Section of Medicine

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DISCUSSION ON SARCOIDOSIS

Dr. J. G. Scadding:

The first difficulty which confronts us in discussing sarcoidosis is that of definition. Many authors of reviews of the subject have side-stepped this difficulty by starting with a historical review of the gradual development of the concept of sarcoidosis as a systemic disorder, which they substitute for any attempt at formal definition. There are only two generally agreed common features between such diverse conditions as the skin lesions described by Hutchinson (1877), Besnier (1889) and Boeck (1899, 1905), the pulmonary changes described by Schaumann (1914) and others, the eye lesions by Heerfordt (1909), the bone changes by Jüngling (1919), the frequent lymphadenopathy, hepatomegaly and splenomegaly, and the rarer changes in the kidneys, in endocrine glands, in the central nervous system, the mucosæ of the respiratory and alimentary tracts and elsewhere; these two common features are the frequent concurrence of two or more of these manifestations, and a common histological pattern. Accordingly, only these two features can be mentioned in the definition. I suggest the following:

Sarcoidosis is a disorder which may affect any part of the body, but most frequently the lymph nodes, liver, spleen, lungs, skin, eyes and small bones of the hands and feet, characterized by the presence in all affected organs or tissues of epithelioid cell tubercles, without caseation, with little or no round-cell reaction, becoming converted in the older lesions into a rather hyaline featureless fibrous tissue. Even though it may be stated quite correctly as an addendum to the definition that, at present, knowledge of the cause or causes of sarcoidosis is incomplete, the inclusion in the definition itself of the statement that "sarcoidosis is a disease of unknown ætiology" (Ricker and Clark, 1949) leads to logical difficulty; for if, as may well be the case, sarcoidosis can be caused by more than one agent, the discovery of one of them would involve the elimination of the group of cases caused by it from the category "sarcoidosis" so defined. Accordingly, no statement whatever about ætiology can be made in the definition.

The clinical manifestations of sarcoidosis are so numerous that it is difficult to obtain a reliable assessment of the frequency of involvement of various organs and tissues; every series is biased, both by the interests of the person observing it, and by the criteria which he adopts for diagnosis. My own series naturally contains a high proportion of patients with prominent intrathoracic manifestations. I have analysed certain aspects of the 142 cases of sarcoidosis which I saw first between 1938 and December 1955. Fig. 1 shows the reasons for which these patients first came under medical care. The high proportion of those whose disease was first discovered as a result of routine radiography, or because of respiratory

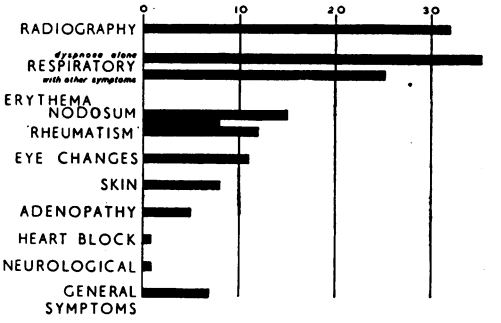

FIG. 1.—Earliest manifestations in 142 cases of sarcoidosis. "Radiography" indicates those patients who were symptom-free when routine radiography revealed abnormality in the lungs or hilar lymph-nodes. The "bridge" between "erythema nodosum" and "rheumatism" indicates the 8 patients who had both these manifestations concurrently.

symptoms is almost certainly a reflection of my known interests. The group whose first symptom was erythema nodosum or "rheumatism" is of some interest. There were 19 of these; 8 had both erythema nodosum and rheumatism, 7 had erythema nodosum alone, and 4 rheumatism alone. The good prognosis of these cases is worth emphasizing. Of 14 who were first observed long enough ago to permit an estimate of the outcome, 11 are well with normal chest radiographs, and 3 have only very slight residual disability. 17 of them had bilateral hilar lymph-node enlargement without lung shadows when they were first seen, and most patients presenting with this radiological finding do well.

The age and sex distribution of these 142 cases is shown in Fig. 2. The ages recorded are those at which the first detected manifestation appeared; e.g. if a patient had an iridocyclitis at the age of 22, and was seen by me with lung changes at the age of 27, he is recorded in the 20–25 year age group. There is no difference in age distribution between the sexes, but there are rather more females (78) than males (64).

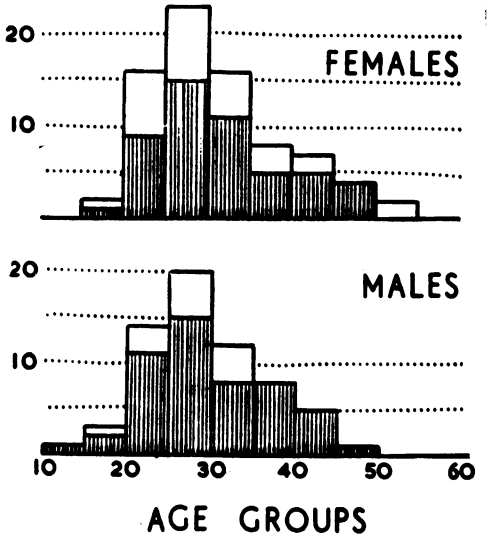

FIG. 2.—Age at apparent onset in 142 cases of sarcoidosis. The ages recorded are those at which the earliest manifestations were detected.

