

## Infectivity of Secondary Dapsone-resistant Cases<sup>1</sup>

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The problem of primary and secondary dapsone resistance has been highlighted by a large number of studies (1-6, 11-15, 20). There has been a worldwide increase in the problem (23). Recently, the issue of the infectivity of cases of secondary dapsone resistance has been raised (22). It is currently assumed that primary dapsone-resistant cases arise because of infection from secondary dapsone-resistant cases (18). If this is so, the incidence of primary dapsone resistance must be high among contacts of secondary dapsone-resistant cases who develop leprosy. This study looks into the incidence rates of leprosy among household contacts of 113 secondary dapsone-resistant cases diagnosed between 1970 and 1982.

### MATERIALS AND METHODS

Data from 113 cases of secondary dapsone-resistant leprosy with 598 contacts were analyzed. These cases were proven to have secondary dapsone resistance (SDR) by the Division of Laboratories of the Schieffelin Leprosy Research and Training Centre at Karigiri, India, using the mouse foot pad technique.

The information on the household contacts was obtained from contact survey registers of the cases from the time of registration, i.e., between 1970 and 1982.

Incidence rates of leprosy among contacts were defined as cases arising among household contacts found free of leprosy at least once before the onset of the disease. Co-prevalent cases of leprosy were household contacts diagnosed as having leprosy the first time they were examined. These were not considered as true incident cases but as co-prevalent cases, which could have arisen due

to a common source of infection outside the household (1).

For the calculation of incidence rates, person years at risk were used, as in earlier studies (7-9, 16).

### RESULTS

**Response to dapsone monotherapy.** The age and sex of the 113 primary cases is given in Table 1. These 113 primary cases of leprosy had 598 household contacts, of whom 81 were classified as co-prevalent cases (CPC) and 22 as incident cases (IC) of leprosy (total = 103). After excluding the 81 CPC, the incidence rate was studied among the 517 contacts.

Among the 81 CPC, 25 were multibacillary (MB) and 56 were paucibacillary (PB). Seventeen of the PB cases were deleted as migrated or as defaulters, and five PB cases were put directly on multidrug therapy (MDT). The remaining 25 MB cases and 34 PB cases were put on dapsone monotherapy, and were assessed for their responses to treatment (total = 59) (Table 2).

Of the 22 incident cases, 2 were MB and 20 were PB. Two of the PB cases migrated, and four PB cases were put on MDT directly. The remaining 2 MB cases and 14 PB cases put on dapsone monotherapy were assessed for their responses to treatment (total = 16).

Combining the CPC and IC, there were 27 MB and 48 PB cases who were assessed for their responses to dapsone monotherapy (total = 75).

All of the 16 incident cases studied, including the two MB cases, showed good responses to dapsone monotherapy. Among the 59 CPC studied, there were two MB cases who did not respond satisfactorily to dapsone monotherapy; they were confirmed to be dapsone resistant using mouse foot pad studies. One MB case who showed a slow response to dapsone was put on MDT before mouse foot pad studies were done. Thus, there were two and possibly three dapsone-resistant cases among the 27 secondary (CPC and IC) MB cases studied.

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TABLE 1. Age and sex of the 113 primary cases.

Sex	Age			Total
	20	20-39	≥40	
Males	1	22	65	88
Females	0	12	13	25
Total	1	34	78	113

None of the 48 secondary PB cases were suspected of being dapsone resistant (DR).

**Incidence rate of leprosy among household contacts of the 113 DR cases.** The 113 dapsone-resistant cases had 517 household contacts (after exclusion of 81 CPC). The 517 household contacts contributed 5074 person years at risk. Twenty-two incident cases of leprosy developed over the period of surveillance of 2 to 12 years, giving an incidence rate of 4.3/1000 person years at risk (PYR) (Table 3).

The profile of dapsone resistance to different strengths of dapsone in the mouse diet is given in Table 4. Of the 113 DR cases, 65.6% had bacilli which were resistant to concentrations of 0.01% of dapsone in the diet; 13.3% were of moderate dapsone resistance.

### DISCUSSION

The incidence rate of leprosy among household contacts of MB cases in an earlier study in the same area was 4.8/1000 PYR<sup>(10)</sup>. The incidence rate among household contacts of the dapsone-resistant cases was similar (4.3). This difference was statisti-

TABLE 3. Incidence rate of leprosy among household contacts of 113 dapsone-resistant cases.

No. dapsone-resistant cases	113
No. household contacts	598
No. incident cases	22
No. co-prevalent cases	81
Person years at risk	5074
Incident rate	4.3

cally not significant. The comment<sup>(22)</sup> that bacteriological evidence suggests that dapsone-resistant cases of leprosy are more infectious, in relationship to transmission of leprosy within households, needs to be further studied.

Earlier studies on the prevalence of dapsone resistance in the same area indicated that 3% of the MB cases on treatment were proven to be dapsone resistant<sup>(1-5)</sup>. Among 75 contacts who developed leprosy and were put on monotherapy in this study, there were two cases of proven dapsone resistance among 27 MB contacts who developed leprosy. This gives a rate of 7-11% as the prevalence of dapsone resistance among household contacts who developed MB leprosy.

