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# *Mycobacterium leprae* in Muscle

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## INTRODUCTION

There are few references in the literature to the presence of *M. leprae* in muscle.

The earlier references (Babes, 1901; Klingmüller, 1930) describe *M. leprae* in the vicinity of, but not within, smooth muscle in the dermis —the arrectores pilorum muscle. More recently, Neves (1961) reported that bacilli and globi were frequently to be found between the fibres of these muscles. Hashizume and Shionuma (1965), in an electron microscopic study of lepromatous changes in the iris, reported finding *M. leprae* in and between the smooth muscle cells of the iris. Also in an electron microscopic study of leprosy lesions, Nishiura *et al.* (1960) reported the finding of *M. leprae* in the smooth muscle cells of blood vessels.

There are still fewer references in the literature to the presence of *M. leprae* in striated muscle. Ishihara (1959) reported 4 cases with myositis interstitialis leprosa where lepromatous infiltration was present between striated muscle fibres. Convit *et al.* (1960) reported 4 cases of lepromatous myositis in which *M. leprae* were found in lepromatous infiltrate between striated muscle fibres; they also stated that most of the bacilli stained irregularly. Some bacilli, however, were found within muscle cells, and some of these were solid staining.

## PERSONAL OBSERVATIONS

In this Centre, only a few opportunities of examining biopsies of striated muscle taken from the limbs of lepromatous patients have presented themselves during the past few years. In none of these have bacilli been seen in muscle fibres, although they were found in the neurovascular tissue and in accumulations of histiocytes between muscle bundles.

By contrast, in biopsies of skin and other tissues, bacilli have been found not only between smooth muscle cells but also within the cells themselves. Furthermore, it is noted that in patients undergoing treatment with dapsone (DDS) or other antileprosy drugs, the bacilli in the muscle cells may stain less irregularly than those in the surrounding infiltrate. Such bacilli are found both in the arrectores pilorum muscles and in muscle fibres in the walls of the larger blood vessels. Organisms in these sites might be the origin of the relapses that may occur when treatment is stopped before it should be. Thus, in biopsies obtained from patients with lepromatous or near-lepromatous leprosy, when the skin smears no longer contain bacilli, we at this Centre habitually look for bacilli (particularly solid staining forms) in smooth muscles in the skin.

In biopsies from the face, deep enough to include bundles of striated muscle, no bacilli were found in any of the muscle fibres examined, although they were present in the infiltrate and neurovascular tissue between them, and in the overlying arrectores pilorum muscles.

It would thus appear that, in man, smooth muscle, rather than striated muscle, may be a preferential site for the multiplication of *M. leprae*. It is, therefore, considered important to publish details of some unusual findings in biopsy material containing smooth muscle sent for examination to this Centre.

BIOPSY 1. Received in August, 1967, from Uganda. The specimen came from a male with active lepromatous leprosy who was receiving dapsone. Circumcision had been advised on clinical grounds. At operation, a small mass was found in the foreskin; the whole of the excised foreskin was therefore put in fixative and sent for microscopical examination. A report was requested on the nature of the mass, which was suspected to be either a lepromatous nodule or a tumour. On examination, the mass was indeed a lepromatous nodule, but it was noticed that

