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Evaluation of "Chemical Isolation" in 1,168 Leprosy Patients' Homes [1, 2]

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In recent years many leprologists have considered the possibility of evaluating statistically, through epidemiologic studies, the concept of "chemical isolation" which is understood as the supposed power of sulfone treatment to reduce to nil (within four to six months) the infectiousness of the leprosy patient with respect to the transmission of viable bacilli ([7, 20, 22, 27]). Such studies are extremely important in view of the fact that chemotherapy is at present the only widely accepted measure used to protect susceptible people against leprosy ([1, 3, 5, 6, 8, 9, 12]).

In the view of many authors, this mentioned hypothesis has been confirmed by some laboratory findings such as the fall of the Morphologic Index (MI) from four to six months after initiation of treatment ([13]) and/or the loss of viability of *Mycobacterium leprae* after three months of treatment even on minimal dosage ([17, 18, 19]), as assessed by mouse foot pad inoculations ([15, 16]).

Many other leprologists do not agree with these criteria ([14]). Levy ([11]) observed that "it is unquestionably extremely hazardous to extend the results in the mouse to man" and Bechelli and Guinto ([4]) say "final proof of the relationship between the MI and contagiousness can come only from prolonged and well planned epidemiologic studies."

This study presents an evaluation of "chemical isolation" through a retrospective study of a large group of household contacts of leprosy patients.

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[2] Presented at the Tenth International Leprosy Congress, Bergen, Norway, 14 August 1973 (IJL **41** [1973] 612-613). This study was done at the PAHO/WHO Center for Research and Training in Leprosy and Related Diseases, Instituto Nacional de Dermatología, Venezuela.

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MATERIALS AND METHODS

Comparable groups from 7,232 contacts from homes of 1,168 leprosy patients (LL & BB and TT & I), born before treatment (Group A) and born after treatment (Group B) of the index case had begun, were investigated. Ongoing studies will extend the study to more patients' homes.

It is important to point out that the protection to be evaluated is the protection conferred by the routine treatment that is given to the patient in the field, including the factor of possible failures in regularity with which this treatment is taken.

Families of patients registered from 1948 to 1968 were studied in order to obtain comparable groups of contacts before and after beginning treatment of the index case, with ages (as of December 1972) ranging from 5 to 24 years (Tables 1 and 2).

Thus, of two contacts born in 1952, whose sick relatives were registered in 1949 and 1956 respectively, both were 20 years old in December 1972. However, the first contact belonged to Group B while the second belonged to Group A.

In order to avoid the negative effect of the varying periods of observation in the comparison of groups included in Tables 1 and 2, the rates were calculated per 1,000 persons/year. Thus, in Table 1, among the 10-14 age group, 320 contacts produced 17 cases during 1.812 years of observation, with a rate of 9.4 per 1,000 persons/year. One thousand contacts belonging to this age group observed during one year would, therefore, produce 9.4 cases.

In addition, the study was extended to the whole group (Table 5) of Group A and Group B contacts, both of open (LL & BB) and closed (TT & I) cases, based on the fact that the variations in involved variables, such as age and period of observation, are spread at random in the same proportion among Group A and Group B contacts, since we were managing large numbers.

The data for this study was found in the

TABLE 1. *Morbidity in contacts of LL and BB index cases.*

Age (years)	GROUP A				GROUP B			
	Contacts	Cases	Years of observation	Rate × 1,000 persons per year	Contacts	Cases	Years of observation	Rate × 1,000 persons per year
5-9	76	1	351	2.8	392	7	2,239	3.1
10-14	320	17	1,812	9.4	306	8	2,860	2.8
15-19	491	41	3,225	12.7	182	8	2,044	3.9
20-24	493	27	3,545	4.8	56	1	797	1.3
Total	1,380	86	8,933	9.6	936	24	7,940	3.0

$p < 0.01$ = the difference between the rates 9.6 and 3.0 is statistically significant.

case histories of 19 centers of the Departmento de Dermatología Sanitaria of Ministerio de Sanidad de Venezuela. Statistical significance was established by means of the standard curve method.

RESULTS

In two groups of contacts, which were comparable with regard to age in December 1972, born before (Group A) and after (Group B) dapsone treatment of the LL or BB case had begun (Table 1), Group A for age groups of ten years and over had higher incidence rates as compared to the same ages in Group B. For ages 5-9 the incidence rate was less for Group A. This may be explained by the fact that in that group the observations never began at birth so we lost the chance to register some incipient forms that generally disappear spontaneously.

