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Antibodies to a Synthetic Analog of Phenolic Glycolipid-I of *Mycobacterium leprae* in Healthy Household Contacts of Patients with Leprosy[1]

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Subclinical infection in leprosy can be detected by methods of cellular immunology, most convincingly by *in vitro* techniques ([13, 20]). However, for application in large-scale field studies these methods have definite disadvantages, being either too sophisticated, as is the case with the *in vitro* tests, or requiring a second visit to the examined person, as skin tests do. Furthermore, methods of cellular immunology are unsuitable for the detection of early lepromatous disease because they cannot differentiate between the state of anergy in the lepromatous patient and the negative immune responses in persons without exposure to leprosy.

When the first antibody assays with antigen from *Mycobacterium leprae* were developed ([1, 7, 15]) interest arose immediately in their potential use for the detection of subclinical infection in leprosy with special emphasis on the diagnosis of early lepromatous disease. Examination of clinically healthy household contacts of patients with leprosy revealed that antibodies to *M. leprae* antigen may be demonstrated ([1, 3, 19]). However, a definite drawback of these methods is the need to pre-absorb the tested sera with different mycobacterial antigens in order to achieve sufficient specificity within the test.

The discovery of the phenolic glycolipid-I (PGL-I) of *M. leprae* ([17, 18]), having a high degree of specificity for this species, and its introduction to the serology of leprosy ([4, 9, 18, 24, 29]) therefore represented a major development. The first serological examination of household contacts of leprosy patients with PGL-I, by Buchanan and his coworkers ([6]) and by Ulrich and her coworkers ([28]), showed that antibodies to this antigen could be detected in healthy contacts. These studies were of a preliminary nature and, in addition, the authors did not

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investigate the influence of the type of leprosy in the index patient on antibody formation in the contacts.

We have examined the antibody responses to a synthetic analog of PGL-I in a well-defined study group, one of which we had previously investigated for cellular immune responses at the Armauer Hansen Research Institute in Addis Ababa, Ethiopia, namely, household contacts of lepromatous and tuberculoid patients and carefully chosen controls from a leprosy-endemic area in Ethiopia.

POPULATION AND METHODS

Study area and study population

A detailed description of the population and area under examination has already been given in a previous paper ([20]). The study was conducted in the Gurage area of Ethiopia which lies southwest of Addis Ababa. The prevalence rate of leprosy in this area has been estimated to be 2.5 per thousand. Twenty percent of the registered patients had lepromatous leprosy. *M. tuberculosis*, which is common, and *M. avium* and *M. gordonae* act also as mycobacterial sensitizers in this area ([23]). Medical services are provided by Attat Hospital with its outpatient clinics and by Gura Mission Station.

Study groups

A patient contact group and a control group were identified on the basis of index persons who had come for treatment to the outpatient clinics of Attat Hospital or Gura Mission Station. A total of 30 households were examined in the period between February 1975 and January 1976.

Index persons with leprosy for the patient contact group. Fifteen patients with a confirmed diagnosis of leprosy who had received regular treatment for less than 2 years were selected as index patients. They were diagnosed and classified according to the criteria given by Ridley and Jopling ([25]). A microscopic examination of smears from nasal discharge for acid-fast bacilli (AFB) was also performed. Seven of the patients were classified as tuberculoid (BT and BB/BT) and eight patients as lepromatous (BL and LL). Among the lepromatous patients, five were considered to have "active" disease [bacterial index (BI) between 4.0 and 5.0; morphological index (MI) between 3% and 8%; AFB in nasal discharges] and three were considered to have "inactive" disease (BI between 2.0 and 3.0; negative MI; no AFB in nasal discharges).

