PRIMARY TUBERCULOSIS OF THE CONJUNCTIVA*†

BY

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THE response evoked by the tuberculous infection of a tissue has been classically divided into two forms: the progressive childhood (primary) type and the adult (secondary) type. In the child, tuberculous infection of the lung causes a small circumscribed caseous and often calcifying lesion in any part of the lung, and there is prominent involvement of the regional lymph nodes. In contrast, the adult lesion is subapical, larger, and is not associated with any macroscopic lymphadenopathy.

It has long been believed that the childhood form of tuberculosis represented a first infection, whilst the adult type was due to a re-infection, the response in the latter being modified by previous experience of tuberculosis. This belief was based upon experimental evidence, the results of population surveys, and the clinical behaviour of the disease.

(1) *Experimental Evidence.*—Koch (1891) demonstrated in guinea-pigs that previous tuberculous infection modified their response to experimentally-induced tuberculosis. Igersheimer (1922) observed a similar phenomenon in guinea-pigs when he produced tuberculous conjunctivitis by instilling tubercle bacilli into their conjunctival fornices. He found that those animals which had no previous experience of tuberculosis developed a conjunctivitis with local lymphadenopathy. On the other hand, others with concurrent tuberculosis elsewhere did not develop lymph node involvement.

(2) *Population Surveys.*—Surveys have shown that in the earlier part of the 20th century a vast majority of the urban population had experienced tuberculosis by adult life.

(3) *Clinical Behaviour of the Disease.*—It was consistently observed in the past that the childhood form of tuberculous infection occurred only in early life whereas the adult form was seen in later life. The adult form occurred in children only if they had previously experienced tuberculosis.

More recently, however, there has been an increasing awareness that tuberculous infection before adulthood is no longer the rule. In 1949, 50 per cent. of the population of England and Wales were Mantoux positive by the age of 16 years and 70 per cent. by the age of 20 years (Logan and Benjamin, 1957), while in 1962, only 24 per cent. of London school children were Mantoux-positive by the age of 15 years (Hartston, 1962). In spite of this recent decline in the incidence of tuberculosis in children and adolescents, there has not

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been the expected increase in the incidence of the progressive childhood form of tuberculosis in adults. Although a first pulmonary tuberculous infection may evoke, in an adult, the classical primary or progressive childhood response, it is very rare, and it usually produces the classic lesion of adult life without lymphadenopathy. On the basis of this last observation, Rich (1951) concluded that there was an increase of natural resistance to tuberculosis with maturity, and a few years later Florey (1962) stated that the difference between childhood and adult tuberculosis was associated with the intrinsic changes in the reaction of the body with age. It seems therefore that the tissue response to tuberculous infection is determined both by the patient's age and by his previous experience of tuberculosis.

The following five patients with primary tuberculosis of the conjunctiva are described in order to determine whether the changing response of the lung to tuberculosis with age is reflected in the behaviour of conjunctival tuberculosis, with particular reference to the presence or absence of lymphadenopathy, and the morphology of the conjunctival lesion. The effect of previous experience of tuberculosis upon this conjunctival response will also be discussed. The clinical details are shown in the Table.

TABLE
DETAILS OF FIVE PATIENTS WITH PRIMARY TUBERCULOUS CONJUNCTIVITIS

Patient No.	Age (yrs)	Sex	Site on Conjunctiva	Morphology of Lesion	Lymph-adenopathy	Confirmatory Laboratory Tests	Evidence of Primary Nature
1	12	M	Right upper tarsal	Nodular	Parotid and submandibular	Z.N. +ve Culture +ve	Chest x ray normal
2	14	M	Left bulbar and lower tarsal	Oedema and congestion ↓ Nodules	Parotid	Z.N. +ve	No history of tuberculosis No chest x ray available
3	16	M	Left upper tarsal	Ulcer with local hyperaemia	Parotid	No a.f.b. seen	Chest x ray normal
4	25	F	Right upper tarsal	Ulcer with local hyperaemia	Parotid and submandibular	Z.N. +ve Culture +ve	Chest x ray normal
5	32	M	Right lower fornix	Hyperaemia and oedema ↓ Ulcer	Parotid	Z.N. +ve Culture +ve	Chest x ray normal

Case Report (Case 5, Table)

A 32-year-old solicitor presented at Moorfields Eye Hospital with a 14-day history of swelling of the right side of the face and a slightly sore red right eye for 10 days.