The incidence rate in the group which had ages from 5-9 years instead of being 2.8 should be three times higher (9.3) perhaps, the same as in the other age groups. The difference should indicate the number of lost diagnoses. Considering the global rate, we can see that in Group A the prevalence was more than three times higher than in Group B which means that treatment of a case conferred a good degree of protection (about 66%). Nevertheless, we consider that the rate in Group B was elevated, especially in the 15-19 age group.

This prevalence could be explained by the persistence of the contagiousness of the cases under treatment and/or by the possibility of exposure outside the home to open untreated cases ([2]). In order to establish the value of both possibilities in producing the prevalence in Group B, we have considered the morbidity among contacts 5-24 years old in Groups A and B from TT and I patients' homes (Table 2). We may appreciate that in Group B the rate was nil and consequently, if LL and BB patients under treatment behaved the same as TT and I patients, the rate in the Group B contacts of LL and BB cases should also be nil.

We have also studied the infection rate in Group B contacts of LL and BB patients ac-

TABLE 2. *Morbidity in contacts of TT and I index cases.*

Age (years)	GROUP A				GROUP B			
	Contacts	Cases	Years of observation	Rate × 1,000 persons per year	Contacts	Cases	Years of observation	Rate × 1,000 persons per year
5-9	73	—	249	—	278	—	1,441	—
10-14	266	3	1,450	2.1	182	—	1,493	—
15-19	353	1	2,217	0.4	106	—	943	—
20-24	350	9	2,270	4.0	23	—	267	—
Total	1,042	13	6,186	2.1	589	—	4,144	—

TABLE 3. *Morbidity among contacts of LL and BB index cases (1,972) according to the interval between the beginning of treatment and the birth of the contact.*

Interval (years)	Contacts	Mean age	Contact cases	Years of observation	Rate × 1,000
0-4	546	12.7	17[a]	4,862	3.5
5-9	268	11.3	5	2,166	2.3
10-14	96	10.0	2	750	2.7
15-19	25	9.3	—	158	—
20-24	1	8.0	—	4	—
Total	936	11.9	24	7,940	3.0

[a] The 17 cases appeared: 0 years—5 cases; 1 year—3 cases; 2 years—4 cases; 3 years—1 case; and 4 years—4 cases.

cording to the interval between the beginning of treatment and the birth of the contact. As seen in Table 3, all of the morbidity appeared in the groups with less than 15 year intervals and the higher modified rate belonged to the 0-4 age group. This indicates that the persistence of contagiousness was greater in the 0-4 age group due to the slow action of dapsone, since the chances of contagion outside the home must be equal in each group, if the average ages of the groups were sufficiently comparable. When the infection in the 0-4 years group was analyzed, it was found that there was no preference for a particular year since the observed differences were not statistically significant.

When the age of onset of the disease in contacts was considered in both Group A and Group B (Table 4), it was apparent that most of the cases were 15 years old or less, especially under ten years, as was expected in view of the fact that they were adequately controlled contacts. There also appeared to be an apparent predominence of TT and I cases in Group B but actually they were similar ($p = 0.4237$).

When all the contacts in this study were taken into account (Table 5) it was found that both Group A and Group B presented a higher rate among contacts of LL and BB

TABLE 4. *Contact case age at onset and type of leprosy acquired.*

Age at onset of disease (years)	GROUP A				GROUP B			
	LL & BB	TT & I	Total	% TT & I	LL & BB	TT & I	Total	% TT & I
0-4	—	14	14	100.0	—	9	9	100.0
5-9	6	29	35	82.9	5	9	14	64.2
10-14	4	20	24	83.3	—	—	—	—
15-19	1	11	12	91.7	—	1	1	100.0
20-24	1	—	1	0	—	—	—	—
Total	12	74	86	86.0	5	19	24	79.2

$p = 0.4237$. Thus the difference between the percentages of TT and I cases, 86.2 among Group A and 79.2 among Group B, is not statistically significant.

TABLE 5. *Morbidity in contacts according to the form of leprosy of the index case.*

Index case type	GROUP A			GROUP B		
	Contacts	Cases	%	Contacts	Cases	%
LL & BB	3,170	293	9.2	1,074	23	2.1
TT & I	2,253	71	3.2	715	1	0.1
Total	5,423	368	6.8	1,789	24	1.3
p			<0.01			<0.01

patients. This fact was surprising in Group B since both groups were exposed to the same risk in their homes as well as to untreated open cases outside the home. From a statistical concept of large numbers, the second possibility would be of the same value in both groups since the factors which we have not taken into account must be accounted for similarly in both groups.