Patient contact group. The patient contact group consisted of those people, devoid of leprosy themselves, who had lived in one of the 15 households with a leprosy patient before this patient had been subjected to regular treatment. Altogether, we examined 54 household contacts of lepromatous patients and 39 household contacts of tuberculoid patients. Among the contacts of lepromatous patients, 35 had been exposed to a patient with active disease with a median duration of exposure of 7 months (range 3–60 months) and 19 to a patient with inactive disease with a median duration of exposure of 35 months (range 18–123 months). The duration of known exposure to the lepromatous index patient was less than 1 year (median 6 months; range 3–7 months) in 20 contacts and more than 1 year (median 32 months; range 18–123 months) in 34 contacts.

Index persons without leprosy for the control group. For each index person with leprosy a person without leprosy was selected as the index person for the corresponding control household.

Control group. The control group consisted of members of the 15 control households. Altogether, 99 control persons were included in the study.

Examination of the households

The complete examination of each household member included a physical examination for signs of leprosy and the taking of samples for laboratory tests, namely, slit-skin smears from one earlobe, smears from the nasal discharge, and venous blood. The patient contact group and the control group were comparable with regard to the distribution of sex and estimated ages.

Laboratory methods

Microscopic examination of skin smears for AFB. Skin smears were processed and scored for BI and MI in a routine fashison.

Microscopic examination of smears from nasal discharge. Material from nose blows was smeared onto slides and processed in

the same manner as a skin smear. Slides were labeled as positive when AFB were seen and as negative when no AFB were seen within a 5-minute search.

Histological examination of skin biopsies. Biopsies were taken from skin lesions suspected to be due to leprosy, and then processed and classified according to Ridley and Jopling ([25]).

Enzyme-linked immunosorbent assay (ELISA). We used the procedure described by Cho and his co-workers ([9]) with some modifications. Microtiter plates (96 F Nunc Immuno Plate II, 4-42404) were coated with 100 μl per well of the synthetic analog of PGL-I described below diluted 1:3000 in ammonium acetate/ammonium carbonate buffer, pH 8.2, overnight at 37°C. Blocking was performed by the addition of phosphate-buffered saline (PBS) with 1% bovine serum albumin (BSA) and 0.5% gelatin, 100 μl per well, overnight at 4°C. The plasma diluted 1:100 in PBS with 0.5% BSA plus 0.2% gelatin and 0.1% Tween 20 was added and incubated for 1 hr at 37°C. For control, tests were made in parallel with antigen blank wells to ensure that positive readings were, in fact, due to specific interactions between antibodies and the antigen. Following that, 100 μl of anti-human immunoglobulin M (IgM)-peroxidase conjugate reagent (DAKO P 215) diluted 1:1000 in PBS/BSA/gelatin/Tween was added and incubated for 1 hr at 37°C. Finally, 100 μl of ABTS-substrate (Boehringer Mannheim 102 946) was added. Between each step of the assay, the plates were washed three times in PBS/BSA/gelatin/Tween. The optical density (OD) was read in an automatic ELISA reader at 405 nm waiting until the OD of a standard lepromatous serum pool (LSP), used for reference and diluted 1:100, was about 1.0. The results are expressed as antibody activity in percent of the activity of the LSP. Values below 6% of LSP could not be reliably determined, thus rendering the antibodies unrecognizable for the purposes of our study.

Antigen. As a substitute for the native PGL-I, we used a synthetic analog containing the same terminal sugar epitopes (PGL-I_{SA}). Synthesis of this antigen has been described ([8]). The correct chemical name is: *O*-(3, 6-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-*O*-(α-L-rhamnopyranosyl)-(1 → 9)-oxynonanoyl-BSA. The trivial, operational name is: disaccharide-octyl-BSA (D-O-BSA). This antigen is water soluble and therefore better suited for the ELISA technique. Chatterjee and her co-workers have demonstrated ([8]) that this synthetic analog is comparable to the native PGL-I with regard to sensitivity and specificity.

