Indeterminate Leprosy

TO THE EDITOR:

I wonder why Dr. Browne in his letter ([1]) on indeterminate leprosy in cases of doubt accepts the advice of Dr. Pettit "to temporize" and "to await indubitable signs of leprosy," without first referring to other means of diagnosing indeterminate leprosy. To my experience each lesion suspected of being indeterminate leprosy should be examined by sweat testing rather than by histopathology or sensory tests. The absence of sweating, visualized by 5% o-phthalaldehyde in xylene ([2]) provides convincing evidence of indeterminate leprosy. This test is easier to carry out than pilocarpine injections with iodine and starch as the indicator.

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Reply to Dr. Klokke's Letter

TO THE EDITOR:

The short answer to Professor Klokke's letter is that by the time the "absence of sweating" (not its diminution) is present in a hypopigmented skin lesion, the clinical appearances are pathognomonic to the experienced clinician. Characteristic, but nonspecific anhidrosis does not give the indubitable evidence of the leprous origin of the lesion as does the demonstration of acid-alcohol-fast organisms in typical situations in the nerve fibrils coursing in the deep dermis.

The less experienced clinician or the less experienced histopathologist is, in my opinion, well advised to await indubitable signs of leprosy.

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Foam—the Result of an Interaction Between Unactivated Macrophages and Dead *Mycobacterium leprae*?*

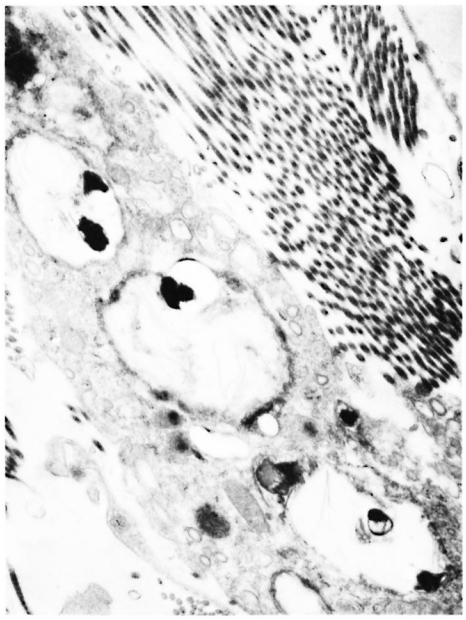
TO THE EDITOR:

The foam in lepromatous leprosy has been the object of study for many years, and it has been said that it consists of phospholipids and fatty acids ([2, 4, 7, 9, 10]). Recently, in an important communication by Hunter and Brennan, it was shown that armadillo-derived *Mycobacterium leprae* contain a phenolic glycolipid that "may be responsible for the electron transparent foam which surrounds the leprosy organism in infected tissue" ([6]).

Light- and electron-microscopic studies of the structure of lepra cells have shown that the opaque droplets seen around *M. leprae* in the early stages of the infection coalesce in the later stages to produce foam containing degenerating bacilli ([1, 8, 12]).

Several suggestions have been made with

* Dr. Charles C. Shepard kindly served as Acting Editor regarding this communication.—RCH



THE FIGURE. Electron micrograph of a macrophage showing several cross sections of *M. leprae* surrounded by electron-transparent material which causes the foamy appearance of the cytoplasm (×30,000).

regard to the origin of foam. It was thought that foam may arise from the effect of the intracellular invasion and proliferation of *M. leprae* on the cytoplasm of the cell ([5, 9]). It was also suggested that it was the breakdown product of the degenerating *M. leprae* ([11]) or the result of abnormal lipid metabolism of the cells ([7]). Recently in an ultrastructural study of the growth of *M. leprae* and *M. lepraemurium* in nude mouse macrophages, it was found that *M. leprae* produced foamy structures and *M. lepraemurium* produced cystalline material. It was suggested that the foamy structures were made up of a substance produced by the multiplication of *M. leprae* in suitable host cells ([3]).

We have injected 10^7 autoclaved armadillo-derived *M. leprae* intradermally into nude mice. The sites were biopsied at the end of four weeks. Each biopsy was divided into two parts. One was fixed in 10% formalin for light-microscopic study and the other was further divided into 1 mm cubes and fixed in 2% glutaraldehyde at 4°C for electron-microscopic study.

In the light-microscopic examination, a few small collections of mononuclear cells were seen around capillaries in the dermis. The cells were mostly macrophages, although a few lymphocytes were seen. The cytoplasm of the macrophages on careful examination revealed a foamy appearance. Acid-fast stain showed bacilli inside the macrophages. An electron-microscopic study of the biopsy showed that the macrophages contained large phagosomes containing fragmented bacilli surrounded by a large amount of electron-transparent material characteristic of foam (The Figure).

There are two possibilities to explain the presence of foam in the macrophages in this study. It may be produced by the dead (autoclaved) *M. leprae* as a reaction of the macrophages to the constituents of the bacilli, or it may be from the inoculum itself because most of the purification methods are not successful in completely removing foam from the bacilli. Further studies are being planned to rule out this latter possibility.

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Co-incident (Simultaneous) Dapsone Sensitivity and Dapsone-resistant Leprosy

TO THE EDITOR:

It was interesting to read the letter of Dr. McDougall and Dr. Felton Ross [IJL **50** (1982) 214–215] concerning co-incident (simultaneous) dapsone sensitivity and dapsone-resistant leprosy. They ask whether leprosy workers in other parts of the world have observed findings similar to theirs.

This occurrence was first proved by workers from the British Medical Research Council's unit in Sungei Buloh, Malaysia, in the initial series of papers which proved the existence of sulfone-resistant leprosy.

Our Indian patient No. 5075 was No. 1 in the first seven cases we studied for resistance ([2]) and also No. 1 in the more detailed report printed in 1966 ([3]). Although the sensitivity tests that were first performed found him to have a strain of dapsone-sensitive organisms, his Morphological Index did not diminish as much as might have been expected after six months on injectible DDS (600 mg weekly).

This case was reported in much greater detail in 1968 as "A Case of 'Partial' Resistance" ([1]) which describes how his Morphological Index fluctuated wildly while on sulfone treatment. In March 1963 the biopsies (we always took two from different sites) showed definite active lepromas and he was treated with 300 mg of dapsone twice weekly. About eight months later further biopsies seemed quiescent although Dr. Ridley noted "one more than the other." In April 1964 however the biopsies again showed definitely active leprosy. In the next eight months he had a severe bout of erythema nodosum leprosum which we believe is associated with successful anti-mycobacterial therapy, yet by February 1965 the biopsies still showed definite evidence of activity. At that time he was put on clofazimine therapy and from then on got steadily better by all criteria—clinical, bacteriological, and pathological.

We were treating a patient whose initial lesions showed dapsone sensitivity but who improved and then got worse while under treatment—the skin plaques got smaller but a diffuse skin infiltration appeared.

In those early days we were not yet able to recognize the clinical appearance of sulfone-resistant leprosy, but in retrospect it is obvious that this patient had some lesions containing resistant organisms and others with sensitive organisms. We said in our summary that it was likely that more cases of this type will be found. Apparently this is now the case.

We must therefore accept that resistant leprosy may be due to two things:

1) The development of a resistant clone in a patient most of whose bacilli are sulfone-sensitive. It is a moot point whether this clone develops because of inadequate therapy or whether it was always there and