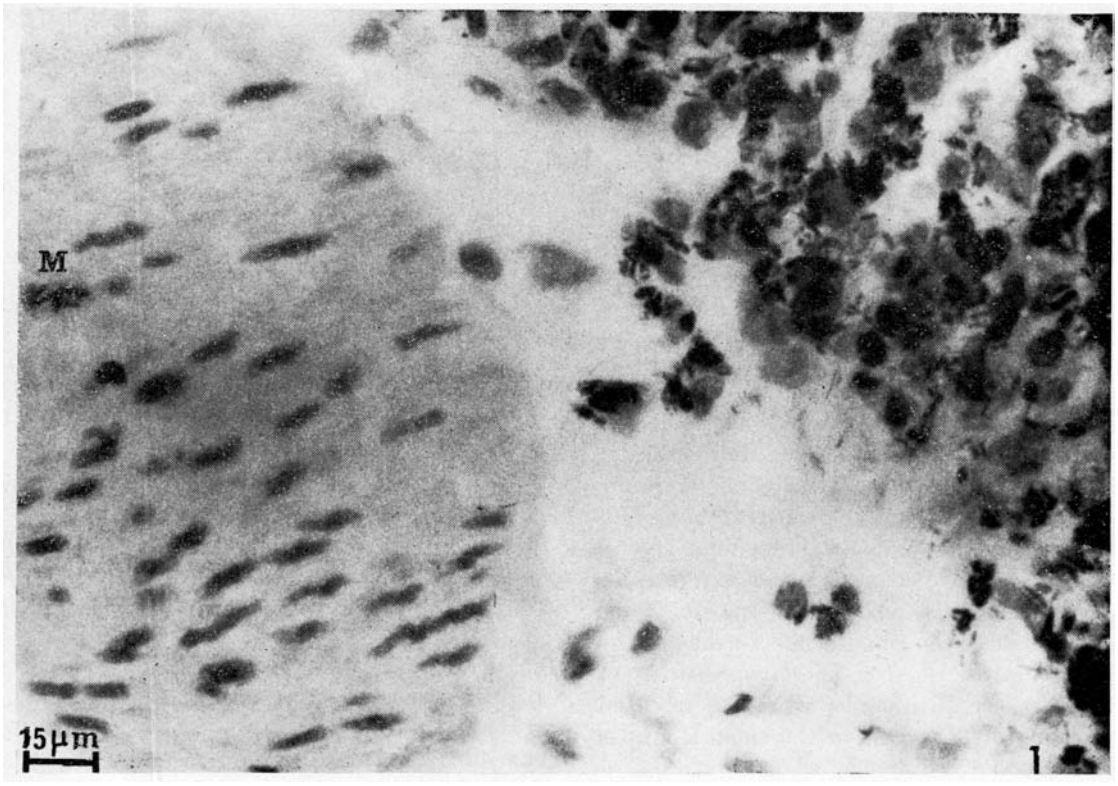


FIG. 1

Human foreskin. Two obliquely cut smooth muscle bundles. One fibre in healthy bundle, left, contains a micro-colony of solid-staining *M. leprae* (M). Neighbouring muscle bundle, right, nearly exhausted, contains irregularly staining *M. leprae*, lymphocytes and plasma cells.

the foreskin contained a large number of smooth muscle bundles. *M. leprae* were present in considerable numbers in the lepromatous infiltrate, most of them staining irregularly with carbol fuchsin. Many of the muscle bundles also contained bacilli, most of them apparently lying within muscle cells; by contrast, most of these organisms were solid staining (Fig. 1).

Because of this finding, biopsies were requested from this same patient of skin from the scrotum for the dartos muscle, from the face for facial muscle, and from the forearm to include some of the underlying striated muscle. Meanwhile the patient experienced episodes of acute reaction; the dose of dapsone had consequently first been decreased, and then stopped altogether.

The small piece of striated muscle from the forearm was found not to contain bacilli. Nevertheless, in the overlying skin and arrectores pilorum muscles numerous bacilli were present. Comparable observations were made in the biopsy containing muscles of the face, but here bacilli in the arrectores muscles were fewer than in the forearm. Numerous bacilli were present in the lepromatous infiltrate in the scrotal dermis and in the dartos muscle bundles. Some dartos muscle fibres contained micro-colonies of *M. leprae*, and others globi of solid-staining bacilli contained in vacuoles within the sarcolemma (Fig 2).

In all the specimens examined from this patient, it was noteworthy that no inflammatory cells could be seen invading or surrounding the solid-staining bacilli present within the bundles of smooth mucles. Those bundles in which the bacilli were most numerous and which were most disorganised, however, did contain in-


FIG. 2

Human scrotum. Smooth muscle fibres containing numerous solid-staining *M. leprae*. No inflammatory cells are present.