TABLE 1. *Antibody responses in the ELISA to the synthetic analog of phenolic glycolipid-I (PGL-I_{SA}) in household contacts of patients with leprosy and controls.*

	No. persons with antibodies to PGL-I_{SA} (% of LSP)[a]		
	<6%	≥6%	Total
Contacts of			
Lepromatous patients	31	23	54
Tuberculoid patients	31	8	39
Controls	66	33	99
Total	128	64	192

[a] Antibody activity expressed as percent of the activity of a standard lepromatous serum pool (LSP) used for reference.

Plasma samples. Plasma samples had been stored in a lyophilized state and were reconstituted to a final dilution of 1:100.

Lepromatous serum pool. The lepromatous serum pool consisted of sera from 30 lepromatous patients who were either newly diagnosed or who had been treated for less than 6 months.

Statistical analysis

Statistical analysis was performed using the Chi-square test for $R \times C$ contingency tables. A p value of 0.05 or less was chosen as an indication of statistical significance.

RESULTS

The antibody responses to PGL-I_{SA}, expressed as a percent of LSP, in household contacts of patients with different types of leprosy and in the control group are presented in Figure 1. The distribution of the antibody responses in the different contact groups appears similar, with no detectable antibodies in the majority of the sera and a rather small spread of the quantifiable antibodies only up to 18% of LSP. For statistical evaluation, persons with no detectable antibodies to PGL-I_{SA}, i.e., antibody values

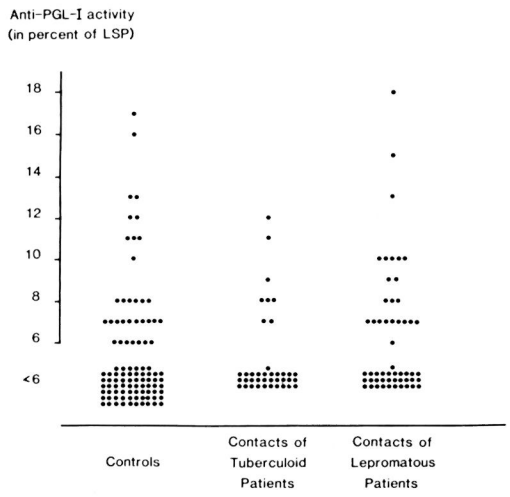

FIG. 1. Antibody responses to the synthetic analog of phenolic glycolipid-I (PGL-I_{SA}) in the ELISA in household contacts of lepromatous patients, household contacts of tuberculoid patients, and controls. Antibody activity is expressed as percent of the activity of a standard lepromatous serum pool (LSP) used for reference.

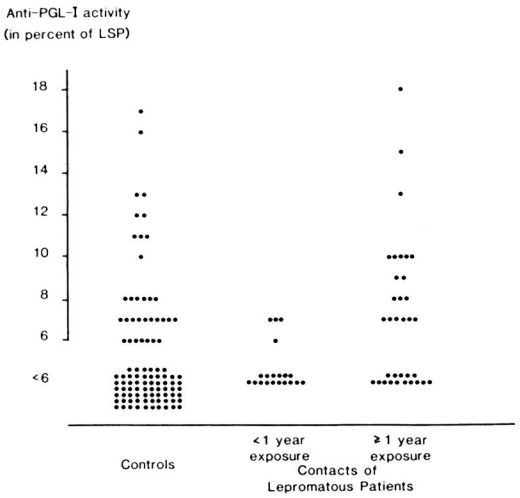

FIG. 2. Antibody responses to the synthetic analog of phenolic glycolipid-I (PGL-I_{SA}) in the ELISA in contacts with different durations of exposure to a lepromatous patient in the household and in controls. Antibody activity is expressed as percent of the activity of a standard lepromatous serum pool (LSP) used for reference.

of <6% of LSP, were grouped together as "nonresponders" and persons with antibody values of >6% of LSP as "responders." Table 1 shows that there are more responders among the contacts of lepromatous patients than among contacts of tuberculoid patients and controls, but these differences are not statistically significant ($\chi^2 = 4.97$; d.f. = 2; $p > 0.05$).

