

Susceptibility to Leprosy and Serum Atypical Pseudochoolinesterase¹

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It has been observed that when scoline is used as a muscle relaxant in leprosy patients undergoing surgery, apnea of more than normal duration results (20). Whether these patients had low levels of pseudochoolinesterase or the enzyme presents as an atypical variant has not been determined. Low cholinesterase activity was observed by Lehmann and co-workers (4,5) in patients who had prolonged apnea following suxamethonium chloride. Lehmann and Ryan (11) pointed out that in some patients the low enzyme activity was not the result of disease but of a hereditary factor, and Kalow (8) has shown that the activity of the enzyme was not only low but qualitatively altered owing to a hereditary change in the enzyme itself. He introduced the term "atypical" to designate the altered enzyme. Kalow further showed that the atypical enzyme variant can be reliably distinguished from the typical serum cholinesterase by the dibucaine number (D.N.). On the basis of the D.N., any given population can be divided into three groups. Those with a D.N. above 70 form the highest percentage and are said to have the typical type of esterase. In a very small percentage of subjects, the D.N. is below 40 and their sera is said to possess the atypical esterase. In the intermediate group with a D.N. between 40 and 70, the serum is thought to have both typical and atypical enzymes. Genetic and biochemical evidence suggest that the first two groups of subjects, each with one or the other of the two enzymes, are homozygotes for one or the other of a pair of allelic genes, and that the third group probably has a mixture of the

two enzymes and represents the heterozygotes.

Many authors have suggested the possibility of genetic factors influencing susceptibility to leprosy. There are studies to show a greater incidence of leprosy in O type blood group individuals than in the B type group and in monozygotic twins rather than dizygotic twins (6,7,12,17). There are no studies to determine the presence of an atypical variant of the pseudochoolinesterase in leprosy patients. Studies on serum cholinesterases in healthy Indians are few (2,3,9,14,21). A preliminary study conducted to determine whether there is any abnormality or deficiency of the cholinesterase by Thomas and Job (19) showed a significantly greater prevalence of the atypical enzyme among lepromatous leprosy patients than in normal subjects. This paper is the result of a study of cholinesterase in a larger sample of leprosy patients and normal controls to assess and confirm the findings of the earlier report.

MATERIALS AND METHODS

The method adopted for the estimation of pseudochoolinesterase and D.N. was the technique of Steinitz *et al* (18) which is a modification of the method of Rappaport and associates (16).

The control population for the study consisted of those who attended the Christian Medical College Hospital, Vellore for minor complaints and routine check-ups, blood donors, staff and medical students of C.M.C. The subjects were chosen after a thorough physical examination to rule out anemia, thyrotoxicosis, liver disease, diabetes, malignancy and other significant pathologic change. Record was also made of any similarity of blood types in the family. A total of 720 patients, male and female, with ages ranging from 20 to 55 years formed the control population.

Sera of leprosy patients was obtained from 721 patients having ages varying from 4 to 55 years who attended the Schieffelin

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Leprosy Research Centre and other leprosy clinics organized by the Christian Medical College at nearby villages. The patients were examined and the type of leprosy classified according to Ridley's classification. There were 420 lepromatous and 301 tuberculoid patients. In 436 of these cases, a skin biopsy and lepromin test confirmed the classification.

RESULTS

Estimations of esterase level and D.N. were performed in 720 control and 721 leprosy patients. The cholinesterase values ranged from 56 to 120 units with an average mean of 84.4 in normal, and 78.6 in leprosy patients. There was no statistical difference in the esterase levels between leprosy patients and normal controls. There was also no significant difference in esterase levels between male and female patients.

Tables 1 and 2, and Figure 1 show the dibucaine number results in the samples studied. Among the normal samples analyzed, 701 of 720 had a D.N. above 70 (97.36%), that is, having the typical pseudo-cholinesterase enzyme. The atypical esterase as depicted by a D.N. below 40 was found in one person only. The intermediate group with a D.N. between 40 and 70 consisted of 18 persons (2.5%).

The leprosy patients taken as a whole showed that 400 (55.48%) had a D.N. above 70. The intermediate groups with a D.N. between 40 and 70 consisted of 291 individuals (40.36%), whereas those with a D.N. below

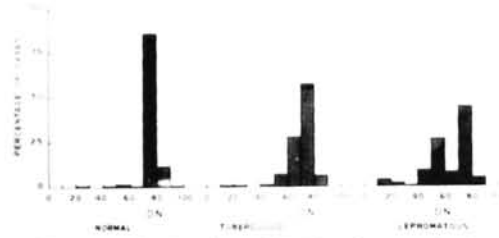


FIG. 1. Distribution of D.N. of normal tuberculoid and lepromatous cases.

40 comprised 30 persons (4.16%). The distribution of D.N. at all three levels, that is, above 70, 40-70, and below 40, among leprosy patients was significantly different compared with the normal population studied ($p < 0.001$, Table 2).

Of the 301 tuberculoid leprosy patients studied, 191 (63.46%) had a D.N. above 70; 105 (35.9%) had a D.N. between 40-70; and 2 (0.66%) had a D.N. below 40. The difference in the D.N. between the 40-70 and the above 70 groups as distributed between normal and tuberculoid patients was significant ($p < 0.001$), however, there was no significant difference between the control population and the tuberculoid patients in the below 40 value group. There was significant difference in the D.N. distribution at all levels between tuberculoid and lepromatous patients (Table 2).

DISCUSSION

Cholinesterase values obtained in this study of the normal sera were 56 to 120 units which is in conformity with other stud-

TABLE 1. Distribution of D.N. levels among normal and leprosy patients.

