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Innervation of Muscle in Leprosy with Special Reference to the Muscle Spindle[1,2]

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One of the characteristic features of the neuropathy of lepromatous leprosy is stated to be the preservation of the commonly elicited deep tendon reflexes (9). This suggests the integrity of the reflex arc related to the large proximal limb muscles. Interest in muscle pathology in leprosy has recently been revived following experimental (11) and human (8) evidence of parasitization of striated muscle fibers in this disease. Furthermore, there have been isolated reports of bacillary presence in relation to the muscle spindles in leprosy (5, 6). It seemed of interest, therefore, to study changes in muscle spindle innervation not only in commonly denervated but also in proximal muscles in lepromatous leprosy.

MATERIALS AND METHODS

Biopsies were obtained from the flexor carpi ulnaris (F.C.U.) muscle in eight patients, and from the biceps in six in bacillated cases of leprosy belonging to the BL and LL groups. Preoperative neurologic examination showed these muscles to be of normal power, and the biceps jerk to be retained. The specimens were obtained from as near the motor point as possible not only to visualize the extrafusal innervation, but to improve the yield of muscle spindles, a requirement of particular importance in large muscles such as the biceps. The biopsy specimens were divided into two parts, one of which was processed for routine histologic studies (using H & E and Fite-Faraco stains) and the other treated by the method of Barker and Ip (1) for demonstration of the innervation pattern in whole amounts. A total of ten spindles from the F.C.U. and four from the biceps were sufficiently well-impregnated to be available for study of the innervation pattern.

RESULTS

H & E and Fite-Faraco stains. As a reflection, perhaps, of the unimpaired clinical function none of the biopsy specimens (either from F.C.U. or biceps) showed the groupwise atrophy suggestive of denervation. Six out of eight muscles showed a moderate degree of diffuse nuclear increase. Frank inflammation, whether localized to the endomysial and perimysial spaces or invading muscle fibers, was present in three specimens from F.C.U. and one from the biceps. These sections showed frank interstitial myositis or muscle fiber phagocytosis and degeneration.

Bacilli. Acid-fast bacilli were detected not only in the infiltrating macrophages but also in the striated muscle fibers and in relation to the sarcoplasmic nuclei. Muscle spindle infiltration and bacillation were also frequent (4/8 F.C.U. and 1/6 biceps), the organisms being found in almost every spindle in the respective sections. They were present variously in the thickened and infiltrated capsule, in the intrafusal space, in the intrafusal muscle fibers and, of course, in the intrafusal nerves—in short, in all the components of the muscle spindle (Figs. 1a, 1b).

Innervation. *Extrafusal.* The following features were noted in relation to innervation of the extrafusal fibers: a) clearly defined single end plates showing the characteristic finger-like terminals. These could confidently be regarded as normal; b) enlargement, dark staining and smudginess of the fiber terminals (Fig. 2A): c) preterminal and ultraterminal thin (probably unmyelinated) sprouts ending either in fine immature terminals, or freely on the muscle fiber (Fig. 2B). Accessory end plates were only occasionally identified.

Intrafusal. Gross abnormalities were detected only infrequently in the muscle spindle preparations. It is possible, also, that

