sitive enough to reliably assess the differences among the various systems investigated.

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REFERENCES

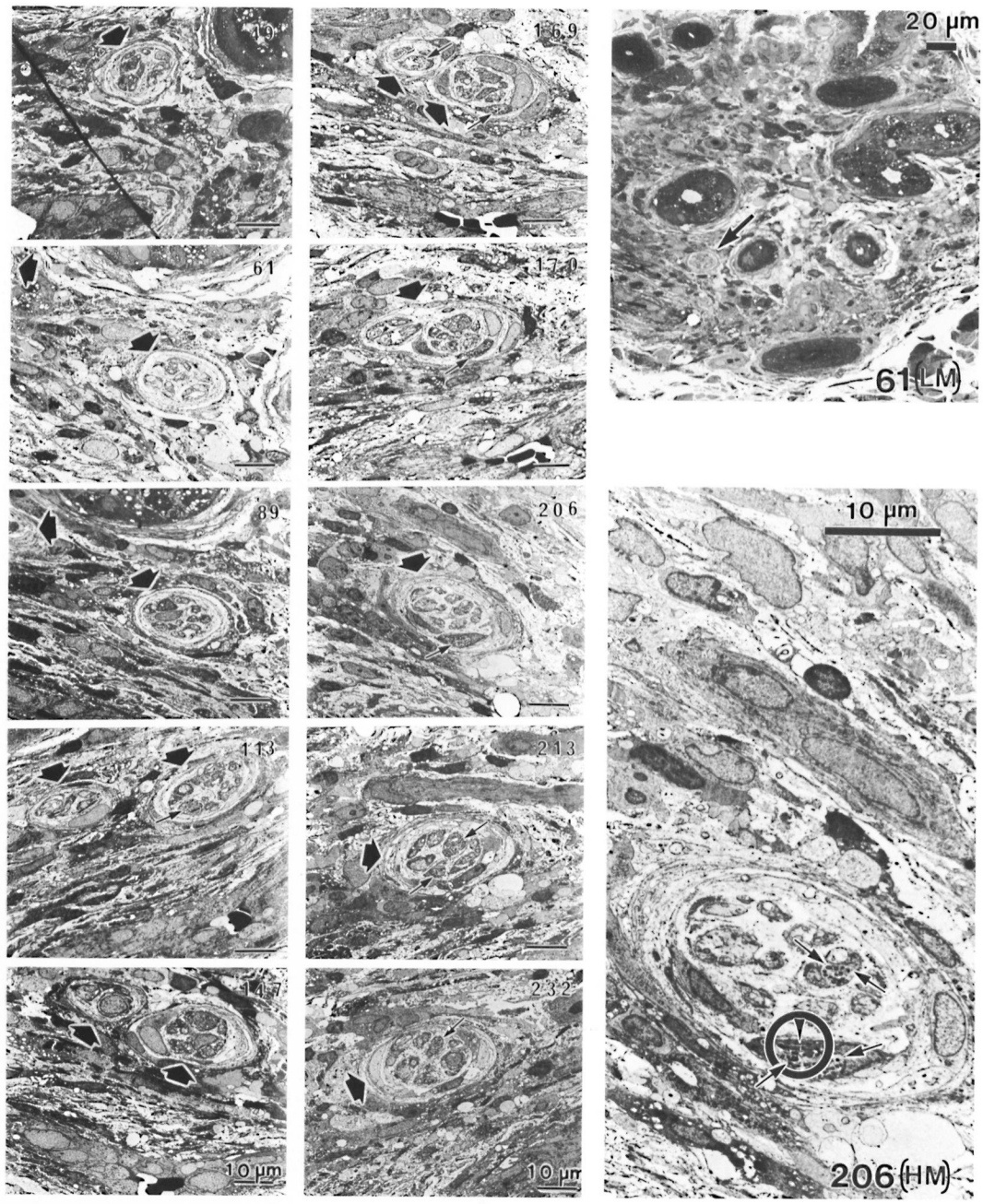
1. Ellner, J. J. and Daniel, T. M. Immunosuppression by mycobacterial arabinomannan. Clin. Exp. Immunol. **35** (1979) 250–257.
2. Krishna, P., Mishra, R. S. and Nath, I. Phenolic glycolipid-I of *Mycobacterium leprae* induces general suppression of *in vitro* concanavalin A responses unrelated to leprosy type. J. Exp. Med. **165** (1987) 239–244.
3. Lemieux, S., Gosselin, D., Lusignan, Y. and Turcotte, R. Early accumulation of suppressor cell precursors in the spleen of *Mycobacterium lepraemurium*-infected mice and analysis of their *in vitro*-induced maturation. Clin. Exp. Immunol. **81** (1990) 116–122.
4. Lowrie, D. B. The macrophage and mycobacterial infections. Trans. R. Soc. Trop. Med. 77 (1983) 646–655.
5. Mehra, V., Mason, L. H., Fields, J. P. and Bloom, B. R. Lepromin-induced suppressor cells in patients with leprosy. J. Immunol. **123** (1987) 1813–1817.
6. Mosmann, T. Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays. J. Immunol. Methods **65** (1988) 55–63.