There was no previous history of major illness and his general health was good; 6 months previously he had been to Yugoslavia and Greece, and one month previously he had returned from a 3-week holiday in Majorca.

Examination.—There was an obvious solid swelling 2 inches in diameter in front of the right ear; it was fixed to the underlying structures but not to the overlying skin (Fig. 1).

FIG. 1.—Case 5, showing right pre-auricular lymphadenopathy.

There was oedema and hyperaemia of the lower bulbar conjunctiva and to a lesser degree of the tarsal conjunctiva (Fig. 2).

FIG. 2.—Right eye of Case 5, showing tuberculous ulcer in lower fornix with localized conjunctival inflammation.

Within 5 days the hyperaemia had largely settled on the bulbar conjunctiva and an ulcer had appeared in the lower fornix. The gland had become fluctuant and attached to the overlying skin, but there were no skin changes.

Investigations

- (1) Full blood count normal. The erythrocyte sedimentation rate was raised to 30 mm. in the first hour (Westergren).
- (2) The Wassermann reaction and Kahn test were negative.
- (3) Chest x ray showed no evidence of active tuberculosis or old primary lesion.
- (4) Mantoux test strongly positive in 1 : 10,000.
- (5) Culture—there was no growth of bacteria on blood agar or fungus on Sabouraud's medium.

(6) A biopsy was taken of the edge of the ulcer. Sections showed a granulomatous reaction with prominent caseation, typical Langhans giant cells, epithelioid cells, and lymphocytes. Ziehl-Neelsen stain revealed acid and alcohol-fast bacilli morphologically indistinguishable from tubercle bacilli (Fig. 3).

FIG. 3.—Photomicrograph of histological preparation from Case 5 stained with haematoxylin and eosin.
A. Lymphocyte and epithelioid cell infiltration and giant cells. $\times 100$.
B. Giant cell and epithelioid cells. $\times 350$.

Tubercle bacilli were cultured in 4 weeks on a Lowenstein Jensen slope from scrapings of the ulcer.

Injection into a guinea-pig of material from the lesion produced a typical tuberculous primary complex.

No evidence of active tuberculosis was found in his family.

Treatment.—The cold abscess was incised, curetted, and closed by primary intention, and the patient was treated with systemic para-amino salicylic acid, isoniazid, and streptomycin.

The conjunctival lesion healed in 3 weeks, but a small sinus in front of the ear persisted for a further 4 weeks.

Four other cases of tuberculous conjunctivitis have been seen at this Institute in the last few years (Cases 1–4, Table), which have been considered to be primary in nature on the basis of normal chest x rays (including apical views). All these patients had a positive Mantoux reaction. This was, however, expected as all cases presented initially with a well-established lymphadenopathy of at least 2 weeks' duration. In all the patients the conjunctivitis was localized and unremarkable in comparison with the lymphadenopathy when the patient presented, and, although the conjunctival lesion healed rapidly with treatment, in no case did the regional lymph node heal in less than 5 months.

Discussion

Two of the patients presented here are adults and yet the tuberculous lesion in each case was associated with prominent lymphadenopathy. The presentation of the disease and its response to treatment in the adults were identical to the disease behaviour in the three younger patients.

Four other adult patients with primary conjunctival tuberculosis have been described in the last 15 years: Anhalt, Zavell, Chang, and Byron (1960) 36 years; Donegan (1950) 27 years; Sykowski (1950) 30 years; von Berger (1953) 44 years. They all presented with a classical primary complex typified by prominent lymphadenopathy.

Furthermore, tuberculous conjunctivitis may be associated with a regional lymphadenopathy even if it represents a re-infection. Eyre (1912) personally observed

tuberculous conjunctivitis associated with lymphatic involvement in two patients who had a previous history of tuberculosis (Cases 12 and 13). Moreover, it is probable that those of his patients who were over 20 years old (Cases 5, 10, 11, and 26) would have had a previous tuberculous infection since they were drawn from an urban population. Similar cases have been described by Poulard (1903), Kalt (1906), Magitot and Rossano (1937), and Bezançon, Delarue, and Wolinetz (1938).

