

## SARCOIDOSIS OF THE EYE\*†

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SARCOIDOSIS (Boeck's sarcoid; Besnier-Boeck disease; benign lympho-granulomatosis; uveo-parotid fever; Heerfordt's disease) has been defined as:

A disease in which the lesions have a characteristic histological appearance consisting of epithelioid cell tubercles, as a rule clearly defined within the affected tissue, with only slight round cell infiltration in their vicinity, without central caseation, with or without Langhan's type giant cells, and with or without peculiar inclusion bodies within these cells, proceeding in the older lesions to conversion into hyaline fibrous tissue; these histological appearances must be present in all affected tissues. (Robb-Smith, 1952).

**Pathology.**—The structural changes which may commonly affect the skin, bones, lymph glands, lungs, and eyes, and rarely almost any tissue of the body, result from the formation of small nodules, composed of epithelioid cells, which never show necrosis. Some lymphocytes may be present around the nodules, and a few giant cells may be found which contain small refractile bodies. Healing follows by organization and fibrosis, but calcification does not occur.

**General Signs.**—Skin nodules and enlargement of the lymph glands are commonly seen, X-ray examination of the bones shows characteristic rarefaction, especially in the phalanges, and radiological examination of the chest shows the diffuse fibrosis of the lungs and enlargements of the mediastinal lymph glands which is present in nearly all cases of the condition. The parotid salivary gland may be enlarged, and palsy of the facial nerve may be a sequel. The submaxillary salivary gland and the lacrimal gland are also affected in some patients giving the syndrome of von Mickulicz. Nodular lesions may occur more rarely, in almost all the tissues of the body. Laboratory investigation often reveals an increase of the erythrocyte sedimentation rate, and an elevation of the serum globulin. A very common finding, and one which some authorities suggest is present in all cases of sarcoidosis, is an anergy to tuberculin. No skin reaction occurs as a result even of large intracutaneous doses of the tuberculin, and the injection of B.C.G. vaccine does not induce a positive skin reaction to tuberculin in most cases. In Great Britain, therefore, where almost all adults show a positive Mantoux test, a negative reaction should always lead to the suspicion that sarcoidosis may be present.

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**Ocular Signs.**—Sarcoidosis may occur in any part of the eye or ocular adnexa, but the uveal tract is the part most frequently affected. Nodules appear in the iris which may when fully formed, be large and more vascular than those of tuberculosis (Laval, 1952). Large clear keratic precipitates are present, often situated peripherally, and posterior synechiae may occur. The inflammatory reaction may be acute, subacute, or chronic. Choroidal lesions occur rarely, and the retina may be involved; lesions of the latter structure are sometimes accompanied by periphlebitis. Swelling of the parotid gland in association with uveitis, fever, and general malaise is the syndrome of uveoparotid fever.

**Aetiology.**—The essential feature of sarcoidosis is a hyperplasia of mesenchymal cells to form histiocytes and epithelioid cells. Present evidence suggests that this can only occur as a response to infection by, or sensitivity to, members of the mycobacterium group. The difference between tuberculosis and sarcoidosis seems small in some cases (Merz, 1952). The granulomata which form in response to beryllium appear, according to some authorities, to have different histological characteristics, and it is stated that this lesion must be regarded as a separate condition.

**Diagnosis.**—The clinical characteristics, the radiological appearances, the anergy to tuberculin, and the rise of serum globulin, indicate the nature of the condition, though the final test should, where possible, be histological examination of one of the lesions either of the skin or of a lymph gland. It is possible that some cases cause symptoms and signs only in the eye, and that these may be regarded, in error, as cases of non-specific uveitis.

#### Case Reports

(1) **Aged 20.**—Admitted to the Eye Sanatorium, Swanley, on August 2, 1951, with a history of painless congestion of the left eye with blurred vision for 4 months. The right eye was normal. The left eye, in which vision was hand movements, showed a ciliary staphyloma near the limbus above, a large iris nodule, and large pale keratic precipitates. The Mantoux reaction was negative to 1:100 O.T. and remained so even after B.C.G. vaccine. Cervical, axillary, and mediastinal lymph glands were enlarged, and biopsy showed the typical histological changes of sarcoidosis. In October, 1952, the condition of the left eye started to settle, coinciding with the beginning of a prolonged course of subconjunctival injections of cortisone. The iris nodule had disappeared from the left eye on December 9, 1952, and visual acuity was 6/36.

(2) **Aged 58.**—Admitted to the Eye Sanatorium, Swanley, on June 16, 1951, with a history of left uveitis of 3 months' duration. There was dryness of the mouth, and both eyes showed evidence of keratitis sicca. There was no evidence of uveitis in the right eye, but the left showed profuse keratic precipitates. No iris nodule was seen. The Mantoux reaction was negative to 1:100 O.T. and remained so after injection of B.C.G. vaccine. Radiological examination of the chest showed diffuse reticulation of the lungs, an appearance compatible with sarcoidosis. The condition of the left eye improved markedly after a period of general rest, and local treatment to the eye with atropine drops.

