Risk of Paucibacillary Leprosy Patients Released from Control Relapsing with Multibacillary Leprosy[1]

Kumar Jesudasan and Melville Christian[2]

A study on 2027 paucibacillary (PB) patients, of whom 1701 were followed up ([2]), suggested that the lepromin test is one of the most useful indicators to determine the risk of relapse in PB leprosy patients. The above study showed that lepromin-negative patients had a statistically higher risk of relapse ($p < 0.01$) than did lepromin-positive patients. The present paper examines the risk of developing multibacillary (MB) leprosy among the lepromin negative patients who relapsed.

Bernandi, *et al.* ([1]) have suggested that PB patients who are Mitsuda negative should be considered as multibacillary leprosy patients for purposes of treatment since immunologically they are potentially multibacillary.

Ferreira (personal communication) recommended that lepromin-negative PB patients ideally be put on a therapeutic regimen similar to that used for MB leprosy.

MATERIALS AND METHODS

This study has been done using data which have already been described ([2]). During the period 1975 to 1979, 2027 paucibacillary (PB) patients were released from control (RFC) after varying periods of dapsone monotherapy. They all had a minimum of 4½ years to over 15 years of treatment with dapsone monotherapy. During the follow-up visits in 1979 and 1980, 1701 of the patients (95%) who were available (excluding 57 dead, 179 migrated) were seen and examined for relapse. These 1701 patients contributed a total of 5254 person years at risk (PYR). Fifty-one patients relapsed, giving a relapse rate (RR) of 9.7 per 1000 PYR (or 3%), and these 51 patients were further investigated in the present study.

The study included only PB patients who were classified as indeterminate (Ind), tuberculoid (TT), or borderline tuberculoid (BT) leprosy. The classification used was the clinical classification of Ridley and Jopling ([4]), with modifications as suggested by Job and Chacko ([3]). A skin smear was taken at the time of RFC; only skin smear negative patients were considered for release from control. The classification was the one at registration of the patient. Lepromin or histopathology was not used at registration in classifying the patients. Histopathology was also not used in classifying the patients who relapsed.

The Mitsuda lepromin test was done using 0.1 ml of solution containing 160 million bacilli (from human sources) per ml injected intradermally. The reading was taken four weeks later. The lepromin test was done at the time of assessing patients before releasing them from control. At this time it was seen that 41% of these patients clinically classified as indeterminate leprosy at registration were lepromin test negative (a lepromin reading of 5 mm or less after four weeks). Similarly, 33% of the tuberculoid and 43% of the borderline tuberculoid patients were also lepromin negative.

Polar tuberculoid patients cannot have a negative lepromin reading. Hence in the original paper ([2]) it was suggested that clinical classification per se was not accurate enough as done under field conditions. Secondly, clinical classification also has changed over time, with a better understanding of its correlation with histopathological and immunological parameters. The patients in this study were registered between 1963 and 1975. Some of the patients who were clinically classified as paucibacillary were probably potentially multibacillary patients picked up in the early evolutionary stages of multibacillary disease due to an active case finding program.

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[2] K. Jesudasan, M.B.B.S., D.T.P.H., Ph.D. (Lond.), Associate Epidemiologist; M. Christian, M.B.B.S., D.T.M.&H., Dip.Epid. (Prague), Chief, Branch of Epidemiology and Leprosy Control, Schieffelin Leprosy Research and Training Center, Karigiri 631106, South India.

TABLE 1. *Relapse rate by lepromin status.*

Lepromin	No. patients	No. relapses	PYR[a]	RR[b]
Positive	981	18	2824	6.4
Negative	550	29	1877	15.5

[a] PYR = Person years at risk.
[b] RR = Relapse rate per 1000 PYR.

There were also problems in classifying some of the patients who relapsed. Five of the 10 patients classified as MB had a BI of 1+ or less. This was because the patients released from control were actively followed up. The diagnosis of relapse often was made early in the re-evolution of the disease, hence the low BI. All of these patients were lepromin negative and, correlating their clinical picture with their lepromin status, the classification was made as MB. One patient showed no clinical evidence of relapse at all. A skin smear taken (as was taken in 77% of patients followed up) showed a BI of 1+ on routine and selected sites. Hence this patient, who was lepromin negative, was classified as MB. The terms nonlepromatous (NL) and paucibacillary (PB) leprosy are used synonymously.

