Sarcoid tumors of the skin with report of a case of the Boeck type / by George Henry Fox and Udo J. Wile.

17.

SARCOID TUMORS OF THE SKIN WITH REPORT OF A CASE OF THE BOECK TYPE.

By George Henry Fox, M.D., New York,

and

Udo J. Wile, M.D., New York.

Reprinted from The Journal of Cutaneous Diseases for July, 1911.

REBMAN COMPANY
1123 Broadway
NEW YORK

SARCOID TUMORS OF THE SKIN WITH REPORT OF A CASE OF THE BOECK TYPE.*

GEORGE HENRY FOX, M.D., New York,
and
UDO J. WILE, M.D., New York.

UNDER the name of sarcoid tumors Kaposi,[1] in the fifth edition of his "Lehrbuch der Hautkrankheiten," provisionally grouped mycosis fungoides, lymphoderma perniciosum and sarcomatosis cutis. His object was to point out the nosological relation between sarcoma and certain granulomata of probable infectious origin. Spiegler,[2] Max Joseph,[3] Fendt[4] and others adopted the name, but restricted it to a group of neoplasmata composed of round cells and characterized by a limited growth and comparative benignancy. In 1899, Boeck[5] published in THE JOURNAL a notable article on "Multiple Benign Sarcoid of the Skin." In this he reported a hitherto undescribed dermatosis for which he claimed a characteristic and unmistakable clinical as well as histological appearance. Cases of an identical or similar nature have since been reported by observers in various countries and a rather extensive literature on the subject of this rare disease has already developed. In America the only cases reported are those of Gottheil[6] and Pollitzer.[7] Since his first communication Boeck[8,9] has reported a series of cases and elaborated on his early observations. In 1904, Darier and Roussy[10] described under the name of subcutaneous sarcoid, an affection closely resembling that of Boeck though differing from it in various anatomical and clinical features. From their cases and those reported by others and from the various discussions of the subject of sarcoid tumors, it is evident that while the clinical features of this group are sufficiently characteristic to render a diagnosis easy, there is a notable variation in the histopathology.

Great credit is due to Darier[11] for an exhaustive study of the subject of both cutaneous and subcutaneous sarcoids and of their relationship to sarcoma, lymphoderma and tuberculosis. From a careful review of the literature he arrives at the conclusion that the reported cases may be classified under four distinct types, as follows:

1. The multiple benign sarcoid of Boeck.
2. The subcutaneous sarcoid of Darier and Roussy.

*Read before the 35th Annual Meeting of the American Dermatological Association, Boston, Mass., May 25-27, 1911.

3. The nodular sarcoid of the extremities resembling erythema induratum.

4. The sarcoid of Spiegler and Fendt which, unlike the above mentioned types, shows no relationship to tuberculosis, but seems rather akin to the neoplastic lymphoderma.

The Boeck type of sarcoid may present one or more large nodules, or occur in the form of numerous papules, or one or more infiltrated plaques. It usually occurs upon the face, back, shoulders, and extensor aspects of the arms. The general health seems but little affected and subjective symptoms are slight if present. The tumors are firm and elastic, reddish or purplish in color, may show delicate peripheral telangiectases and occasionally slight scaling. Under glass pressure, according to Boeck, the nodule is seen to be composed of minute grayish-yellow foci, which appearance led him in his later writings to use the term, "miliary lupoid." The course of the disease is chronic and the lesions never ulcerate or soften. When involution occurs a central umbilication forms, with gradual flattening of the periphery until a pigmented area or slight atrophic scar remains.

In this type the histological picture is quite as characteristic as the clinical picture, although some deviations do occur from the description originally given by Boeck. The sections show the presence of sharply circumscribed, deep-seated nodules, which fill the perivascular lymph spaces and which are separated one from the other by connective tissue septa, which seem to have been pushed aside by the growing infiltration. The cell type is epithelioid, with faintly staining nuclei. At the periphery are seen lymphocytes in varying numbers, few plasma cells and scattered here and there giant cells having many nuclei, and rarely giant cells of the true Langhans type. The elastica is well preserved in the connective tissue septa, but is quite absent from the centre of the nodules and arterioles may be seen traversing the latter. There is never microscopic evidence of caseation necrosis. As typical for the disease as any one factor and perhaps the most constant finding, is the involution of the nodules under the influence of prolonged arsenical medication.