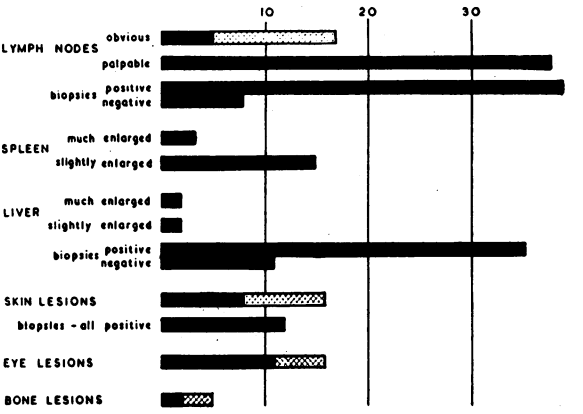

FIG. 3.—Clinically observed extrathoracic manifestations in 142 cases of sarcoidosis. The cross-hatched areas represent the cases in which lymph nodes, skin, eyes and bones became involved while the patients were under observation after the diagnosis had been established.

Fig. 3 shows the clinically observed extrathoracic manifestations in this series. Biopsy confirmation of the diagnosis was obtained in 101 of the 142 cases; it was obtained first from lymph-node biopsy in 39, from liver biopsy in 35, from biopsy of skin lesions in 12, and from biopsy of bronchial mucosa in 5. Other sites from which histological evidence was obtained included 2 infiltrated scars, 3 subcutaneous nodules, an infiltrated nasal mucosa, and a nodule in the breast. Biopsy of the lung and of hilar nodes at thoracotomy and of the liver at laparotomy were each responsible for confirmation in one patient. When superficial lymph nodes are palpable, they offer the most favourable available tissue for biopsy; 39 out of 46 nodes removed, or 85%, have shown specific changes. My experience with liver biopsy has been similar to that of others; 35 out of 46, or 76%, of those performed in patients eventually accepted as suffering from sarcoidosis having proved confirmatory. The relative rarity of notable enlargement of the liver and spleen and of the bone lesions of the hands and feet is noteworthy. The request for radiographs of the hands, in the hope that they will provide evidence of sarcoidosis in obscure cases, has always in my experience proved futile. Only 2 patients had changes in the bones of the hands when I first saw them, and both of these had also obvious skin lesions; in 3 others, radiographic changes appeared in the bones while they were under observation after the diagnosis had been established.

Intrathoracic manifestations.—I have prepared a summarized account (Fig. 4) of these in 102 cases which I have followed for not less than two years; the period of observation extends up to a maximum of fourteen years, though few cases have been followed more than seven years. The cases are grouped according to the radiographic changes when I first observed them. Of 16 patients who had enlarged hilar nodes at that time, 15 now have normal chest radiographs, and only one has slight residual radiographic abnormality; all are symptom-free. 6 of them developed diffuse mottling in the lungs before final resolution. Among the 32 patients who, when I first saw them, had both enlargement of hilar nodes

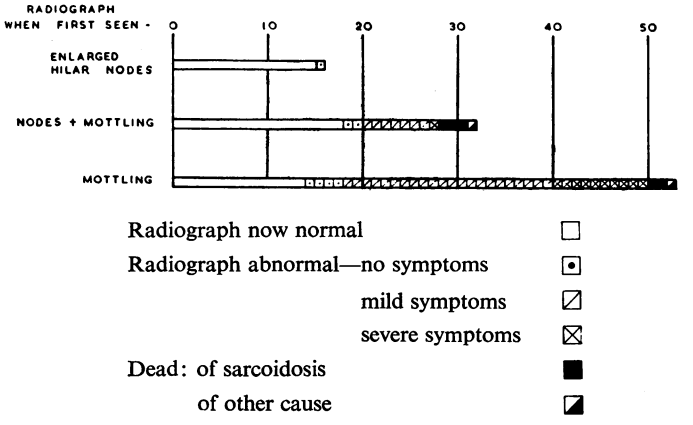

FIG. 4.—Lung and hilar lymph-node changes in 102 cases of sarcoidosis, followed not less than two years, grouped according to the radiographic changes at the beginning of the period of observation.

