A Study of Early Leprous Skin Lesions.

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The initial lesion in leprosy

The problem of the initial lesion in leprosy is one which cannot even yet be considered settled. Danielssen (quoted by Hansen) states that he has seen, at the very beginning of the disease, 'a slight vaso-motor disturbance indicated by a bluish-red reticular appearance most clearly marked on changes of temperature.' Sticker (1897), having found acid-fast bacilli morphologically similar to Mycobacterium leprae in the nasal secretions of 128 cases of leprosy out of a total of 153 examined, concluded that the nasal mucosa is the seat of the primary lesion. The value of this observation has been largely discounted by the work of Mc.Donald (1903) and of Brinckerhoff & Moore (1909) in Hawaii, & more recently of Wade & Solis (1927) in the Philippines.

In Sticker's original paper there is no accurate account of the clinical condition of each member of the group of patients examined and it seems probable that his sample was unduly weighted by the inclusion of a large number of advanced nodular cases in whom positive nasal findings are, of course, common. There is, however, one type of case in which the nasal mucosa may be the seat of the primary lesion, namely, the type in which the onset of the disease is of an explosive nature and is heralded by the simultaneous appearance of multiple lesions at different parts of the body surface. This type of case is, in our experience at least, relatively uncommon and we are accordingly driven to look elsewhere for a possible seat of the primary lesion.

The frequency with which depigmented patches on the skin manifest themselves as first-noticed lesions in dark-skinned races has been noted by various workers. Rogers & Muir (1925), in an analysis of first-noticed lesions in 252 Indian patients, found that depigmented patches constituted the apparent primary lesion in 212 (84.1%). Gomez, Basa, & Nicolas (1922) in their studies in the Philippines, have also emphasised this point.

A striking example was recently seen in a family of six children who appeared at the Leprosy Outpatient Clinic, the School of Tropical Medicine & Hygiene, Calcutta. The eldest boy was an early nodular case (Muir's B^2 type) in whom abundant acid-fast bacilli could be demonstrated particularly in the lobules of the ears. All the other children showed typical depigmented patches of various sizes & shapes. Swabs from the nasal mucosae of all the children (including the eldest boy) were negative for the specific organism.

Classification of depigmented patches.

In a recent study (Henderson 1929) we found that depigmented patches can be classified roughly into five groups.

(a) The first variety - which we may describe as the peri-follicular type takes the form of a collection of discrete pin-head-like spots occurring around the mouths of the hair follicles. In addition to the loss of pigment there is a mild degree of hyper-keratosis around the mouths of the hair follicles and a distinct sensation of roughness is conveyed to the palpating finger. This peri-follicular type of lesion is, in our experience, of recent occurrence: that shewn at PLATE 1 is according to the statement of the patient, an intelligent woman, only of 15-20 days' duration.

(b) The second variety, which may be regarded as a further development of the peri-follicular type, presents itself as a more or less uniformly depigmented area of varying size (PLATE 1) The edge of the patch may shade off into apparently normal skin or it may show a zone of peri-follicular depigmentation. The latter appearance is indicative of a progressive lesion & where it occurs in a patch which has hitherto shown more or less uniform loss of pigment, it suggests a reactivation of the disease process. Broken stunted hairs can be detected throughout this type of lesion & variable degrees of keratosis are commonly present. Such patches vary considerably in duration but they are commonly of much longer standing than the peri-follicular type. Those which have existed for

years showing no tendency either to extend or to regress are essentially of the nature of scars.

(c) The third variety of depigmented patch is merely an extension of the simple flat depigmented patch described above. It takes the form of a large plaque-like lesion covering a considerable area of a limb, usually the extensor aspect, or a large portion of the trunk; well-marked keratosis, amounting in some cases to a condition similar to ichthyosis is frequently met with. Plaque-like lesions are very chronic; that shewn at PLATE 2 is of at least 20 years' duration.

(d) The zone type of patch represents a transition stage between the true depigmented patch and what we may call the erythematous lesion. The appearance is that of a flat depigmented patch bounded either wholly or partially by a raised erythematous border (PLATE 3)

(e) The mottled type of patch is not very common in untreated cases. It takes the form of a depigmented patch in which there is a return of pigment around the mouths of the hair follicles. This type of lesion is much more frequently observed in cases undergoing treatment & arises as a result of the application of counter-irritants to patch in which depigmentation was more or less uniform (PLATE 4)

Clinical attributes of the depigmented patch.

(a) Depigmentation. This varies in degree, tending naturally to be more marked in dark skinned patients; nevertheless variations in the degree of depigmentation occur in subjects whose skins are of approximately equal tint. In general, recent patches show relatively a greater degree of loss of pigment than those of longer standing. It would appear that there is a partial restoration of the pigment forming function of the skin in certain quiescent & long-standing cases even in the absence of treatment. Lesions of the palms & soles show a less striking loss of pigment than those elsewhere owing to the fact that the natural deposition of pigment in the hands & feet is less in amount than on the body surface generally. Depigmentation in leprosy is relative, not absolute,

and is very seldom comparable in degree to that seen in leucoderma. We have, however, frequently seen complete loss of pigment occurring in part of the area covered by a depigmented patch. This is, in practically all cases, traumatic in nature, the result of injury by caustics, fire/as etc., a result of loss of tactile sensibility in the part.

(b) Anaesthesia to light touch. This is a variable feature; it is very commonly present in the simple flat depigmented patch & in the plaque type of lesion; paraesthesia is, in our experiente, a more common finding that superficial anaesthesia in the peri-follicular patch. In zone lesions there is usually anaesthesia at the centre with paraesthesia at the periphery. In the relatively few examples of the mottled patch that we have been able to examine anaesthesia has been present; in these cases treatment was apparently of some value in stimulating recovery of the pigment forming function of the skin. In general, lesions of the limbs are more frequently anaesthetic/than those of the trunk. A small point, but one of some practical importance in testing for superficial anaesthesia is that the stimulus applied must be adequate to the area stimulated. We have seen cases diagnosed as 'leprosy' on the strength of supposed anaesthesia of the palms & soles but on examination we found that the anaesthesia was probably due to the application of sub-minimal stimuli.

(c) Para-and hyperkeratosis & distortion of the hair follicles have already been noted. Anhydrosis also is commonly present in depigmented patches & there may be compensatory hyperidrosis in the immediate neighbourhood. Alterations in deep sensibility & in the appreciation of painful stimuli are frequently met with & the same is true of perversions of thermal sensibility.

These clinical attributes of the depigmented patch are merely touched on in passing. For a more adequate description the works of Rogers, Muir, Wade & his colleagues and Monrad-Krohn should be consulted. The classical observations of Hansen, Looft & Danielssen are in the main as true today as they were half a century ago.

Histo-pathology of the depigmented patch.

The histological appearances vary with the type of depigmented patch examined, but the predominant feature in all such lesions of relatively recent onset is the proliferation of cells morphologically indistinguishable from endothelial cells. In the earlier type of patch this cellular proliferation is limited to certain well defined areas, viz: central portions of the papillae of the corium, along the hair follicles frequently splitting the arrector pili muscle from its attachment to the hair follicle and infiltrating the connective tissue between the fibres of the muscle, surrounding the sweat & sebaceous glands and spreading along the lines of the subpapillary & corial lymphatic plexuses. In slightly more advanced lesions one finds that the cell proliferation is not so rigidly confined to the areas mentioned above but that it now fills up the papillae of the corium, forms a mantle of varying thickness around hair follicles, sweat & sebaceous glands and invades those areas of corium immediately adjacent to the lines of the subpapillary & corial lymphatic plexuses (PLATE 5)

Another feature of interest in the depigmented type of lesion is the increase in numbers of the so-called "mast" cells. These cells are present in normal connective tissue and when stained by Ziehl Neelsen's method they appear as small irregularly oval or spindle-shaped structures containing dark red or purplish granules. In many of the depigmented patches that we have examined there was a definite increase in numbers of these cells. A point of some practical importance is the ease with which extra-cellular collections of "mast" cell granules (an artefact incidental to the preparation of the tissue for microscopic examination) may be mistaken for aberrant forms of Myco bacterium leprae. Sections stained by Levaditi's silver method from

patches in which depigmentation is a well marked clinical feature, show a diminution in the concentration of melanin pigment granules particularly in the basal cell layer of the epithelium (PLATES 6 and 7).