However, when the contacts of lepromatous patients are divided according to the duration of their known exposure to the index patient, a different picture emerges. Figure 2 shows the antibody responses to PGL-I_{SA}, expressed as a percent of LSP, in contacts with <1 year's exposure and contacts with ≥1 year's exposure. Clearly, contacts of lepromatous patients with ≥1 year of exposure have antibodies to PGL-I_{SA} more often than contacts with <1 year of exposure and the controls. Detectable antibodies to PGL-I_{SA}, i.e., antibody value of >6% of LSP, were present in 19 of 34 contacts with ≥1 year's exposure to a lepromatous patient but only in 4 of 20 contacts with <1 year's exposure and in 33 of 99 controls without exposure to leprosy in the household (Table 2). The differences among the three groups are statistically significant ($\chi^2 = 8.28$; d.f. = 2; $p < 0.05$). These differences were still apparent when the data were stratified for sex and age (the age groups being 6–14 years, 15–49 years, and 50 and more years), although statistical significance was not reached in all comparisons due to the small numbers involved.

A division of the contacts of lepromatous patients according to the state of disease activity in the index patient at the time of examination is presented in Table 3. The contacts of lepromatous patients with inactive disease had antibodies to PGL-I_{SA} more often than contacts of patients with active disease and the controls. However, the differences were not statistically significant ($\chi^2 = 4.25$; d.f. = 2; $p > 0.05$).

A division of the contacts with ≥1 year's exposure to a lepromatous patient according to their sex revealed that females had detectable antibodies to PGL-I_{SA} more often (12 of 18) than males (7 of 16) but the difference is not statistically significant ($\chi^2 = 1.8$; d.f. = 1; $p > 0.05$). In the control group, females also had antibodies to PGL-I_{SA} more often than males (24 of 55 and 9 of 44, respectively). These differences are statistically significant ($\chi^2 = 5.82$; d.f. = 1; $p < 0.05$).

TABLE 2. *Antibody responses in the ELISA to the synthetic analog of phenolic glycolipid-I (PGL-I_{SA}) in contacts with different duration of exposure to a lepromatous patient in the household and in controls.*

	No. persons with antibodies to PGL-I_{SA} (% of LSP)[a]		
	<6%	≥6%	Total
Duration of exposure to lepromatous patient			
≥1 yr	15	19	34
<1 yr	16	4	20
No exposure	66	33	99
Total	97	56	153

[a] Antibody activity expressed as percent of the activity of a standard lepromatous serum pool (LSP) used for reference.

TABLE 3. *Antibody responses in the ELISA to the synthetic analog of phenolic glycolipid-I (PGL-I_{SA}) in contacts with household exposure to lepromatous patients with different disease activity at the time of the examination and in controls.*

	No. persons with antibodies to PGL-I_{SA} (% of LSP)[a]		
	<6%	≥6%	Total
Exposure to lepromatous patient with			
Active disease	23	12	35
Inactive disease	8	11	19
No exposure	66	33	99
Total	97	56	153

[a] Antibody activity expressed as percent of the activity of a standard lepromatous serum pool (LSP) used for reference.

A division of the contacts with ≥1 year of exposure to a lepromatous patient according to their age showed that detectable antibodies to PGL-I_{SA} were present in 6 of 12 persons of the age group 6–14 years, in 12 of 17 persons of the age group 15–49 years, and in 1 of 5 persons of the age group of 50 and more years. In the control group, detectable antibodies were present in 10 of 28 persons of the age group 6–14 years, in 21 of 57 persons of the age group 15–49 years, and in 2 of 14 persons of the age group of 50 and more years.