and mottling in the lungs, or who had diffuse mottling at that time with earlier radiographic evidence of preceding hilar node enlargement, 18 have resolved completely and are well, 2 still have some residual radiographic abnormality, but are symptom-free, 7 have mild symptoms, 1 has severe symptoms, 3 have died of sarcoidosis, and 1 of unrelated disease. Among the 53 who had generalized mottling of the lung fields when I first saw them, and in whom there was no record of previous enlargement of hilar nodes, the course has been even less favourable. 14 are well, with normal radiographs, 4 have some radiographic abnormality but no symptoms, 22 have mild and 10 have severe symptoms; 2 have died of sarcoidosis and 1 of an unrelated disease. There seem to be two possible explanations of these observations. One is that there are two distinct groups of cases of pulmonary sarcoidosis; one starting with hilar lymph-node enlargement and liable to proceed later to diffuse lung involvement, but in any case having a strong tendency to spontaneous resolution; and the other starting with diffuse lung involvement and tending to lead to fibrosis. The other possible explanation is that the patients who, when I first saw them, had diffuse lung involvement represented the residue of a very much larger group who had in the past had symptomless and undetected hilar lymph-node enlargement. I have no evidence to suggest which of these two explanations is correct. It remains a fact of immediate clinical importance that patients first coming under observation with enlarged hilar lymph nodes only can be given a generally good prognosis, and that there is no indication, as far as I can see, to use cortisone or corticotrophin in an attempt to modify the course of the disease at this stage.

Fig. 5 shows the tuberculin sensitivity in the 140 of these 142 cases in which it was

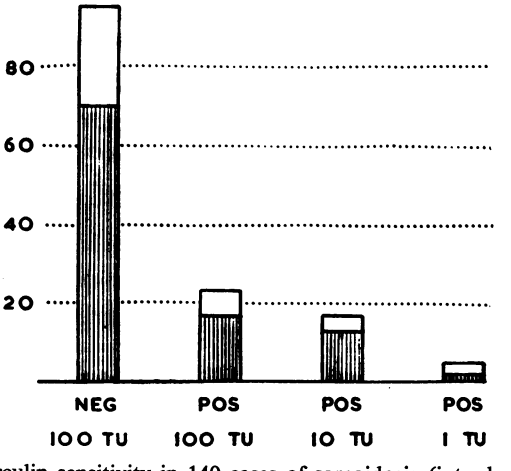

FIG. 5.—Tuberculin sensitivity in 140 cases of sarcoidosis (intradermal test with old tuberculin or P.P.D.).

precisely recorded. In the other two (both early in the series) the Mantoux test was recorded as "negative" without a note of the dose of tuberculin used. 68% were negative to 100 T.U., and the proportion is the same whether or no cases without histological evidence are included. This proportion is, of course, much higher than would be found in a group of the same age-distribution in the general population. It is also much higher than was found by my colleague, Dr. Clifford Hoyle, either in his own series of cases of sarcoidosis, or in a series of cases of Hodgkin's disease (Hoyle *et al.*, 1954). It is clear that the negative Mantoux test in sarcoidosis does not necessarily represent complete absence of tuberculin sensitivity; in some cases with negative Mantoux tests, reactions to tuberculin can be elicited by cortisone, either systemically or locally (Pyke and Scadding, 1952), or by using a depot tuberculin (Seeberg, 1951). It is perhaps significant that when tuberculin tests are done routinely in patients with established pulmonary tuberculosis, a few cases will be found to produce no reaction even to 100 T.U. I have records of several such cases, and a series of 11 has been reported by Mascher (1951).

There is no certain knowledge of the ætiology of sarcoidosis, or even of whether it forms an ætiologically homogeneous group. Controversy about its relation to tuberculosis continues. My own opinion is that the condition as seen in this country is a variety of tuberculosis. Of the 142 cases which I have analysed, no fewer than 14 have produced tubercle bacilli at one time or another. Bacilli were found in sputum, gastric contents or laryngeal swabs in 10 of them while they were still in a "sarcoid phase", in 7 on culture, and in 3 on direct microscopy only; in one of the latter, tubercle bacilli were subsequently cultured from lung tissue *post mortem*. In these 10 patients there was no change in the clinical or radiological picture at the time the bacilli were found; the Mantoux test was, and remained, negative to 100 T.U. in 8 of them, negative to 10 T.U. but positive to 100 T.U. in one, and positive to 10 T.U. in one. In one patient, tubercle bacilli had been cultured from a cervical adenitis four years before the sarcoid phase began. In 3 patients, the finding of tubercle bacilli in the sputum was accompanied by a change to a frankly caseating phase with development of tuberculin sensitivity. The existence of intermediate cases between caseating tuberculosis and sarcoidosis is another important piece of evidence; it has seemed to me quite arbitrary where the dividing line between these two categories should be placed, so that I believe that there is not in fact a clear division.

The usual failure of antibacterial treatment to produce any readily observable effect in sarcoidosis does not disprove this view, since the very indolent type of tuberculosis which is accompanied by low tuberculin sensitivity also may not respond in any obvious way to antibacterial drugs. Similarly the response which is often observed to cortisone cannot be used as an argument against a tuberculous ætiology, since in a number of cases of indolent tuberculosis, an immediate response to cortisone, combined with antibacterial drugs, may be observed. While thus expressing my opinion that sarcoidosis in this country is usually due to tuberculosis, I try to keep an open mind about the possiblity that some cases may be due to other causes, and that in other parts of the world other causes may even be more frequent; and the definition which I have suggested allows for this possibility, by imposing no logical bar to the addition of an adjective indicative of ætiology to the term sarcoidosis if the evidence justifies it.