Microscopic study of depigmented lesion reveals surprisingly little reaction on the part of the tissues to the invasive process. Lymphocytes can be seen among the proliferation endothelial cells but fibroblasts are not a prominent feature in the early stages. In the chronic quiescent type of patch the appearances are essentially those of scar formation with fibrosis & sclerosis along the lines of previous cellular proliferation (PLATE 7 Fig.3).

The zone type of lesion which we have described as a variety of the depigmented patch appears to us to represent in the histological sense a transition stage between the true depigmented patch & the erythematous lesion. The microscopic appearances are therefore more conveniently described along with those of the erythematous lesion (vide infra).

The relationship of the specific organism of leprosy Mycobac-terium leprae, familiarly known as the leprosy bacillus, to the depigmented patch is an interesting and somewhat puzzling one. Hansen (1900) states that Looft first demonstrated the specific organism in leprous macules in 1891. Lesage & Thiercelin (1900) failed to find leprosy bacilli in the skin of an advanced case of anaesthetic leprosy either during life or at autopsy. Hopkins (1917) states that leprosy bacilli are rarely found in macules & this is the view held by the majority of workers. We think, however, that there is one point to which sufficient attention has not been paid in investigations regarding the presence or otherwise of the specific organism in the type of lesion we are considering & that is the age of the lesion or lesions in question. As an instance of this the case reported by Lesage & Thiercelin already quoted may be referred to. From their clinical description it is obvious that their case was a very advanced "maculo-anaesthetic" one in which the lesions (trophic ulcers, deformities of the extremities and the macules on the skin) were due, not to active leprosy at the time of examination but to the ravages of past disease. One is not, therefore, surprised [illegible] examination failed [illegible] of the

presence of organisms. Our own experience, however, coincides with that of other workers on this point. We have examined a large number of microscopic sections of portions of skin removed under local anaesthesia from early depigmented patches; a standardised method of staining was used but on very few occasions were organisms found and then only after prolonged search. One seems justified in concluding, therefore, that the specific organism of leprosy can only rarely be detected in depigmented patches by our present methods of staining.

This inability to find acid-fast organisms in early leprous lesions has raised the question as to whether there may be a non-acid fast form of the organism which is not demonstrable by our present tinctorial methods. Emile Weil (1905) & others have shewn that Mycobacterium leprae may lose its acid-fast properties especially in old lesions & we have been able to shew that the same thing happens on inoculating the organism into a non-susceptible animal. A heavy suspension of the human leprosy organism inoculated intradermally into a white rat shews at the end of 24 hours complete loss of acid-fast properties. By a modification of Unna's Thymen Victoria Blue-Safranin Stain the organism appears as dark blue or reddish brown rods, threads & granules, we are following up this line of work on naturally acquired human lesions; some interesting & it is hoped, fruitful results have already been obtained. If these are confirmed on repeated experimentation they will form a subject for publication but any further reference is meantime premature. In this connection also an observation of Unna (1896) calls for comment. This worker found acid-fast granules & clumps of granules thickly permeating the epithelium of the coil glands and the lymph spaces surrounding the glands. Such granules he believed to be 'bacilli altered by the secretion of the coil glands'. We have, however, been able to demonstrate similar appearances in sections of normal skin & it appears to us more probable that the acid-fast granules permeating the epithelium of the coil glands are products of the secretion of those glands altered in the process of fixing & preparing the tissue while those in the lymph spaces surrounding the glands are extruded granules of "mast" cells.

Uncertainty still exists regarding the exact nature of the cellular response to invasion of the tissues by Mycobacterium leprae; this uncertainly is, we think, very largely due to the confusing terminology which has accumulated with reference to macrophage cells, particularly those of the connective tissues. We have referred to a proliferation of endothelial or endothelial-like cells including therein the true endothelium of the blood capillaries & lymphatic channels & also the morphologically similar cells lying free in the connective tissues. These last may be denominated wandering endothelial phagocytes and Sabin (1925) in her latest work derives them definitely from the endothelial cell. These are the cells which in more advanced lesions of the nodular type become crammed with the specific organism of the disease, assume the well known 'foamy' appearance & are then usually called "lepra" cells.

Relationship between clinical picture & histo-pathological appearances.

When we come to the correlation of the pathological with the clinical findings we are on much more difficult ground largely owing to the lack of precise knowledge regarding the anatomy & physiology of the skin.

Depigmentation. The exact mode of pigment formation in the skin is still under debate. Briefly there are two views, (1) that held by English & certain American dermatologists to the effect that the formation of the normal skin pigment, melanin, takes place in the basal layer of the epithelium and (2) the view of Bruno Bloch (1917), Acton (1922) & certain of the Continental observers that pigment formation is a function of certain specialised cells, the melanoblasts, lying in the upper part of the corium, the pigment reaching the epithelium by lymphatic drift. Recent work has demonstrated that melanin or its precursor is a derivative of protein decomposition.& hence that it is closely bound up with intestinal metabolism. Disturbances in pigment formation may therefore result from abnormalities in two directions (a) abnormalities of protein metabolism, (b) interference with the transport of the pre-melanin substance or substances to the melanoblasts - or to the cells of the basal layer of the epithelium. So far as we can judge there is no ~~xxxxxxxxxx~~ interference with protein metabolism in the early stages of leprosy; the partial depigmentation of the lesions under discussion would appear to be due to the mechanical action of the proliferated endothelial cells interfering with the blood & lymph supply to particular areas & hence interfering also

with normal pigment deposition in these areas.

Sensory Nerve Disturbances. The varieties of sensory disturbances most commonly met with in the earliest stages are hyperaesthesia & paraesthesia either or both of which may be present before any lesion is definitely discernible - followed by analgesia anaesthesia & loss of thermal sensation. Presumably there is irritation of the sensory receptors in the skin followed by inhibition of these structures as the disease spreads in the skin & up the fine nerve terminals. The early onset of analgesia is a feature of interest; it might be imagined that pain being a form of "protopathic" sensibility would not be affected at such an early date as the sensations of light touch & slight temperature discrimination which are subserved by the more highly differentiated "epicritic" fibres. There are two possible explanations, (1) the nature of the pain receptor, which is believed to exist as a free axon termination without a surrounding capsule, thus differing from the fibres connected with other cutaneous sensations which commonly end in more complicated end-organs. (2) The second possible explanation is provided by the recent work of Adrian(1926). This worker has shewn that the pain receptor is characterised by a very brief duration of the discharge which results from weak stimuli; he suggests that these brief discharges may not be adequate to evoke the pain response but may serve instead for momentary sensations of contact. We may imagine, therefore, that the pain receptor, lacking the protection afforded to the other receptors by the possession of a surrounding capsule is damaged at an earlier date by the leprotic cell proliferation in the papillae of the corium: the threshold of adequate stimulation is raised & stimuli which should be interpreted as painful are interpreted as sensations of contact only.

Hair follicle & cutaneous gland disturbances. Distortion of hair follicles & absence of sweat & sebaceous secretions are explicable on purely mechanical grounds viz., the marked cellular proliferation around these structures leading to interference with their nutrition & function.

Hyperkeratosis & Parakeratosis. Irregularities in cornification are partly "central" and partly of "peripheral" origin. Where the condition is a mild one, the explanation is probably to be found locally viz; as a result of deficient blood supply to the particular area. Where, however, there

is an ichthyotic-like condition, there is probably in addition depressed thyroid function; clinical evidence of such depression can be obtained in a large number of our patients, especially during the colder periods of the year.

The erythematous type of skin lesion.

