

# Relapse in Lepromatous Leprosy<sup>\*†</sup>

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The investigation based on a follow-up study of 125 lepromatous cases living in their natural environment and followed up for about 6 years, showed a relapse rate of 3.22% per year. It was also found that all the relapses occurred among those who, after becoming negative, either were very irregular in taking treatment or sought no treatment. The risk of relapse was found to decrease progressively with the number of years that passed after the patients attained a bacteriologically negative state.

## Introduction

The term relapse is derived from the Latin word "relapsus", and according to Dorland's medical dictionary it means "return of the disease after its apparent cessation". The main difficulty is not in understanding this definition, but in how to define apparent cessation (or subsidence) particularly in a disease like leprosy. In lepromatous leprosy it has become the practice to base cessation of the disease on bacteriological negativity. The situation is even more difficult in non-lepromatous leprosy. Further, unless relapse is qualified so as to indicate whether it occurred under treatment or not, it is not fully meaningful. Similarly, risk of relapse calculated without reference to the period of exposure to risk, as is often done, gives an incorrect picture.

## Review of Past Work

Published well-documented data on the rate of occurrence of relapse in leprosy are not many, to the extent that we do not know clearly at present the risk of relapse a patient runs under various conditions such as, the patient's original clinical and bacteriological status, the regularity of treatment during the active phase of the disease, the continuation of treatment and its regularity after he becomes bacteriologically negative, the patient's age and sex, and the stress factors faced by the patient. Erickson (1950), in a study of 33 arrested cases from Carville which he followed-up for periods ranging from 6 months to 5 years, found a relapse rate of 45% (5 out of 11) among patients who discontinued

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sulphone treatment after becoming negative, and 4.5% (1 out of 22) among patients who continued treatment. Lowe (1954), on the basis of a follow-up of 139 lepromatous cases from Eastern Nigeria, reported a relapse rate of 10.8%, the period of follow-up ranging from a few weeks to 5 years (average 22 months). Rodriguez (1959) has reported on relapse in the Philippines both among sanatorium cases and out-patients discharged earlier from sanatoria. From his figures the relapse rate for in-patients works out at 4.5% for 3½ years (46 out of 1027) under conditions of irregular treatment; for out-patients the rate was 3% (3 out of 101). The relapse rate was highest among those who had been negative for 6 months to 2 years, and lowest among those who had been negative for more than 2 years. The rate was also low in the first 6 months of negativity. He has also compared his relapse rates of 3 to 4% in 3½ years in the sulphone era with relapse rates observed earlier among chaulmoogra-treated negative lepromatous cases. He had found that in the period of chaulmoogra treatment the relapse rates ranged between 30 and 40% among those completing the first 5 years of negative period while by 10 years, the rate reached 75%. Quagliato *et al.* (1961), working with cumulative coefficients, found that the cumulative probability of suffering a relapse during the first 3½ years was 18.9%, whereas for the first 6½ years this figure was 26.4%. They also found that the relapse rates for cohorts of patients discharged between 1949 and 1952 was higher than that for cohorts of patients discharged between 1953 and 1959. From the figures provided by the authors the relapse rate works out at 8.4% per year for those discharged between 1949 and 1952, and 6.3% per year for those discharged between 1953 and 1959. Torsuev *et al.* (1965) reported 45 relapses among 187 patients followed-up for up to 18 years (crude relapse rate 24.1%), and considered that the relapses were due to various factors, such as inadequate or prematurely discontinued treatment, long intervals between courses of treatment, over-treatment with large doses of sulphones, and other factors such as intercurrent diseases, physical strain, or abuse of alcohol. Recently, Quagliato *et al.* (1968), on the basis of a retrospective study of 807 lepromatous cases registered between 1946 and 1968, reported that the 5-year cumulative relapse rates ranged between 7.7 and 14.4% for lepromatous cases of different types under regular treatment; while the rates for those under irregular treatment ranged between 10.9 and 28.4%. Similarly the 10 years and over cumulative relapse rates in patients under regular treatment ranged between 19.6 and 27.8% for different types of lepromatous cases, and for those under irregular treatment the figures ranged between 45.0 and 62.4%. Basto and Barbosa (1968) reported a relapse rate of 20% in about 9 years for lepromatous cases under treatment.

From the various figures quoted above it can be seen that it is very difficult to compare one set of figures with another, as the different studies are based on different methods of calculation and different assumptions. However, from a review of the above 10 studies the following general inferences can be drawn. (1) Relapse is a common feature in lepromatous leprosy. (2) Patients with negative lepromatous disease who discontinue treatment or are irregular in taking treatment run a higher risk of relapse, which may range between 1 to 6% per year under different conditions, whereas those who continue treatment run a much lower risk, which may range between 0.5 to 2.5% per year. (3) The risk of relapse decreases with the passage of time (although cumulative relapse rates will show increase with passage of time). (4) Well established and more extensive disease tends to relapse more often than less extensive.