It would appear, therefore, that a patient with tuberculous conjunctivitis may have involvement of the regional lymph nodes independent of his age or previous experience of tuberculosis.

Excluding conjunctival tuberculosis resulting from the spread of infection from lupus vulgaris, the morphological characteristics of the conjunctival lesions in tuberculous conjunctivitis have been considered to fall into four groups (Eyre, 1912):

- (1) *Ulcerative*.—Localized ulceration associated invariably with lymphadenopathy.
- (2) *Nodular*.—Localized area of conjunctivitis containing multiple nodules which later ulcerate. Lymphadenopathy was usual.
- (3) *Hypertrophic granulomatous*.—Massive flattened granulations commonly associated with lymphadenopathy.
- (4) *Pedunculated*.—Pedunculated mass without lymphadenopathy.

Eyre (1912) made this classification on the basis of 160 cases of tuberculous conjunctivitis, both first and re-infections, which he had collected from the previous medical literature, with a further 29 cases personally observed. He made no attempt to correlate the morphology of the lesions with the patient's previous experience of tuberculosis. There is no striking age difference between the patients of the different groups, and in all four groups are found patients who are at an age at which they might have had a previous tuberculous infection. (All the cases described in this paper fall into Groups 1 and 2.)

There appears, therefore, to be no constant relationship between the presentation and behaviour of the disease in the conjunctiva, and the patient's age or previous experience of tuberculosis.

This suggests that attempts to re-classify the morphology of the lesion in respect of these last two factors are unlikely to be successful.

The clinical behaviour of conjunctival tuberculosis is, therefore, much less dependent on the patient's age and previous experience of tuberculosis than is observed in pulmonary tuberculosis.

Summary

(1) A detailed report of a 32-year-old white male patient with primary conjunctival tuberculosis has been given, and four further cases briefly described.

(2) It has been found that, in tuberculous conjunctivitis, lymphadenopathy may occur irrespective of the patient's age or previous experience of tuberculosis.

(3) The morphological presentation of the conjunctival lesion is also independent of the patient's age or experience of tuberculosis.

(4) It is concluded that conjunctival tuberculosis behaves quite differently from tuberculosis of the lung.

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REFERENCES

- ANHALT, E. F., ZAVELL, S., CHANG, G., and BYRON, H. M. (1960). *Amer. J. Ophthalm.*, **50**, 265.
 BEZANÇON, F., DELARUE, J., and WOLINETZ (1938). *Ann. Anat. path.*, **15**, 215.
 DONEGAN, J. M. (1950). *Amer. J. Ophthalm.*, **33**, 1117.
 EYRE, J. W. H. (1912). *Lancet*, **1**, 1319.
 FLOREY, H. W. (1962). In "General Pathology", 3rd ed., p. 1027. Lloyd-Luke, London.
 HARTSTON, W. (1962). Cited by Perry and Holmes Sellors (1963).
 IGRSHEIMER, J. (1922). *Klin. Mbl. Augenheilk.*, **69**, 226.
 KALT, E. (1906). *Bull. Soc. franç. Ophtal.*, **23**, 284.
 KOCH, R. (1891). *Dtsch. med. Wschr.*, **17**, 101.
 LOGAN, W. P. D., and BENJAMIN, B. (1957). In "Tuberculosis Statistics for England and Wales, 1938-1955". General Register Office. Studies on Medical and Population Subjects, No. 10. H.M.S.O., London.
 MAGITOT, A., and ROSSANO (1937). *Bull. Soc. Ophtal. Paris*, p. 383.
 PERRY, K. M. A., and HOLMES SELLORS, T. (1963). "Chest Diseases", vol. 2, p. 249. Butterworths, London.
 POULARD, A. (1903). "Adénopathies dans les infections oculaires", pp. 85-95. Thèse No. 367, Paris.
 RICH, A. R. (1951). "The Pathogenesis of Tuberculosis", 2nd ed., p. 771. Blackwell, Oxford.
 SYKOWSKI, P. (1950). *Amer. J. Ophthalm.*, **33**, 1291.
 VON BERGER, G. P. (1953). *G. ital. Oftal.*, **6**, 385.