DISCUSSION

In an area endemic for leprosy, healthy persons with more than 1 year's exposure to a lepromatous patient in the household had antibodies to *M. leprae* antigen significantly more often than healthy household contacts of tuberculoid patients and healthy persons without household exposure to leprosy. We interpret the increased prevalence of antibodies to PGL-I_{SA} in these contacts of lepromatous patients as an indication of specific sensitization to antigens of *M. leprae* because previous studies have clearly demonstrated the high degree of species specificity of this antigen [8] and its native relative [4, 9, 29]. Even the possible small degree of crossreactivity with other mycobacteria [5, 8] is unlikely to have influenced our results, given the similar sensitization to these locally important mycobacteria [23] in the patient contact and control groups described earlier [20]. The presence of antibodies to *M. leprae* antigen in a significant proportion of healthy contacts therefore provides further evidence that subclinical infection with *M. leprae* is common. Thus, our findings confirm the results of Buchanan and his co-workers [6] and of Ulrich and her co-workers [28] and furthermore extend the observations with regard to the influence of the type of leprosy in the index patient. A significantly greater prevalence of antibodies to *M. leprae* antigen could be demonstrated among contacts of patients with lepromatous leprosy with exposure of more than 1 year, but not among contacts of tuberculoid patients. This is in line with the results of studies with other antibody assays [3, 19, 26], with the results of an investigation of the lymphocyte transformation responses to *M. leprae* antigen in contacts [20], and with earlier epidemiological studies which have clearly shown the key role of lepromatous leprosy for the propagation of the disease [12, 14]. The fact that some antibody studies [2, 22] could not demonstrate an association between the type of leprosy in the index patients and the antibody responses in their contacts is likely related to differences in the selection of the patient contact and control groups and to differences in the sensitivity of the antibody assays used.

It was surprising, though, that in our study the degree of sensitization to *M. leprae*, as indicated by the prevalence of antibodies to PGL-I_{SA}, did not parallel the degree of probable infectivity of the lepromatous index

patient at the time of examination. Household contacts of lepromatous patients did not have antibodies to PGL-I_{SA} more frequently when the index patients were "active," i.e., highly bacilliferous, than when they were "inactive," i.e., having a comparatively low bacillary load. This finding is in contrast to data on lymphocyte transformation responses in the same study group ([20]). These latter studies had shown a clear association between the sensitization to *M. leprae* antigen in the contacts and the degree of presumed infectivity of the lepromatous index patient.

On the other hand, we found in this present study an association between the prevalence of antibodies to *M. leprae* antigen in the healthy contacts and the duration of known exposure to the lepromatous index patient. Household contacts with more than 1 year's exposure to the patient had antibodies to PGL-I_{SA} significantly more often than contacts with less than 1 year's exposure. In this context, it is of interest that antibodies to *M. leprae* antigen in experimentally infected armadillos became detectable about 6 months ([27]) to 1 year ([16]) after inoculation with leprosy bacilli while, on the other hand, conversion of the lymphocyte transformation responses to *M. leprae* antigen in occupational contacts had already occurred 3 to 6 months after first exposure to leprosy patients ([13]). Our data imply that in healthy leprosy contacts antibody formation to *M. leprae* antigen does not, in contrast to the development of cellular immunity, constitute an immediate response to the exposure to leprosy bacilli.

Antibodies to *M. leprae* antigen were found in a number of persons in each of the age groups examined when the exposure to lepromatous leprosy in the household had exceeded 1 year. These results are in line with data from studies with other antibody assays ([1, 3]). The fact that in our study already half of the contacts of the youngest age group had developed antibodies to *M. leprae* antigen reflects both the early exposure to leprosy bacilli and the good sensitizing capacity at this young age. The previously examined lymphocyte transformation responses to *M. leprae* antigen gave comparable results ([21]).

No influence of sex on the antibody responses in contacts of leprosy patients was found in our study or in other studies ([1, 3]). The previously examined lymphocyte transformation responses to *M. leprae* antigen had been significantly greater among males in contact with an active lepromatous patient than among females of the same group ([21]). Thus, our previous and present studies do not provide any evidence for an impaired capacity of males to develop cellular immune responses to *M. leprae* nor for augmented humoral immune responses to this antigen in males. Therefore, our data do not offer an explanation of why males ultimately account for about two thirds of the lepromatous patients in our study as well as elsewhere ([12]).