This type of lesion represents, from the histological point of view the next step in the progress of the disease. We wish to state very clearly at the outset that we are speaking in the histological sense only; every depigmented patch does not, even in the absence of treatment develop into an erythematous lesion. Not only so but the actual onset of the disease may be signalised by the appearance of erythematous lesions or even of nodules without a previous history of the existence of a depigmented patch or patches.

Naked eye and microscopic appearances.

On naked-eye examination this type of skin lesion is found to be divisible into two sub-types, (a) the uniform type in which there is a slightly raised and uniformly erythematous infiltration of the skin of varying dimensions, (Plate 8), and (b) the zone type of lesion, larger on the whole, and in which there is a flat and partly depigmented area of skin surrounded either wholly or in part by a raised and erythematous border (PLATE 3). This last subtype has already been described as a variety of the depigmented patch between which and the true erythematous lesion it represents histologically a transition stage.

Examination for the presence of the cardinal signs of leprosy viz. superficial anaesthesia and the presence of Mycobacterium leprae results in findings which are rather variable. In the raised and uniformly erythematous plaque there is commonly either a slight blunting of the sense of superficial touch or the actual presence of paraesthesia, while in the zone type of lesion absolute loss of superficial touch sensibility is the rule in the centre with blunting of sensation or the presence of paraesthesia in the raised erythematous border. The specific acid-fast bacterium can be detected in a larger proportion of instances than is the case in the simple flat depigmented patch but even in the erythematous lesion a negative finding is not uncommon, and organisms, if present, can be detected in small numbers only. Another

clinical feature of interest is the frequency with which one can detect a small thickened branch of a cutaneous nerve in association with this type of lesion (PLATE 9)

Histopathology of the erythematous lesion

There is a much greater degree of endothelial cell proliferation in this type of lesion than occurs in the depigmented patch. This cellular invasion does not however result in the complete swamping of the normal tissues of the skin such as one sees in the more advanced nodular lesions. There is definite evidence of reaction on the part of the tissues so that the endothelial cell invasion is broken up into small and more or less isolated foci by circumscribing collections of fibroblasts, young connective tissue & lymphocytes. With the notable exception that central caseation is very rarely found, the microscopic appearances closely resemble tubercle formation; this similarity is further heightened by the very frequent presence of large multinucleated cells both in this type of skin lesion and in the thickened branches of cutaneous nerves connected therewith (Plates 10 and 11).

The morphology of the large multinucleated cell is a variable one. There is no clear cut margin, the borders of the cell are prolonged into irregular strands fusing imperceptibly with the reticulum between the surrounding endothelial cells. The protoplasm of the cell is finely granular, occasionally vacuolated and faintly eosinophil. The number and position of the nuclei vary; in those cases in which they form a ring around the periphery of the cell the latter presents an appearance indistinguishable from that described as typical of the tuberculous giant cell. The nuclear elements stain blue with haematoxylin and shew a vesicular structure; a well marked mucleolus is sometimes seen. In these respects they closely resemble the nuclei of the surrounding endothelial cells. Care is necessary to avoid mistaking sections of sweat glands, capillaries and the apices of hair follicles for large multinucleated cells.

A survey of the literature revels that Klingmuller, Jodassohn and several other workers have noted 'tuberculoid' changes in leprous lesions which appear to be very similar to those described above. The designation 'tuberculoid' applied by these workers is unfortunate from several points of view for it has been seized on by certain dermatologists - working

incidentally in parts of the world in which leprosy is not endemic - as a basis of argument that the changes described are really tuberculous in nature & that they do not occur in leprosy uncomplicated by tuberculosis. Against this argument the following facts may be cited:-

1. The frequency with which this type of lesion is seen in leprosy practice in an endemic area. In the Leprosy Outpatient Clinic at the School of Tropical Medicine & Hygiene, Calcutta, examples of erythematous lesions occurring in undoubted cases of leprosy may be encountered on almost any day that the clinic meets & we have repeatedly confirmed the histological picture in portions of such lesions excised under local anaesthesia. While admitting that the incidence of tuberculosis is high in Calcutta this frequency is, we submit, more than can be accounted for by an error in random sampling.

2. Preversions of superficial sensation, an almost constant finding in erythematous skin lesions of true leprotic origin, are not, in our experience, common in tuberculous affections of the skin.

3. We are not aware that thickened branches of cutaneous nerves have been described in association with tuberculous skin lesions. Such a finding is relatively common in erythematous leprotic lesions & the histological changes in such nerves are similar in kind - including multinucleated cell formation to those occurring in the associated skin lesions.

Relationship between Clinical findings & histopathological appearances.

Here again, as in the depigmented patch, speculation bulks rather largely in our argument. Our conclusions such as they are, may, however, be worth recording:- In the early flat depigmented patch in which the organisms, as demonstrable by our present methods of staining, are very few in number, the reaction of the tissues even in extensively anaesthetic & depigmented areas, is surprisingly slight; invader & victim are living in a state of mutual quiescence. In those cases in which the disease advances to the next stage - the stage of the erythematous lesion - there is a much more determined effort on the part of the organisms to gain a foothold in the tissues. This effort is resisted actively by the tissues

as evidenced by the proliferation of fibroblasts, the formation of young connective tissue & the breaking up of the cellular invasion into more or less isolated foci. The leprotic 'follicle' is a much more vascular structure than the corresponding lesion in tuberculosis, for which reason central caseation seldom occurs. There is, however, interference with the nutrition of certain of the invading endothelial-like cells comprised in the foci & while we cannot at present bring forward any proof in support of the hypothesis, we would suggest, both from clinical & pathological considerations, that the multinucleated cell in leprosy is derived by a fusion of proliferated endothelial-like cells & that it represents in the first instance an attempted defence mechanism on the part of such cells against impending destruction. The phenomenon certainly occurs at the critical point in the course of the disease, mid-way between the mild, chronic, & almost stationary condition represented by the flat depigmented patch & the extensive virulent infiltration of the tissues manifested in the advanced nodular case.

Summary & Conclusions.

1. An attempt has been made to give a brief clinical & histological account of the findings in early leprous skin lesions. For this purpose we have considered such lesions under two main headings - the depigmented patch & the erythematous lesion. We are conscious that this division is rather artificial - as all such divisions are apt to be but we think that for descriptive purpose its adoption is justifiable. Furthermore our studies have been carried out mainly on Indian patients and it may be objected to that our findings cannot, in the nature of things, have a more general application. We do not consider that this objection can be upheld. We have had opportunities of observing early leprous skin lesions in fair-skinned Anglo-Indians, in Chinese & in a few Europeans & while certain of the clinical appearances naturally differ from those presented by the more deeply pigmented Indian, the underlying histological changes are essentially similar.

2. We have further attempted to correlate the clinical findings with the histological picture & to give an explanation for certain of the clinical phenomena described.

