment of this test has been recommended in doubtful cases of tubercle of the choroid, the percentage of such cases in which a positive result is obtained would probably, however, be much smaller.

The length of time which might have to elapse before any certainty could be arrived at by this procedure would seem to considerably detract from its practical utility. Three weeks is the usual time after inoculation that tuberculous nodules first show themselves in the rabbit, but their appearance may be delayed considerably longer.

Tubercle of the iris is liable to be mistaken for other forms of non-pigmented growth arising in that structure such as—simple granuloma; syphilitic nodules; the nodules of ophthalmia nodosa; the tubers of leprosy; or sarcoma.

A simple granuloma of the iris may be distinguished from a tuberculous nodule by its originating from a prolapse of the iris through a perforation in the cornea, either traumatic or the result of ulceration, also by its subsequent progress, it tending quickly to develop into fibrous tissue without any disintegration or caseation.

The nodules which appear in the iris in connection with secondary syphilis, and the true gummata which appear in the later stages of that disease, are both liable to be mistaken for tubercle, and the latter solitary conglomerate tubercle. The history or the presence of other symptoms of either tubercle or syphilis often serves to differentiate between the two conditions. If the patient is under 20 years of age the affection is most likely to be tuberculous, if over 20 it is most likely syphilitic. The nodules met with in the iris in secondary syphilis are, like the miliary nodules of tubercle, generally situated at its pupillary or ciliary margin, the syphilitic nodules have usually, however, a distinctive rusty hue. A syphilitic gumma differs from a tuberculous mass in being more vasculous. If any doubt exists in deciding between the syphilitic or tuberculous character of an iritic swelling, the rapidity with which it disappears under anti-syphilitic treatment will serve to settle the diagnosis.

<sup>(1)</sup> *Rev. Méd. de la Suisse Romande*, XXIII, 1803, p. 223.

A case of ophthalmia nodosa with nodules in the conjunctiva, episcleral tissue, and iris, might be mistaken for one of disseminated tubercle, both from the clinical appearance and histological characters, of the new growths. Microscopically giant cells of the Langhans type and epithelioid cells as in tubercle are met with, the distinguishing feature is the presence of the caterpillar's hair in the centre of the nodule. The history of contact with a caterpillar likely to excite the affection would be obtained in ophthalmia nodosa and the affection would have started in one of the three months (August, September, or October) in which those caterpillars exist.

The granulomatous masses which appear in the iris or ciliary body in connection with leprosy present much the same clinical appearances as a tuberculous growth, and are often associated with iritis. The age of the patient and the presence or absence of other symptoms of leprosy are usually sufficient to establish the diagnosis. Leprosy never starts as a primary affection of the intra ocular structures.

A leucosarcoma of the iris, though a rare affection, might be mistaken for a solitary mass of tubercle. The points which help to differentiate the two affections are : The position of the growth, tubercle being generally located at the ciliary or pupillary margin, a sarcoma starting in any part ; the number of blood vessels, a tuberculous mass is devoid of blood vessels, though those around may be enlarged, in a sarcoma they are fairly numerous ; the age of the patient, tubercle being usually an affection of youth and sarcoma of later life ; the presence or absence of other evidence of tubercle.

Tubercle of the ciliary body, especially when it arises in the lymph spaces external to the ciliary muscle, may involve the sclerotic and give rise to a raised patch in the ciliary region covered by injected blood vessels which presents a dusky violet hue. Such a patch when seen by itself might very probably be regarded as one due to simple episcleritis. When due to tubercle other nodules shortly make their appearance in other parts of the uveal tract and serve to clear up the diagnosis.

The diagnosis of disseminated miliary patches of tubercle in the choroid when associated with general tuberculosis or with meningitis present no difficulties.

The diagnosis of the tuberculous or non-tuberculous character of patches of effusion into the choroid, when there is no evidence of tubercle, and where no history of syphilis is to be obtained, is, as has been already stated, attended by much uncertainty.

The situation of such patches near the periphery of the fundus,

and the presence around them of much pigmentation, are generally regarded as characteristics which are in favour of a syphilitic origin. Not uncommonly large solitary patches are met with in the vicinity of the optic disc or yellow spot in which the diagnosis of tubercle seems probable, but in which no confirmatory evidence is obtained. They are not attended by much disturbance of pigment and at first not associated with vitreous opacities, though later some floating strands may be seen and dots of keratitis punctata, due probably to the extension of the disease to the retina and exudate from its surface.

A conglomerate mass of tubercle of the choroid may give rise to symptoms closely simulating those of an intra-ocular malignant growth, either a glioma of the retina or a sarcoma of the choroid. Indeed, in some cases, from the clinical appearances alone, it is impossible to differentiate between the two affections.

Some difficulty in diagnosis may also arise between conglomerate tubercle of the choroid and those other conditions which simulate glioma of the retina, to which the term "pseudo-glioma" has been applied, *viz.*, a plastic cyclitis with detachment of the retina; or a persistence of the central hyaloid artery of the vitreous, which continuing to carry blood terminates in a mass of fibrous tissue, atypically developed vitreous, at the back of the lens.

In all these conditions a light coloured reflex is obtained from a mass behind the lens with blood vessels in it or on its surface. In the last-named condition the reflex from behind the lens is of a greyish colour and densest in the centre, becoming fainter towards the margins; in the extreme periphery by reflected light the red reflex of the fundus can often be seen in all directions. There are, moreover, usually present other congenital defects, such as a microphthalmic condition of the eye, or persistent tags of pupillary membrane, which help to differentiate it for conglomerate tubercle of the choroid.

If the light-coloured reflex is due to detachment of the retina, with a mass of conglomerate tubercle or a malignant growth behind it, the blood vessels seen will be the retinal vessels. The big trunks will be in the centre, and they will branch and become smaller as they proceed outwards.

If the light-coloured reflex is due to a cyclitic membrane, the result of plastic cyclitis, the blood vessels seen in it will come from those of the ciliary body, the largest ones will be external and they will divide and become smaller as they approach the posterior pole of the lens.

