An average of 14 fibers per funicle with multiple axonal myelination, observed in the mice with *M. leprae* infection followed by DDS treatment, was striking as compared to nerves of mice with only *M. leprae,* only DDS, and normal, age-matched controls kept under similar conditions. Although the exact cause for such abnormal myelination is not very clear, we can speculate that the unmyelinated fibers and their Schwann cells, which are known to be affected following *M. leprae* infection ([4]), have shown abnormal regenerative activity following DDS treatment.

Abnormalities such as a) swelling of the axons, b) tangential arrangement of the axons, c) the presence of miniature axons as well as d) partial or total loss of individual ensheathment by the Schwannian processes of the axons within the myelin ring system suggest that the myelination had commenced following partial disorganization of a parent unmyelinated fiber unit.

There is no definitive evidence, such as degenerating myelinated fibers or myelin debris, to suggest that there was prior axonal degeneration of myelinated fibers. It is therefore unlikely that multiple axonal myelination is a regenerative activity following axonal degeneration. Waxman ([5]) suggests that the branching of a single axon within its myelin sheath would result in myelination of multiple axons. On the other hand, Brown and Radich ([1]) have shown a number of axons lying outside the myelin ring system. They propose that the multiple axonal myelination is a focal phenomenon occurring within one internodal length of myelin along the course of an otherwise unmyelinated bundle of axons. This is also the opinion of Okada, *et al.* ([2]). Our own observations favor the proposition by Brown and Radich ([1]).

Our material does not give any evidence to suggest that such fibers degenerate in the course of time. In this mouse leprosy we have a unique experimental model of selective involvement of unmyelinated axons and their Schwann cells in the initial stages of infection. Therefore it is speculated that occurrence of multiple axonal myelination in this model is a misguided regenerative response following partial denervation of unmyelinated fiber groups, implicating a defective Schwann cell axon interaction.

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Theophylline-sensitive and Theophylline-resistant E-rosette-forming Cells in Leprosy

To the Editor:

The heterogeneity of surface markers on lymphocytes and their relations to functions have been amply demonstrated ([5, 6, 10]). Recently, changes in the T cell subsets in leprosy patients have come under study, using different kinds of markers ([1, 7, 11, 12]). One of the standard markers for T lymphocytes, E-rosette formation, is considered to identify the total T cell population (ERFC). But

THE TABLE. *Theophylline-sensitive (TheS) and theophylline-resistant (TheR) ERFC in controls and leprosy patients.*

Group	No.	Total ERFC % (mean ± S.D.)	TheR ERFC % (mean ± S.D.)	TheS ERFC % (mean ± S.D.)	Ratio TheS ERFC/ TheR ERFC % (mean ± S.D.)
Controls	33	60.21 ± 4.36	50.36 ± 3.71	9.84 ± 2.23	0.19 ± 0.04
Patients					
1	12	57.08 ± 5.03	47.83 ± 5.95	9.25 ± 4.43	0.19 ± 0.10
2	10	37.20 ± 8.95[a]	24.60 ± 6.96[a]	12.60 ± 3.13[a]	0.53 ± 0.16[a]
3	8	40.25 ± 9.69[a]	26.25 ± 7.99[a]	14.00 ± 4.98[a]	0.57 ± 0.28[a]
4	10	59.04 ± 8.63	36.50 ± 6.51[a]	22.90 ± 4.43[a]	0.63 ± 0.14[a]
5	8	59.37 ± 2.82	51.50 ± 2.67	7.87 ± 2.69	0.15 ± 0.06

[a] Significantly different from control values when analyzed by Student's *t* test, $p < 0.01$.

under some conditions, this population can be subdivided by altering the rosetting technique. Theophylline, perhaps through its effect on cAMP metabolism, causes the loss of ERF ability in 15–20% of the total peripheral blood T cells ([4]). Dosch and Gelfand ([2]) concluded that the theophylline sensitive ERFC (TheS ERFC) population contained cells with a suppressive effect on T help for antibody production *in vitro*; while the theophylline-resistant ERFC (TheR ERFC) cells included those able to help in the same response. However, Peterman, *et al.* ([8]) showed that neither population was suppressive in *in vitro* proliferative response to specific antigen but that for optimal, or perhaps any, response, it was necessary that both populations be present, and in an appropriate ratio. Considering the interest in the regulation of T cell activities in leprosy, we have investigated the proportions of these two T cell subsets in leprosy patients and in healthy Vietnamese controls.

Forty-eight leprosy patients, classified according to the Ridley-Jopling scale on clinical grounds, were studied. They were divided into five groups: 1) 12 tuberculoid patients, treated with DDS for 2 or more years; 2) 10 lepromatous patients with a heavy bacterial load (++) on the 0–4+ Dharmendra scale, without erythema nodosum leprosum (ENL), treated with dapsone (DDS) for more than 5 years; 3) 8 lepromatous patients with a heavy bacterial load (++), without ENL, treated with DDS for 2–3 years; 4) 10 lepromatous patients with a light bacterial load (+), without ENL, treated with DDS for 1–2 years; and 5) 8 lepromatous patients with a recent ENL reaction, treated with DDS for 1–2 years. The controls consisted of 33 apparently healthy blood donors from the blood transfusion service in Hanoi.

Peripheral blood lymphocytes were separated on Ficoll-Hypaque and tested for ERFC as described by Jondal, *et al.* ([3]). Triplicate tubes were set up for total ERFC and for TheR ERFC; the latter were incubated in the presence of $10^{-3}M$ theophylline. Two hundred cells were counted for each tube, and the numbers given are the means of the triplicate counts. TheS ERFC were calculated as the difference between total and TheR ERFC (The Table).

In this group of patients, there was no difference between the tuberculoid leprosy patients and the controls in the proportions of TheR and TheS ERFC. Patients in groups 2 and 3, with heavy bacterial loads, but not those in group 4, with light bacterial loads, had significantly reduced total ERFC compared to the controls. This is in agreement with our previous study on ERFC in leprosy patients ([11]). In all three groups of lepromatous patients without ENL, there were significant changes in the proportions of TheR and TheS ERFC; in all of these groups there were relatively more TheS ERFC, whether they had been under treatment for a rather long or a shorter time. In the fifth group, lepromatous patients with ENL, the total ERFC and the TheR ERFC were not significantly different from the healthy controls.

The relative lack of responsiveness to certain antigens by T cells of lepromatous leprosy patients is well known; explanations for

its initiation and maintenance are less well understood. There is evidence for activity of suppressive cells in some experimental systems ([9]), and some studies have been aimed at identifying possible changes in the makeup of the lymphocyte subpopulations which could be involved in such activities ([1, 7, 11, 12]). In this study, we have demonstrated significant differences in the proportions of two subpopulations of T cells between lepromatous patients without ENL and controls. Patients at the tuberculoid end of the spectrum and those with ENL were not different from controls in this respect. Since all of the patients had been treated with DDS, the change in the balance of T cell subpopulations is not likely due to treatment. If, as was suggested by Peterman, *et al.* ([8]), the proportions of these two subsets are important in the generation of appropriate antigen-specific immune responses, this study would support the idea that there are long-lasting changes in the composition of the T cell population in lepromatous leprosy patients, which may be related to the immune status of the host with respect to the infection.

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