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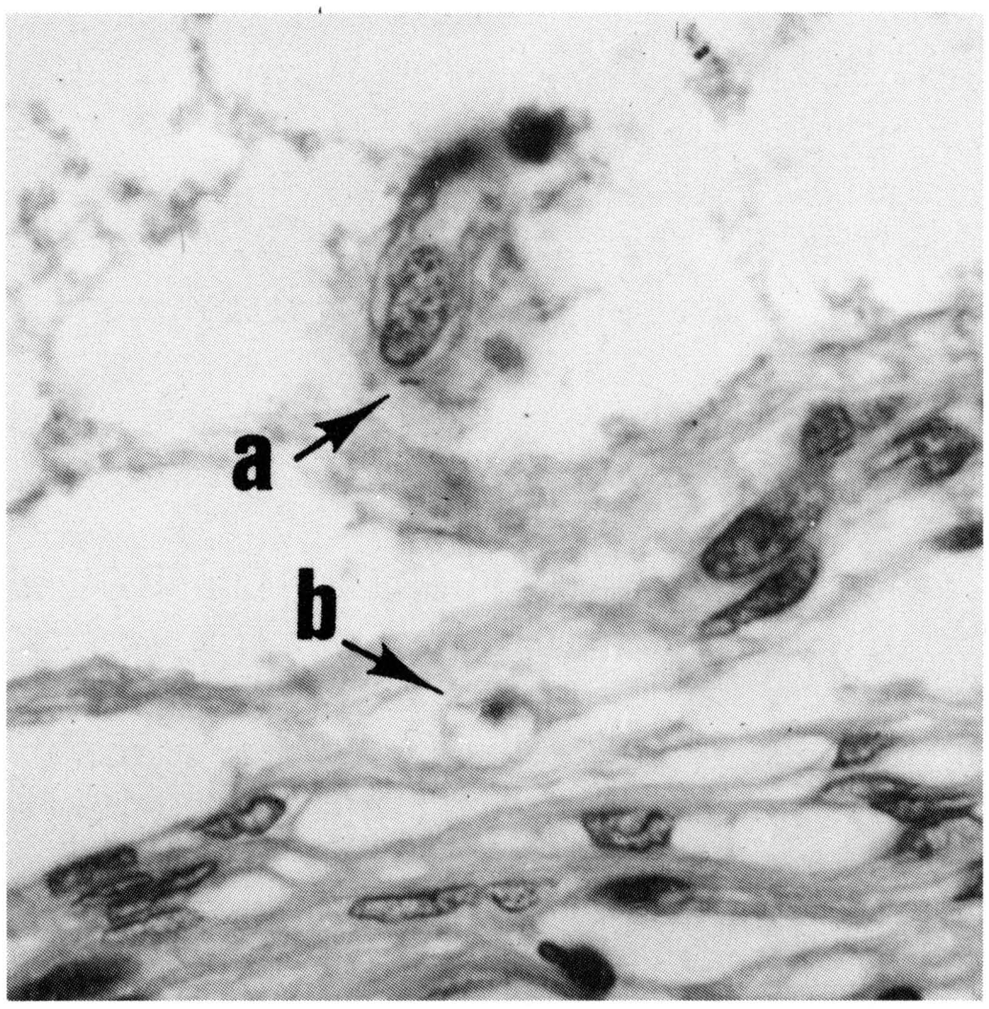

FIG. 1. Arrows indicate AFB located in macrophage in the intrafusal space (a), and in the capsular cells of a muscle spindle and adjacent fusal nerve bundle (b). Fite-Faraco, ×230.