Posterior synechiæ or a pupillary membrane the result of iritis are frequently met with in connection with conglomerate tubercle of the choroid. They were present in cases 3, 4 and 17

in this report ; they also occur in association with plastic cyclitis, but are rare, or if they occur at all, do so only in the late stages of intraocular malignant growths.

In plastic cyclitis, where the exudation has undergone organisation and contraction, the root of the iris is usually retracted and the angle of the anterior chamber deepened. In intra-ocular malignant growths and conglomerate tubercle of the choroid, the lens and iris get pressed forwards as the mass in the posterior part of the globe increases in size, so that the anterior chamber becomes shallow, its angle becomes closed, and the tension of the eye increased.

Increase of tension in cases of conglomerate tubercle of the choroid has been recorded by Lubousky <sup>(1)</sup> and Posey <sup>(2)</sup>, and was present in cases 3, 4 and 13, included in this report.

It is said that, due to the necrotic changes which take place in a tuberculous mass in the choroid, the tension of the eye may be decreased. In some cases of glioma of the retina the eyeball shrinks and the tension becomes minus. So it will be seen that the state of the tension of the globe is of little value in distinguishing between these two diseases.

The age of the patient seldom affords any very material assistance in diagnosis. Zur Nedden <sup>(3)</sup> found the age of patients suffering from tuberculous tumours of the choroid to vary between  $1\frac{1}{2}$  and 62 years. One occurring in early life is liable to be mistaken for glioma of the retina and in late life for sarcoma of the choroid. Dupuy-Dutemps <sup>(4)</sup> considers that between 6 and 20 years of age the probability would be in favour of the affection being tuberculous, it being too late for glioma, and too early for sarcoma. The latest age at which glioma of the retina manifested itself in a series of 60 cases collected by the writer was 7 years, and the earliest age at which he met with sarcoma of the choroid in a series of 103 cases was 15 years.

The rapidity with which the sclerotic becomes involved and perforated, as pointed out by Zur Nedden, forms one of the most striking characteristics of conglomerate tuberculous growths of the choroid, and is often of the greatest diagnostic importance. Dupuy-Dutemps found in several cases scleral perforation noted as early as 3 weeks to 4 months ; sometimes, however, specially in adults, it is much slower.

Of the cases of conglomerate tubercle of the choroid recorded in this report, perforation of the sclerotic had occurred in case 17, a child aged one year, in whom the affection of the eye had

<sup>(1)</sup> *Arch. of Ophth.*, XXIX, 1900, p. 278.

<sup>(2)</sup> *Tr. Am. Oph. Soc.*, X, 2, 1901, p. 244.

<sup>(3)</sup> *Klin. Monatsbl. für Augenheilk.*, XII, 2, 1903, p. 351.

<sup>(4)</sup> *Archiv. d'Ophtal.*, XXIV, 1904, p. 309.

only been noted 3 months. In case 3, a child of 2 years, the sclerotic was extensively invaded and staphylomatous, and the eye affection had been noted only 10 weeks. In case 12, a child of 2 years, the sclerotic was invaded posteriorly but not perforated, though the affection had been noted  $8\frac{1}{2}$  months.

As in tubercle of the iris the presence or absence of tuberculous lesions in other parts of the body often affords valuable assistance in arriving at a diagnosis.

Tubercle of the retina occurring in the nerve-head might in the early stages be mistaken for optic neuritis, or in the later stages for a malignant intraocular growth.

The amount of the swelling of the nerve-head and its intense whiteness generally serve to distinguish tuberculous disease from a simple inflammatory or œdematous condition of it. In case 10, in this report, in which one eye was removed for tubercle of the iris, what was described as intense optic neuritis was seen in the other eye with some hæmorrhages in the retina, it subsequently completely subsided and full vision was obtained. There is some doubt as to whether this patient had a tuberculous growth in his nerve-head, or only a simple optic neuritis, he was very ill at the time the eye was removed, but his health improved shortly after and remained good.

To distinguish tubercle of the nerve-head from a malignant growth, much which has already been said as to the diagnosis of such growths from conglomerate tubercle of the choroid applies. How strikingly similar the appearances presented ophthalmoscopically by a sarcoma of the choroid and a tuberculous mass involving the nerve-head may be, was well exemplified by two cases shown at the Ophthalmological Society of the United Kingdom last session, coloured illustrations of which appear in its *Transactions*.\*

\*Vol. XXV. Pls. II. and X

The one case was reported by Simeon Snell, it was that of a man, aged 27, in whom a swelling  $2\frac{1}{2}$  disc diameters in size, and irregularly circular in form, was seen overlaying and completely obscuring the optic disc. The most prominent part of this swelling was seen with + 11 D. lens. Blood vessels coursed over its surface and there were hæmorrhages and yellowish white dots to be seen on it. The eye was excised and examined pathologically by the writer, who found a spindle celled sarcoma arising from the choroid around the optic disc and extending with a knob-like protuberance 5 mm. inwards towards the centre of the globe. The retina was adherent to the apex of the growth and had hæmorrhages in it. The other case was a girl, aged 15, shown by R. E. Bickerton, in whom a large white globular swelling, with woolly margins below and on the outer side, was seen in the situation of the optic disc. It had numerous blood vessels on its surface. The highest point of the swelling measured 10 dioptries. The vision of the eye was reduced to  $\frac{1}{10}$ . After six months the swelling had almost entirely disappeared, some irregularly shaped white areas and dots, over which the retinal vessels coursed, being, however, left behind. The vision had improved and was  $= \frac{6}{8}$ . There was no absolutely definite proof that the swelling in this case was tuberculous, but there was nothing in the history of the case to suggest it was syphilitic, and the way in which it disappeared showed clearly it was not a malignant growth.

## TREATMENT.

### *Remedial.*

It has already been pointed out that some cases of intra-ocular tuberculosis proceed to caseation, perforation, and disintegration of the eyeball; whilst in others the nodules of disease absorb, become replaced by fibrous tissue, and the sight of the eye, although usually impaired, is not lost. Presuming that the favourable termination of the latter cases is due, at any rate to some extent, to a superior power of resistance on the part of the individual attacked, remedial treatment, especially in early cases, should do all that is possible to aid and to increase these natural protective forces.