The second type, described by Darier and Roussy, is a rarer form of sarcoid, and presents painless, subcutaneous, round or oval nodules of a hazel-nut or walnut size. These occur exclusively on the trunk, particularly the upper portion. But three such cases are recorded by Darier, all occurring in adults. Histologically, this

form differs from the Boeck type in presenting an even closer resemblance to tuberculosis. The nodules are composed of epithelioid cells and lymphocytes, with numerous giant cells; the changes are less circumscribed and distinctly more infiltrating than in the Boeck form; but despite these differences the processes in the main seem very similar.

A third group, suggested by Darier, includes cases resembling very closely the erythema induratum of Bazin and to which he has given the name, "sarcoides noueuses et nodulaires des membres." The cases in this group are more numerous than in the other two; they occur principally in adult women, are chronic in course, and present, as a rule, hazel-nut-sized, reddish or purplish tumors, and infiltrations on the arms and legs, the extensor surfaces being a special site of predilection. Such cases have been described as sarcoid by Pelagatti,[12] Thibièrge and Bord[13] and by Darier himself. Many other authors have also described such cases, but have classed them as atypical examples of Bazin's disease. Remembering that true Bazin's disease may occur on the arms, body or even on the face, it is hard to separate this group of sarcoids from erythema induratum. Indeed this group further differentiates itself from the other sarcoids by occasional ulceration, and by the almost constant positive tuberculin reaction; furthermore, in isolated instances, Ravaut and Thibièrge, [14] Carle,[15] and Colcott Fox,[16] were able to demonstrate tuberculosis in inoculated animals, and Philippson[17] succeeded in demonstrating tubercle bacilli in one case.

Darier's fourth type of sarcoid tumors embraces the cases of Spiegler and Fendt with round cells and non-tuberculous structure, which might be regarded as lymphogranulomata. In this group the lesions occur as purplish-red tumors lying deep in the cutis, chronic in course, exhibiting no tendency to ulceration and affected usually by arsenical medication. They have, except for a single fatal case reported by Spiegler, the same good prognosis as the Boeck and Darier form. Histologically, they show aggregations of round cells more or less circumscribed, at times enclosed in a capsule of connective tissue. Giant cells and epithelioid cells occur in but small numbers. It is highly probable that many if not all of the so-called cured cases of sarcomatosis cutis belong to this group, which is readily distinguished from true sarcomatosis cutis by the extreme malignancy of the latter and its tendency to invade the inner organs.

That combination pictures of these several groups may occur is a point insisted upon by Darier. The following case, for example,

conforms, in its clinical aspect, identically with the diffuse form of the Boeck sarcoid type, while its histology shows variations which distinguish it somewhat from this form.

Mrs. A. F., twenty-five years of age, born in Switzerland, gave the following history. About three years ago, while in the fifth month of pregnancy, a small, firm, reddish papule was noticed on the forehead. The lesion, which was slightly pruritic, gradually increased in size until it looked like a ringworm, for which it was treated. It disappeared when the baby was born, but on cessation of nursing three months later, three similar lesions appeared upon the forehead and cheeks. They were of a reddish hue and slightly elevated. Within a year they increased in size, while new ones gradually developed until the upper portion of the face presented a mottled-red appearance, with here and there slight scaling. Two years ago the patient was pregnant again for about two weeks (as alleged by a midwife) and during this period the eruption on the face became redder. Upon the return of menstruation the face grew paler and looked much better than before the irregular menstruation. About this time a few lesions similar to those on the face, though somewhat smaller, appeared on the left chest and upper portion of the left arm. Since then new lesions have developed upon the chin and lower portions of the left cheek.