7. Nath, I., Curtis, J., Sharma, A. K. and Talwar, G. P. Circulating T-cell numbers and their mitogenic potential in leprosy—correlation with mycobacterial load. Clin. Exp. Immunol. **29** (1977) 393–400.
8. Navalkar, R. G., Patel, P. J. and Kanchana, M. V. Studies on immune response to *Mycobacterium lepraemurium*. Int. Arch. Allergy Appl. Immunol. **62** (1980) 423–431.
9. Ramasesh, N., Adams, L. B., Franzblau, S. G. and Krahenbuhl, J. L. Effects of activated macrophages on *Mycobacterium leprae*. Infect. Immun. **59** (1991) 2864–2869.
10. Rojas-Espinosa, O. Active humoral immunity in the absence of cell-mediated immunity in murine leprosy: lastly an explanation. Int. J. Lepr. **62** (1994) 143–147.
11. Rojas-Espinosa, O. and Estrada, P. S. Immunology of leprosy: cellular anergy to *Mycobacterium leprae*. Arch. Invest. Med. **20** (1989) 335–341.
12. Rojas-Espinosa, O., Vega, R., Oltra, R. A., Arce, P. P. and Nuñez, A. Transitory macrophage activation in the granulomatous lesions of *Mycobacterium lepraemurium*-induced lepromatoid leprosy in the mouse. Int. J. Lepr. **56** (1988) 428–436.
13. Touw, J., Stoner, G. L. and Belehu, A. Effect of *Mycobacterium leprae* on lymphocyte proliferation: suppression of mitogen and antigen responses of human peripheral blood mononuclear cells. Clin. Exp. Immunol. **41** (1980) 397–405.