The natural protective power of an individual may be promoted:—(a) By increasing the number of white corpuscles in the blood. (b) By increasing the amount of what Ehrlich has termed the “tuberculotropic substances” in the serum. These act either by increasing its agglutinative power, which brings about immobilization and conglomeration of the bacilli; or by rendering the bacilli more liable to be attacked by the leucocytes, the so-called “opsonic power” of Wright.

(a) An increase in the number of leucocytes in the blood is promoted by a liberal allowance of food, especially of proteid, and by an abundance of fresh air and sunshine, all of which, as in other forms of tuberculosis, should form essential elements in the treatment of patients with intra-ocular tuberculosis.

Abadie<sup>(1)</sup> writing recently on the treatment of tuberculous iritis, lays considerable stress on the importance of inunctions of cod-liver oil and guaiacol, together with the feeding of the patient on raw meat, or a muscular extract called “Carnine Lefrancq.” He records two cases of recovery which were, in addition, treated internally with “iodogenol,” an organic compound of iodine.

(b) The agglutinative power of the blood has been shown by Koch and Wright to be increased by injections of tuberculin.

Wright’s test of opsonic power consists in the incubation in a capillary tube of a mixture of the patient’s serum, leucocytes, and tubercle bacilli, and estimating after fifteen minutes the degree of phagocytosis which has taken place.

Wright has shown that the amount of “opsone” in the blood of tuberculous patients is generally low, and that it can be increased by the injection of tuberculin at properly spaced intervals.

The tuberculin introduced by Koch in 1890, consisting of a glycerine extract of old cultures of tubercle bacilli, filtered free

(1) *Archives d’ophtalmol.*, XXIV, 1904, p. 129.

from germs, has been used experimentally in tubercle of the eye in rabbits and in the treatment of some cases of the disease in man. Unfortunately, the experiments have produced very different results in the hands of different observers. This is shown from the following passage taken from Bossis' work on "Tuberculosis of the Iris."

As experiments always precede the application of methods, Elvidio Gasparini and Ferruccio Mercanti, in May, 1891, made known the results of their experiences on this subject. They selected albino rabbits, their tissue being more suitable for microscopical examination owing to the absence of pigment, and made three series of experiments.

In the first series : injections into the anterior chamber of healthy rabbits of Koch's lymph, two rabbits ;

In the second series : the same experiment in rabbits previously inoculated with ocular tuberculosis, twenty-five rabbits ;

In the third series : the same experiment in rabbits which were at the same time inoculated with tuberculosis, eight rabbits.

In the rabbits of the first series there was opacity of the cornea after forty-five minutes, the epithelium in places became detached. The next day it re-formed and a fibrinous mass appeared in the anterior chamber. Three days later the eye became normal in appearance.

In the rabbits of the second series, damage to the cornea and conjunctiva, iris and ciliary body extensively altered.

In the rabbits of the third series, in which it cannot be objected that the treatment was commenced too late, infection directly followed. Eleven days after the inoculation the first symptoms of tuberculosis of the iris appeared. The results were therefore nil.

The conclusions that the authors draw from their experiments on ocular tuberculosis are the following :—

1.—Tuberculin introduced into the conjunctival sac, or injected into the anterior chamber, acts as an irritant substance.

2.—It has no action on experimental tuberculosis or on the bacilli. On the contrary, it gave rise to inflammatory reaction, exudation, and infiltration of leucocytes into the tissue surrounding the tubercles, reaction which aggravated the condition of the eye.

3.—It has no action on the development of tuberculosis, even at its commencement.

Numerous observers have made the same experiments, and have arrived at different results. We can only quote their conclusions. For more ample details reference should be made to the very interesting work published by Dr. Kostenitsch in the *Archives of Experimental Medicine* of M. Charcot.

Donitz has arrived at the following results :—1st. Tuberculin is a sure and certain cure against the tuberculosis produced in the eye of a rabbit.

2nd.—Tuberculin makes its influence apparent only when tubercle can be found microscopically in the eye.

3rd.—The first effect of the tuberculin is an intense transitory inflammation of the eye.

4th.—Later, under the influence of the tuberculin, the inflammation of the eye subsides.

5th.—If before the commencement of the treatment the eye presents no grave lesions, it is possible to preserve sight. If the opposite is the case, the eye becomes atrophic.

6th.—Tuberculin should be used in increasing doses sufficient always to produce a decided reaction.

The best initial dose, according to Donitz, is 0 gr. 003, repeating every third day an increased injection rising to 0 gr. 04.

The results of Pfuhl, of Sattler, of Baumgarten are less brilliant. Alexander, Popoff, Weiss, Czaplowski and Roloff obtained no result ; likewise Wissmann. Kostenitsch ends his excellent work thus :—

"Tuberculin, whatsoever be the dose, large or small, however administered, never

cures or lessens the local tuberculosis excited in rabbits by the dead tubercle bacilli. Administered in strong doses it produces injurious suppuration and does not tend to the encystment of the tubercle bacilli. Hence the conclusion that its administration as an antituberculous remedy in man ought to be abandoned."

Case 5 included in this report came under the care of my colleague, Mr. Waren Tay, in January, 1891, shortly after the introduction of Koch's tuberculin and just at the time when such high hopes were entertained respecting it. In the course of a month 10 injections were made, beginning with a dose of 1 milligram, and gradually increasing to 7 milligrams. The total amount injected was '028 grammes. The whole course of the disease in the eye was most carefully watched. At first there were four distinct nodules at the pupillary border of the iris. These during the treatment gradually became confluent, the mass resulting increasing in size, and, ultimately, before excision, it involved the whole iris, filled the anterior chamber, and invaded the cornea.

In 1897 Koch introduced the substance known as "tuberculin R," which contains dead bacilli ground up and suspended in the fluid in the proportion of 10 milligrammes of solid substance in each cubic centimetre. It sets up a weaker reaction than the original tuberculin. Its use is therefore not attended with the same risk of causing a generalisation of the disease.