(3) **Aged 26.**—Admitted to the Eye Sanatorium, Swanley on May 23, 1952, with

a history of recurrent uveitis of 3 years' duration in both eyes, and of scarring of one lung, visible on radiological examination. Both eyes showed a mass of pale keratic precipitates. The Mantoux reaction was negative to 1:100 O.T. and some enlarged cervical glands were found to be present. This patient discharged herself from hospital before treatment could be completed.

(4) **Aged 30.**—Admitted to the Eye Sanatorium, Swanley, on December 17, 1951, with a history of recurrent uveitis of 10 years' duration in both eyes, and of an attack of pneumonia 9 years before. Both eyes showed old keratic precipitates and a few small nodules were present in the right iris. Posterior cortical lens opacities were present in both eyes. The Mantoux reaction was negative to 1:100 O.T. but became positive to the same dose of O.T. after an injection of B.C.G. vaccine. No change in the ocular condition followed 3 months' treatment in hospital, and the condition remains unsettled.

(5) **Aged 28.**—Admitted to the Eye Sanatorium, Swanley, on July 2, 1951, with a history of bilateral uveitis of 2 years' duration. Pale keratic precipitates were present in both eyes. The Mantoux reaction was negative to 1:100 O.T. but became positive to the same dose after an injection of B.C.G. vaccine. Radiological examination of the chest showed lesions compatible with mild sarcoidosis. The eye condition improved slightly during 4 months' stay in hospital.

(6) **Aged 38.**—Admitted to the Eye Sanatorium, Swanley, on July 30, 1951, with a history of bilateral uveitis of 3 years' duration. Large clear keratic precipitates were present in both eyes. The Mantoux reaction was negative to 1:100 O.T. but became positive after an injection of B.C.G. vaccine. Radiological examination of the chest showed lung changes suggestive of sarcoidosis. There was improvement both of the ocular and general condition during a stay of 3 months in hospital.

(7) **Aged 23.**—Admitted to the Eye Sanatorium, Swanley, on June 6, 1951, with a history of recurrent uveitis in both eyes of 4 years' duration, and of iris nodules present in the left eye for one year. Both eyes showed old keratic precipitates and some nodules were present in the left iris. The Mantoux reaction was negative to 1:1000 O.T. Radiological examination of the hands showed changes suggestive of sarcoidosis in the phalanges. Considerable improvement in ocular condition occurred during 4 months' stay in hospital.

### Discussion

Sarcoidosis must be regarded as a tissue reaction to a foreign agent which is introduced into the body. This is possibly a hypersensitivity reaction of certain cells of the body analogous to that which is believed to occur in uveitis, or it is possibly a direct reaction to a toxic agent. One body of opinion believes that this sensitizing or toxic agent is related to the mycobacterium group, but in this series of cases, little evidence of tuberculous infection was found. In Great Britain, however, the Mantoux reaction is positive in almost all adult persons, and the possibility of a subclinical tuberculous infection in these cases of sarcoidosis cannot be excluded. Typical cases of sarcoidosis show characteristic changes in the lymph glands, lungs, and eyes, as well as in other parts of the body, but consideration must be given to cases showing less typical and less widespread signs. No cause is found for many cases of uveitis, and in the presence of a negative Mantoux reaction the possibility of sarcoidosis should always be considered. The diagnosis is confirmed by the presence of enlarged lymph glands, shadowing of the lungs on radiological examination, and a raised serum globulin, as

well as by the development of iris nodules, and by the large transparent peripheral keratic precipitates which are found so frequently in this condition. Absolute proof depends upon the histological appearances of an excised lesion.

Tuberculin anergy in sarcoidosis is a constant finding. It is due to the presence in the skin of a substance which has been called anticutin and which prevents a hypersensitivity reaction to injections of tuberculin. Anticutin remains in the skin even when its hypersensitivity is increased by the injection of B.C.G. vaccine.

The cause of sarcoidosis is uncertain and treatment cannot, therefore, be based on logical principles. Cases treated at the Eye Sanatorium, Swanley, on a regime of general rest have improved, though since the disease seems to be chronic in many cases, complete cure does not occur in the 3-6 months which they spend as patients. The use of cortisone appears to have been beneficial in some cases, and this would support the thesis that hypersensitivity is a cause of the condition. ACTH may also be useful (Ozazewski and Bennett, 1952). In some cases the condition may persist for many months or even years, but the ultimate prognosis for vision appears to be good.

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