

CORRESPONDENCE

This department is for the publication of informal communications that are of interest because they are informative and stimulating, and for the discussion of controversial matters.

The Possible Significance of the Club-forms of *Mycobacterium leprae*

TO THE EDITOR:

Dr. Waters¹ points out that the occurrence of relapses in patients in whom the bacilli appear to be completely fragmented is not to be taken as evidence against the view that nonsolid bacilli are dead. The regeneration might have arisen from undetected solid organisms, located possibly in nerve or muscle, and he draws an analogy with subacute bacterial endocarditis. All this is quite true, but, nevertheless, there is an alternative possibility, viz., that nonsolid organisms might not be a homogeneous group. All the evidence, quoted by Waters, points to the fact that they are nonreproductive, and that the vast majority of them are dead; but a universal negative is hard to prove.

Our object in writing this note is to draw attention once more to the club forms of metachromatic granules of *Mycobacterium leprae*,^{2, 3, 4} which are universally ignored by current methods of reporting morphology. In Ziehl-Neelsen-stained films clubs appear as dark red swellings, single or multiple, at some point in the bacillary rod. They are seen in some, but not all, lepromatous patients. They differ significantly from granules in being most numerous during the active phase of generation. With treatment, numbers quickly diminish. For a

time more or less isolated clubs may be found, especially in the globi, but eventually they disappear or at least their presence in smears becomes erratic. After prolonged treatment of a few years, clubs may reappear, but only in those patients in whom they were present before treatment. At first they may be smaller than formerly, about the size of a granule, but they are dark staining and invariably spherical. Later they may enlarge to their former size, and perhaps remain dormant for a long period.

We have had the opportunity of following the development of bacilli in smears in 3 patients at the time that a relapse has taken place. Clubs have been present in all of them and have preceded the reappearance of solid rods. In the earliest stage of the relapse one sees isolated clubs, short "comma-shaped" organisms in which there is a club with a tail, and isolated short rods with clubs. One gains an impression that a new rod is issuing from the club, though the impression would be hard to prove. Equally, it cannot be claimed that the comma-shaped organisms have arisen by binary fission of preexisting solid rods; they do not lie in clumps or even in pairs, and some of them are exceedingly short. Later, elongated rods with clubs are seen in clumps and multiplication of the conventional sort is then evident (Figure 1). It has already been postulated that club forms are concerned in some way with regeneration of *M. leprae*.²

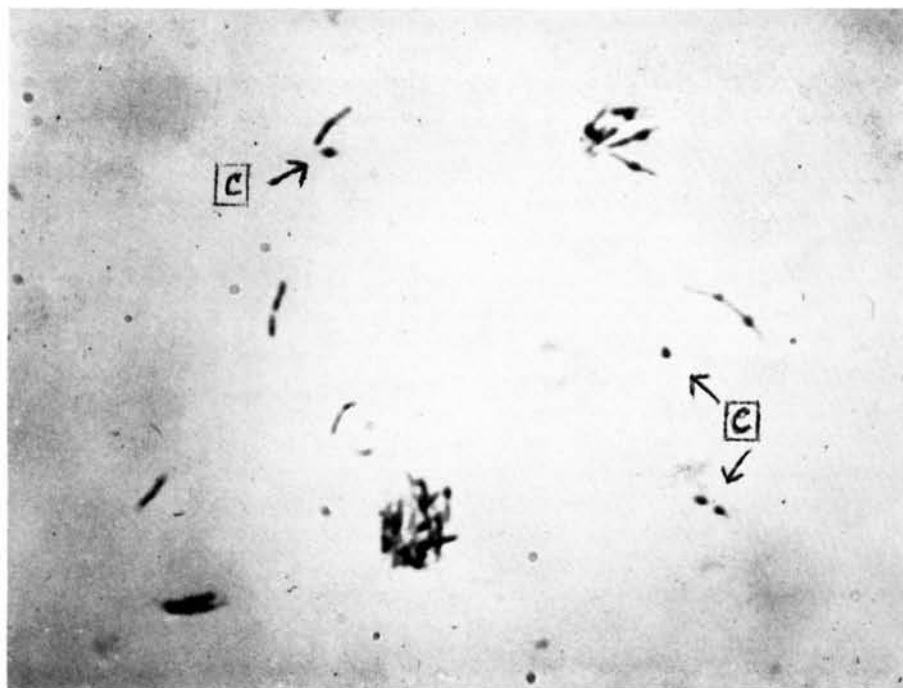
Club forms are less easy to detect in paraffin sections, though they are more likely to be visible by phase contrast. They are destroyed by homogenization of tissue

¹ WATERS, M. F. R. Significance of fragmented leprosy bacilli. *Internat. J. Leprosy* **35** (1967) 518-520.

² SOUZA ARAUJO, H. C. The morphology of *Mycobacterium leprae*. *Leprosy Rev.* **30** (1959) 80-84.

³ DENNY, O. E. A microscopic study of *Mycobacterium leprae*. *Internat. J. Leprosy* **2** (1934) 275-278.

⁴ WISE, M. J. Club-forms of *Mycobacterium leprae*. *Leprosy Rev.* **34** (1963) 68-72. See also Erratum p. 112.



and are lost, therefore, to electron microscopy when this form of processing is used.⁴ By their nature they are hard to investigate. The observations reported here need confirmation, and if confirmed they would raise as many problems as they would solve. Nor is it clear whether clubs are at any stage related to the L-forms which have been postulated in leprosy,¹ but whose existence remains to be proved. However, more might be learned about the known risks of relapse if it was customary to record the presence of clubs whenever they are seen in smears.

In conclusion there are three facts that

seem fairly definite: (1) Clubs occurring on solid rods are associated with the generative phase of *M. leprae*. (2) Clubs or morphologically identical structures can exist in an isolated state, in which form they are distinct from either granules or solid rods. (3) Clubs are associated in some way with the early phase of regeneration in at least some patients who relapse.

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