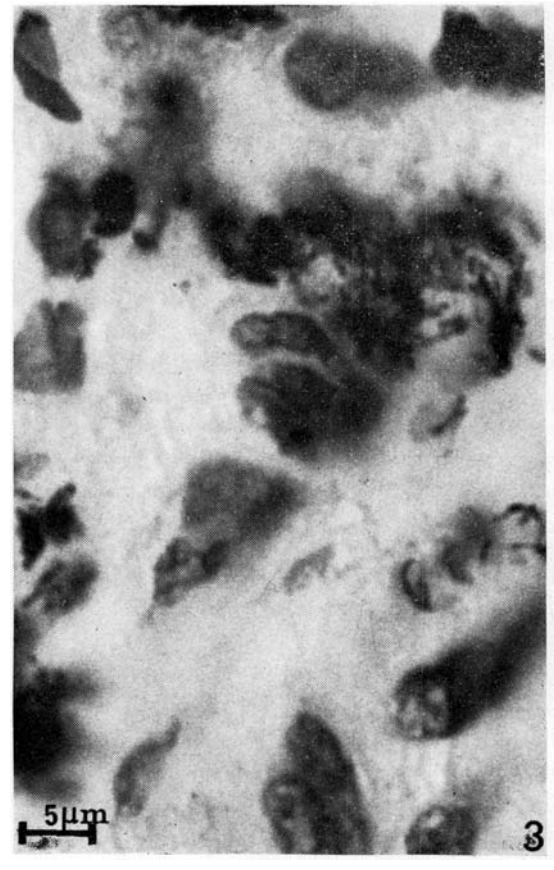


FIG. 3

Human nipple (male). Exhausted smooth muscle cells. Inflammatory cell nuclei lie close to irregularly staining *M. leprae*.

All Figs. are from sections stained with haematoxylin and cold carbol fuchsin.

flammatory cells invading and around them. Even in these bundles, solid-staining bacilli were present in the muscle fibres that were still intact.

BIOPSY 2. Received August, 1967, from Nepal. This specimen was from a male patient with active lepromatous leprosy, who had gynaecomastia. The biopsy included part of the nipple, containing bundles of smooth muscle. Solid staining bacilli were seen in those muscle fibres that were intact; muscle bundles with intact fibres containing bacilli were neither surrounded nor invaded by inflammatory cells. Exhausted muscles were full of irregularly staining bacilli, and contained inflammatory cells (Fig. 3).

## DISCUSSION

It is well known that *M. leprae* multiply in Schwann cells, where they may be temporarily immune from attack by lymphocytes and plasma cells. By contrast, when present in histiocytes, they are usually surrounded by inflammatory cells and are seen to be undergoing digestion. The observations reported above suggest that protection is also afforded to organisms in smooth muscle cells. This would appear to be an important finding, since organisms in nerves and smooth muscle are not

so likely to be sampled in smears as are those in lepromatous skin infiltrate. In some cases, falsely low values for the Bacteriological Index (B.I.) and the Morphological Index (M.I.) may well be obtained. If solid-staining organisms are confined to sites from which smears are never taken, e.g., the scrotal dartos muscle, or the small voluntary muscle fibres in the palm of the hand or the sole of the foot, then the B.I. and the M.I. from skin smears may be even more misleading. These findings may account for the relapses that occur in patients taking dapsone irreguarly, or who stop taking dapsone before they should. Under such conditions, the living organisms in smooth muscle and Schwann cells might well begin to multiply without restraint and then to spread throughout the body.

These observations suggest that leprosy workers should be on the look-out for solid-staining bacilli in smooth muscle in all patients suffering from leprosy that is towards the lepromatous end of the spectrum. Smooth muscle is abundant in the scrotum, in facial skin and in other hairy skin sites. Care should, therefore, be taken to include hair follicles in skin biopsies.

It is not yet known if *M. leprae* are able to multiply more readily in smooth than in striated muscle in man. The observations of Rees and Weddell (1968) that *M. leprae* multiply and are found in large numbers in certain striated muscle fibres of mice, immunologically crippled by thymectomy and total-body irradiation, are of interest and importance. Leprosy bacilli may well reside and multiply in striated muscle in man, but it will be difficult to obtain sufficient biopsy material to test this hypothesis. However, Rees and Weddell (1968) have already reported, in a preliminary study, that bacilli are present in striated muscle in a proportion of patients with lepromatous leprosy. Current work (Rees and Weddell, 1968, personal communication) suggests that they probably multiply only in one kind of striated muscle (B fibres) in mice, and this may well be the case in man also. Until this supposition is confirmed, skin biopsies that include smooth muscle are to be preferred to those that do not.

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FOOTNOTE

While this article was being prepared for the press, attention was directed to the paper by Job *et al.* entitled 'Leprous myositis—a histopathological study,' which appeared as Abstract No. 137 in Session XI in the Ninth International Leprosy Congress, London, 1968, and which is to be published in the *International Journal of Leprosy*, Vol. 26, No. 4 (II). In this paper, Job reports the finding of *M. leprae* in the fibres of striated muscle, but more abundantly so in the fibres of smooth muscle, particularly those which are subcutaneously placed.

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