When first seen at the New York Skin and Cancer Hospital over a year ago, the patient was evidently in good general condition and had remained so throughout the course of the disease. Her digestion was excellent and she slept well. The circulation was not perfect, as shown by a chronic passive hyperæmia of the hands and a tendency to cold feet. Examination of the blood and urine showed nothing abnormal. A tuberculin test (von Pirquet) was followed by a slight reaction. The Wassermann test was negative. At this time the clinical diagnosis was that of an unusual form of erythematous lupus. At a meeting of the New York Dermatological Society in October, 1909, the patient was presented and several members thought that the eruption might be syphilitic. At a later meeting, after three months of "mixed treatment" she had shown but little if any improvement and the diagnosis of lues was forsaken and the question of lepra was considered. Lotio alba was prescribed at the hospital clinic and was followed by a slight improvement in the patient's appearance. The dull-red hue of the tumors was decidedly lessened, but there still remained a lumpy condition with some pigmentation and a marked venous congestion on exposure to cold. Most of the lesions had extended peripherally and had a depressed centre. They were discolored and varied from a small pea to a bean in size and were always more prominent at each menstrual period. The eruption persisted until a series of injections of arsenate of soda was given, when a notable improvement took place. A four per cent. solution was used, the dose being increased stead-

ily from five to twenty minims and then steadily decreased. About forty injections were made during a period of two months.

When the patient was last examined (Feb. 15, 1911), the face presented, at first glance, a somewhat uneven appearance. There were numerous elevations upon the forehead and cheeks, interspersed with atrophic pits and hollows of varying size and form. Some of these were pigmented and some of recent development were of a faint reddish hue (Fig. 1). Though these looked like cicatrices, there had never been any ulceration throughout the course of the disease. Here and there a slight induration or flattened nodule could be felt upon passing the finger over the surface, but there was a notable absence of the firm tumors which were present a year ago. Upon the deltoid region of the left arm there was a slight mottling of the skin where the eruption had practically disappeared.

Two lesions were removed from this patient; one, a bean-sized infiltrate from the left cheek, and a second, of about the same size, from the forehead. The sections were run through alcohol of increasing strength, blocked in celloidin and stained with eosin-hæmatoxylin, polychrome-methylene blue, orcein-polychrome-methylene blue and methyl-green-pyronin (Unna-Pappenheim). It must be remarked at this juncture that the two lesions did not show identical pictures. The difference lay in the presence in the cheek tumor of a fair number of giant cells, whereas in the lesion from the forehead, giant cells were of extremely rare occurrence. From this fact we conclude that the cheek lesion represented an older focus. In other respects the lesions were histologically identical and they presented the following picture:

The epithelium, except for a slight thinning in places, shows no change from the normal; the papillary layer is likewise normal. Beginning about the level of the base of the sebaceous glands and extending through the entire remainder of the derma and including the subdermal fat, are circumscribed nodules and more diffuse masses of cells, separated from each other by trabeculæ of connective tissue; indeed, some are almost seen encapsulated by connective tissue fibres (Fig. 2). In places the infiltrate surrounds blood vessels, in others it is found completely enclosing sweat coils and a large nerve trunk, seen in cross section, is also closely pressed upon by the infiltrating cells. In no instance, however, is the structure of either gland, nerve or vessel invaded by the new growth, nor is there any evidence of pressure atrophy of these structures. This fact, as characteristic and illustrating the benignity of the lesion has been noted and described by Boeck, Kren and Weidenfeld[18] and others. Under high power the predominating cell is seen to be a young connective tissue cell with a large vacuolated nucleus and a small amount of protoplasm (Fig. 3). It must be remarked here that under the low power the predominating cell appears to be a large lymphocyte; careful study, however, reveals not this cell but an unusually small type of the epithelioid

cell. Many larger epithelioid cells also occur, a number of plasma cells and a much larger number of lymphocytic elements than has been described in other cases of sarcoid. Indeed the scarcity of this cell is spoken of by Boeck and others as quite characteristic for the histopathology of the lesion. Giant cells are present in fair numbers in the lesion from the cheek, but are extremely few in the lesion from the forehead. They are of two types, the larger number seems to be due to degeneration of a few closely clumped cells, with retention of their nuclei (Fig. 3); in addition to these, however, a few Langhan giant cells do occur. An arrangement into typical tubercles, resembling tuberculosis, is seen in some of the nodules from the older lesion. A curious feature, and one described as characteristic for the lesion, was demonstrated in sections stained for connective tissue. The elastica is pushed aside and upward by the advancing nodules so that the subpapillary layer is seen as a dense mass of elastic fibres. Within the nodule itself are seen numerous fine capillaries and small vessels, and the elastic tissue representing their walls is the only remnant of this tissue remaining within the infiltrating mass. In not any single instance is there any evidence of caseation or necrosis, as in tuberculosis. Bacteria were entirely absent in all the sections examined.

