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A Study of Blood Groups and Leprosy in the Population of Colonia Tovar, Venezuela[1, 2]

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As a preliminary trial for a larger study of genetic polymorphism and leprosy, a survey of ABO blood groups was undertaken among leprosy patients and nonleprotic controls in the isolate of Colonia Tovar in Venezuela.

STUDY AREA

Colonia Tovar is located in a valley covering approximately 13 square miles, at an altitude of 6,000 feet in the State of Aragua, in the northern part of Venezuela. The population constitutes a genetic isolate, consisting almost exclusively of persons of German ancestry, descendants of immigrants who settled in the valley between 1843 and 1856. It is said that these settlers numbered 146, representing 110 patronyms. For the most part they originated from a few villages in the Black Forest, Germany. Since then the population has lived in a state of relative isolation, no road having connected the valley to the rest of the country until the 1950's.

The surrounding mountainous area is almost unpopulated, except for a few scattered families of Creole extraction, born of Spanish and/or Indian ancestry. The result has been high inbreeding of the group. Apart from shopkeepers and skilled workers, who live around the church, the population is scattered in small farms in the valley or foothills. The households are often constituted by three generations, grandparents, parents and children.

The German population of the region, however, is not limited to Colonia Tovar. As the population increased over the last hundred years, a few satellite hamlets developed in nearby valleys beyond the mountains. As the years passed, some people moved to the nearest Creole villages or even to the city of La Victoria. Cultural, linguistic and breeding characteristics have been diluted progressively as the distance from the center of the settlement increased. Recently, with the opening of a road connecting Colonia Tovar and Caracas, important changes have commenced in the community, which is now rapidly losing its earlier characteristics. The village has a health center, with a physician in charge, helped by three auxiliary-nurses.

Census data are extensive and apparently close to complete, the whole population having been followed up for the last 12 years by the Servicio de Dermatología Sanitaria (leprosy service) of Aragua State. The data include distribution of the population by household, with information on sex, age and family relationship for each member of the household. In 1962 census estimates gave a total German population of 1,028 in Colonia Tovar (1,107 have left the isolate and live elsewhere).

The prevalence of leprosy in the community is high. It is not known how and when the disease was introduced. A survey made in 1942 revealed 32 confirmed cases of leprosy and 9 suspects among 808 persons examined ([6]). Cases were sent to the Cabo Blanco Leprosarium, near Caracas, where at one time 29 patients from Colonia Tovar

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were isolated. In 1950 Convit ([3]) found 113 cases among 1,126 persons examined, who constituted nearly all the population at that time. The prevalence, therefore was 100.4/1,000, a figure in sharp contrast to the prevalence in the rest of the State of Aragua, 1.35/1,000.

After 1950, several surveys were made again by Convit *et al.* ([1,2,4]), in connection with studies of lepromin-reactivity in the population. Thirty-two more cases were found, some of which had escaped detection in earlier surveys. In 1962 an examination of the German population of Colonia Tovar revealed only two cases not yet registered ([5]).

SAMPLING AND TECHNICS

Sampling methods. Although random sampling from lists prepared beforehand from the registers of leprosy in the División de Dermatología Sanitaria of the Ministerio de Sanidad y Asistencia Social in Caracas, was intended, the procedure soon appeared to be unworkable for practical and psychologic reasons. Although the cooperation given by the personnel of the local health center, as well as by the sanitary inspectors of the Servicio de Dermatología Sanitaria (leprosy service) was excellent and dedicated, summons of the selected individuals yielded few attendances. It should be remembered in this connection, that this population had been subjected to numerous surveys, especially skin testing, over the past few years.

Cases and controls in the German isolate were therefore included in the sample as volunteers. The population was invited to cooperate in the survey. In addition, blood specimens were taken from individuals attending the local health center. Advantage was taken also of a local survey of the handicapped for rehabilitation, conducted concurrently among the leprosy patients.

Specimens from the Creole population were obtained as opportunity arose in Colonia Tovar and the nearby city of La Victoria. The sample consisted of mothers attending the well-baby clinics at the local health center, persons submitted to serologic test for syphilis on the occasion of request for travel authorization, and persons attending the dispensary of El Consejo and the Servicio de Dermatología Sanitaria in La Victoria for conditions other than leprosy.

Characteristics of the sample. The age distribution of cases and controls is given in Table 1 by ethnic groups, disease status, and sex. Among the Germans, 58.0 per cent of the individuals were under 40 years of age, in contrast to 65.2 per cent among the Creoles. The patients were on the average older than the controls, 48.1 per cent of the patients being under 40, in contrast to 64.9 per cent of the controls.