Tuberculin R has been used experimentally in rabbits and for the treatment of tuberculosis of the iris in man by Schieck (<sup>1</sup>). The results of his experiments in rabbits he sums up as follows:—

- (1) T. R. tuberculin has no immunising effect.
- (2) It is not able in every case of experimentally induced tuberculous disease of cornea and iris to bring about healing.
- (3) At all events, the course of the disease is not unfavourably affected.
- (4) Recovery may occur without the use of tuberculin, especially if the pupil has become excluded and occluded; this leads to alteration in the nutrition of the anterior parts of the eye, and the tubercle bacillus no longer thrives.

Schieck obtained better results when he employed it in tubercle of the iris in man than in rabbits; this he attributes to the fewness of the bacilli present in the former, which permits of their becoming more readily surrounded by scar tissue and encysted.

Schieck has used tuberculin in five cases. With tuberculin T. R. he began with a dose of 0,002 milligrammes and increased it alternate days by 0,001 mg. Improvement began, in some cases immediately the injections were commenced, in others there was at first an increase in the intensity of the symptoms, which was followed by subsidence and recovery.

Another possible method of treating tuberculosis with remedial

(<sup>1</sup>) *Arch. f. Ophth.*, Vol. L 1900, 2, p. 247.

agents, besides increasing the natural resistive power of the individual, is to make an attack directly on the bacilli themselves by means of antiseptics. The obvious difficulty of this method in dealing with intra-ocular tuberculosis is the introduction of a sufficiently powerful antiseptic into close enough proximity to the bacilli to kill them without disorganising the eye.

The remarkable tolerance which the eye has for iodoform introduced into the anterior chamber was shown as the result of an accidental occurrence during a cataract extraction by Berry <sup>(1)</sup> in 1892, and as the result of experiments on rabbits by Ostwalt <sup>(2)</sup> in 1897.

In the same year Ammann <sup>(3)</sup> described a case of irido-ciliary tuberculosis of one eye, which he treated first with sub-conjunctival injections of an iodoform-vaseline salve, 1 : 5, and afterwards, the tuberculous process having advanced, with sterilized iodoform powder introduced into the anterior chamber. A decrease in the size of the tubercles of the iris was then noticed. A second introduction of iodoform was made, but in spite of this, the disease advanced, and the eye was enucleated. The histological appearances of tubercle were found on microscopical examination, but no bacilli.

The amelioration of the affection, although of only limited duration, produced in this case by the iodoform, led Weill <sup>(4)</sup> to make a series of experiments. In rabbits whose eyes had been infected with tubercle, he introduced iodoform, sterilized in the following way :—place the iodoform in a 3% solution of carbolic acid for 48 hours. Pour the acid off. Plug the receptacle with sterilized cotton, put it in an oven with a constant temperature of 40° C. to dry and to free it from the remnants of carbolic acid.

The iodoform, thus prepared, was introduced into the anterior chamber through a puncture in the cornea, by means of canula and blunt trocar. Weill summarises the results of his experiments as follows :—

(1) Sterilized iodoform is slowly taken up from the anterior chamber, even if the boundaries of the latter are diseased.

(2) It undoubtedly exercises a mitigating influence, not only in an eye in which tuberculous material is simultaneously introduced, but also in those eyeballs in which the iris has previously been tuberculous.

(3) It is probable that the tuberculous process in eyeballs already tuberculous would have been less intense if the inoculation could have been made more thorough and kept free from unexpected deleterious complications.

<sup>(1)</sup> *Trans. Ophth. Soc. of U.K.*, XIII, 1893, p. 222.

<sup>(2)</sup> *Arch. f. Augenheilk.*, XXXV, 1897, p. 308.

<sup>(3)</sup> *Klin. Monatsbl. f. Augenheilk.*, XXXV, 1897, p. 135.

<sup>(4)</sup> *Archives of Ophth.*, XXVIII, 1899, p. 133.

(4) Iodoform inoculation may bring about at least a temporary retardation of the tuberculous invasion, and afford sufficient time to build up the general system enough to resist the invading bacillus. It is not incompatible with other remedies, but, on the contrary, needs them as adjuncts.

(5) It is applicable in acute as well as in chronic cases.

Weill points out that owing to the extraordinary predisposition which it is known that rabbits possess for tuberculous affections, it is probable that more beneficial results would be obtained in the human subject.

In a later article <sup>(1)</sup> Weill has recorded a case of a man, aged 21, who presented the clinical symptoms of tuberculous iritis, and whose condition seems to have been considerably benefited by the introduction of iodoform into the anterior chamber.

The insertion of the iodoform into the eye is considerably facilitated by the method employed by Haab of mixing it with sterilized gelatine into the form of small rods or flat discs.

### *Operative Treatment.*

If in any case it could be definitely determined that an intra-ocular affection was a primary tuberculosis, it would seem a most reasonable procedure to advise removal of the eye for the prevention of any general infection.

Although many observers write as if they were confident that when tubercle occurs in the eye it is not unfrequently the primary seat of the disease, there are probably few, if any, who would recommend excision of an eye so affected, if it retained useful vision, which did not seem likely to become permanently impaired. Nearly all, however, would probably agree in the advisability of excising an eye which had become disorganised by tuberculosis, whether primary or secondarily affected by the disease. It is difficult to see how, if the globe has not been perforated and the disease has not extended into the optic nerve, anything but good can result from the removal of an entire focus of it encapsuled in such a structure as the sclerotic.

Rogman <sup>(2)</sup> in a recent paper, points out the danger, when the sclerotic is ruptured or staphylomatous, of laying open a tuberculous focus during excision and disseminating the bacilli in the field of operation. He reports nine instances where the tuberculous process, which had been without general manifestations prior to the removal of the eye, seemed to be stimulated by the operation, and, assuming an active form, occasioned death from meningitis.

When perforation of the sclerotic has taken place, or the optic

<sup>(1)</sup> *American Journal of Ophthalm.*, XX, 1903, p. 95.

<sup>(2)</sup> *Société belge d'Ophthalmologie*, Ap., 1903.

nerve has become extensively invaded, it is probably best, as recommended by Moissonnier<sup>(1)</sup>, not to rest content with excision of the eyeball, but also to exenterate the orbit.