To sum up briefly, we are dealing clinically with a case of extremely chronic, benign, non-ulcerating tumor formation, the lesions occurring in an otherwise healthy woman, occupying the face, neck, shoulders, and outer side of the upper arm and disclosing themselves as pea to almond-sized, red or violet colored infiltrations, which under the influence of arsenic tend to disappear, leaving as a residue brownish pigmented, slightly atrophic areas. Under glass pressure the lesions reveal themselves as composed of several minute, brownish-yellow foci. In every single detail this description tallies with the form "en plaques" of the Boeck type of sarcoid; the clinical diagnosis is thus unquestionable. The histological picture, however, does not agree in every respect with the Boeck type of sarcoid. Notably is this the fact in the presence in our case of a relatively large number of lymphocytes and an unusually small type of the predominating connnective tissue cell. The tumor under the low power does resemble a lymphogranuloma, rather than a connective tissue tumor, but careful study under greater magnification reveals the fact that this picture is only apparent and that connective tissue elements do predominate. Darier, who has seen slides from our case, regards the microscopic picture as an example of atypical sarcoid. A case not unlike our own in its histopathology is described by Urban.[19]

A word might here be interposed as to nomenclature. The great resemblance to tuberculosis in structure and the presence, macro-

scopically, of the miliary foci, has led Boeck to rename the lesion "benign miliary lupoid." While the ætiology is still in doubt, the name lupoid is open to the same objection as that of sarcoid. It has the advantage, however, of separating the disease from the older Kaposi sarcoid, which, while it includes undoubtedly under this heading the lupoid tumor, included also other neoplasmata which had nothing to do with the disease in question. The name benign miliary lupoid, therefore, is to be preferred to the term sarcoid.

The theory that the sarcoid is a tuberculide or possibly due to a low-grade infection with the tubercle bacilli, was advanced by Darier and Roussy. The theory is based on the histopathology mainly. The weight of clinical evidence it must be admitted is against rather than for this view. There are about thirty-one cases in the entire literature. In only one of these were acid-fast bacilli found (Boeck) and in this instance not in the lesion, but in the nasal secretion and it seems by no means sure that they were tubercle bacilli. Winckler,[20] in an analysis of seventeen cases, found positive evidence of tuberculosis elsewhere in the body in six cases; against this, however, is the fact that only about one-third of the entire number of the thirty-one cases reacted positively to tuberculin. In the five cases of Darier, Kreibich,[21] and Opificius,[22] although positive tuberculin tests were elicited, careful inoculation experiments failed to demonstrate the tuberculous nature of the disease. It is quite conceivable that in these cases the patients may have had tuberculous foci elsewhere in the body, entirely independent of their sarcoid condition. A single positive inoculation experiment, however, is recorded by Morawetz.[23]

On the other hand Kren and Weidenfeld[18] inoculated twelve guinea pigs from their two cases, all unsuccessfully for tuberculosis; furthermore, none of the inoculated animals reacted to tuberculin administered one or two months after inoculation. In Boeck's eight cases none reacted positively to tuberculin. A point much against the tuberculous nature of the disease is the entire absence of ulceration and necrosis in contrast to other forms of cutaneous and visceral tuberculosis, and, moreover, differing thus from the tuberculides in which necrosis is the rule. The therapeutic result of arsenic in the treatment of the disease, has, we believe, no analogy in other tuberculous processes. In view of these facts, therefore, one must conclude that although some of the sarcoid cases seem to stand in certain relation to tuberculosis, the entire group must, until a closer relationship is established, be regarded as connective tissue tumors of obscure ætiology.

The prognosis as regards life in the sarcoids is good. Only two cases, those of Mazza,[24] terminated fatally and in one of these, at least, the patient's age at the time of the disease (64 years), without doubt was the important factor in the fatal issue. An extremely interesting and inexplicable fact is the large predominence of women affected as against men; of the thirty-one cases (including our own) twenty-three were females. The analogy in this respect to Bazin's disease is suggestive.

From a purely objective standpoint, leprosy, leukæmia cutis, syphilis, lupus erythematosus nodularis, erythema induratum and lupus pernio must be differentiated when studying a case of sarcoid. The typical history and unique histopathology of sarcoid, however, together with the characteristics of the other diseases brought out in their histories, readily enable one to establish the diagnosis. Aside from the remarkable therapeutic effect of arsenic before mentioned, the X-ray, calomel, and tuberculin are reported by Darier as causing the lesions to disappear.