The fact that antibodies to PGL-I_{SA} were detected in one third of the persons without household exposure to leprosy is in line with data from Brett and her co-workers ([4]) and Buchanan and his co-workers ([6]) who similarly found antibodies to native PGL-I in control persons from leprosy-endemic areas. Antibodies in healthy persons without known exposure to leprosy in the household may, in part, result from past or present subclinical infection with leprosy bacilli due to unknown exposure in the community. Another contributing factor may be polyclonal B-cell activation, as suggested by Brett and her co-workers ([4]). As we have discussed earlier, some of the antibody activity may also be due to crossreactivity with other mycobacteria ([5, 8]) present in our study area as indicated by skin-test responses ([23]) and lymphocyte transformation responses ([20]). Our finding of a comparatively high prevalence of antibodies to PGL-I_{SA}, considered to have a high degree of specificity, also in healthy noncontacts emphasizes the necessity to always include carefully chosen controls from the same endemic area in studies of leprosy contacts in order to ensure comparability of the study and control groups with respect to factors which are intangible or currently unknown.

For purposes of leprosy control, it is highly desirable to identify those persons in whom the detected antibodies to *M. leprae* indicate early lepromatous disease. In our study, the antibody levels in the contacts were all comparatively low in relation to the lepromatous serum pool used as a reference.

Therefore, it seems unlikely that any of the contacts had already acquired early lepromatous disease at the time of the examination; the negative skin smears of those contacts reinforce this interpretation. However, the study of Douglas and Worth ([11]) with *M. smegmatis* antigen, which included a follow-up examination after 2 years, has demonstrated that rather quick changes in the antibody status and the related clinical status can occur. One would, in accordance with the findings of Dharmendra and Chatterjee ([10]), expect future lepromatous patients among those contacts who have antibodies to *M. leprae* antigen but no accompanying cellular immune responses. Further studies based on much larger study groups and incorporating cellular immune responses as well as careful follow-up examinations are necessary to ascertain the significance of antibodies to *M. leprae* antigen in an individual leprosy contact.

SUMMARY

Fifty-four household contacts of lepromatous patients, 39 household contacts of tuberculoid patients, and 99 control persons were examined with an enzyme-linked immunosorbent assay for their antibody responses to phenolic glycolipid-I (PGL-I) of *Mycobacterium leprae* using a synthetic analog (PGL-I_{SA}) with the same terminal sugar epitope, namely, *O*-(3, 6-di-*O*-methyl-β-D-glucopyranosyl)-(1 → 4)-*O*-(α-L-rhamnopyranosyl)-(1 → 9)-oxynonanoyl-BSA. This study was conducted in the Gurage area of Ethiopia in 15 households with a leprosy patient and 15 matched control households.

Household contacts with more than 1 year of exposure to a lepromatous patient had antibodies to PGL-I_{SA} significantly more often (19 of 34 persons) than did household contacts with less than 1 year of exposure to a lepromatous patient (4 of 20 persons), household contacts of tuberculoid patients (8 of 39 persons), and persons without exposure to leprosy in the household (33 of 99 persons). No significant association was found between the prevalence of antibodies to PGL-I_{SA} in the household contacts and disease activity in the lepromatous index patients at the time of examination; nor was there a significant association between antibody responses and age or sex of the contacts.

The increased prevalence of antibodies to *M. leprae* antigen in healthy persons with more than 1 year of contact with a lepromatous patient provides further evidence that subclinical infection in leprosy is common, and is related to the type of leprosy in the index patient. The fact that antibodies to PGL-I_{SA} were detected in one third of the persons without household exposure to leprosy emphasizes the necessity to always include comparable controls from the same endemic area in studies of leprosy contacts.