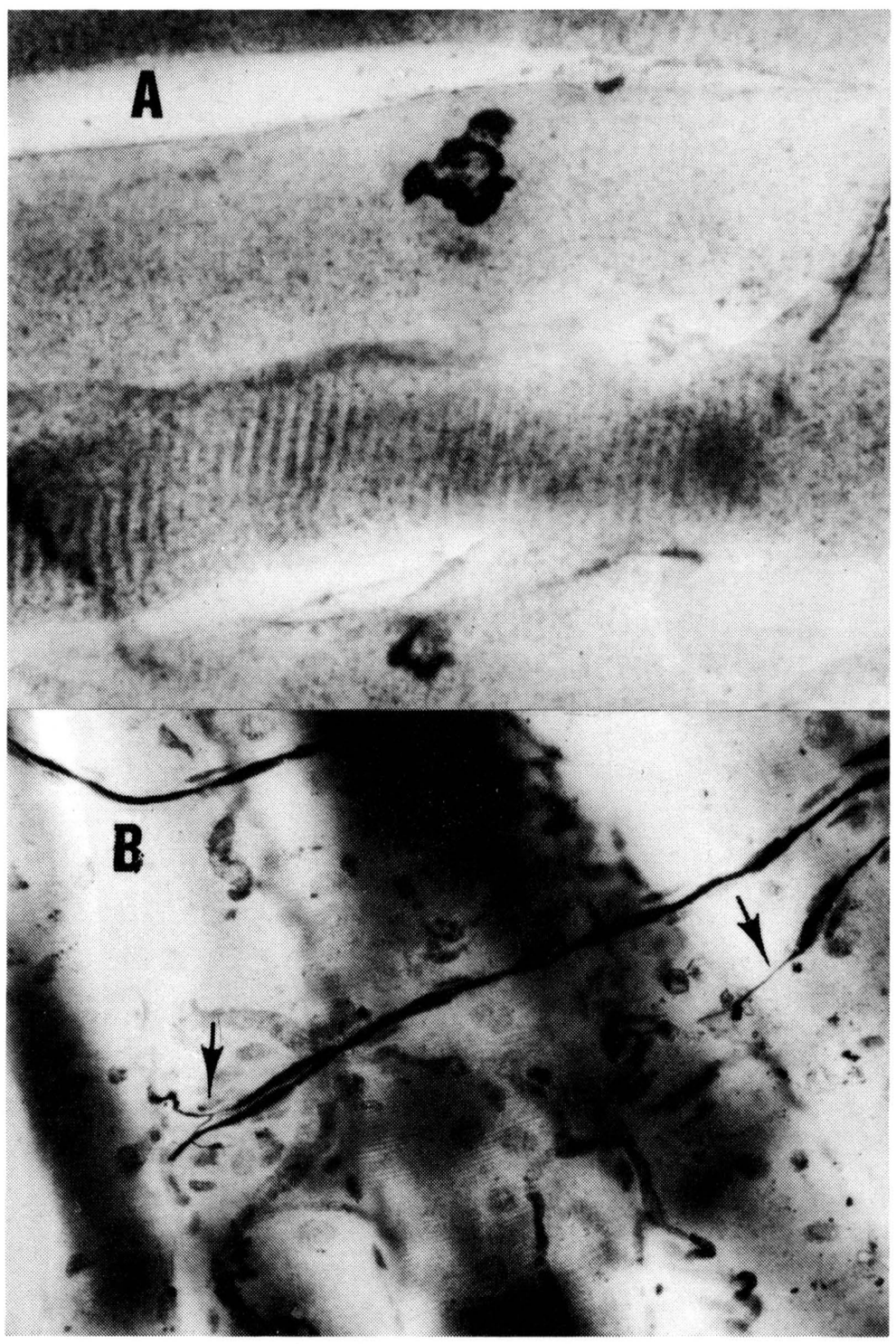

FIG. 2. Abnormalities of extrafusal innervation (A) smudginess of outline and loss of normal finger-like projections in end plate; (B) preterminal and ultraterminal probably unmyelinated sprouts ending freely on muscle fiber (right arrow) or in immature end plates (left arrow). Method of Barker and Ip, 1963, ×92.

mild degrees of change may be overlooked in a structure which even normally has a complicated innervation pattern. Features which were considered suspicious were: a) increased tortuosity and beading of the sensory fibers at the equatorial arborization (Fig. 3A); b) beading of the motor fibers, particularly striking terminally (Fig. 3B), c) enlargement of the motor end plates best seen in those of the extrafusal type;