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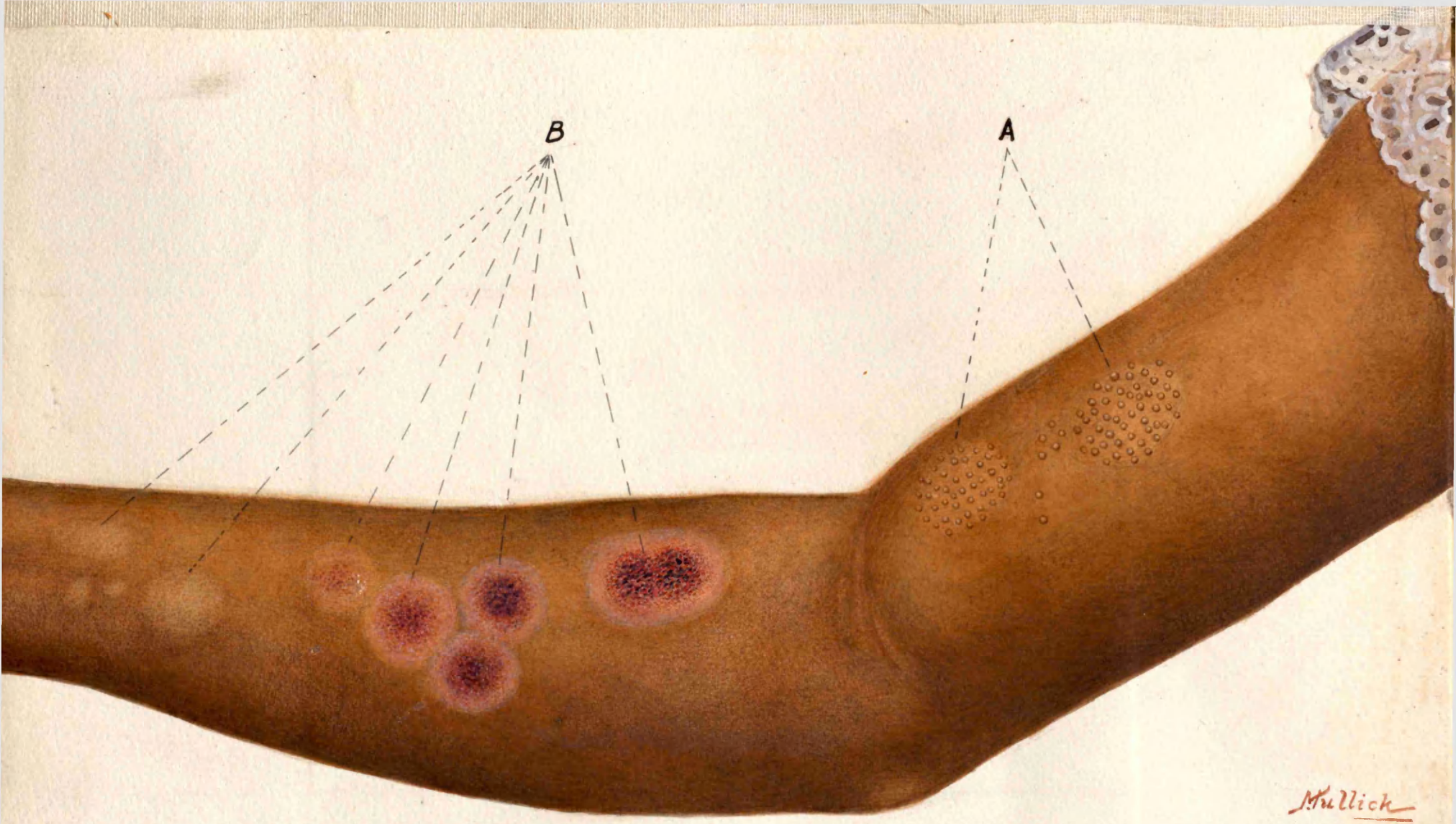

PLATE. 1.

Perifollicular lesions (A) and depigmented patches (B). The reddish blue colour on the latter is due to the application of Ung. Chrysarobin, the result of a diagnosis of "Ringworm" made elsewhere.

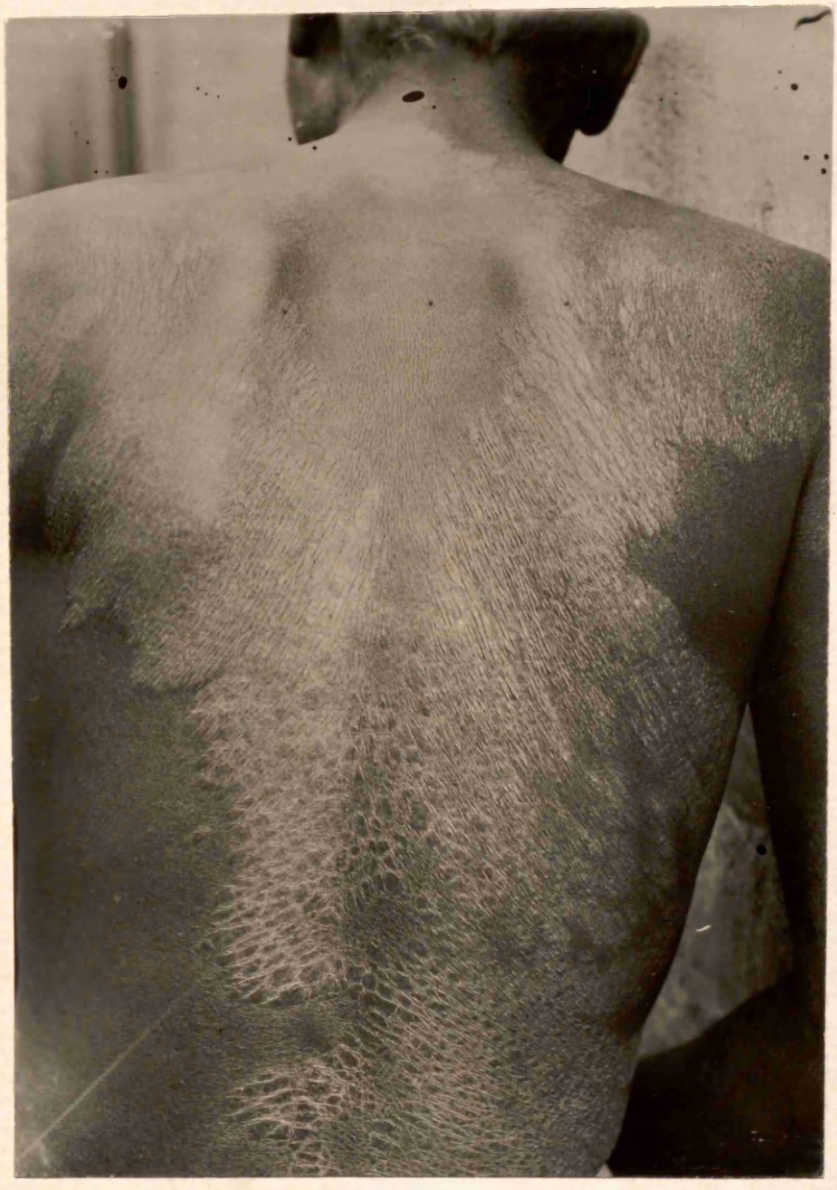

PLATE 2.

Plaque type of Depigmented patch.

