LEPROSY SPREAD IN URBAN AREA, PART II: REACTIVITY OF SOLUBLE ANTIGEN (SA) IN THREE DIFFERENT GROUPS OF LEPROSY CONTACTS IN SÃO GONÇALO RIO DE JANEIRO STATE BRAZIL

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ABSTRACT - In three different groups of leprosy contacts there were observed results of intradermoreaction to the soluble antigen (SA). In urban area endemic for leprosy (prevalence rate of 2,87 per 1.000 inhabitants) there were studied three groups:
1) intradomiciliary contacts or living together with a case for more than one year; 2) neighboring contacts or extradomiciliary one's; 3) inhabitants in the areas far from the focus. Thirty nine per cent of the 1.569 intradermoreactions were positive. It was demonstrated an association between the positiveness of the intradermoreaction and the proximity of the infection source, with the age and the time of residence in the same dwelling. The SA was considered a good instrument for the identification of the groups of risk for leprosy, although the findings do not quantify its predicting value in the individual diagnosis of the infection.

Key words: *Leprosy. Urban area. Soluble antigen. Inquiry. Contacts. Morbidity. Epidemiology. São Gonçalo, RJ, Brazil.*

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1 - INTRODUCTION

The lack of knowledge on the mode of transmission of leprosy and the period between infection and clinical manif estations after exposure to **Mycobacterium leprae**[16,20,31] has been raising difficulties for epidemiological studies being under taken, and in some cases also for the development of control measures against the endemic.

Mechanisms determining clinical manifestations depend not only on the individual immune system but also on unleashing or predisposing factors[3,20]. The elucidation of the control model requires some previous knowledge

on risk factors as well as on the characteristics of infected individuals. Therefore, there is a need for identifying infected individuals, something that in other endemics can be confirmed by the immune response through skin tests-

Positive response to Mitsuda lepromin Is one of the available indicators for the host's cell immunity against **M.leprae**[27,21,26,31]. However, its low specificity[5,28,17,26] due to interference generated by cross-reactions with other mycobacteria and the lack of association with leprosy prevalence rates[2,3,4,5,6,12,25] do not allow the use of such indicator in 'infection studies, despite the importance of its negative response for the evolutional prediction of clinical forms[27,13,15,20].

The use of Soluble Antigen (SA) from purified bacilli of infected armadillos has also limitations due to cross-reactions with other mycobacteria, although it reveals an association between infection in intra-domiciliarycontacts[22,32].

Considering that the SA is of great interest for epidemiologic studies of **M.leprae** infection, this paper is aimed at showing the results of SA intradermoreaction response during the survey carried out in the county of São Gonçalo according to age, sex, length of time living in the dwelling and proximity to the source of exposure.

2 - MATERIAL AND METHODS

The study was carried out in the county of São Gonçalo, Rio de Janeiro, since this is an endemic area for leprosy with focal distribution of cases and exclusively urban characteristics, as described in elsewhere[(1)].

The proximity to the cities of Rio *de* Janeiro and Niteroi, associated with poor opportunities of better work conditions, have led more and more people choosing to book for a job in other urban centers- In relation-to migratory characteristics, 46% of the population are migrants. Of these, 59% live in the county for over 10 years.

The study of the magnitude of the endemic in this county from 1967 to 1987 consisted in the analysis of data obtained from files kept by the three major units assisting leprosy cases in the area. Reports follow general lines which have been developed by the Leprosy Control Program, whose planning, techinical rules definition and managerial procedures are attributed to the State Secretariat of Health through its Sanitary Dermatology Coordinating Committee. All activities are developed according to guidelines set up by the National Divison of Sanitary Dermatology - Ministry of Health[7].

An aerophotometric map containing the description of the census tract was used to define low, mean and high prevalence areas- The cases were marked, yielded to the reporting made in December 1987 in streets corresponding to addresses provided by the primary care Unit were marked in this map[1].

Participants Members: The selection of 203 Index case dwellings was made by the systematic drawing of one out of each five cases included in the nominal list of the active reporting by date of detection. The peripheral population sample was obtained selecting 203 core dwellings with no reported case of leprosy. The number of core dwellings selected at random in each tract corresponded to the overall number of dwellings within the tract. For the selections of each dwelling, one street was chosen at random and numbers were assigned to each dwelling- Then the core dwelligs were picked out.

Group I, or intra-domiciliary contacts, consists of relatives and/or people living together with the index case under the same roof [(26)].

Group II, or extra-domiciliary contacts, includes all individuals living in 4 adjoining households in relation to infected individuals, that is, neighboring contacts.

Group Ill, or the peripheral population, consists of individuals living in 5 dwellings located in census tracts with no reported case of leprosy.