The pathological work in connection with this paper was undertaken in the laboratory of the Beth Israel Hospital. For the privileges of the laboratory the authors are indebted to the courtesy of Dr. E. Moschcowitz.

BIBLIOGRAPHY.

1. Kaposi. *Lehrbuch der Hautkrankheiten*, 5th ed., 1899, pp. 909-916.
2. Spiegler. *Arch. f. Dermat. u. Syph.*, 1894, xxvii, p. 163.
3. Joseph. *Arch. f. Dermat. u. Syph.*, 1898, xlvi, p. 177.
4. Fendt. *Arch. f. Dermat. u. Syph.*, 1900, liii, p. 213.
5. Boeck. *Jour. Cut. Dis.*, 1899, xvii, p. 543.
6. Gottheil. *Jour. Cutan. Dis.*, 1902, xx, p. 400.
7. Pollitzer. *Jour. Cut. Dis.*, 1908, xxvi, p. 15.
8. Boeck. Festschrift zu von Moritz Kaposi, 1900, p. 153.
9. Boeck. *Arch. f. Dermat. u. Syph.*, 1905, lxxiii, Nos. 1-3, p. 71.
10. Darier et Roussy. *Ann. de dermat. et de syph.*, 1904, v, pp. 144-347.
11. Darier. *Monatsh. f. prakt. Dermat.*, 1910, l, p. 419.
12. Pelagatti. *Gior. ital. d. mal. ven.*, 1907, xlviii, p. 425.
13. Thibièrge et Bord. *Ann. de dermat. et de syph.*, 1907, viii, p. 113.
14. Thibièrge et Ravaut. *Ann. de dermat. et de syph.*, 1899, x, p. 513.
15. Carle. *Lyon Méd.*, 1901, xcvi, p. 358.
16. Fox, Colcott. *Brit. Jour. Dermat.*, 1893, v, p. 225.
17. Philippson. *Gior. ital. d. mal. ven.*, 1898, xxxiii, p. 61.
18. Kren und Weidenfeld. *Arch. f. Dermat. u. Syph.*, 1909, xclx, p. 79.
19. Urban. *Arch. f. Dermat. u. Syph.*, 1910, ci, p. 175.
20. Winkler. *Arch. f. Dermat. u. Syph.*, 1905, lxxvii, p. 3.
21. Kreibich und Kraus. *Arch. f. Dermat. u. Syph.*, 1908, xcii, p. 173.
22. Opificius. *Arch. f. Dermat. u. Syph.*, 1907, lxxxv, p. 239.
23. Morawetz. (Ref. Pöhlmann) *Arch. f. Dermat. u. Syph.*, 1910, cii, p. 121.
24. Mazza. (Ref. Darier) *Monatsh. f. prakt. Dermat.*, 1910, l, p. 419.

DISCUSSION.

Dr. Pollitzer said that this contribution of Drs. Fox and Wile, upon the subject of sarcoid tumors of the skin, was especially welcome because it presented in such a complete manner both the clinical and histological features of a case of this kind. Of course, the last word on the subject had not been said, although we had learned a good deal about these so-called sarcoid tumors, chiefly through the studies of Darier. The histological resemblance of the growths to tuberculosis, was perhaps their most interesting feature. Dr. Pollitzer said that when he saw Dr. Fox's patient about a year or so ago, he did not get the impression that it was clinically a case of sarcoid. The common skin lesion in sarcoid was a flat or irregularly discoidal infiltration of the skin, while in this case the lesions were deeply seated, and were rounded and apparently spherical in outline. That, however, was a matter of no very great importance in view of the microscopic structure of the lesions which he had had an opportunity of inspecting.

The case, he understood, improved very rapidly under arsenic, and practically recovered. While this was the rule, one should not get the impression that arsenic might be looked upon as an absolutely specific therapeutic test in this disease, as mercury was in syphilis. While arsenic cured a large proportion of these patients, it failed in some instances. The speaker said that in the case which he presented at the International Dermatological Congress in New York a few years ago, the patient failed to improve at all under arsenic, in spite of large doses hypodermatically and long-continued treatment. That patient had since died of tuberculosis.