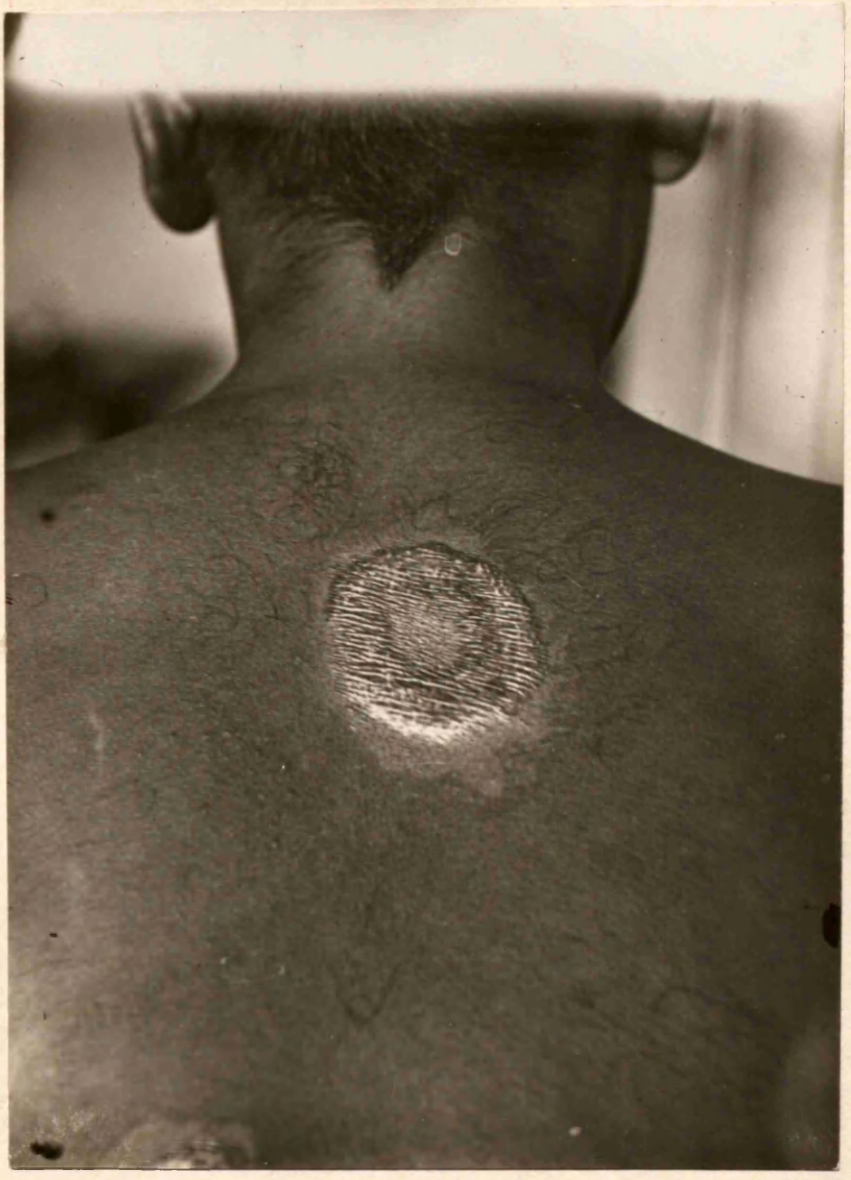

PLATE 3.

Zone type of Depigmented patch.

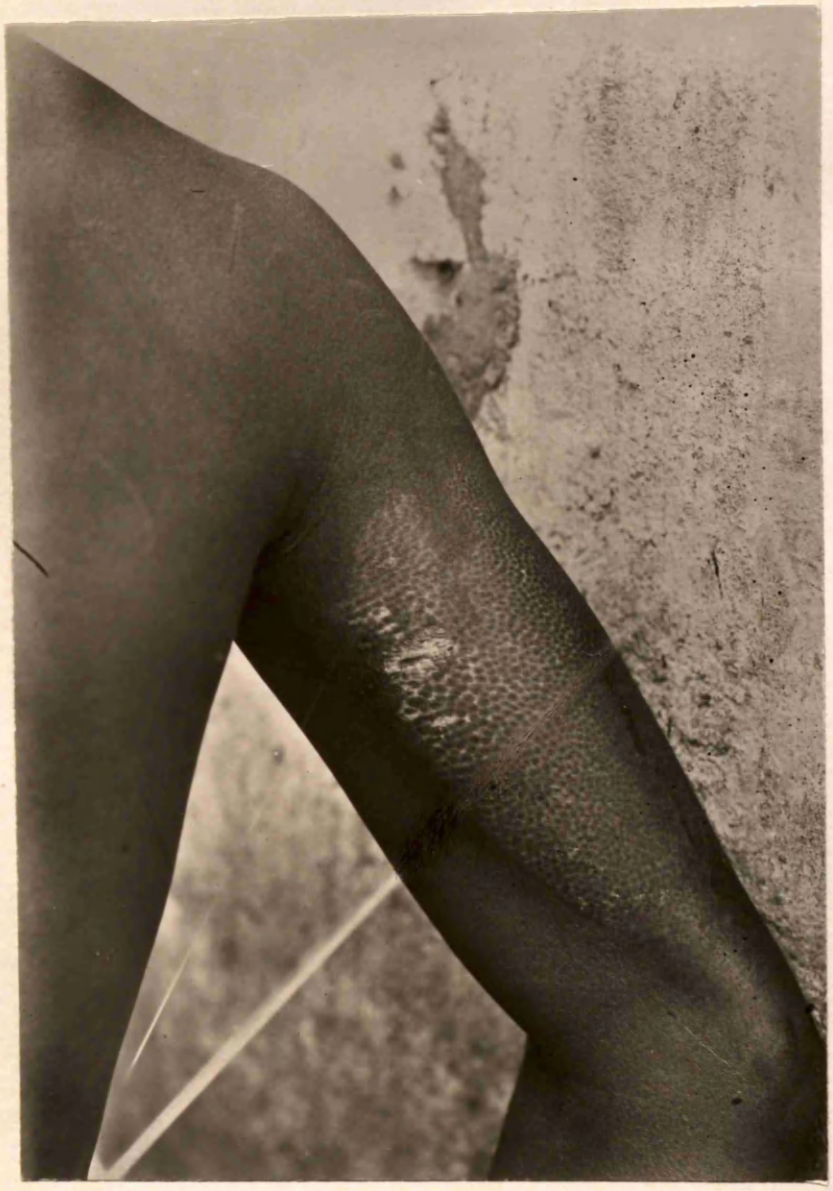

PLATE 4.

Mottled type of depigmented patch.

PLATE 5.

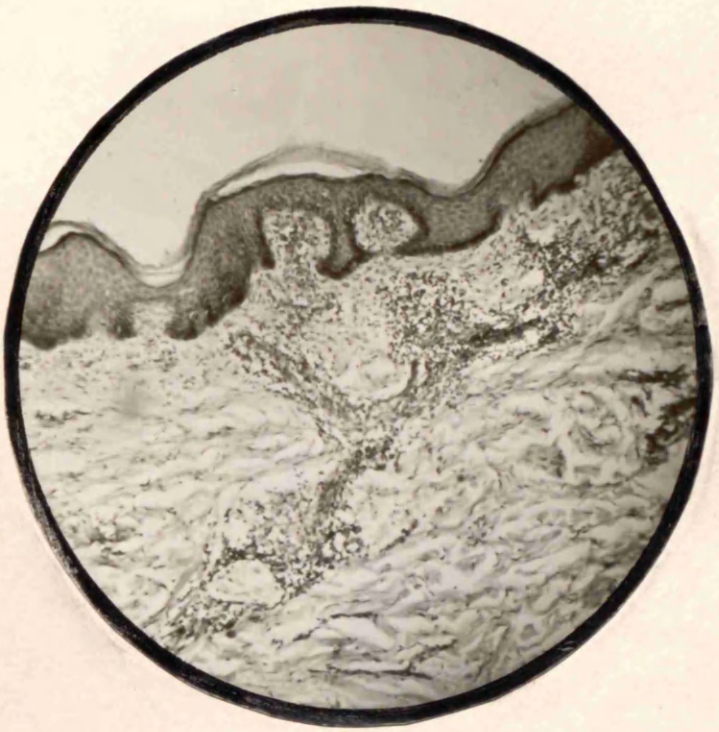

Fig. 1. Early depigmented patch showing cellular proliferation in papillae of corium and along subpapillary plexus. Haematoxylin and eosin. Zeiss eyepiece K7, obj. ⅔ inch.