In case No. 17 recorded in this report, the sclerotic was perforated and the orbital tissues involved; after excision, tuberculous growths continued to form in the orbit. The case ended fatally, the child dying in convulsions a month after the operation.

A. Hill Griffith<sup>(2)</sup>, who made an analysis of 32 recorded cases of tuberculosis of the iris, says:

"Of three cases in which no operation was done, two died of general miliary tuberculosis, three months and five weeks respectively after the onset of the eye affection, the third with symptoms of tuberculous meningitis, nine weeks after the beginning of the eye disease. Two cases, in spite of enucleation, died with symptoms of brain disease, one six months and the other nine months after removal of the eye. These two were the only deaths out of 27 cases in which enucleation of the bulb was performed. Several cases, however, developed manifestations of tubercle after the operation; for example, one showed a tumour on the upper jaw which proved to be a lymph gland undergoing degeneration, in another caseous ulcers developed on the legs, and a third showed hemiplegia and epileptiform spasms three months after enucleation, along with the presence of a granular mass at the operation wound. Information in regard to the state of health some years after operation was mostly wanting. It was noted however, that one case was well six years after enucleation." Hill Griffith states that he is of opinion that it has been shown that in many cases lives have been saved by the operation. He adds, however, that he would only urge enucleation where the eye was lost, or there was danger of sympathetic disease or where the tuberculosis was markedly progressive in character. "Considering," he says, "how difficult, if not impossible, it must often be to determine that the disease is primary, I hold that in the present state of our knowledge we are not justified in extirpating every bulb affected by tuberculosis with the object of preventing general infection."

Of the 18 cases of intra-ocular tuberculosis recorded in this communication, in all of which enucleation of the eye was performed, the after-history is unknown in four. One case, above referred to, in which the sclerotic was perforated and the orbital tissues involved, ended fatally; in four others the after-history, so far as it has been ascertained, extends only for a few weeks after the operation, but the health of each patient during that time showed marked improvement.

(1) *Archives d'Ophthal.*, XXIV, 1904, p. 438.

(2) *Trans. Ophth. Soc. of U.K.*, X, 1890, p. 90.

In the remaining nine cases, the after-results have been ascertained for a much longer period.

|                   |                                  |       |                       |
|-------------------|----------------------------------|-------|-----------------------|
| Case 10           | was alive                        | 11    | years after operation |
| „ 12              | „ „                              | 10    | „ „ „                 |
| „ 5               | „ „                              | 7     | „ „ „                 |
| Cases 8, 15, & 16 | were „ between                   | 4 & 5 | „ „ „                 |
| Case 1            | was „                            | 3     | „ „ „                 |
| „ 18              | „ „                              | 1     | „ „ „ , and           |
| „ 11              | is said to have "grown up" well. |       |                       |

Cases 1, 8, 11, 16, and 18, so far as could be ascertained, developed no other symptoms of tuberculosis after enucleation of the eye. Case 5 had an enlarged gland removed from the neck. Case 10, developed lupus of the face and a tuberculous ulcer of the conjunctiva. Case 12 is said to have shown signs of phthisis; and Case 15 had enlarged glands in the neck.

The above cases go to prove that the prognosis as regards life after excision of an eye for intra-ocular tuberculosis, when no perforation has occurred, is very favourable. That this favourable result is really to some extent due to the removal of the eye is shown by the marked improvement in the health of the patients immediately after the operation. Several of the children were losing flesh or were generally ill previous to the excision of the eye, and rapidly picked up afterwards.

It must be borne in mind, however, when the eye is not removed, that a fatal termination does not always occur. This we know by reference to the accounts of cases published by older writers, before the practice of excising such eyes was so generally adopted.

In tuberculosis of the iris a removal of the diseased part by the operation of iridectomy has frequently been tried; on this subject Hill Griffith writes as follows:—

“In contrast with the good results obtained by enucleation, we find that in the eight cases where attempts had been made to remove the growth by iridectomy, enucleation had later on to be performed in every case. The position of the growth at the ciliary border of the iris, the early implication of the ciliary body, and the rapid multiplication of foci prevent the probability of any good attending iridectomy. Treitel, however, records a case of cure from iridectomy, but only after the operation had been thrice performed; on the second occasion for recurrence, and the third time for increased tension; and his case was, as pointed out, exceptional in regard to the portion of iris affected.”

A second successful case treated by iridectomy is recorded by Schneller <sup>(1)</sup>, and a third more recently by Terson *père* <sup>(2)</sup>;

(1) Ueber einen Fall von geheilter Iristuberculose. Halle, 1888.

(2) *Annales d'oculistique*, T. CXXI, 1904, p. 119.

It was the case of a child in which both the iris and a portion of the ciliary body were involved. The tuberculous mass was removed with loss of a small amount of vitreous. A cataract afterwards formed and was extracted. Fifteen years after the operation there had been no return of the disease in the eye and the patient could distinguish large objects with it.

In the two cases included in this report (Nos. 2 and 7) in which an iridectomy had been performed, a microscopical examination of the seat of the incision after enucleation showed invasion of the wound by tuberculous growth.

It is only in a very limited number of cases of tubercle of the iris that an iridectomy would have a possible chance of success—so frequently the root of the iris at its junction with the ciliary body and in the region of the ligamentum pectinatum is involved. When this is the case, the entire removal of the affected part becomes impracticable without enucleating the whole eyeball. A few cases are met with where the affection commences at the pupillary border, and if there was only one nodule so situated, or if more than one they were lying close together, the whole area involved might be excised with a piece of the iris. Even then the grasping of the nodule with the forceps and the withdrawal of it through the wound would be liable to set free some bacilli, and thereby to cause infection of the freshly incised surface. After such a procedure, it would, therefore, probably be a wise precaution to introduce some iodoform into the anterior chamber.