If treated BB and LL patients behaved the same as TT and I cases, the rate in both groups would be practically the same. Nevertheless, the observed difference (2.0%) is statistically significant ($p < 0.01$) which might indicate a persistence of the contagiousness of the LL and BB patients under treatment.

Table 2 suggests that TT and I cases are, to a certain degree, contagious and that "chemical isolation" eliminates infectiousness.

The 0/1000 rate among household contacts in Group B of TT and I index cases indicates that exposure outside the home to open untreated cases was not an important source of disease since both those contacts in Group A and Group B (2.1 per thousand rate) underwent the same risk of exposure to open cases outside the home. Nevertheless, the above noted infection rate for Group B (2.1 per thousand) was due to the untreated closed cases (TT & I) living in the home.

It is concluded that treatment of open cases confers a degree of protection (66%) to household contacts. The residual rate (33%) may be attributed, at least in part, to the persistence of contagiousness of the patients. For this reason, from an epidemiological point of view, bacteriologically positive LL and BB patients under treatment cannot be regarded as noncontagious. Nevertheless, they may be considered as being less contagious. The protection among TT and I household contacts is apparently complete. However, the small size of this group does not permit a firm conclusion to this effect.

SUMMARY

"Chemical isolation" (treatment of open cases as a measure of control for transmission between contacts) is evaluated by a retrospective study of 7,232 household contacts of 1,168 leprosy patient homes. Contacts comparable in age and type of exposure were arranged in subgroups according to whether they were born before (Group A) or born after (Group B) beginning treatment of the index cases had begun. Additionally, the whole group of contacts, both of open (LL & BB) and closed (TT & I) cases were evaluated.

Among comparable contacts of LL and BB cases, the infection rate in the contacts before initiation of treatment is higher than in that of contacts after initiation of treatment. The protection afforded by the treatment to the exposed group (Group B) is on the order of 66%.

The morbidity occurring in the group born after the initiation of index case treatment apparently results from partial persistence of infectiousness of the case under treatment.

RESUMEN

Se evalúa el "aislamiento químico" (tratamiento de casos abiertos como medida de control de la transmisión entre contactos) en un estudio retrospectivo de 7232 contactos domiciliarios en 1168 casas de pacientes con lepra. Los contactos comparables en lo que respecta a edad y tipo de exposición, fueron separados en sub-grupos en relación a si habían nacido antes (Grupo A) o después (Grupo B) del comienzo del tratamiento del caso índice. Además, se evaluó todo el grupo de contactos, tanto de casos abiertos (LL y BB) como cerrados (TT e I).

En contactos comparables de casos LL y BB, la tasa de infección en los contactos de antes del inicio del tratamiento es más alta que en los contactos posteriores al inicio del tratamiento. La protección que recibió el grupo post-tratamiento es del orden del 66%.

La morbilidad que se observó en el grupo nacido después del inicio del tratamiento del caso índice, aparentemente se debe a una persistencia parcial de la infectividad de los casos bajo tratamiento.

RÉSUMÉ

On a évalué la valeur du traitement des cas ouverts comme mesure de contrôle pour la transmission de la lèpre entre les contacts (autrement appelés isolement chimique), en menant une étude rétrospective de 7.232 contacts domiciliaires répartis dans 1.168 maisons de malades de la lèpre. Des contacts comparables quant à l'âge et au type d'exposition ont été divisés en sous-groupes, selon qu'ils étaient nés avant (groupe A) ou après (groupe B) que le traitement ait été entamé chez le cas index. De plus, on a évalué l'entièreté du groupe de contacts, tant les

contacts de cas ouverts (LL et BB) que les contacts de cas fermés (TT et I).

Lorsque l'on compare des contacts assortis de cas LL et de cas BB, le taux d'infection parmi les contacts avant le début du traitement chez le cas index est plus élevé que le taux d'infection observé chez les contacts nés après le début du traitement. La protection conférée dans le groupe exposé au traitement (groupe B) est de l'ordre de 66 pour cent.

La morbidité survenant dans le groupe né après le début du traitement du cas index provient appremment d'une persistance partielle du caractère infectieux des cas en traitement.

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