Subjects	D.N.	Above 70		40-70		Below 40		Total	
		No.	%	No.	%	No.	%	No.	%
Normal		701	97.36	18	2.5	1	0.14	720	100
Lepromatous		209	49.78	183	43.57	28	6.6	420	100
Tuberculoid		191	63.46	108	35.88	2	0.66	301	100
All leprosy		400	55.48	291	40.36	30	4.16	721	100

TABLE 2. Statistical analysis of results.

Subjects	D.N.	Above 70		40-70		Below 40	
		Normal	TT leprosy	Normal	TT leprosy	Normal	TT leprosy
Lepromatous		$p = .001$	$p = .001$	$p = .001$	$p = .05$	$p = .001$	$p = .001$
Tuberculoid		$p = .001$	—	$p = .001$	—	NS	—
All leprosy		$p = .001$	—	$p = .001$	—	$p = .001$	—

ies⁽³⁾. No statistically significant difference in cholinesterase values was observed between normal subjects and leprosy patients. The distribution of the D.N. in the normal subjects in the present study was in conformity with studies done in India and elsewhere^(1, 10, 13, 15). In the case of leprosy patients there was a statistically significant difference in the distribution of the D.N. at all three levels when compared to normal subjects. The difference in distribution of the D.N. was more marked in lepromatous leprosy patients alone when compared with normal subjects. That the number of patients with the atypical enzyme (D.N. below 40) was significantly more in lepromatous leprosy patients is especially noteworthy. There was no significant difference among the tuberculoid patients and normal patients with regard to the D.N. below 40 group.

Thus, the distribution of the D.N., which indicates the nature of the cholinesterase enzyme, was significantly different in the lepromatous leprosy patients as compared with the normal population and the tuberculoid leprosy cases.

In this study it was found that the incidence of the atypical enzyme is significantly greater among lepromatous leprosy patients than in normal subjects or tuberculoid leprosy patients. That the susceptibility to leprosy is influenced by various genetic factors has been suggested by many authors but none of the studies have been conclusive⁽²²⁾. We propose from our findings that, since there is a greater incidence of the atypical enzyme in the lepromatous leprosy cases, the presence of this enzyme or deficiency of the typical enzyme may make a person more susceptible to leprosy. Further studies on contacts of leprosy patients having a low D.N. are in progress. An alternative hypothesis postulated is that the disease itself has altered the enzyme pattern in the patients. This is possible to substantiate only by again screening the same population that are exposed to leprosy after five years and comparing the esterase levels and the D.N. then with what has already been recorded.

SUMMARY

The pseudocholinesterase levels and the nature of the enzyme as shown by the dibucaine number (D.N.) were estimated in 720 controls and 420 lepromatous leprosy patients, and 301 tuberculoid leprosy patients.

There was no statistical difference in the esterase levels between leprosy patients and normal controls. But the distribution of D.N. was significantly different in the leprosy patients compared to the normal population studied. The D.N. below 40 indicates the samples with the atypical pseudocholinesterase—the presence of which is genetically determined. The distribution of samples with D.N. below 40 was significantly higher in the lepromatous leprosy patients compared to the normal population or tuberculoid leprosy patients. It is proposed that since there is a greater incidence of the atypical enzyme in lepromatous leprosy cases, the presence of this enzyme or the deficiency of the typical enzyme may make a person more susceptible to leprosy.

RESUMEN

Los niveles de pseudocolinesterasa y la naturaleza de la enzima demostrada por el "numero dibucaine" (D.N.) fueron estimados en 720 controles normales y en 420 pacientes con lepra lepromatosa y en 301 pacientes con lepra tuberculoides. No diferencias estadísticas en los niveles de esterases fueron observados entre pacientes leproso y los controles normales. Pero la distribución del D.N. fue significativamente diferente en pacientes leproso comparados con la población normal estudiada.

El D.N. por debajo de 40 indica la presencia de colinesterasa atípica, cuya presencia es determinada genéticamente. La distribución de muestras con D.N. por debajo de 40 fue significativamente mayor en pacientes con lepra lepromatosa comparados con la población normal o con pacientes con lepra tuberculoides. Desde que existe mayor incidencia de la enzima atípica en casos de lepra lepromatosa, se propone que la presencia de esta enzima o la deficiencia de la enzima típica puede hacer a una persona más susceptible a la lepra.

RÉSUMÉ

Chez 720 témoins, chez 420 malades atteints de lèpre lépromateuse, et chez 301 sujets tuberculoïdes, on a procédé à une estimation des niveaux de pseudocholinestérase ainsi qu'à une évaluation de la nature de cette enzyme telle qu'on peut l'étudier par le nombre dibucainique (D.N.). On n'a observé aucune différence significative dans les niveaux d'estérase relevés chez les malades atteints de lèpre et chez les témoins normaux. Par contre, la distribution du nombre dibucainique était significativement différente chez les malades de la lèpre comparée à la population normale. Un D.N. inférieur à 40 révèle les échantillons qui ont une pseudocholinestérase atypique,

dont la présence est déterminée génétiquement. La distribution des échantillons présentant un D.N. en-dessous de 40 était significativement plus élevée chez les malades atteints de lèpre lépromateuse que chez les sujets normaux ou les malades tuberculoïdes. Puisque la prévalence de cette enzyme atypique est supérieure dans la lèpre lépromateuse, la présence de cette enzyme ou la déficience d'une enzyme atypique peut signifier qu'une personne est plus susceptible à la lèpre.

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