PLATE XXIX.—To Illustrate Article by Dr. George Henry Fox and Dr. Udo J. Wile.

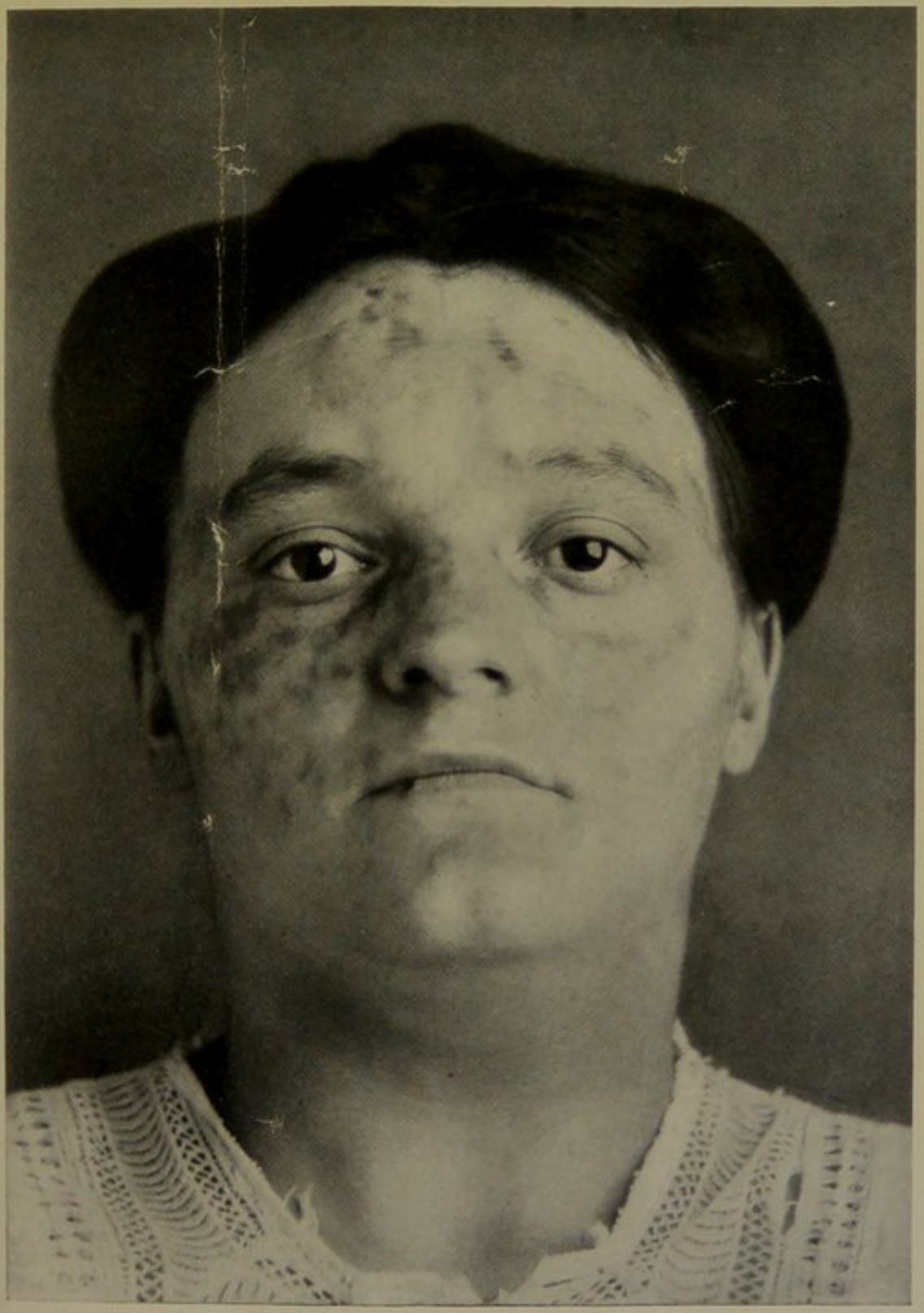

Fig. 1.

Sarcoid.

PLATE XXX.—To Illustrate Article by Dr. George Henry Fox and Dr. Udo J. Wile.