Skin tests were made in individuals aged 7 to 60 years living in the previously selected dwellings for over one year, also considering the following criteria: they should not be pregnant (females), should not be infected with any disease other than leprosy, and should voluntary choose to take part in the study.

Reactions to the skin test using the SA were assigned the dependent variable. Variables included in the analysis were: study group (dummy variable), age, sex, and length of time living in the dwelling. Softwares used for data processing were Epiinfo[14] and Multlr[9] The study of 2 x 2 tables association was made using Mantel-Haenszel's Chi-squared.

REAGENT: The Soluble Antigen (SA)[11,13] used in the study was provided by the Biomedical Institute of Venezuela. It was prepared from **M.leprae** suspension obtained from experimental lesions in armadillos and purified according to DRAPPER'S method (IMMLEP protocol 3/79). Protein contents were determined using LOWRY'S method adjusted to 2.5 ug/ml.

For anticen administration, 0,1 ml was intradermally inoculated at the upper part of the rigth forearm. Response to the antigen was checked 48 hours after inoculation with the induration being recorded in millimeters by a standardized examiner[(21)]. Reactions with 10 mm or more were taken as positive.

3 - RESULTS

In 1569 intradermoreactions, 238 belong to intra-domiciliary contacts (Group I), 662 to extra-domiciliary contacts (Group II), and 669 to the peripheral population (Group III).

The age average of individuals included in this inquiry was 27 years. Among them, 624 were men and 945 women.

Forteen per cent of soluble antigen administrations failed to be read since the reading team was not awaited by the participants in their houses.

The proportion of positive individuals, i.e., those with reaction equal to or over 10 mm, was 39,1%. The prevalence of positive reactors in the intra-domiciliary group was 1,43 times higher than that of extra-domiciliary contacts and 1,69 times that of the peripheral population group (Table I)

According to table 2, the identification of index cases by clinical form shows that the prevalence of SA positive response in intradomiciliary contacts of multibacillary cases and paucibacillary cases was 59,2% and 52,2% respectivelly.

Analysing the association between length of time living in the studied dwelling and SA positive response in the three groups, it was found that in the overall sample 46,2% of individuals livingthere for over 11 years were positive, whereas for those living there for less than 6 years it was 34,9%. Considering the intra-domiciliary group alone, this rate for the former is as high as 59.1%, against 37.5% for the latter (table 3).

Figure 1 shows the influence of age over intradermoreaction mean induration. There is an increase in the 7-11 and 12-19 age groups, whatever the stratum(I, II or III), it was noticed that Group I, or intra-domiciliary contacts, reaches its maximum peak in the 20-39 age group. In all three groups the mean induration tends to decrease slowly after 20-39 years of age.

With regard to the prevalence of positive reactors by age Table 4 shows that in all three groups most positive reactors belong to the 20-39 age group. The prevalence of positive cases in individuals aged 7-11 years is 24,3% for extra-domiciliary contacts, 23,8% for the peripheral population and 51.7% for individuals living close to leprosy patients. No matter the age group, intra-domiciliary contacts have higher positivity rates than both extra-domiciliary contacts and the peripheral population.

Results yielded by the logistic regression model point to an association between skin test positive response to SA and the proximity to the source of infection, age and lenght of time living in the dwelling. The odds ratio of having a positive skin test the intra-domiciliary group was 2.36 in relation to the peripheral population. Concerning the extra-domiciliary group, the odds ratio was 1.28. With respect to the association of age and positive response to the antigen in individuals aged over 20 years, the odds ratio was 1.41 compared to individuals aged less than 19 years. Living in the same dwelling for over 11 years showed odds ratio of 1.43 in relation to other residents. There was no association of positive response to SA with sex. No significant interaction was found in the analysis of the proposed variables (table 5).

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TABLE 1 - Prevalence of Soluble antigen positive response in the studied groups São Gonçalo - Rio de Janeiro - 1988

Groups	NUMBER OF TESTS PERFORMED	PREVALENCE OF POSITIVES	ODDS RATIO	ODDS RATIOLIMITS a= 0.05
INTRADOMICILIARY	238	55.7	2.59	1,89 OR 3,51
EXTRADOMICILIARY	662	38.9	1.30	1,03 OR 1,64
PERIPHERAL POPULATION	669	32.9	———	—

TABLE 2 - Soluble antigen response in intrahousehold contacts according to clinical form of index cases São Gonçalo - Rio de Janeiro - 1988

Soluble Antigen Response of Intrahousehold Contacts \ Clinical form of index cases	* MB		** PB		TOTAL	
	Nº	%	Nº	%	Nº	%
Negative	56	40.8	44	47,8	100	43.6
Positive (≥ 10 mm)	81	59.2	48	52,2	129	56.4
TOTAL	137	100.0	92	100.0	229	100.0