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Dr. Peter Kerley:

The sarcoid granuloma has now been described in a wide variety of infectious diseases (bacterial, viral, fungoid and protozoan) in benign and malignant neoplasms, in occupational and collagenous diseases and in blood dyscrasias. It is accepted that it is a non-specific allergic tissue reaction to a great variety of agents so its finding by no means establishes a firm diagnosis of the systemic disease known as Boeck's sarcoidosis. The real incidence of systemic sarcoidosis is unknown but I would estimate that for every case presenting with symptoms, there are at least 5 detected by mass radiography without symptoms. Sarcoidosis has only recently been included as an entity in the mass radiography classification for England and Wales. Although detailed figures are not yet available, it appears that between four and five hundred cases per annum are being discovered.

The commonest initial finding is symmetrical enlargement of the bronchial glands and, for some unknown reason, the hila often swing outwards, even in the early stages before there is any fibrosis to pull them out (Fig. 1). This symmetrical splaying of the hila is often permanent and is a useful diagnostic point. The paratracheal and bifurcation groups are less frequently involved and very large mediastinal tumours are unusual. I have only once seen a glandular mass which was strictly unilateral and remained so.

The glandular stage may remain the only manifestation and may disappear quickly or persist for years. The shortest period I have seen is two months and the longest eight years. Pulmonary and systemic spread usually follow the glandular phase but occasionally iritis or uveo-parotid fever precede the intrathoracic lesions.

The relationship between sarcoidosis and erythema nodosum has been firmly established by Löfgren and in his series of 212 cases there was a remarkably high incidence in young pregnant women. In 3,000 routine antenatal X-rays last year I found 3 cases, 2 with glandular enlargement alone and 1 with glandular enlargement and pulmonary infiltration. In 1 pulmonary lesions spread during the pregnancy and have persisted unaltered after the birth of the child.

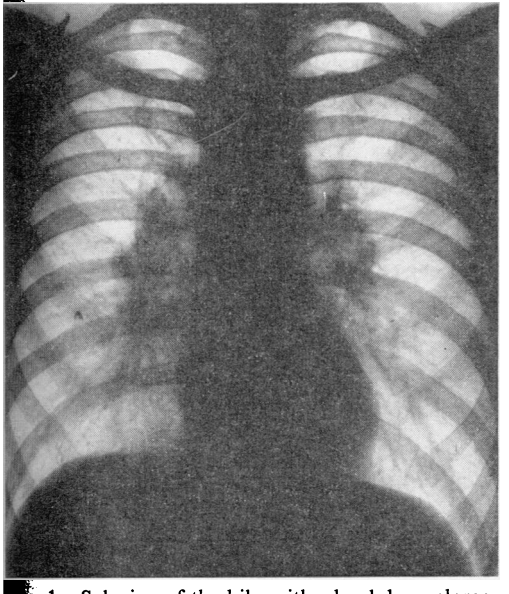

FIG. 1.—Splaying of the hila with glandular enlargement in sarcoidosis.

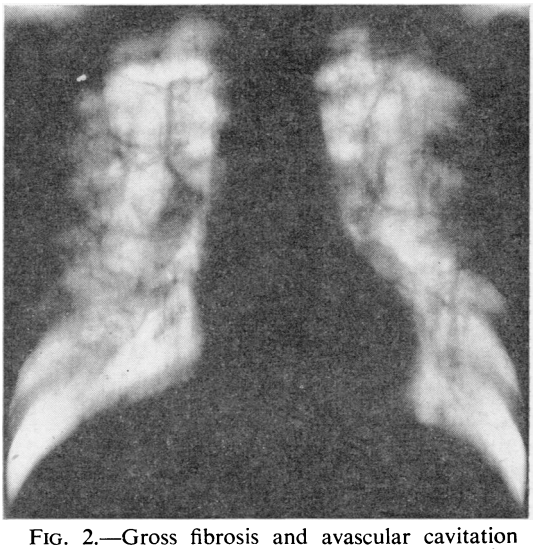

FIG. 2.—Gross fibrosis and avascular cavitation five years after bronchial gland enlargement which had been overlooked.

In 1953-54 there was an epidemic of erythema nodosum in adults in two counties of Northern Ireland and Dr. J. W. Winchester, the area radiologist, wrote to me that he had found 30 cases running the course of sarcoidosis. The region is very sparsely populated, with no large towns in it and no facilities for an extensive field survey. Dr. Winchester made what enquiries he could and writes that there were many more cases treated at home or untreated. He questioned the water supplies as a source of infection and for what it is worth he has found out that in the majority of cases the water supply was a well of the shallow type in the garden. Michael, in a recent survey of 300 cases in America, explains

the higher incidence in negroes, 22–1, not on a racial but on a geographical basis, most of them coming from the rural South and he suggests soil and water studies. There is clearly a need for an epidemiological survey in this country.

