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EDITORIALS

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SARCOIDOSIS AND LEPROSY[1,2]

Sarcoidosis has been described in one or another of its different phases as "Boeck's sarcoid," "lupus pernio" (Besnier), "benign miliary lupoid" (Boeck), and "osteitis tuberculosa multiplex cystoides" (Jungling). On the continent of Europe it is usually called "Morbus Besnier-Boeck."

The clinical resemblance between sarcoidosis and tuberculoid leprosy can be striking. Histologically also it may be difficult to differentiate the two conditions. Although nerve changes point to leprosy, several authors have stated that sometimes it is impossible, on histologic grounds, to distinguish between the two diseases. Boeck himself provided a good example of this confusion when he made the diagnosis of sarcoidosis on a histologic section of tuberculoid leprosy shown to him by J. Jadassohn. As early as 1897, Boeck ([1]) maintained that the histologic picture in his first case of sarcoid was of a special character, distinct from that of ordinary tuberculosis of the skin. He found the histologic changes of sarcoidosis so characteristic that, on several occasions, he is said to have exclaimed "a glance down the microscope is enough for the diagnosis!" Later experience has shown that this is not true. Similar histologic pictures can be produced by a number of different agents, e.g., tubercle bacilli, lepra bacilli, spirochetes, fungi, silicates, beryllium, pine pollens, and other foreign bodies. For a long time, however, the view was held that a diagnosis of sarcoidosis in a lesion could be made on the basis of the histologic structure alone.

It seems probable that the diagnosis of sarcoidosis has been made wrongly several times in the past in cases of leprosy. For this reason I have studied a few of the earlier reports of cases of sarcoidosis by well-known dermatologists. Indeed I found that the diagnosis of sarcoidosis was made wrongly in the past in cases of leprosy by

[1]Received for publication February 24, 1965.
[2]Guest editorial.

Boeck ([2,3]), Kyrle ([9]), and others. I published the results of this investigation recently ([6]). At approximately the same time Kalkoff and Holtz ([4]) reported a case of "sarcoidosis," known to them since 1957, which proved to be a case of leprosy. They wrote: "It seems possible that in Germany, among cases diagnosed as sarcoidosis, still other cases of leprosy occur." Their supposition was soon confirmed. A patient, whose case was reported at a meeting in East Germany, was re-examined at their request and found to suffer from leprosy.

That these errors in the diagnosis of sarcoidosis have occurred, and still do occur, is chiefly due to the fact that the disease is not well defined. The etiology of sarcoidosis is still controversial. There are two main concepts. Some consider sarcoidosis to be a single disease of unknown etiology, while others contend that it is a syndrome that can be caused by many agents, some known (e.g., tubercle and leprosy bacilli, silicates, beryllium, zirconium, histoplasma, and pine pollens) and others still unknown.

The supporters of the syndrome theory consider the cases of known etiology (tuberculosis, leprosy, silicates, beryllium, etc.) as belonging to the *syndrome* of sarcoidosis. They classify these cases as tuberculous sarcoidosis, sarcoid leprosy, beryllium sarcoidosis, etc. Those who consider sarcoidosis to be a single disease due to an unidentified specific agent, exclude the cases resembling sarcoidosis that are caused by a known agent. Actually, as long as a known agent can be demonstrated, and it is clearly stated to which concept of sarcoidosis one adheres, there need not be much misunderstanding. Practical difficulties arise in cases resembling sarcoidosis, that could be caused by an agent known to cause some well-known disease, but in which the agent has already been destroyed. One of the characteristics of a sarcoid reaction is that the causative agent often has disappeared.

Unless the right investigations are made at the right time, the etiologic agent is unlikely to be demonstrated in an individual case, although indirect evidence on its nature may be obtainable. Under these circumstances it is possible that such cases may be considered as being caused by an unidentified specific agent. It is very difficult, however, and often impossible to decide in an individual case that it is *not* caused by a known agent.

For instance, in tuberculoid leprosy, with histologic sarcoid structure (better called "sarcoid leprosy"), often no acid-fast bacilli can be found. If some organisms are actually present, however, they can easily be missed in routine histologic sections unless special investigations or staining methods are used. Especially when the initiating organism is small or lacks a readily stained structure, as in leprosy, tuberculosis, histoplasmosis, etc., it may be difficult to demonstrate this organism.

Silicates also can easily be missed. According to Shelley and Hurley [13] foreign doubly refractile material is not always seen in silica granulomata. If the silica was in colloidal form or had become colloidal, only micro-incineration studies will disclose its presence. Such investigations are seldom carried out. The same considerations apply in the case of beryllium granulomata.

As long as the controversy exists, it seems advisable to leave open both conceptions of the etiology of sarcoidosis. In this respect the definition proposed by Scadding [11] is acceptable. He suggests the following: sarcoidosis is a disease characterized by the presence in all affected organs of epithelioid cell tubercles without caseation, the older lesions of which tend to become converted into hyalinized fibrous tissue. Scadding purposely leaves out any comment on the etiology. I would propose adding to this definition an explanatory note on the etiology, stating that a difference of opinion exists over the question whether sarcoidosis is caused by a still unknown agent or by many agents, some known and others unknown.

I consider sarcoidosis as a reaction pattern occurring in certain individuals who possess the peculiar quality of responding under certain circumstances to one or a few of several agents with a sarcoid rection (terrain sarcoidique). One of these agents can be the leprosy bacillus, which in certain individuals evokes a sarcoid reaction. The difference between the tuberculoid and lepromatous types of leprosy is presumably determined by the constitutional reactivity of the patient. This difference of reactivity can be shown by means of the lepromin test, which usually is positive in tuberculoid leprosy and negative in lepromatous leprosy. Comparably, the Kveim test detects the peculiar reactivity of persons who are liable to develop sarcoidosis. There is a great resemblance in this respect in the nature of the lepromin and the Kveim tests, which I have discussed in several papers [5-8]. I have obtained positive Kveim tests also in patients with tuberculoid leprosy. At the Third International Conference on Sarcoidosis, held in Stockholm, September 1963, Nobechi [10] also reported positive Kveim reactions, with a suitable Kveim antigen, in leprosy. I consider tuberculoid leprosy as belonging to the syndrome of sarcoidosis. Evidence for this view was brought forward by myself [7], Scadding [12] and others at the above-mentioned conference. At this conference, devoted to sarcoidosis, there was still considerable disagreement on the definition of sarcoidosis. This is regrettable because this controversy is chiefly responsible for the "errors" in the diagnosis and it holds up the advancement of knowledge on the pathogenesis of sarcoidosis.

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[Editor's Note: *A Comprehensive Bibliography on Sarcoidosis 1878-1963, prepared by W. Mandel, J. H. Thomas, D. T. Carman, and J. P. McGovern, giving 3,592 references, has recently been distributed as U.S. Public Health Service Publication No. 1213 (Bibliography Series No. 51), under the sponsorship of the National Library of Medicine, Bethesda, Maryland, 20014. E.R.L.*]