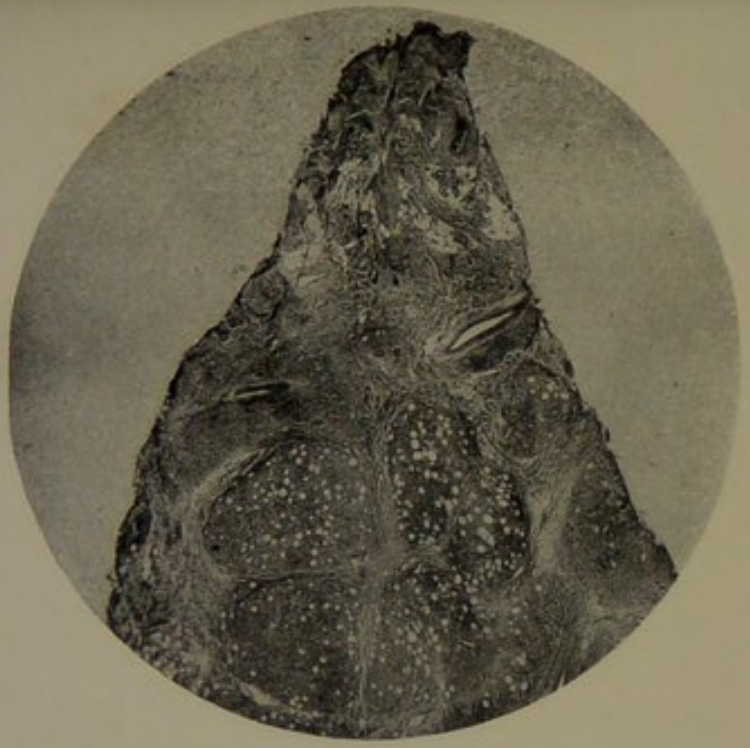

Fig. 2.

Sarcoid.

Showing sarcoid nodules separated by connective tissue septa.

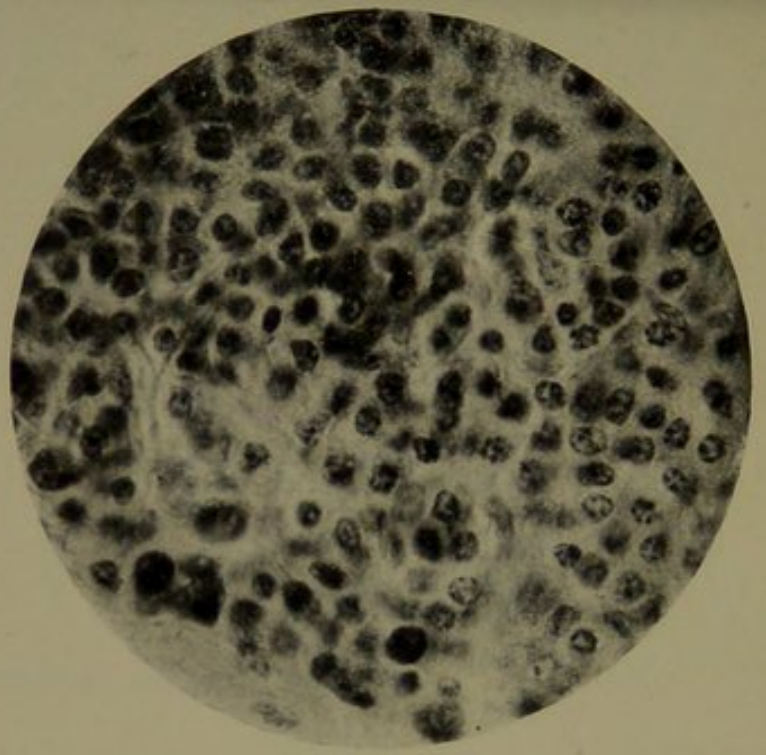

Fig. 3.

Sarcoid.

Showing small type of epithelioid cell.

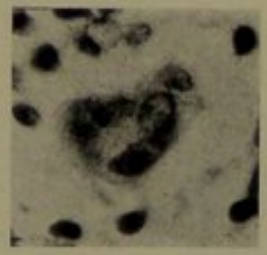

Fig. 4.

Sarcoid.

Giant cell from centre of nodule.

ROYAL COLLEGE OF SURGEONS OF ENGLAND
14 DEC 11