It is generally assumed that the asymptomatic cases do well but an occasional one deteriorates. Fig. 2 is that of a boy who had enlarged glands five years previously—these were overlooked and he has now gross fibrosis and avascular cavitation with dyspnœa. The need for continual observation of these cases is obvious.

The pulmonary changes usually appear after the glandular enlargement. In most cases the spread is slow over six to twelve months or even longer; exceptionally, the lungs are diffusely involved in a month or less. The pulmonary lesions as seen radiologically are of three distinct types. In the commonest the nodes are widely scattered but not clumped. They are of unequal size, some being only 1 mm. and others 3 or even 4 mm. They seem to favour the middle zones or rather the dorsal segments of the lower lobes but if antero-posterior views and tomographs are made numbers of them are found in other areas. Fig. 3 is type 1 which is often accompanied by type 2 when some interstitial change occurs and a coarse linear pattern appears along with the mottled nodules. This striation should not be interpreted as fibrosis or the precursor of fibrosis for it can disappear as completely as the other lesions. The third type is a true miliary disease with all the nodules equal in size and the whole of both lungs involved. Type 3 is indistinguishable from many other miliary diseases but I think that types 1 and 2 if accompanied by splaying of the hila are characteristic of sarcoid. It is very unusual for only one segment or one lobe to be involved and I have seen this only twice following glandular enlargement.

Occasionally, large round nodules like tuberculomata or metastases occur. These have an odd distribution which should arouse suspicion. Large lumpy deposits, similar to those in the liver and spleen, are very unusual in the lungs.

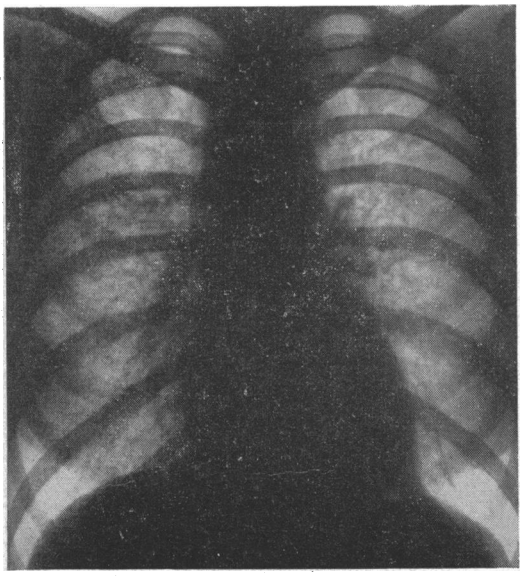

FIG. 3.—The common type of pulmonary sarcoidosis. Note the main distribution of the lesions in the middle zones (lower lobes) and the varying sizes of the nodules.

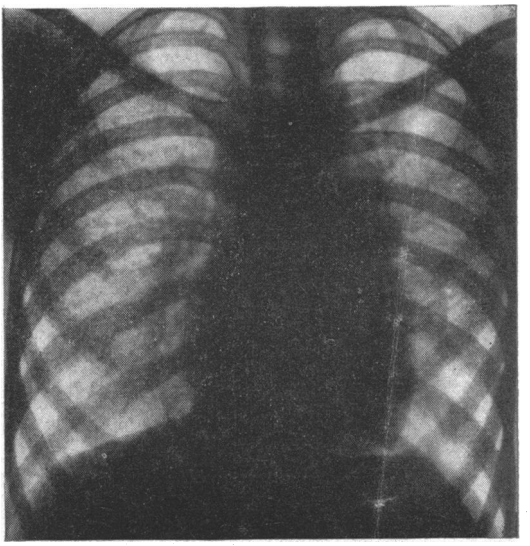

FIG. 4.—Sarcoidosis with nodular and interstitial changes. Eventual reversion to a normal picture.

If fibrosis develops, the extent to which it occurs cannot be estimated from the preceding changes. A most extensive lesion may leave patchy fibrosis limited only to a lobe or one or two separate segments. Basically, all forms of pulmonary fibrosis look alike with long fibrinous strands and traction on vessels and the mediastinal structures. Some get focal emphysema with a honeycomb lung and some develop large avascular cavities. There are two interesting features about sarcoid fibrosis: (1) There is never calcification in it which serves to distinguish it from tuberculous fibrosis, and (2) there is seldom, if ever, pleural fibrosis. Pleural fibrosis with a shaggy mediastinum and diaphragm is common to all the late pneumoconioses and many of the chronic pulmonary infections resulting in fibrosis but sarcoid seldom involves the serous membranes. Even in the acute fulminating fatal cases the serous membranes escape. The only case I have seen with pleural fibrosis was

in a patient who developed sarcoidosis after he had recovered from active pulmonary tuberculosis.