RESULTS

Mitsuda lepromin positive patients had a relapse rate (RR) of 6.4 per 1000 person years at risk and lepromin-negative patients had a RR of 15.5 per 1000 PYR (Table 1). Lepromin-negative patients had a significantly higher RR ($p < 0.01$) than lepromin-positive patients.

Of the 51 patients who relapsed, 18 (35%) were lepromin positive, 29 (57%) were lepromin negative; the lepromin reading was not available in 4 (8%) patients.

Among the 29 patients who were lepromin negative, 11 relapsed with multibacillary leprosy. The remaining 18 (of the 29) were also lepromin negative but were classified as PB because clinically they had only few lesions and were skin smear negative. None of the 18 lepromin-positive patients relapsed with MB leprosy (Table 4).

The risk of developing multibacillary leprosy in lepromin-negative patients who relapsed was statistically significantly higher than among lepromin-positive patients ($p < 0.01$).

TABLE 2. *Change in type of relapsed patients.*

Initial classification	Classification at time of relapse				Total
	IND	TT	BT	MB	
IND	4	4	3	2	13
TT	2	16	5	7	30
BT	2	1	2	2	7
Total	8	21	10	11	50[a]

[a] Total 51 relapses. Initial type of one patient uncertain, hence not included in table.

TABLE 3. *Bacterial index (BI) of the 11 relapsed patients with MB leprosy.*

BI	No. patients
0.1–0.5	2
1+	3
2+	4
4+	1
Not available	1
Total	11

DISCUSSION

In the earlier study on relapse rates among nonlepromatous patients ([2]), 37.7% of PB patients were lepromin negative. Bernardi, *et al.* ([1]) suggested that PB patients who were lepromin negative were potentially MB patients. This study showed that the risk of relapse with MB leprosy was significantly higher among lepromin-negative PB patients than in lepromin-positive patients who relapsed. This raised the question of how

TABLE 4. *Lepromin status in relation to classification at relapse.*[a]

Lepromin result	Clinical classification at relapse		Total
	MB	PB	
Negative (0–5 mm)	11	18	29
Positive (>5 mm)	0	18	18
Total	11	36	47[b]

[a] Chi-square value 6.9, 1 df ($p < 0.01$).
[b] Of the 51 total patients, lepromin reading not available for 4.

lepromin-negative PB patients, should be treated in the first place. The World Health Organization (WHO) ([5]) has suggested a uniform regimen of treatment for all paucibacillary leprosy patients.

Our present findings suggest that a uniform treatment regimen with dapsone monotherapy may result in lepromin-negative PB patients relapsing with MB leprosy. It is probably better to use lepromin, where feasible, for operationally classifying PB patients as lepromin positive (true PB) and lepromin negative (potentially MB) patients. Even though the present findings are in relationship to dapsone monotherapy, there may be implications regarding the WHO ([5]) regimen in PB leprosy. This regimen is based on the bacterial load, which is low in paucibacillary leprosy, and the potent bactericidal action of rifampin. This regimen will be adequate for lepromin-positive PB patients, especially those with a single or few lesions. However, whether this same short-term chemotherapy would suffice in lepromin-negative paucibacillary patients, especially those with multiple lesions (who could be potentially multibacillary), needs to be carefully evaluated.

SUMMARY

We studied 51 paucibacillary patients who had relapsed after cessation of dapsone monotherapy. Among the 51 relapses, the lepromin-negative group had a significantly higher risk of relapsing with multibacillary leprosy compared with the lepromin-positive group of patients. The significance of these findings is discussed.

RESUMEN

Se estudiaron 51 pacientes paucibacilares que habían recaído después de suspender su monoterapia con dapsona. Entre los casos que recayeron, los pacientes lepromino-negativos tuvieron un mayor riesgo de recaer con lepra multibacilar que los pacientes lepromino-positivos. Se discute el significado de estos hallazgos.

RÉSUMÉ

On a étudié 51 malades paucibacillaires qui avaient présenté des récidives après l'interruption de la monothérapie par la dapsone. Parmi les 51 récidives, le groupe des malades présentant une réaction négative à la lépromine témoignait d'un risque significativement plus élevé de faire une rechute se manifestant sous la forme d'une lèpre multibacillaire que les malades positifs à la lépromine. La portée de ces observations est discutée.

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