In the 18 cases of the intra-ocular tuberculosis included in the following table, the eyeball was excised, and the specimens were preserved in the laboratory at the Royal London Ophthalmic Hospital, where the writer had the opportunity of examining them.

| Case | Date and Name of Surgeon.                                      | Name of patient and age. | Eye affected. | Apparent starting point of affection in eye.                                                                                   | Other structures in the eye involved.                                                                                                                                                                                                   | History of the eye affection.                                                                                                                                          | General health of patient.                                                                                                                          | Family history.                                                                                                                    | Subsequent history.                                                                                             |
|------|----------------------------------------------------------------|--------------------------|---------------|--------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| 1.   | Recorded by Lawford, R.L.O.H. Reports, 1888, Vol. XII, p. 149. | Daisy J., 1 yr.          | R.            | Choroid which is everywhere greatly thickened. Giant cells and necrotic areas. Finding of bacilli doubtful.                    | Retina has in great part disappeared. Vitreous shrunken and infiltrated. Ciliary body much changed. Ciliary processes only here and there recognizable. Iris thickened and infiltrated, adherent to lens capsule. Optic nerve inflamed. | Three weeks before excision eye blood-shot, cornea hazy and eyelids swollen.                                                                                           | A first child, weakly since birth, bottle fed since a month old. No acute or serious illness.                                                       | Father and other members of her family healthy. Mother very delicate, suffers from winter cough. A maternal aunt died of phthisis. | Health decidedly improved soon after removal of the eye, and three years after the operation in perfect health. |
| 2.   | Recorded by Lawford, R.L.O.H. Reports, 1888, Vol. XII, p. 151. | Rose W., 8 months        | R.            | Iris, the lowest part of which was the thickest. Giant cells and necrotic areas. No bacilli found though carefully looked for. | Iris and ciliary processes largely replaced by growth. Scattered areas of small cell accumulation in choroid. Cornea at seat of iridectomy incision thickened and invaded by tuberculous growth.                                        | Two nodules the size of a pin's head first noted in iris. An iridectomy performed. Three months later eye excised on account of increased swelling of iris and cornea. | Fourth child born at full term. Weakly and ailing since a month old. Bottle fed. For some months discharge from ears and a "breaking out" on scalp. | Father died of acute phthisis 7 months previous to excision of patient's eye. Mother in good health.                               | Patient's health improved after operation. Further history unknown.                                             |

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| 3. | Recorded by Treacher Collins, R.L.O.H. Reports, 1892, Vol. XIII, p. 367. | Robert V., 2 yrs. | R. | Choroid which is completely replaced by new growth, with caseating areas and giant cell systems. Bacilli not found.    | Sclerotic invaded by tuberculous growth. Retina detached and infiltrated with round cells. Vitreous shrunken and fibrous. Iris inflamed, adherent to lens capsule. Giant cell systems and caseating areas in central portions of optic nerve. Lens misshapen.                 | Affection of eye noted 10 weeks. General injection. Posterior synechia. A small hyphema and a yellowish reflex from behind lens. T.+. Condition diagnosed as glioma of retina.                                                                            | Measles 12 months previous to excision. For two weeks before operation child ill with headache and sickness. | Consumption in father's family. | Illegitimate child, another of the mother's children had had some manifestations of tuberculosis. After operation patient had an enlarged gland in one arm, which subsequently disappeared. Further history unknown. |
| 4. | Spicer. Nov., 1891.                                                      | Edward B. 3½ yrs. | R. | Choroid which at the posterior part is much thickened and contains some typical giant cell systems and necrotic areas. | Retina detached from the optic disc to ora serrata: posteriorly it is thickened and infiltrated by tuberculous growth. Tuberculous nodules in posterior part of ciliary body. Vitreous shrunken and infiltrated. Much inflammatory exudate about iris membrane filling pupil. | "Skin" seen on eye after measles. Eye inflamed for three weeks before its removal. Proptosis deep injection and dullness of cornea. Anterior chamber deep. Lens opaque. Posterior synechia. Slight hyphema, T+1. Condition diagnosed as glioma of retina. |                                                                                                              |                                 | A fortnight after operation child quite well.                                                                                                                                                                        |

| Date and Name of Surgeon. | Name of patient and age. | Eye affected. | Apparent starting point of affection in eye.                                                                                                                                                                                                                                                                                                     | Other structures in the eye involved.                                                                                                                                                                                                                              | History of the eye affection.                                                                                                                                                                                                                                                                                                                                                                  | General health of patient.                                                                                               | Family history.                                                                                                      | Subsequent history.                                                                                                                                                                                                                                                                                                                                     |
|---------------------------|--------------------------|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 5. Tay.<br>Jan., 1891.    | Edith B.<br>9 yrs.       | R.            | Iris. Four nodules first seen near pupillary margin at lower part. Typical giant cell systems and necrotic areas. Two rabbits whose eyes were inoculated from the recently excised eye 3 weeks later developed tuberculous iritis. Two guinea pigs whose abdomens where inoculated developed nodules at seat of inoculation and enlarged glands. | The whole iris involved in a thickened mass nearly filling A. C. The ciliary processes and ciliary body on inner surface of ciliary muscle much affected with tubercle. Cornea and sclerotic invaded in region of ligamentum pectinatum. Parenchymatous keratitis. | Two months previous to excision a "speck" noticed in eye which was inflamed. Three weeks later, when first seen, 4 small nodules at pupillary margin, posterior synecchia and keratitis punctata. In the course of one month 10 injections of Koch's tuberculin. Total amount of fluid injected 0.28 grams. Fresh nodules, however, appeared in iris, and ultimately the whole of it involved. | Patient well developed. Strumous appearance, no definite tuberculous glands detected. Lungs healthy, no joint affection. | Father's sister died of phthisis. One of 6 children; four besides patient alive and well, one died of scarlet fever. | Five days after excision of eye an experimental injection of Koch's tuberculin made. Reaction produced temperature rising to 101.5, 18 hours later. No evidence of local reaction could be found anywhere. About 5 years after removal of eye patient had enlarged glands removed from neck. Seven years after removal of eye alive and in good health. |
| 6. Tay.<br>Feb., 1893.    | Bessie S.<br>5 yrs.      | R.            | Iris or ciliary body, both of which are much thickened by new growth, the former being almost entirely replaced by it. Numerous typical giant cell systems: bacilli not looked for.                                                                                                                                                              | Sclerotic and cornea in region of ligamentum pectinatum invaded by tuberculous growth. Perforation has taken place at the upper part. The circumferential space is filled with tuberculous tissue.                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                          | No history of tubercle in mother's family but possible history of tubercle in father's.                              |                                                                                                                                                                                                                                                                                                                                                         |