The bone changes in sarcoid of the phalanges are well known, with a widened trabecular pattern, cysts, expansion of the bone without periosteal reaction and even pathological fractures. It should be emphasized that at autopsy the phalanges have been found to be full of sarcoid with only minor changes in the trabeculation. Some put the incidence of bone lesions at 20% but I have only found it twice in just over 300 cases. It is said to be rare in other bones but on reviewing my cases I have found one in the outer end of the clavicle.

Lesions in other organs which can be radiologically investigated are rare. There are a small number recorded in the gastro-intestinal tract where a submucosal fibrosis with ulceration can simulate carcinoma and ulceration in the œsophagus and stomach and regional ileitis in the small bowel. These can only be suspected to have a sarcoid basis if the clinical findings are suspicious or if the X-ray signs of intrathoracic sarcoidosis are present.

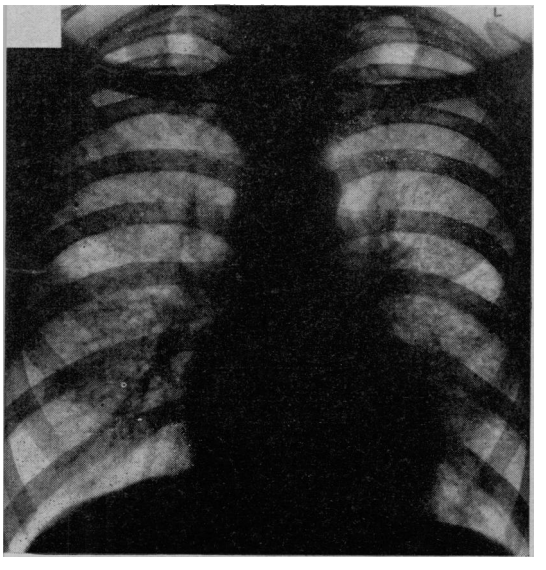

FIG. 5.—True miliary sarcoidosis.

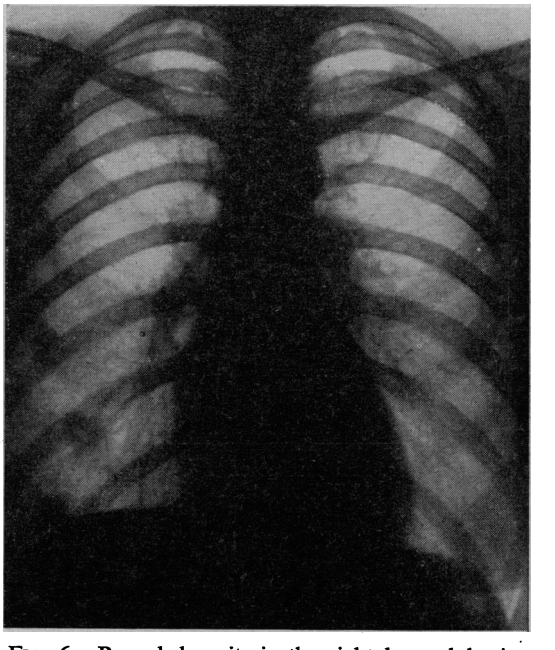

FIG. 6.—Round deposits in the right lower lobe in sarcoidosis. The glands enlarged later.

Involvement of the heart or cardiovascular system is rare but is of great importance since it is one of the immediate causes of death. There are quite a number of cases recorded in which large sarcoid deposits were found in the myocardium at autopsy. There is one recently recorded death with all the classical signs of cardiac ischæmia where autopsy showed myocardial sarcoidosis and fibrosis constricting the coronary arteries. I have seen other cases in young people with heart block and flutter who have had pulmonary manifestations of sarcoidosis. They have shown no radiological evidence of cardiac disease. I have, however, found one case in which the transverse diameter of the heart gradually enlarged up to 3 cm. and subsequently reverted to normal over a period of eighteen months. Cardiac involvement was never suspected in this patient.

There is also a steadily increasing number of cases developing malignant hypertension. The relationship is quite obscure since most of them have not been found to have renal sarcoidosis. Berger and Relman who have studied this aspect intensively think it is due to a disorder of calcium metabolism in sarcoidosis while Ricker and Clark in other cases have found a renal arteritis and periarteritis. In my series there are two cases. One, a boy of 19, was admitted to Westminster Hospital with iritis and a fever of 101° F. Two months later there were pulmonary lesions consistent with sarcoidosis. A diagnosis of sarcoidosis was established and for a brief period he recovered. There was a relapse followed by the rapid development of malignant hypertension, failure and death. Autopsy revealed sarcoid

lesions in glands and in the interventricular septum but none in the kidneys. The total duration of the illness was eighteen months. The second patient developed uveoparotitis five years ago. While this waxed and waned thoracic signs arose, first massive glandular enlargement which receded and was followed by miliary infiltration in both lungs. All these lesions have disappeared but malignant hypertension is now established and resistant to all methods of treatment. In both of these there was gradual insidious cardiac enlargement. A third case with all the clinical features of polyarteritis, fever, leucocytosis, eosinophilia, joint pains and muscular pains had the pulmonary X-ray signs of sarcoidosis and over three years made a complete clinical and radiological recovery on cortisone. Twenty-five years ago in the literature, this combination was described as a particularly fatal type of Hodgkin's disease.