The sample consisted of 448 individuals, including 174 males (38.8%), of whom 52 (29.9%) were cases of leprosy, and 274 females (61.2%), of whom 29 (10.6%) were affected by the disease. Among the 81 cases, 54 (66.7%) were of German extraction, 16 (19.8%) of Creole extraction, and 11 (13.6%) of mixed extraction. Among the 367 controls, 179 (48.8%) were of German extraction, 165 (45.0%) of Creole extraction, and 23 (6.3%) of mixed extraction.

As far as possible, multiple sibs were excluded from the sample, through precise instructions given to the health inspectors screening the individuals for blood testing. Although it is believed that this purpose has been fulfilled to a major extent for those sibs sharing the same household, mostly children, this goal probably was not achieved for old sibs living in different households. Moreover, in the German population, the high degree of inbreeding implies some degree of family relationship among all members of the population.

The diagnosis of leprosy was ascertained from the records of the Servicio de Dermatología Sanitaria (leprosy service) of Aragua State, which for the last few years was in charge of leprosy surveillance in this area. No attempt was made to classify patients with respect to the type of leprosy, since most of them were residual cases.

Technics. The typing was performed immediately after blood withdrawal, with use of grouping cards developed by Becton and Dickinson Co., Baltimore, Maryland. Because of difficulties encountered in drawing blood from leprosy patients with anesthetic hands, and from rural individuals used to hard work, with callous hands, blood was withdrawn from the veins. This

TABLE 1. *Age distribution of study group by ethnic group, disease status, and sex.*

Age	Ethnic group						Disease status				Sex				Total	
	German		Creole		Mixed		Lep. cases		Controls		Male		Female			
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
10–19	30	12.9	25	13.8	5	14 7	7	8.6	53	14.4	27	15.5	33	12.0	60	13.4
20–29	61	26.2	50	27.6	10	29.4	15	18.5	106	28.9	42	24.1	79	28.8	121	27.0
30–39	44	18.9	43	23.8	9	26.5	17	21.0	79	21.5	35	20.1	61	22.3	96	21.4
40–49	42	18.0	25	13.8	4	11.8	22	27.2	49	13.4	32	18.4	39	14.2	71	15.8
50–59	34	14.6	12	6.6	4	11.8	14	17.3	36	9.8	23	13.2	27	9.9	50	11.2
60 & over	13	5.6	3	1.7	1	2.9	3	3.7	14	3.8	10	5.7	7	2.6	17	3.8
Unknown	9	3.9	23	12.7	1	2.9	3	3.7	30	8.2	5	2.9	28	10.2	33	7.4
Total	233	100.1	181	100.0	34	100.0	81	100.0	367	100.0	174	99.9	274	100.0	448	100.0

procedure did not raise any objections. In contrast, first attempts to collect blood from the fingertips were strongly opposed by the population.

The collection of blood and technical handling were carried out by local auxiliaries under the direct supervision of one of the authors for the first 381 specimens. Later on, these procedures were conducted by the auxiliaries alone. All readings were made by one of the authors (M.F.L.).

RESULTS

ABO blood grouping was determined for 444 (Table 2) and D-typing for 377 persons (Table 3).

With respect to leprosy, the results suggested an excess of the O and deficit of the A phenotypes among the cases in the Creole group. No such differences were observed in the German group.

With respect to ethnic origin, the German group, including leprosy cases and controls, showed a higher frequency for the A and lower frequencies for the B and O phenotypes than the Creole group.

When cases and controls were compared without regard to ethnic origin, the phenotypic distributions were remarkably similar.

However, because of the absence or small number of persons with the AB phenotypes in some of the groups (none among the leprosy patients of either ethnic group), no statistical analysis could be applied validly to these results.

Gene frequencies were derived for the German and Creole group. An excess of the A gene (significant at the level $P = 0.05$) was found for the German as compared with the Creole group (Table 4).

DISCUSSION

No differences are readily apparent in the distribution of ABO phenotypes in relation to leprosy, either in the total sample, or in either one of the two ethnic groups forming the study population.