|                                            |                               |                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                         |                                                                                           |                                                                                                                    |
|--------------------------------------------|-------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| <p>8.</p> <p>Gunn.<br/>Oct.,<br/>1893.</p> | <p>Cassie, H.<br/>18 yrs.</p> | <p>which was the pri-<br/>mary seat of the<br/>affection. Numer-<br/>ous typical giant<br/>cell systems.</p> <p>Lymph spaces super-<br/>ficial to ciliary body<br/>on outer side. In<br/>which position were<br/>masses of growth<br/>with necrotic areas<br/>and giant cell sys-<br/>tems.<br/>Bacilli looked for but<br/>not found.</p> | <p>Tuberculous growth<br/>appears to have<br/>spread outwards to<br/>sclerotic and epi-<br/>scleral tissue. It has<br/>also involved the<br/>periphery of iris<br/>and the ligamentum<br/>pectinatum extend-<br/>ing some little<br/>distance into the<br/>cornea. There is<br/>some parenchyma-<br/>tous keratitis.</p> | <p>irregular pupil,<br/>steamy cornea,<br/>shallow a. c. T+I,<br/>V=p. c. only, de-<br/>fective projection.<br/>Large iridectomy<br/>performed and lens<br/>extracted. At that<br/>time left eye un-<br/>affected, later iritis<br/>developed in it, re-<br/>sulting in blocked<br/>pupil and iris bom-<br/>bé. The eye ope-<br/>rated on remained<br/>much inflamed and<br/>the pupil was filled<br/>with lymph at the<br/>time of enucleation.</p> | <p>Patient has never<br/>had any cough and<br/>there is no sign of<br/>tubercle in other<br/>parts.</p> | <p>Father died of con-<br/>sumption. Mother<br/>and two brothers<br/>living and well.</p> | <p>Patient seen 4½ years<br/>after operation in<br/>excellent health and<br/>showing no signs of<br/>tubercle.</p> |
|--------------------------------------------|-------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|

| Case | Date and Name of Surgeon  | Name of patient and age | Eye affected | Apparent starting point of affection in eye                                                                                                          | Other structures in the eye involved                                                                                                                                                                                                                                                                                                                                     | History of the eye affection                                                                                                                                                         | General health of patient                                                                                          | Family history                                                          | Subsequent history                                                                                                                                                                                                                                                                   |
|------|---------------------------|-------------------------|--------------|------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 9.   | Tweedy.<br>Oct.,<br>1893. | Maude S.<br>14 yrs.     | L.           | Lymph spaces superficial to ciliary body up and out. The largest mass of tuberculous growth is situated here, and is in places undergoing caseation. | Tuberculous masses showing typical giant cell systems in sclerotic overlying ciliary body; also in the ciliary processes and root of iris. From the latter situation extension has taken place through the ligamentum pectinatum into the tissue of the cornea at its periphery. Perforation of a protuberance at the sclero-corneal margin occurred during enucleation. | Eye stated to have been "bad on and off" since patient was two years old.                                                                                                            | Thick upper lip and strumous appearance. "Healing whitlow" on left little finger; probably tuberculous dactylitis. | Father died of consumption. One brother and one sister living and well. |                                                                                                                                                                                                                                                                                      |
| 10.  | Tweedy.<br>June,<br>1894. | Fred G.<br>9 years.     | L.           | Iris. A nodule first noticed at the periphery down and out. Typical giant cell systems in growth.                                                    | Ciliary processes involved by tuberculous growths. Some cellular infiltration of cornea. Parenchymatous keratitis. A few opaque dots seen in it clinically.                                                                                                                                                                                                              | About 7 weeks before excision nodule in iris first noticed. One month before excision a very intense optic neuritis in his right eye with large and small hæmorrhages in the retina. | Enlarged glands in neck and some punched out ulcers of leg and thigh.                                              | Father phthisical. A brother stated to have been delicate from birth.   | Patient was very ill at the time of operation but improved afterwards. The swelling of the right optic disc subsided. A month after the operation V=6/6, there was then still some swelling and one small retinal hæmorrhage. Patient was seen by Dr. Sinclair, of Ipswich, in 1901. |

REPORT :  
 "V of R=6/6 Hm.

1.5 D. Disc slightly pale with ill-defined edge. Arteries a little contracted, veins about normal." He has seen him again this year 1905, and found the condition of the eye the same, there was, however, a tuberculous looking ulcer of the conjunctiva of the left lower lid and an enlarged preauricular gland. The patient was fat and in good health; he had several large healed lupoid patches on his face.

Child's health improved markedly after operation. She is said to have grown up quite strong, without showing any other manifestations of tubercle.

"Not thriving." Enlarged cervical glands. About a dozen roundish indolent nodules in the deep layers of the skin, each about the size of a big pea, spread over the body and limbs, one or two on the arms, several on legs. These were scraped out at the same time as the eye was removed.

Patient was treated with mercury for two or three weeks, during which time the nodules were noticed to increase in size.

Ciliary processes involved, much tuberculous growth on one side in the circumferential space. Posterior layers of cornea involved, where a nodule from the iris comes into contact with it.

Iris nodules first noticed at pupillary border down and out. Typical giant cell systems and some areas of caseation. A few tubercle bacilli found.

Female  
 1 yr. and  
 6 mths.