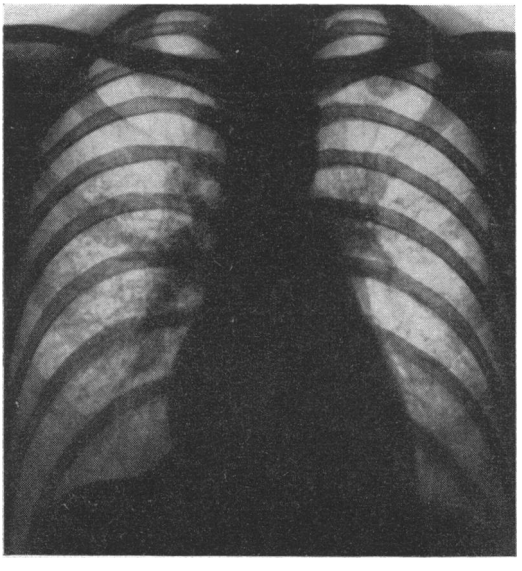

FIG. 7.—Gradual cardiac enlargement in sarcoidosis.

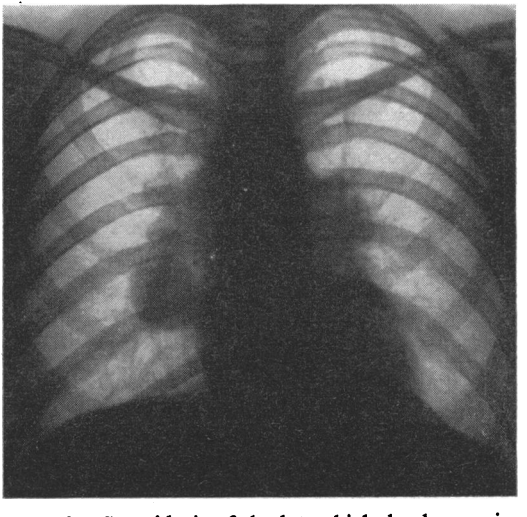

FIG. 8.—Sarcoidosis of the bronchial glands associated with a hydatid cyst.

There are many other bizarre clinical combinations. Brian Taylor and his colleagues have described carcinoma of the lung supervening on pulmonary sarcoid. I have seen one patient who had active pulmonary tuberculosis with a positive sputum, cured by chemotherapy; subsequently she developed asymptomatic pulmonary sarcoidosis and her Mantoux reaction became negative. Another girl, a nurse, who converted from Mantoux negative to positive following BCG inoculation, got systemic sarcoidosis twelve months later and reverted to Mantoux negative.

During the past twelve months the following three combinations have been seen in Westminster Hospital: sarcoid in association with mitral stenosis, sarcoid in association with ankylosing spondylitis and sarcoid in association with a hydatid cyst.

These combinations may be fortuitous or allergic but whatever the ætiology of the disease, it has a significant mortality and may be steadily on the increase.

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Mr. A. G. Cross: *Ocular Sarcoidosis*

Sarcoidosis, which is a granulomatous type of inflammation, may affect any tissue of the body and frequently it involves the eyeball and the ocular adnexa. The eye affection may be the first manifestation of the disease, and it is interesting to recall that the first description of sarcoidosis was written by Jonathan Hutchinson who was a surgeon on the Staff of Moorfields Eye Hospital.

The morbid histology of sarcoidosis is characteristic and its appearances in the eyeball differ in no way from those elsewhere in the body. One part of the eyeball may be affected or there may be generalized infiltration of the granulomatous tissue throughout the whole organ. The ocular adnexa may be affected in association with the disease of the eyeball.

Lesions in the Eyeball

(1) *Uveitis* is the most common ocular lesion of sarcoidosis. This may affect the iris and the ciliary body to give anterior uveitis (iridocyclitis), or the choroid to produce posterior uveitis (choroiditis). Some cases may show a general affection of the whole uveal tract known as panuveitis. The involvement of the uveal tract by sarcoidosis shows certain well-defined clinical characteristics. (*a*) *Anterior uveitis:* Characteristically this is a nodular iritis. Macroscopic nodules of granulation tissue are present in the iris in many cases, and are usually situated near the periphery. Sometimes the nodules may be smaller and they may not be visible to the naked eye, though they can be seen by microscopic examination of sections of the diseased iris tissue. The K.P. are typically very large, confluent, and they have a translucent ground-glass appearance. (*b*) *Posterior uveitis:* Nodular lesions are present in the choroid usually situated near to its periphery. The uveitis of sarcoidosis is frequently, but not invariably, bilateral and it may occur acutely with redness and pain of the eye, or as a more chronic condition when these symptoms are absent. It may lead to all the usual complications of uveitis, including secondary glaucoma and complicated cataract. The inflammation of the uveal tract may be accompanied by sarcoid infiltration of the parotid gland, and this is one cause of the uveo-parotid syndrome (Cross, 1953).