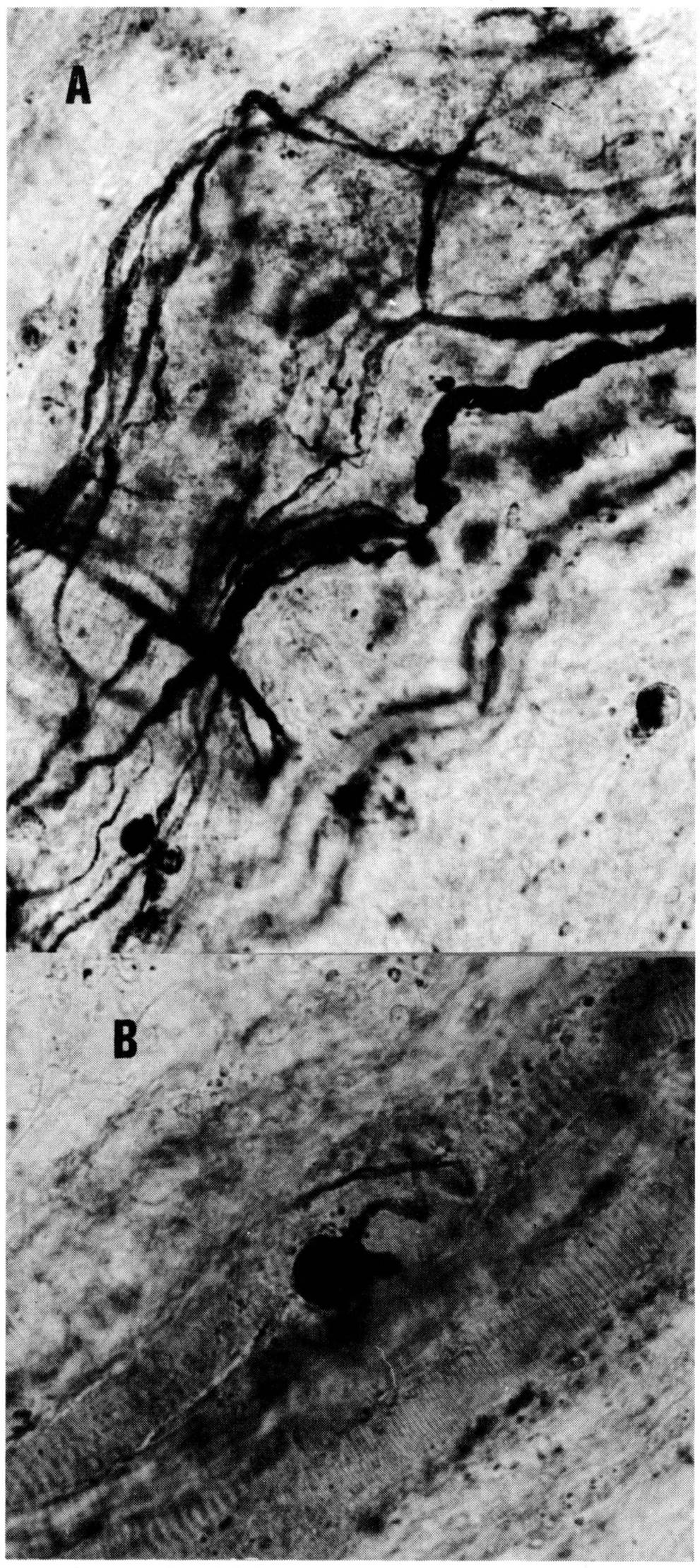

FIG. 3. Abnormalities of intrafusal innervation (A) early changes at equator in the form of thickening and irregularity of primary sensory fiber, (B) fusimotor fiber ending in a bulb. Method of Barker and Ip, 1963, ×184.

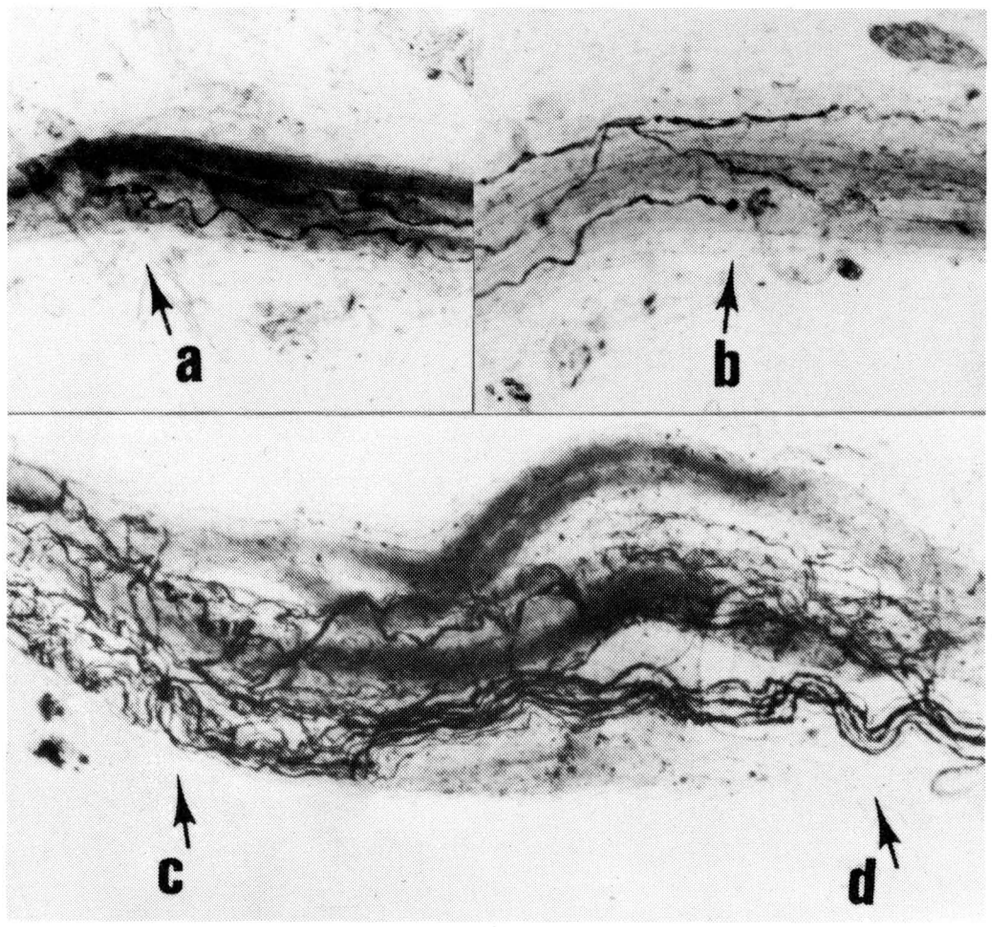

FIG. 4. Composite microphotograph of teased abnormal spindle from biceps muscle in a case of lepromatous leprosy, showing (a) and (b). Two different types of fusimotor endings on gamma fibers near pole; (c) grossly complicated tangles of sensory innervation at para-equatorial region; (d) equator of spindle recognized by absence of intrafusal muscle striations, showing afferent nerve bundle emerging from sensory tangle. Method of Barker and Ip, 1963, ×46.

d) gross disorganization and increased complication of the large (? sensory) arborizing fibers at and adjacent to the equator. This was very striking in one spindle isolated from the biceps muscle (Fig. 4).