* MB = Multibacilary $x^2 = 1.08$
** PB = Paucibacilary $p > 0,10$

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TABLE 3 - Prevalence of soluble antigen positive response according to length of time living in the county of São Gonçalo - Rio de Janeiro - 1988

Groups / Length of time	INTRADOMICILIARY		EXTRADOMICILIARY		PERIPHERAL POPULATION		TOTAL	
	Examined	% Positive	Examined	% Positive	Examined	% Positive	Examined	% Positive
1 - 5 Years	40	37,5	221	35.3	215	34.0	476	34.9
6 - 10 Years	28	71,4	85	50.6	103	30.1	216	43.5
11 e + Years	137	59,1	249	44.6	205	39.5	591	46.2
TOTAL *	205	56.6	555	41.8	523	35.4	1283	41.5
	$x^2 = 8.80$ $p < 0.012$		$x^2 = 7.33$ $p < 0.02$		$x^2 = 2.98$ $p > 0,22$		$x^2 = 14.33$ $p < 0.0007$	

*** Excluding individuals under 11 years of age and individuals whose length of time was not provided.**

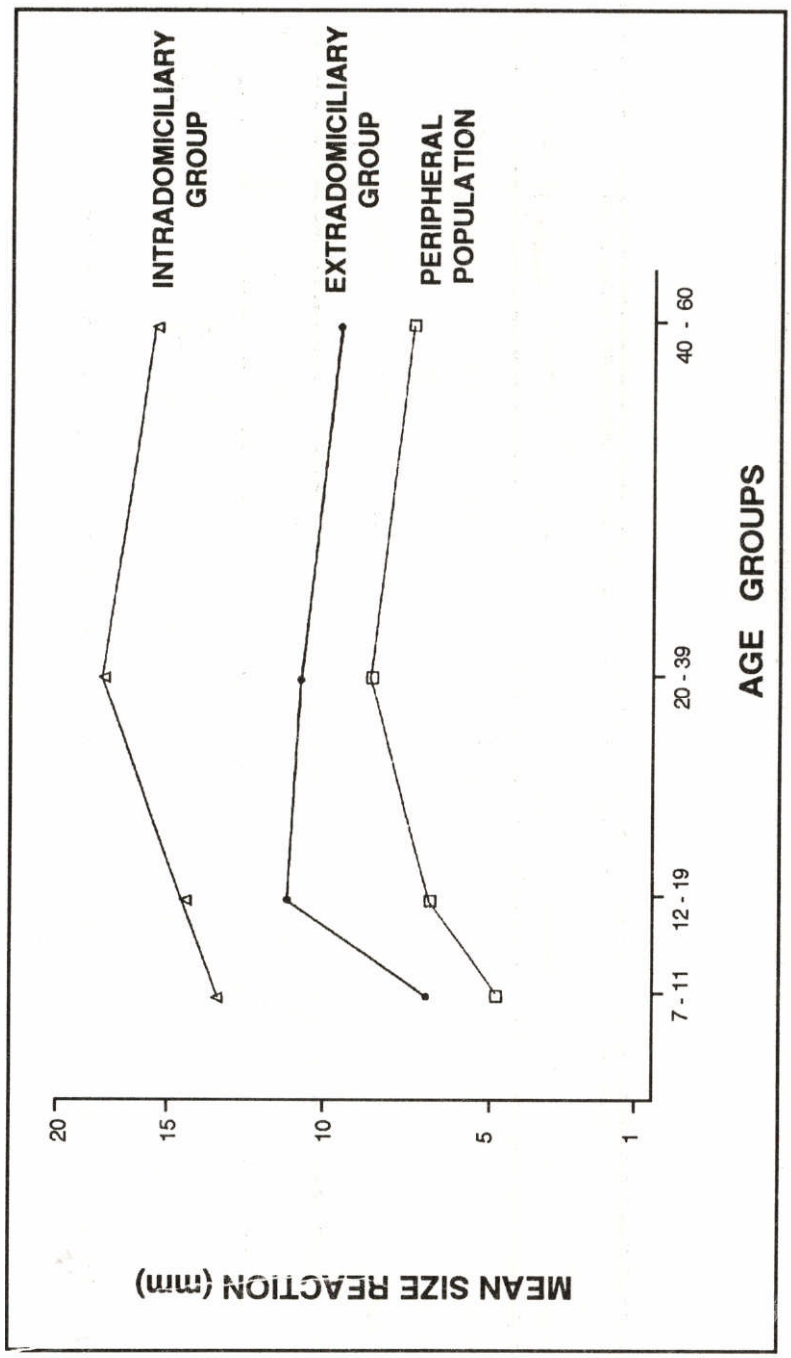

FIGURE I - Mean Size Reaction of sa by age Groups São Gonçalo - 1988 - Rio de Janeiro - Brazil