This is a small study and the data are not conclusive, but they do suggest that there may be more than average sulfone-resistant disease among contacts of secondary sulfone-resistant cases. This needs further investigation. However, the prevalence of dapsone resistance in this study (7-11%) is two to three times higher than similar studies in the same area. The incidence rate of

TABLE 2. Age and sex of the 16 incident cases and 59 co-prevalent cases.

		MB <sup>a</sup>			PB <sup>b</sup>			Totals		
		M <sup>c</sup>	F <sup>d</sup>	T <sup>e</sup>	M	F	T	M	F	T
IC <sup>f</sup>	0-19	0	1	1	3	6	9	3	7	10
	≥20	1	0	1	2	3	5	3	3	6
	Total	1	1	2	5	9	14	6	10	16
CPC <sup>g</sup>	0-19	0	0	0	0	1	1	0	1	1
	≥20	19	6	25	17	16	33	36	22	58
	Total	19	6	25	17	17	34	36	23	59

<sup>a</sup> MB = multibacillary cases.

<sup>b</sup> PB = paucibacillary cases.

<sup>c</sup> M = males.

<sup>d</sup> F = females.

<sup>e</sup> T = totals.

<sup>f</sup> IC = incident cases.

<sup>g</sup> CPC = co-prevalent cases.

TABLE 4. Susceptibility to dapsone of 113 dapsone-resistant cases using the mouse foot pad model.

	No. cases	%
Not sensitive to 0.01% <sup>a</sup>	74	65.5
Not sensitive to 0.001%	15	13.3
Not sensitive to 0.0001%	15	13.3
Resistant (strength not known)	7	6.2
No growth	2	1.7
Total	113	100.0

<sup>a</sup> Percentage weight of dapsone (w/w) in mouse diet.

leprosy as seen is not higher than in previous studies, indicating that household contacts of secondary dapsone-resistant MB cases and those of sulfone-sensitive MB cases are at similar risk.

However, there are methodological issues connected with the exclusion of the co-prevalent cases which have been dealt with in previous studies. Since large numbers of dapsone-resistant cases and their household contacts may not be available for studies, pooling of data from other centers is suggested to provide a clearer picture.

Studies in tuberculosis on isoniazid-resistant tubercle bacilli seem to suggest that these bacilli are less pathognomonic than the sensitive strains<sup>(16, 17, 19, 21)</sup>. Whether or not this is the case with *Mycobacterium leprae* needs further investigation.

The introduction of multidrug therapy in leprosy will to a large extent decrease the problem of drug resistance since a combination of three drugs is being used<sup>(23)</sup>.

#### SUMMARY

The incidence rate of leprosy among 517 household contacts of 113 cases of secondary dapsone resistance with 5074 person years at risk were studied. The incidence rate of leprosy was 4.3 per 1000 person years at risk, which is very similar to the incidence rate (4.8) among household contacts of lepromatous cases. Two, possibly three, cases of primary dapsone resistance were detected among the 27 contacts who developed multibacillary leprosy. There was no evidence of dapsone resistance among 48 paucibacillary leprosy cases assessed when treated with dapsone monotherapy. The possibility that secondary dapsone-resistant cases will infect and will result in an increase in the

number of primary dapsone-resistant cases needs to be investigated further.

#### RESUMEN

Se estudió la incidencia de lepra entre 517 contactos familiares de 113 casos con resistencia secundaria a la dapsona para 5074 personas-año en riesgo. El grado de incidencia de la lepra fue de 4.3 por 1000 persona-año en riesgo, el cual es muy similar al grado de incidencia (4.8) entre los contactos familiares de los casos lepromatosos. Entre los 27 contactos que desarrollaron lepra multibacilar se detectaron 2 ó 3 casos de resistencia primaria a la dapsona. No hubo ninguna evidencia de resistencia a la droga entre 48 casos paucibacilares de lepra tratados con monoterapia con dapsona. Debe de estudiarse más la posibilidad de que los casos con resistencia secundaria a la dapsona puedan infectar y conducir al aumento en el número de casos de resistencia primaria a la dapsona.

#### RÉSUMÉ

On a étudié le taux d'incidence de la lèpre chez 517 contacts domiciliaires de 113 cas de lèpre atteints de résistance secondaire à la dapsonne, qui ont été observés pendant 5074 personne années. Le taux d'incidence de la lèpre a été de 4,4 par 1000 personne années à risques, ce qui fournit une valeur très semblable à celle du taux d'incidence (4,8) parmi les contacts domiciliaires de malades lépromateux. Parmi 27 contacts qui avaient développé une lèpre multibacillaire, on a détecté deux, et même peut-être trois cas de résistance primaire à la dapsonne. Aucune évidence de résistance à la dapsonne n'a été constatée chez 48 cas de lèpre paucibacillaire, alors que ceux-ci étaient traités par la monothérapie à la dapsonne. Des recherches supplémentaires sont nécessaires pour démontrer le caractère infectieux des malades atteints de résistance secondaire à la dapsonne, et leur rôle dans l'augmentation du nombre de cas de résistance primaire à ce médicament.

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