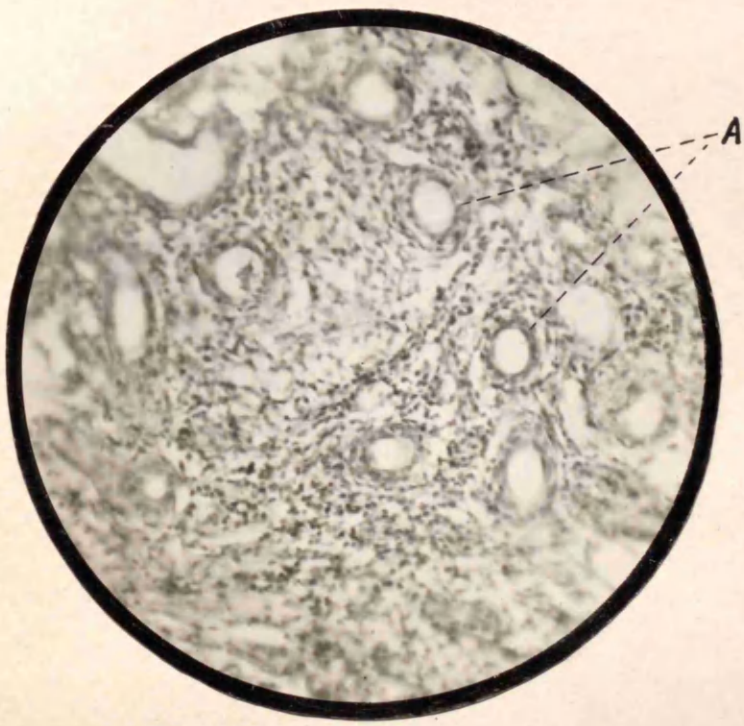

Fig. 2. Depigmented patch showing cellular proliferation around alveoli of sweat glands (A). Haematoxylin and eosin. Zeiss eyepiece K7. obj. 1/6 inch

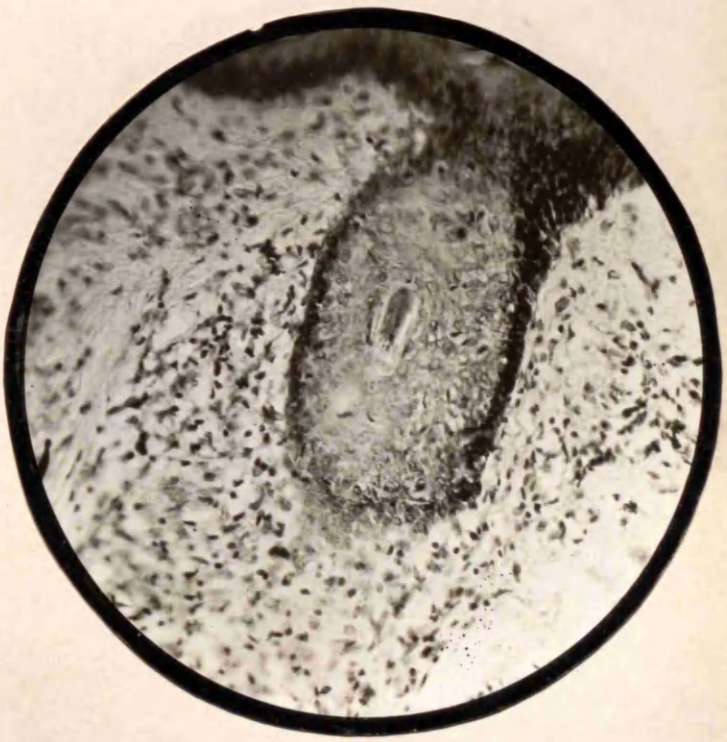

Fig. 3. Depigmented patch showing cellular proliferation around hair follicle. Haematoxylin and eosin. Zeiss eyepiece K7. obj 1/6 inch

PLATE 6.

Fig. 1. Section through healthy Indian skin stained by modified Levaditi's silver stain.

Fig, 2. Section through early depigmented patch stained by modifed Levaditi's silver stain. (Contrast with Fig 1.)

PLATE 7.

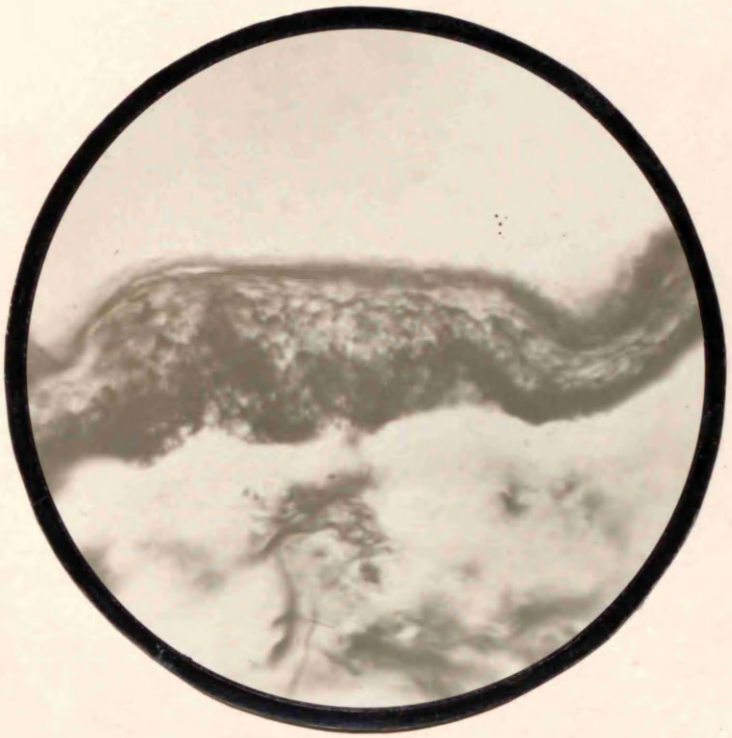

Fig. 1. Section through healthy Indian skin stained by modified Levaditi's silver stain. Zeiss eyepiece K7 obj. 1/6 inch.

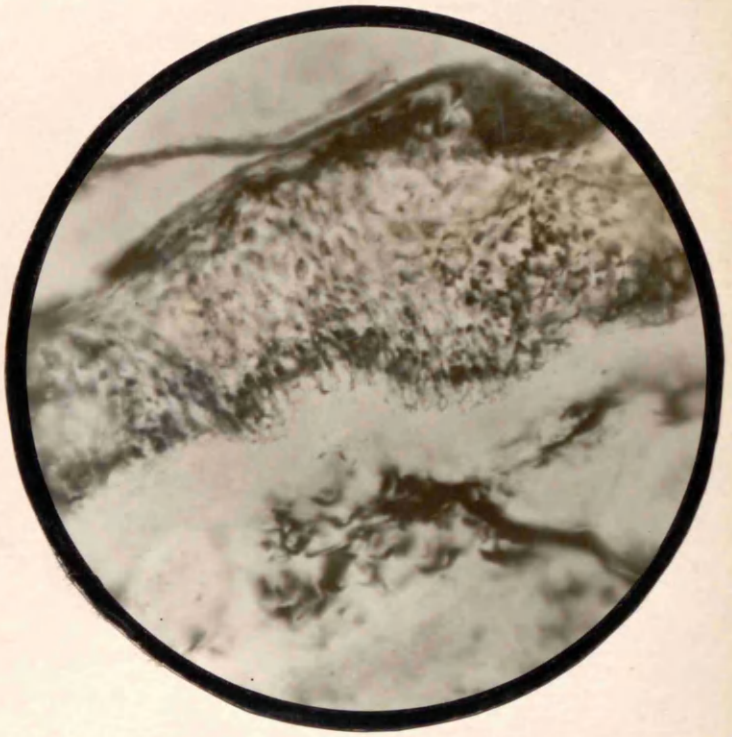

Fig. 2. Section through early depigmented patch stained by mdified Levaditi's silver stain. Zeiss eyepiece K7. obj. 1/6 inch. (Contrast with Fig. 1.)

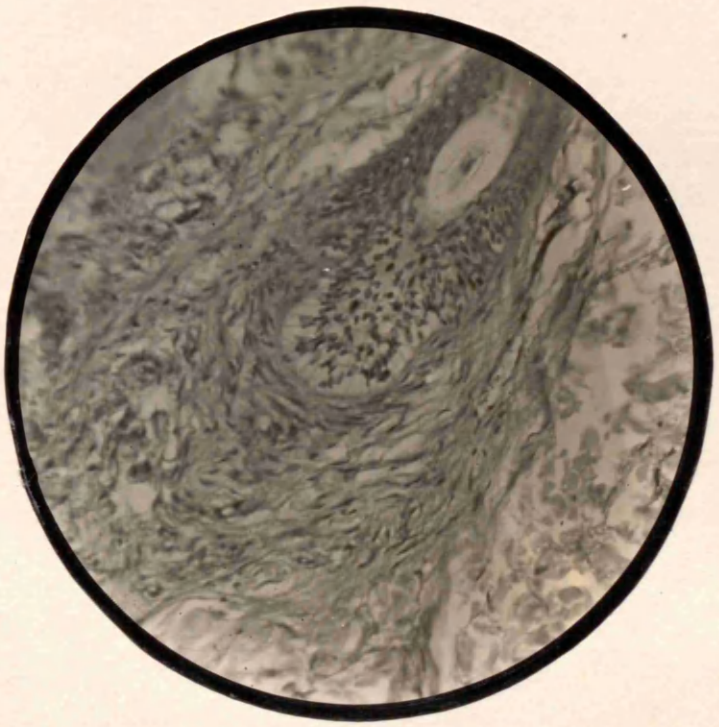

Fig. 3. Section through a chronic depigmented patch showing fibrosis around hair follicle. Stained haematoxylin and eosin. Zeiss eyepiece K7. obj. 1/6 inch. (Contrast with Plate 5 Fig. 3.)