### Materials and Methods

The present investigation of relapse was possible because of a chemoprophylaxis study in Chingleput Taluk (S. India) conducted by the Central Leprosy Teaching and Research Institute at Chingleput, where a number of patients with lepromatous leprosy, who served as index cases for the study, have been regularly followed up both clinically and bacteriologically for about 6 years, and whose treatment status in most cases was also known. The patients were examined every 6 months; several of them were bacteriologically negative and the disease clinically inactive even at the start of the study. A large number who were positive at the start of the study later became negative as the result of treatment. Most of those who became negative during the study period or were negative at the start remained negative subsequently, but a few did become bacteriologically positive again. The length of time for which patients remained negative before becoming positive again varied from 6 months to 5 years. Cases showing negative smears only for a short period may not necessarily be inactive and therefore their subsequent positive status may not necessarily indicate relapse; at any rate we have so far no standard criteria for declaring a case as a case of relapse. In the absence of such criteria we have defined relapse, for the purposes of the study, as the reappearance of acid-fast bacilli (AFB) in skin smears from lepromatous patients who had been negative continuously for 3 years or over, as determined by at least 6 consecutive skin smear examinations performed at half-yearly intervals; the skin smears were taken at 6 sites and examined by standard methods. The number of lepromatous cases which remained negative for 3 years or more and are included in the study was 125. However, the periods of follow-up of these 125 cases were not uniform, as they ranged from 6 months to 2½ years. Therefore, the analyses in the study were based on the calculation of person-years of follow-up, thus giving due weighting to the varying period of follow-up; the relapse rates are calculated per 100 person-years, which is the same as per cent per year.

### Results

The total period of observation of the 125 cases was 279.5 person-years, and the number of relapses among them, by our definition was 9, thus giving a relapse rate of 3.22% per year. When the data are analysed according to regularity and continuation of treatment after becoming negative, it is found that there was no relapse among those who took regular treatment, and that all the relapses occurred among those who either were very irregular in taking treatment or completely neglected to have treatment. The relapse rates are about the same whether the patients were taking treatment irregularly or were completely abstaining from taking treatment. Table 1 shows the relapse rates by treatment status.

Relapse occurred most frequently in the second year of follow-up. In the first and second half-years of the follow-up study, there was no relapse; in the third half-year the relapse rate was 10.3% per year, in the fourth half-year it was 11.9% per year, and in the fifth half-year the rate was only 0.9% per year. Thus the risk of relapse for lepromatous cases appears to decrease considerably 5 years after attaining negativity. All but 13 of the lepromatous cases studied were in males, and all the relapses occurred in male patients. Also, all but 2 of the patients were

TABLE 1  
*Relapse in lepromatous leprosy by treatment status*

Treatment status	No. of cases	Person-years of follow-up	No. of relapses	Relapse rate % per year
Regular (51 to 100%)	43	98.5	0	0.00
Irregular (5 to 50%)	50	114.5	6	5.24
Absent (Less than 5%)	25	52	3	5.77
Not known	7	14.5	0	0.00
Total	125	279.5	9	3.22

adults, and all the relapses occurred among the adults. As the numbers studied are small it is not possible in this group to make age or sex comparisons.

### Discussion

Although the study is not based on a very large number of cases, it has the distinct advantage of a repeated, intensive, and near-complete follow-up of a group of patients with lepromatous leprosy living in their natural environment. The relapse rate for those not taking regular treatment works out at 5.2% per year; this figure is similar to the findings in other studies. The complete absence of relapse among those taking regular treatment was, however, unexpected. In an earlier study (Neelan and Noordeen, 1970) based on routine follow-up of lepromatous patients treated in a mobile treatment unit, we had found that even under regular treatment after becoming bacteriologically negative, there was still a small risk of relapse, to the extent of 0.7% per year (Table 2); on the other hand, in the same study the risk of relapse for those who took irregular treatment was about 4½ times greater, the rate being 3.2% per year. Thus there is no doubt that irregular treatment or cessation of treatment after becoming negative increases the risk of relapse in lepromatous leprosy. Further, the risk of relapse progressively decreases as years pass. In the earlier study we had also found that the risk of relapse was very low after the 6th year of attaining bacteriological negativity and this risk was not affected by whether the patients took treatment regularly or irregularly. This suggests that probably 6 years of treatment, after a case of lepromatous leprosy becomes negative, may be adequate and that the present procedure of advising life-long treatment for lepromatous cases may not be necessary.

### Conclusions

From our study it can be concluded that relapse is a serious problem in lepromatous leprosy, particularly if regular treatment is not taken after becoming bacteriologically negative. However, it also appears to be unrealistic to ask patients with lepromatous leprosy to take life-long treatment, particularly when

TABLE 2\*

*Relapse in lepromatous leprosy by treatment status and period of follow-up*

Treatment status	1 to 3 years			3 to 6 years			Over 6 years			Total		
	Person-years	No. of relapses	Relapse rate	Person-years	No. of relapses	Relapse rate	Person-years	No. of relapses	Relapse rate	Person-years	No. of relapses	Relapse rate
Irregular	48.5	7	14.4	154	12	7.8	494	3	0.6	696.5	22	3.2
Regular	97.5	0	0.0	314.5	3	1.0	1085.5	7	0.6	1497.5	10	0.7
Total	146	7	4.8	468.5	15	3.2	1579.5	10	0.6	2194	32	1.5

\* From Neelan and Noordeen—Relapse in leprosy (under publication).

we know that the risk of relapse decreases with passage of time, and that there is some indication that the very low risk of relapse in later years may not be influenced by treatment status. The problem is particularly serious in centres where large numbers of patients are treated, as for example in leprosy control units. Further work on this problem is suggested.

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