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TABLE 4 - Prevalence of soluble antigen positive response according to age São Gonçalo - Rio de Janeiro - 1988

Groups / Age Groups	INTRADOMICILIARY		EXTRADOMICILIARY		PERIPHERAL POPULATION		TOTAL	
	Examined	% Positive	Examined	% Positive	Examined	% Positive	Examined	% Positive
7 - 11 Years	29	51.7	103	24.3	143	23.8	275	26.9
12 - 19 Years	62	51.6	127	41.7	123	31.7	312	39.7
20 - 39 Years	88	61.4	277	42.2	255	38.8	620	43.6
40 e + Years	55	54.5	146	40.4	138	30.4	339	38.6
TOTAL *	234	56.0	653	38.9	659	32.5	1546	38.7
	$x^2 = 1,77$ $p > 0,62$		$x^2 = 11,14$ $p < 0,01$		$x^2 = 9,89$ $p < 0,01$		$x^2 = 22,39$ $p < 0.00005$	

*** Excluding 23 individuals whose age was not provided.**

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TABLE 5 - Logistic regression parameters for the dependent variable positive response to soluble antigen - São Gonçalo - Rio de Janeiro - 1988

Independent Variables	COEFICIENT	Z	ODDS RATIO	LIMIT OF INTERVAL 0.05		
INTRA-DOMICILIARY GROUP	0,86	5.23	2.36(*)	1.7	OR	3.2
EXTRA-DOMICILIARY GROUP	0,24	2.12	1.28(*)	1.0	OR	1.6
LENGTH OF TIME LIVING IN THE DWELLING	0,36	3.27	1.43	1.1	OR	1.7
SEX	- 0,12	1.14	0.88	0.7	OR	1.0
AGE	0,34	3.05	1.44	1.1	OR	1.7

(*) In relation of prevalence response according to peripheral population group

4 - COMMENTS AND CONCLUSION

The analysis of these results showed that skin test can be períormed in an urban area through home visits. However, losses occurred in the reading of these tests often discourage epidemiologic studies being made[2,23].

As with Mitsuda test, SA positive response being higher in intra-domiciliary contacts than in extra-domiciliary contacts or in the peripheral population indicates organism resistance to **M.Leprae**, despite the conditions determining its reactivity are being unknown up to the moment[30].

The non discrimination of positive response by clinical forms of index case, calls into question their susceptibility, even though right in this stage of the work it is unlikely that we know the actual frequency of false-negative intradomiciliary contacts living together with multibacillary patients. With regard to individuals living together with paucibacillary patients, the lack of knowledge on probable extra-domiciliary exposure sources does not allow a somewhat deeper analysis.

The close relationship between length of time living in the dwelling and prevalence of SA positive response can be explained not only by the source of exposure but also by interference of other environmental mycobacteria[29].

The influence of age agrees with other papers[11,22,32,33]. It appears that the decrease of positive responses in older age groups reflects an individual immunological depletion in the fight mechanism against M.leprae[16,18], resulting in a high case detection rate in this age group'.

Positive response induction by BCG for both Mitsuda[28,26,31] SA[32]ould not explain the low frequency of reactors among children belonging to extra-domiciliary and peripheral population groups since there was no selective vaccination procedure for intra-domiciliary contacts.

In the analysis of the Multiple Logistic Regression the maximum likehood test shows a great residue, thus pointing to the fact that some other factors (interfering variables) for explaning this immune response have not been included in the study.

These findings suggest that the SA is a useful tool for epidemiological studies in the identification of risk groups for leprosy, despite the response to the antigen not expressing a predictive value when analysed at the individual level.

RESUMO - Em três grupos diferentes de contatos de pacientes de Hanseníase foram observados resultados da intradermorreação ao Antígeno Solúvel (AS). Em área urbana endémica para hanseníase (taxa de prevalência de 2,87 por 1.000 habitantes), foram estudados três grupos: 1) Contatos intradomiciliares ou conviventes com um caso por mais de um ano. 2) Contatos de vizinhança ou extradomiciliares e 3) Habitantes nas áreas distantes do foco. Trinta e nove por cento das 1569 intradermorreações foram positivas. Demonstrou-se uma associação entre a positividade da intradermorreação e proximidade de fonte de infecção, com a idade e o tempo de residencia no mesmo domicílio. Considerou-se o AS um bom instrumento para a identificação de grupos de riscos para a hanseníase, embora os achados não quantifiquem seu valor preditivo no diagnóstico individual da infecção.

Palavras-chave: *Hanseníase. Area Urbana. Epidemiologia. Antígeno solúvel. Inquérito. Contatos. Morbidade. São Gonçalo, RJ, Brasil.*

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