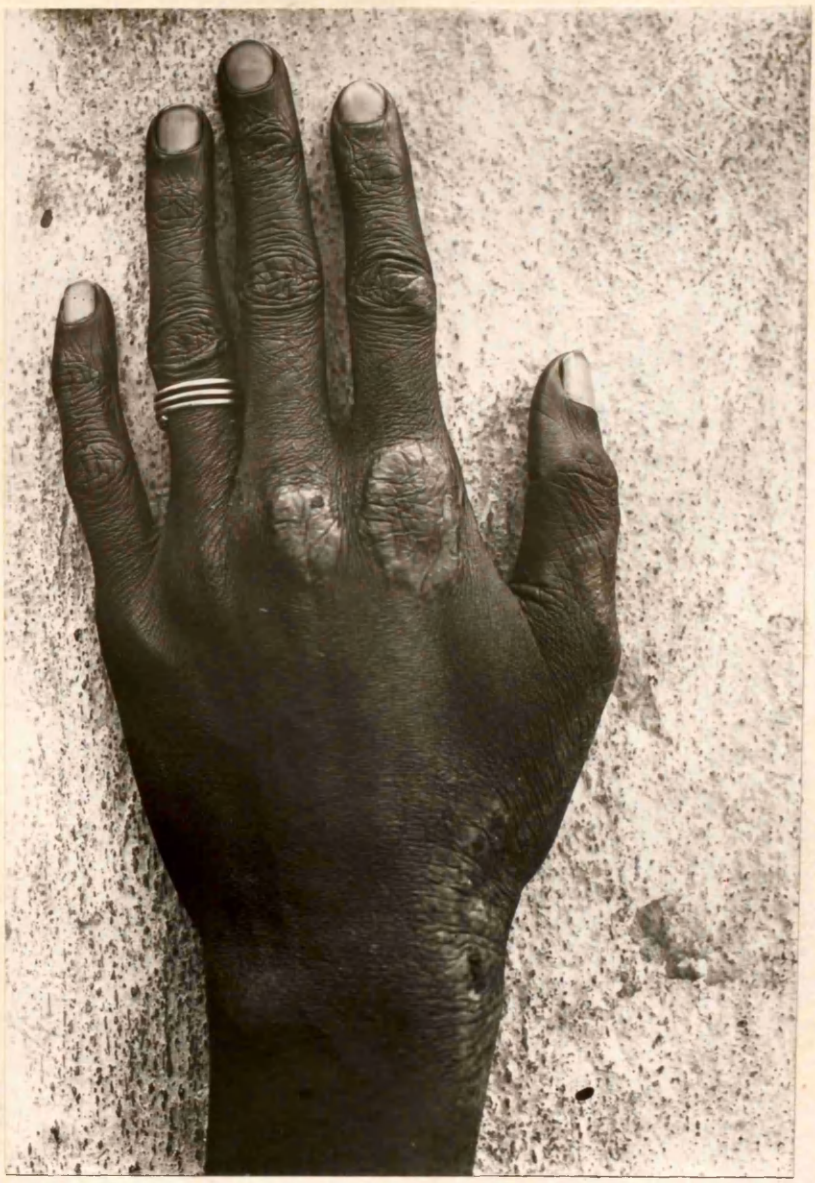

PLATE 8.

Uniformly raised erythematous lesions.

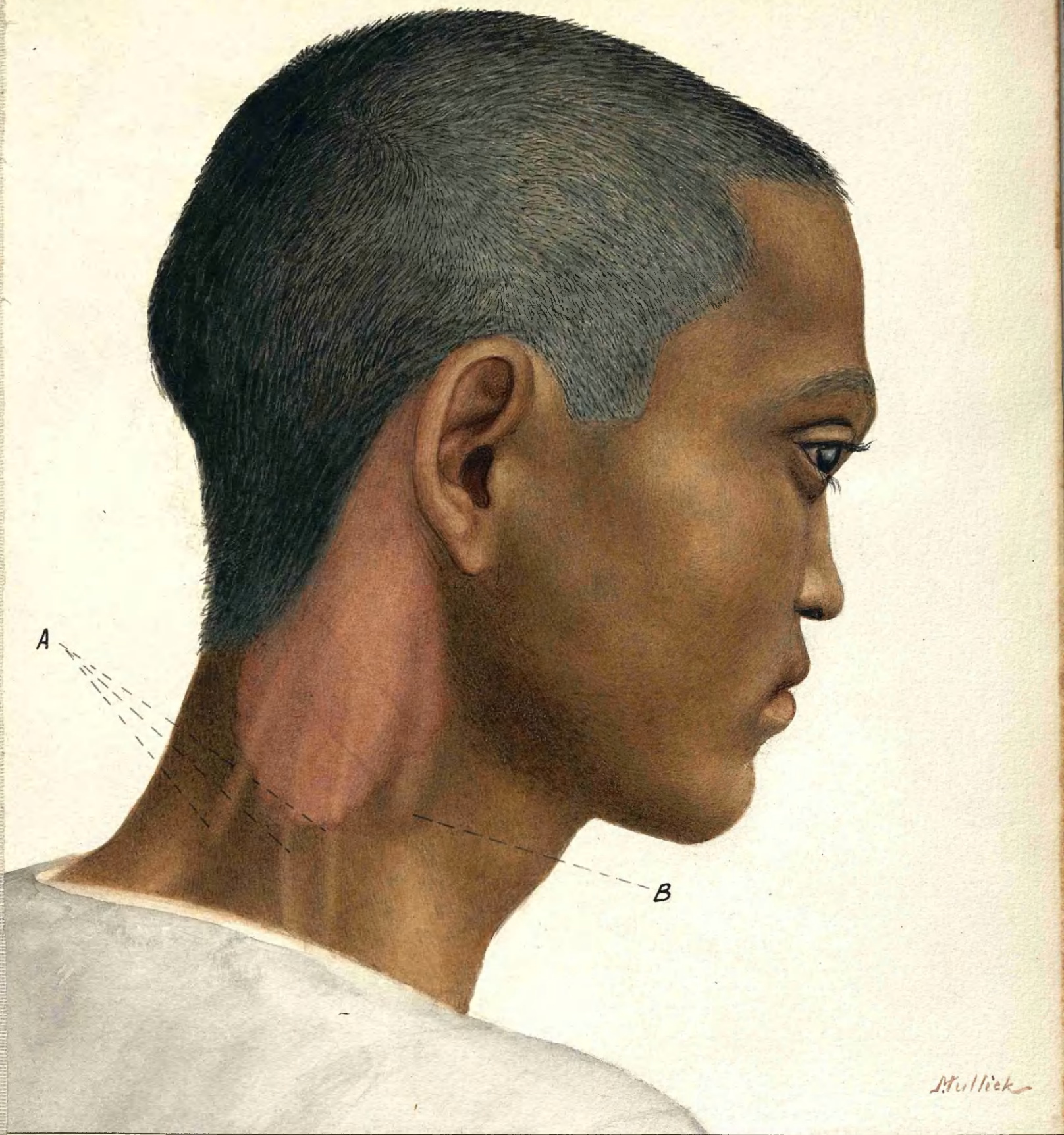

PLATE 9.