If the difficulties of interpretation raised by the small size of the sample, which was insufficient to reveal slight differences in the proportions of phenotypes according to

TABLE 2. *Distribution of ABO phenotypes in leprosy cases and controls, by ethnic group.*

Ethnic group	Disease status	Total	Per cent phenotypes			
			A	B	AB	O
Creole	Leprosy cases	16	25.0	12.5	0.0	62.5
	Controls	165	33.9	10.3	3.0	52.7
	Total	181	33.1	10.5	2.8	53.6
German	Leprosy cases	54	48.1	5.6	0.0	46.3
	Controls	178	48.3	3.9	1.7	46.1
	Total	232	48.3	4.3	1.3	46.1
Mixed	Leprosy cases	10	30.0	20.0	0.0	50.0
	Controls	21	38.1	0.0	0.0	61.9
	Total	31	35.5	6.5	0.0	58.1
Total	Leprosy cases	80	41.2	8.7	0.0	50.0
	Controls	364	41.2	6.6	2.2	50.0
	Total	444	41.2	7.0	1.8	50.0

TABLE 3. *Proportion of $\bar{d}\bar{d}$ phenotypes in cases and controls, by ethnic group.*

Ethnic group	Leprosy cases		Controls		Total	
	No. tested	%	No. tested	%	No. tested	%
Creole	16	0.0	163	6.7	179	6.1
German	53	3.8	123	5.7	176	5.1
Mixed	9	0.0	13	0.0	22	0.0
Total	78	2.6	299	6.0	377	5.3

TABLE 4. *ABO gene frequencies in the German and Creole groups, irrespective of disease status.*

Gene frequencies	Germans	Creoles
O	0.679	0.732
A	0.293	0.199
B	0.031	0.069

disease status or ethnic group, are disregarded, the following remarks can be made in the light of the pilot trial.

The type of the disease should be taken into account. Differences are more likely to be observed between cases classified according to the type of leprosy, i.e., lepromatous *vs* tuberculoid cases, and between lepromatous cases and controls. This is not unexpected, since the lepromatous and tuberculoid types of the disease present contrasting differences with respect to the host-parasite relationship between *M. leprae* and the human organism. It is possible to conceive of host factors, for example, genetic ones, whose role is restricted to or apparent only in lepromatous leprosy. The pooling of leprosy cases without respect to the type of leprosy would readily dilute associations between lepromatous leprosy and genetic characteristics. This requirement calls for a larger sample.

When a household consists of blood relatives, which is generally the case, the genetic constitution of any one individual in the household is probably related to the genetic constitution of the others. Moreover, for a communicable disease where household transmission is important, as was shown to be the case in leprosy, the risk of any one in the household developing leprosy is likely to be associated with the disease status of the others. Therefore, with multiple sampling in the same household, the distribution of genetic factors and the risk of disease might show a spurious association.

Although multiple household sampling has been avoided in this study, the basis for exclusion has been only the household existing at the time of study. Nothing is known of the past structure of the households. Because of the social structure of this community, it is probable that any blood relatives living at present in different households have shared common households in the past, where they might have been exposed to a common risk of contraction of the disease.

SUMMARY

A study of blood groups was conducted among 80 leprosy patients and 364 controls in the German and Creole populations of Colonia Tovar and vicinity, Venezuela. The prevalence of leprosy in the area is 100/1,000 in the German population and 1.3/1,000 in the Creole population.

The sample size was too small to permit statistical analysis of the phenotypic distribution. No difference related to the disease, however, was readily apparent.

The German group showed a significant excess of gene A.

RESUMEN

Se hizo un estudio de grupos sanguíneos en 80 enfermos de lepra y 364 controles en la población alemana y creole de colonia Tovar y sus alrededores, en Venezuela. La prevalencia de la lepra en el área es de 100/1,000 en la población alemana y de 1.3/1,000 en la población creole.

El tamaño de la muestra fué demasiado pequeño para permitir el análisis estadístico de destribución de los fenotipos. No se encontró diferencia aparente, sin embargo, en relación con la enfermedad.

El grupo alemán mostró un exceso significante del gene A.

RÉSUMÉ

Une étude des groupes sanguins a été menée chez 80 malades de la lèpre et 364 témoins appartenant aux populations allemandes et créoles de Colonia Tovar et des environs, au Venezuela. La prévalence de la lèpre dans cette région est de 100 pour mille dans la population d'origine allemande et de 1.3 pour mille dans la population créole.

La dimension de l'échantillon n'a pas été suffisante pour qu'une analyse statistique puisse être pratiquée sur les distributions des divers phénotypes. Toutefois, à première vue, il ne semble pas exister de différence en relation avec la maladie.

Le groupe d'origine allemande témoignait d'un excès significatif du gène A.

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