Gunn.  
 May,  
 1894.

| Case | Date and Name of Surgeon.                                   | Name of patient and age. | Eye affected. | Apparent starting point of affection in eye.                                                                                                    | Other structures in the eye involved.                                                                                                                                                                                                             | History of the eye affection.                                                                                                                                                                                                                           | General health of patient.                                                                                                         | Family history.                                                                                                                                                                                                                                                                                                                                 | Subsequent history.                                                                                                                                                    |
|------|-------------------------------------------------------------|--------------------------|---------------|-------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 12.  | Recorded by Marshall, Trans. Ophth. Soc., 1895, XV, p. 181. | George R. 2 yrs.         | L.            | Probably choroid which is most extensively involved by growth showing giant cell systems and caseating areas. Bacilli looked for but not found. | Retina as such cannot be recognised, it appears to be incorporated in a necrotic mass in the centre of the globe. Nodules of tuberculous growth present in the ciliary processes and the root of the iris. The sclera is invaginated posteriorly. | Eye had been inflamed 6 weeks when patient first seen. The globe was then injected, pupil fixed and eccentric. There was a yellow reflex from the fundus. The eye was excised 7½ months later, it had by that time become filled by a dense white mass. | Patient had always had a weak chest and a cough, but no other illness.                                                             | Patient was the 4th child of a family of 5. The eldest died soon after birth, the other three were living and healthy. The mother was one of a family of 10, 5 of whom died of "bronchitis," when young. The father lost 2 sisters from consumption, and one brother died, aged 24, of hip disease, from which he had suffered since childhood. | Patient seen ten years after removal of the eye, he was said to have enjoyed good health in the meantime. Examination of his chest, however, showed signs of phthisis. |
| 13.  | Silcock, July, 1895.                                        | May H. 1 yr. and 5 mths. | L.            | Choroid at posterior pole or optic nerve head. Giant cell systems and necrotic areas in growth.                                                 | The retina is completely detached except where it is involved in the mass of growth at the posterior pole.                                                                                                                                        | Seen for first time shortly before excision. Complete detachment of retina then denoted. T + 1.                                                                                                                                                         | Patient had been under treatment for 7 months for pulmonary tuberculosis. She still had a cough, looked pale and was losing flesh. | Father died of consumption. Two aunts and one uncle suffering from consumption.                                                                                                                                                                                                                                                                 |                                                                                                                                                                        |

|     |                                                                          |                              |    |                                                                                                                                                |                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                       |                                                                                                                                                                                   |                                                             |
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| 14. | Recorded by Spicer and Marshall. Trans. Ophth. Soc., 1897, XVII., p. 31. | Nellie R. 10 mths.           | L  | Iris at upper and outer part; numerous nodules composed of typical giant cell systems protruding mostly from the anterior surface of the iris. | Tuberculous nodules have extended forwards from the iris and invaded the cornea at the sclero-corneal margin on one side. The ligamentum pectinatum is everywhere infiltrated. Tuberculous growth has involved the anterior part of the ciliary body. | Eye inflamed for 3 months previous to its first being seen. Attack commenced with the appearance of a small speck in the eye. A nodular cheesy looking mass noted in the anterior chamber growing from upper and outer part of iris. A fortnight before excision, the ciliary region began to bulge and the whole cornea became hazy. | Always good health except for a slight attack of thrush with constipation. Always nursed at the breast, fairly well nourished, but fretful and ill.   | Mother healthy but very young and poorly nourished. Married at 17; first pregnancy terminated in a miscarriage; the patient the only living child. No family history of tubercle. | Child's health improved markedly after excision of eyeball. |
| 15. | Treacher Collins December, 1900.                                         | Martin L. 2 yrs. and 9 mths. | R. | The whole iris much thickened by new growths containing giant cells and necrotic areas.                                                        | Ciliary processes involved by tuberculous growth the circumferential space being filled with it. Ligamentum pectinatum invaded. Cell infiltration in cornea, specially its anterior layers, parenchymatous keratitis.                                 | Struck on right eye with a cricket ball when a year and a half old, after which eye was for some time much discoloured. Attended Hospital first 3 months previous to excision; nodules then seen in iris.                                                                                                                             | One of father's uncles died of consumption. Father was suffering from consumption at the time patient's eye was removed; he died of it 3 years later. | Patient seen 4 years and 4 months after removal of the eye. He was in good health, but had enlarged glands at the angles of his jaw.                                              |                                                             |

| No. | Date and Name of Surgeon. | Name of patient and age. | Ref. | Apparent starting point of affection in eye.                                                            | Other structures in the eye involved.                                                                                                                                                                                                                                                                                                   | History of the eye affection.                                                                                                                | General health of patient.                                     | Family history. | Subsequent history.                                                                                                                                |
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| 16. | Tay.<br>Feb. 1901.        | Maria W.<br>8 years.     | R.   | The whole iris much thickened by new growth containing giant cell systems and necrotic areas.           | Ciliary processes involved by tuberculous growth; a large mass fills the circumferential space on one side, displacing the lens to the opposite one. Ligamentum pectinatum invaded. Cell infiltration and new blood vessels in cornea; parenchymatous keratitis.                                                                        | Eye affected four months previous to excision. When first seen appeared to have iritis with hyphema. Blood vessels appeared in cornea later. | No sign of tubercle could be discovered in patient elsewhere.  |                 | Stated to have been in good health and not to have had any illness for 4 years after removal of the eyeball.                                       |
| 17. | Fisher.<br>May, 1902.     | Daisy B.<br>1 year.      | R.   | The choroid which was extensively thickened and contained large caseating areas and giant cell systems. | Sclerotic much invaded by tuberculous growth. At the lower part it has perforated; the tissue external to the sclerotic in this locality much inflamed and adherent to it. Retina very necrotic & scarcely distinguishable. Optic nerve invaded by tuberculous tissue. Iris and ciliary body inflamed, but show no tuberculous nodules. | Eye red for 3 months previous to excision. A month later a lump formed on the inner side of the globe and burst.                             | Two large subcutaneous nodules on the outer side of the thigh. |                 | Patient died about a month after removal of the eyeball from convulsions. There was apparently some recurrence of tuberculous growth in the orbit. |

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| 18. Lawson. Sept., 1904 | R. Arthur T. 4 yrs. | Iris in which there were nodules containing giant cell systems and necrotic areas. | Ciliary processes and circumferential space contain masses of tuberculous growth. The ligamentum pectinatum is invaded. Accumulation of cells have been precipitated on the back of the cornea. | Eye affected about six weeks previous to excision. When first seen 14 days before excision, iris studded with yellowish nodules, lymph in pupil, keratitis punctata, haze of cornea, and T. full. | No previous illness. | Not very well nourished. No affection of lungs. No previous illness. | Tubercle on father's side of family. One sister, aged 8, living and healthy. | In good health a year after the operation. |
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