DISCUSSION

Although the paraffin sections did not reveal any overt neurogenic muscle atrophy, the extrafusal innervation pattern showed several deviations from "normal." According to the criteria of Coers and Woolf ([3]), sprouting and accessory end plates are unequivocal evidence of a pathologic denervation-regeneration process. The detailed studies of Barker and Ip ([2]) on normal young animals, however, led them to the conclusion that these features were indicative of a normally and continuously occurring degeneration-regeneration cycle in motor nerves, similar to that described by Weddell *et al* ([10]) in the cutaneous nerves of normal individuals of all ages. In view of this, we could regard only dark staining and smudginess of the motor terminals without sprouting as abnormal, particularly in the absence of data regarding the normal proportion of sprouted and free terminals in muscles in this age group. This conclusion was strengthened by the fact that it was seen much more frequently in the commonly denervated F.C.U. muscle, as compared to the biceps.

As far as the muscle spindle is concerned, the intravital stained preparations studied by Dastur ([4]) showed no gross abnormalities of innervation. This surprising observation can probably be explained by poor penetration of the staining material (methylene blue), particularly because biopsies in that study were obtained from grossly denervated muscles as well as less affected ones. Abnormalities of spindle innervation were definitely present in the present series, and as Figure 4 shows, were occasionally striking. The excessive coiling, tortuosity and beading of motor and sensory fibers, compare with the features reported in other neuropathies ([7]) and indicate that these are in no way peculiar to leprosy. Further studies should yield information on the evolution of changes in the pattern of innervation with advancing neuropathy.

This study further suggests that though abnormalities in innervation of the muscle spindles are to be expected in a commonly denervated muscle such as the F.C.U., similar observations are the exception rather than the rule in a muscle such as the biceps. Even the strikingly abnormal spindle from the biceps illustrated in Figure 4 must be an isolated phenomenon not compromising the stretch reflex.

The finding of bacilli in all components of the muscle spindle, with the frequency seen in this study, emphasizes again that striated muscles are more significantly involved in lepromatous leprosy than is evident by clinical examination alone.

SUMMARY

The pattern of extrafusal and intrafusal innervation was studied in muscle biopsies from the flexor carpi ulnaris and biceps brachii muscles, which were clinically unimpaired. Smudginess and enlargement of the motor end plates were the most definitely abnormal feature of the extrafusal innervation pattern; the intrafusal fibers, on the other hand, were either unremarkable or showed increased tortuosity, beading and in more extreme cases a grossly complicated intertwining pattern. Bacilli were frequently

found in the spindles, no component being spared. The study emphasizes the significant involvement of striated muscle in leprosy, a fact not always revealed by clinical examination alone.

RESUMEN

Se estudió el modelo de inervación extrafusal e intrafusal en biopsias de los músculos "flexor carpi ulnaris" y "biceps brachii," que no tenían compromiso clínico. Los bordes borrosos y el engrosamiento de las placas terminales motoras fueron las características más anormales del patrón de inervación extrafusal; las fibras intrafusales, por otra parte, no tuvieron nada de extraordinario o mostraron una tortuosidad aumentada, granulación y, en los casos más extremos, un patrón entrecruzado extremadamente complejo. Con frecuencia se encontraron bacilos en los husos, ningún componente fué eximido. Este estudio destaca el compromiso significativo del músculo estriado en la lepra, un hecho no siempre revelado por el examen exclusivamente clínico.

RÉSUMÉ

Le profil de l'innervation a l'intérieur et à l'extérieur des fuseaux a été étudié dans des biopsies musculaires provenant du long fléchisseur du pouce et du biceps brachial, ces deux muscles ne présentant pas de dommages cliniques. Le caractère pâteux et l'épaississement des plaques motrices terminales constituaient la caractéristique anormale la plus notable au niveau du profil d'innervation en dehors des fuseaux; par ailleurs, les fibres se trouvant à l'intéreur des fuseaux ne présentaient aucune caractéristique digne d'être notée, ou bien ne montraient qu'une augmentation du caractère tortueux, de petits épaississements, et dans les cas les plus extrêmes un profil en écheveau fort compliqué. On a fréquemment observé des bacilles dans les bourrelets (spindle), aucune constituant n'étant épargné. Cette étude permet de souligner l'atteinte significative du muscle strié dans la lèpre, fait qui n'est pas toujours mis en évidence par l'examen clinique seul.

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