(2) *Conjunctivitis.*—Sarcoid follicles may be present in the conjunctival fornices, and in the bulbar conjunctiva. Crick, Hoyle, and Mather (1955) have developed the method of biopsy and microscopical examination of the conjunctiva in suspected cases of sarcoidosis, and it seems that this procedure may be useful in the routine examination of suspected but undiagnosed cases.

(3) *Sclera.*—Sarcoidosis may occur in the sclera, and it appears as a localized scleritis which may be accompanied by uveitis. Healing leaves weakened fibrous tissue and this, subsequently may lead to the formation of a staphyloma.

(4) *Cornea.*—The cornea may be involved by a spread of the pathological process from the sclera, and some patients who have suffered a severe uveitis may show the condition known as band degeneration of the cornea.

(5) *Perivasculitis retinæ.*—This condition of inflammation of the retina, particularly around the retinal vessels, which was originally described as Eales' disease, may be due to sarcoidosis. It shows no characteristic features, when due to this condition. It was, for many years, considered to be a tuberculous periphlebitis, but it appears that its ætiology is as varied as that of uveitis and that, in some cases, sarcoidosis may be the responsible agent. Perivasculitis retinæ usually manifests itself by recurrent vitreous hæmorrhage, and hæmorrhages and exudates are present in the periphery of the retina. Organization of the vitreous hæmorrhage may lead to retinitis proliferans and retinal separation. It may be accompanied by uveitis (Cross, 1955).

Lesions in the Ocular Adnexa

(1) *The eyelids.*—Sarcoid lesions may be present on any part of the skin of the body, and the eyelids may be affected. This lesion appears, in some cases, to be an isolated manifestation of the condition.

(2) *The orbit.*—Masses of sarcoid granulation tissue may be deposited in the orbit where they give the signs of an orbital tumour.

(3) *Lacrimal gland.*—Deposits of sarcoid tissue may be present in the lacrimal gland, when the secretion of tears may be reduced, and keratoconjunctivitis sicca may occur.

Diagnosis.—Ocular manifestations of sarcoidosis appear in two groups of patients. (1) *The first group*, having the eye condition as its primary lesion, appear in the Eye Hospitals and in the Ophthalmic Departments of General Hospitals. The ocular condition is diagnosed but its cause may be difficult to identify, in spite of the fact that some of the clinical manifestations of sarcoid are characteristic. Skin lesions may be removed for microscopic examination and enlarged lymphatic glands, when present, may be subjected

to biopsy. Routine X-ray examination of the lungs and, rarely, of the bones may yield confirmatory evidence that sarcoidosis exists, and a negative Mantoux reaction in an adult may be suggestive evidence. Most ophthalmologists do not undertake liver puncture. Serum protein estimation does not appear to be of great value. Some patients in this group may have their eye condition for months or even years before the development of a skin lesion or a lymphadenopathy allows the diagnosis to be made with some certainty. (2) *The second group* comprises patients with established sarcoidosis in whom a lesion appears in the eyes, and in whom it is reasonable to suppose, at least in the majority of patients, that sarcoidosis is the cause of the eye condition. Crick (1955) has reported that, in his series, ocular lesions were found in 33% of proved cases of sarcoidosis.

Treatment.—Eye lesions require general treatment as well as local treatment. Some of these cases have been treated during the past four years at the Eye Sanatorium at Swanley where, under the usual sanatorium regime, they have improved greatly. Local treatment depends upon the site of the lesion in the eyeball. Cortisone used as drops or by sub-conjunctival injection is very valuable in cases of anterior uveitis and scleritis. Some have cleared in a dramatic manner. Patients with posterior uveitis and with perivasculitis retinæ have improved as a result of a course of systemic cortisone. It is very striking that patients with ocular sarcoidosis settle much more effectively if diagnosed and fully treated at an early stage before a fibrosis has caused permanent changes in the tissues of the eye. Patients who have developed such complications as secondary glaucoma and cataract seem to be much more resistant to therapy. This is found also in other diseases of the eyes and of the rest of the body, but it is very marked in cases of ocular sarcoidosis.

Ætiology.—The cause of sarcoidosis and the mechanism of its development appear to be unknown. The relationship to tuberculosis appears definite, but it seems certain that this is not the only cause. The condition can occur at any age, but appears more common in early adult life and in later life. It occurs in all grades of severity from apparently isolated lesions to a generalized affection of the whole body.

The relationship between uveitis and sarcoidosis is of interest. The causes of uveitis are many and the mode of its causation, as of sarcoidosis, is uncertain. Some cases of uveitis, it is supposed, are the result of a sensitivity of the uveal tract to toxins produced elsewhere in the body—whether by infection of the teeth, tonsils, gut, lungs or any other organ. It is attractive to postulate that sarcoidosis develops by a similar mechanism, but that the sensitivity—instead of being restricted to the uveal tract—affects the many other tissues of the body.

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