Electron Microscopic Observations of Small Unmyelinated Nerve Tissue Proper in a Dermal Lesion of a Relapsed Lepromatous Patient

To the Editor:

When scrutinized once again the ultrastructural features of small unmyelinated nerve(s), apart from the dermal peripheral nerves appearing in the negative films of the photomicrographs of the 300 serial semithin sections described previously ([2]), attracted our attention.

The course of this small nerve was traced through the neighboring serial sections, and the observations are summarized in The Table. Ten photomicrographs were selected and are presented in The Figure. A few bacilli were observed in vacuolar spaces located in the axoplasm (← in photos 113, 169, 170, 206,

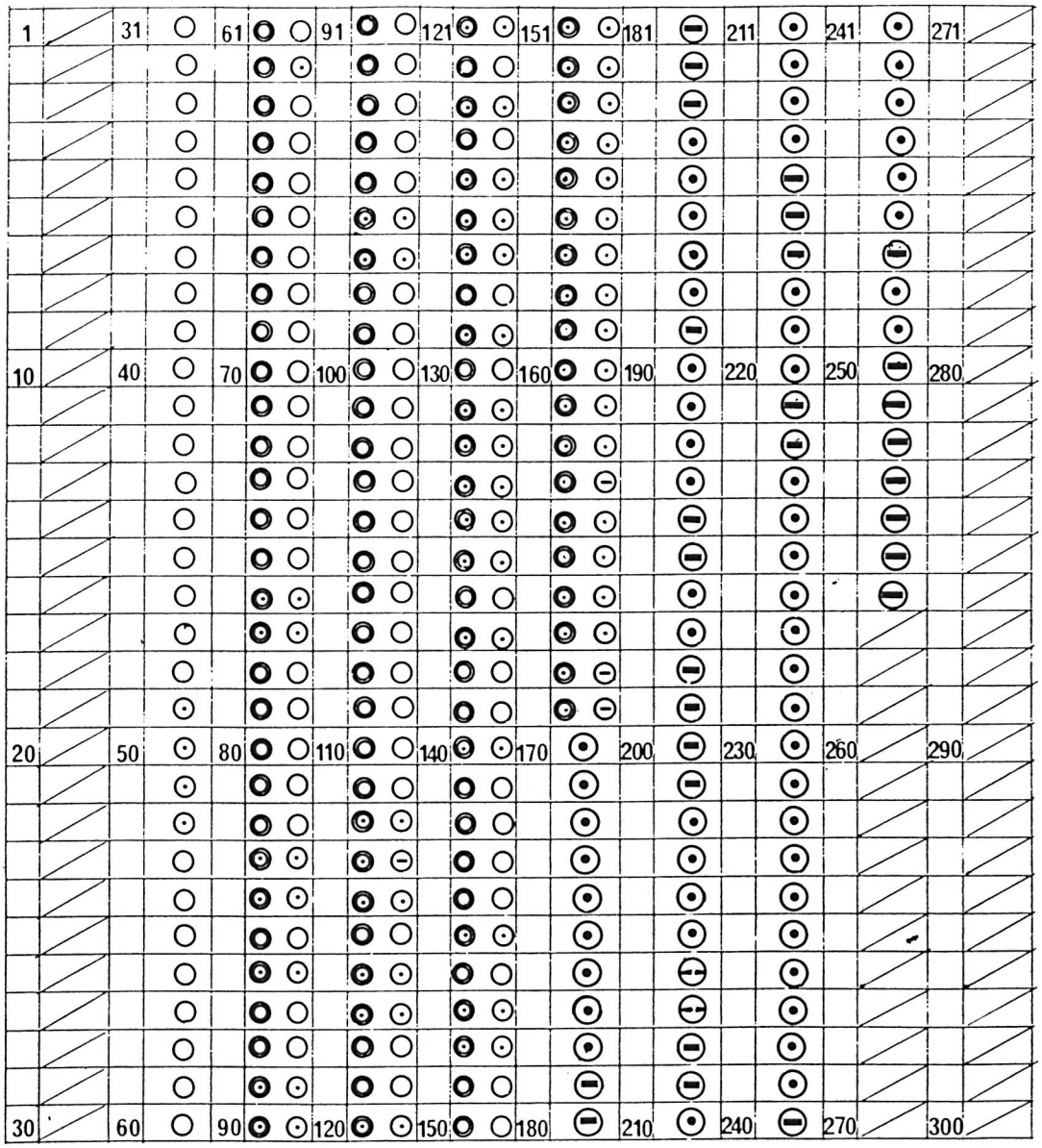


THE FIGURE. Ten photomicrographs of small unmyelinated nerve(s) (SUN) selected from photographs of 300 serial semithin sections published earlier (2). ◖ = Small unmyelinated nerve; ⟵ = a few bacillary cells observed in vacuolar spaces located in axoplasm; 61 [LM] = low magnification photomicrograph of 61 with (⟵) a few bacillary cells observed in vacuolar spaces located in axoplasm; 206 [HM] = high magnification photomicrograph of 206 with (⏲) a bacillary cell caught in the act of division.

213, 232, and 206 [HM] in The Figure). They were diverse and some were seen in the act of dividing (⏲ in photo 206 [HM]). We also saw two nerves joining to form one nerve, or vice versa, as seen in photo 170 in The Table and ◖ in photos 169 and 170 in The Figure.

In the literature it has been emphasized that intra-axonal leprosy bacilli were only to be

THE TABLE. *Distribution of bacilli observed in 300 serial sections of small unmyelinated nerve(s) (SUN) and the course of the nerve(s).*[a]



[a] In photos 1–30 and 257–300, no small unmyelinated nerves seen. In photos 31–60, one small unmyelinated nerve can be seen. In photos 61–169, two small unmyelinated nerves can be seen. In photo 170, one small unmyelinated nerve showing joining of two nerves into one nerve can be seen. In photos 171–260, one small unmyelinated nerve can be seen.

[b] ▱ = Section did not show any small unmyelinated nerves; ○○ = small unmyelinated nerve (SUN); ⊙⊙ = SUN observed containing cross sections of bacillary cells; ⊖ = SUN observed containing longitudinal and cross sections of bacillary cells; ⊖ = SUN observed containing bacillary cell in the act of division.

found in myelinated axons and that none were to be seen in unmyelinated axons [1, 3, 4]. The present observations show that bacilli can be found in unmyelinated axons. Earlier studies, based on the usual electron microscopic examinations, would not have been likely to observe such bacilli since the usual studies do not employ serial sections.