Erythematous patch with thickening of branches of cervical nerve plexus (A) and of great auricular nerve (B.)

PLATE 10.

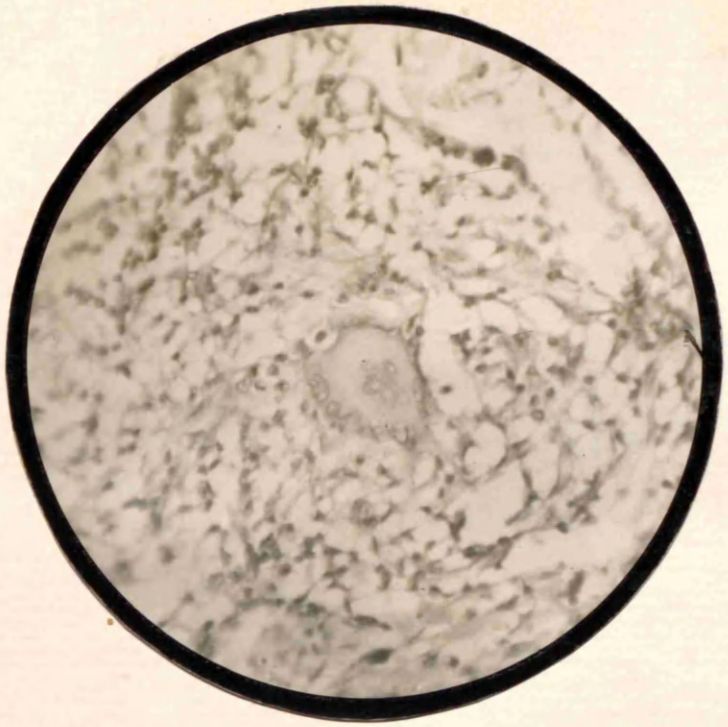

Fig. 1. Section through an erythematous lesion showing giant cell. Haematoxylin and eosin. Zeiss eyepiece K 7. obj. 1/6 inch.

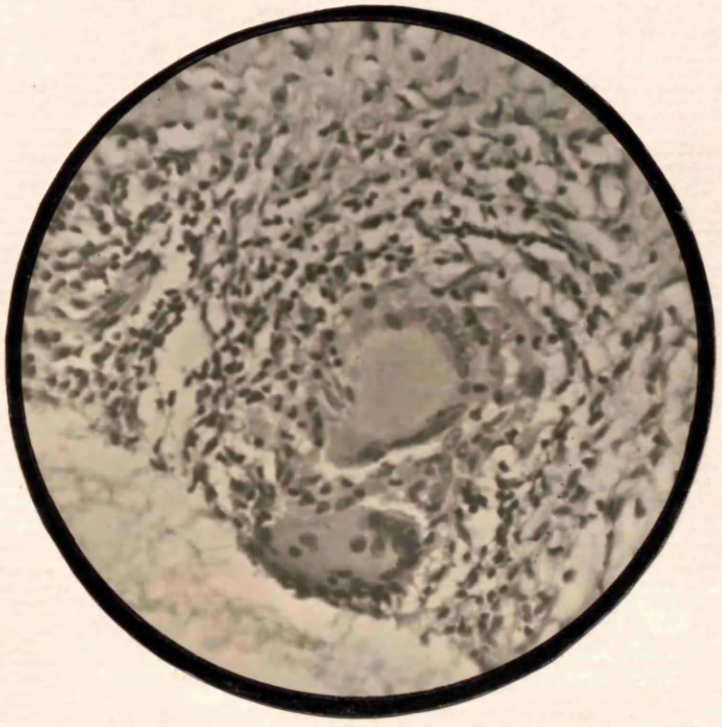

Fig. 2. Section through an erythematous lesion showing giant cells. Haematoxylin and eosin. Zeiss eyepiece K 7. obj. 1/6 inch.

PLATE 11.

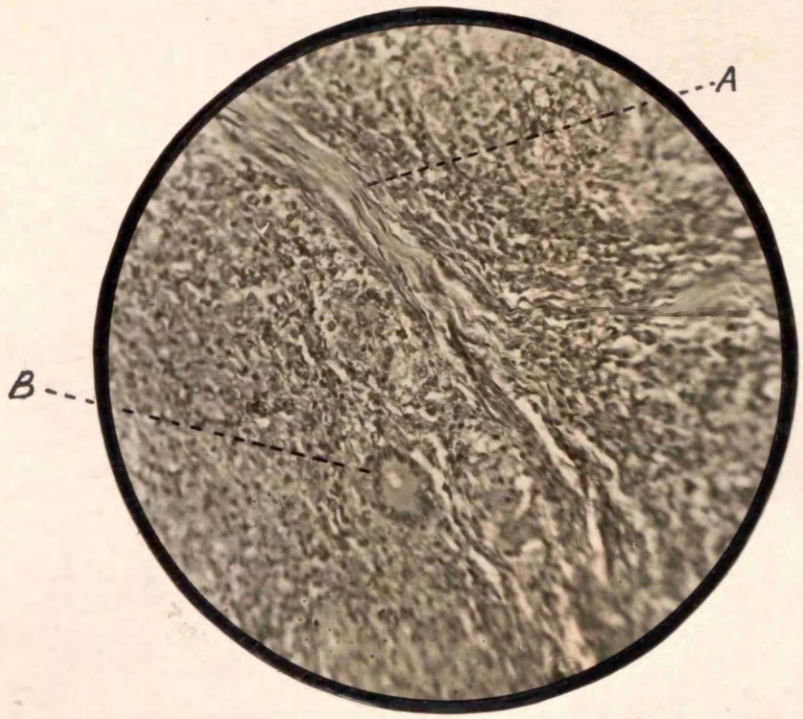

Fig. 1. Section through a thickened cutaneous nerve connected with an erythematous lesion showing considerable fibrosis (A) and giant cell formation (B). Haematoxylin and eosin. Zeiss eyepiece K 7. obj. 1/6 inch.

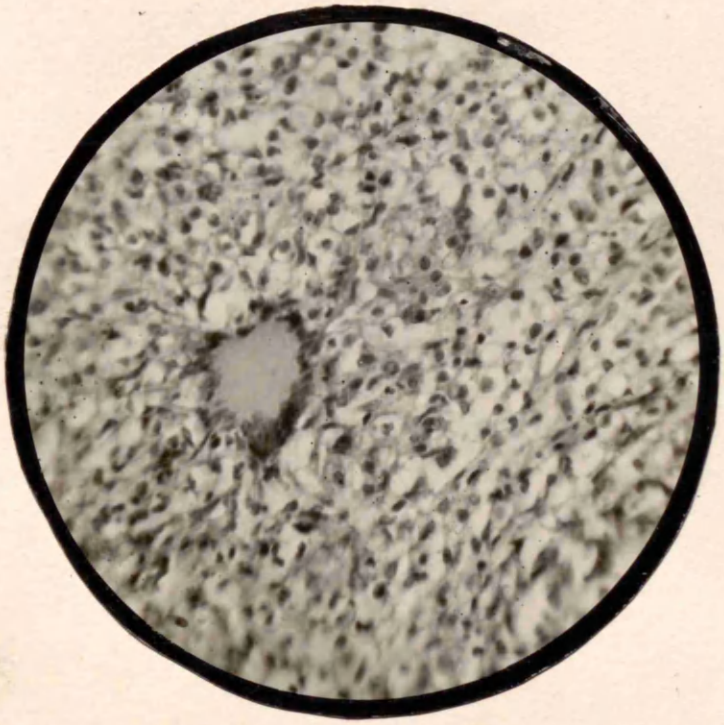

Fig. 2. Section through a tuberculous ovary showing giant cell formation. Haematoxylin and eosin. Zeiss eyepiece K 7. obj. 1/6 inch. (Contrast with Plate 10 and with Plate 11. Fig 1.)