The locations of *Mycobacterium leprae* in dermal peripheral nerves in leprosy patients should be reinvestigated.

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REFERENCES

1. Boddingius, J. The occurrence of *Mycobacterium leprae* within axons of peripheral nerves. Acta Neuropathol. (Berl.) **27** (1974) 257–270.
2. Hirata, T. and Harada, N. Electron microscopic observations of the relationship between peripheral nerve tissue proper and an endoneurial capillary in a dermal lesion of a relapsed lepromatous patient. Int. J. Lepr. **62** (1994) 89–98.
3. Jacob, J. M., Shetty, V. P. and Antia, N. H. A morphological study of nerve biopsies from cases of multibacillary leprosy given multidrug therapy. Acta Neuropathol. (Berl.) **85** (1993) 533–541.
4. Shetty, V. P., Antia, N. H. and Jacob, J. M. The pathology of early leprous neuropathy. J. Neurol. Sci. **88** (1988) 115–131.

Relapse After Long-Term Follow Up of Multibacillary Patients Treated by WHO Multidrug Regimen

To the Editor:

Up to 1993, more than 4 million leprosy patients [5] in the world have completed their treatment with multidrug therapy (MDT) recommended by a WHO Study Group [4] in 1982. Data from routine leprosy control programs have indicated that, after completion of MDT, the relapse rates are well below 1% [1, 6]. However, the low relapse rates must be interpreted with great caution, because the durations of follow up in the majority of patients are relatively short and the relapses after treatment with any rifampin-containing regimens occur late, at least 5 ± 2 years after starting treatment.

Thirty-five multibacillary patients, treated with MDT for 2 years between 1984 and 1986 at the Institute Marchoux, with all drugs administered under supervision, have been seen at least once later than 12 months after completing MDT. Relapse was diagnosed if two or the following three criteria were met: a) increase of bacterial index (BI) by at least 2+ over the previous value, b) occurrence of a definite new leprosy skin lesion, and c) demonstration of viable organisms by mouse foot pad inoculation [2, 3].

After 41.9 ± 12.1 months of follow up, only one patient relapsed for a relapse rate of 2.9% or 0.8 per 100 patient-years [3]. Additional follow up was done. Six additional relapses were diagnosed during the next 2½ years for an overall relapse rate of 20.0% or 3.3 per 100 patient-years. The mean interval between stopping treatment and the appearance of relapse was 62.7 ± 18.7 months, a figure similar to that of relapses after stopping treatment with other rifampin-containing regimens.

To date, the relapsed cases had significantly greater bacterial loads before or at the end of the 2 years of MDT: 38.9% and 41.7% relapsed, respectively, among patients who had an average BI ≥4.0 before MDT or BI ≥3.0 at the end of MDT; whereas the relapse rates were respectively 0% and 8.7% among patients who had an average BI <4.0 before MDT or BI <3.0 at the end of MDT. In other words, relapse was significantly more frequent among patients with BI ≥4.0 before MDT or BI ≥3.0 at the end of MDT.

A full manuscript, analyzing the long-term, follow-up results has been submitted to this Journal.

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REFERENCES

1. ALM Consensus Development Conference on the Chemotherapy of Leprosy. Consensus development statement on the chemotherapy of leprosy. Int. J. Lepr. **60** (1992) 644-652.
2. Jamet, P., Blanc, L., Faye, O. C., Traore, I. and Bobin, P. Relapses after a single dose rifampin in skin smear negative multibacillary patients after dapsone monotherapy. Int. J. Lepr. **62** (1994) 209-214.
3. Marchoux Chemotherapy Study Group. Relapses in multibacillary leprosy patients after stopping treatment with rifampin-containing regimens. Int. J. Lepr. **60** (1992) 525-535.
4. WHO Study Group. Chemotherapy of leprosy for control programmes. Geneva: World Health Organization, 1982. Tech. Rep. Ser. 675.
5. World Health Organization. Progress towards the elimination of leprosy as a public health problem. Weekly Epidemiol. Rec. **68** (1993) 181-188.
6. World Health Organization Leprosy Unit. Risk of relapse in leprosy. WHO document WHO/CTD/LEP/94.1.