RESUMEN

Utilizando un inmunoensayo enzimático (ELISA) se examinaron 54 contactos convivientes de pacientes lepromatosos, 39 contactos convivientes de pacientes tuberculoides, y 99 personas control, con respecto a su respuesta contra el glicolípido fenólico-I (GLF-I) del *Mycobacterium leprae*, usando el análogo sintético GLF-I_{SS}: *O*-(3, 6-di-*O*-metil-β-D-glucopiranosil)-(1 → 4)-*O*-(α-L-ramnopiranosil)-(1 → 9)-oxinonaoil-ASB. Este estudio se realizó en el área Gurage de Etiopia en 15 grupos de convivientes con un caso de lepra y en 15 grupos de no convivientes (control).

Los contactos convivientes con más de 1 año de exposición a un paciente lepromatoso tuvieron anticuerpos contra el GLF-I_{SS} en forma más frecuente (19 de 34) que los contactos con menos de 1 año de exposición (4 de 20 personas), que los contactos convivientes con un paciente tuberculoide (8 de 39 personas), y que las personas sin exposición a la lepra (33 de 99 casos). No se encontró una asociación significativa entre la prevalencia de anticuerpos contra el GLF-I_{SS} en los contactos convivientes y la actividad de la enfermedad en los pacientes lepromatosos; tampoco hubo asociación entre las respuestas en anticuerpos y la edad o sexo de los contactos.

La incrementada prevalencia de anticuerpos anti-*M. leprae* en las personas sanas con más de un año de contacto con un caso lepromatoso, proporciona evidencias de que la infección subclínica en la lepra es común y está relacionada con el tipo de lepra del paciente involucrado. El hecho de que los anticuerpos contra el GLF-I_{SS} fueran detectados en un tercio de las personas sin exposición a la lepra, enfatiza la necesidad de incluir siempre controles comparables de la misma área endémica en estudios de contactos de pacientes con lepra.

RÉSUMÉ

On a examiné 54 contacts domiciliaires de malades lépromateux, 39 contacts domiciliaires de malades tuberculoides, et 99 sujets témoins, au moyen d'une épreuve ELISA, afin d'étudier leur réponse en anti-

corps à l'antigène phénoglycolipidique-I (PGL-I) de *Mycobacterium leprae*. Pour ce faire, on a utilisé un analogue synthétique (PGL-I_{SA}) ayant le même épitope hydrocarboné terminal, à savoir l'*O*-(3, 6-di-*O*-méthyl-β-D-glucopyranosyl)-(1 → 4)-*O*-α-L-rhamnopyranosyl)-(1 → 9)-oxynonanoyl-BSA. Cette étude a été menée dans la région de Gurage en Ethiopie, chez 15 personnes qui partagaient leur domicile avec un malade de la lèpre et chez 15 personnes témoins appariés.

Les contacts domiciliaires ayant plus d'une année d'expositions à un malade lépromateux présentaient des anti-corps au PGL-I_{SA} significativement plus souvent (19 sur 34) que les contacts domiciliaires qui avaient vécu moins d'un an au contact d'un malade lépromateux (4 sur 20), les contacts domiciliaires de malades tuberculoides (8 sur 39), et les personnes n'ayant aucune exposition à la lèpre au domicile (33 sur 99). Aucune association significative n'a été observée entre la prévalence des anticorps au PGL-I_{SA} chez les contacts domiciliaries d'une part, et l'activité de la maladie chez les malades lépromateux au moment de l'examen. On n'a pas davantage observé d'associations significatives entre les réponses d'anticorps, et l'âge ou le sexe des contacts.

La prévalence accrue d'anticorps à l'antigéne *M. leprae* chez les sujets sains ayant plus d'une année de contact avec un malade lépromateux, fournit des arguments supplémentaires pour soupçonner que l'infection infraclinique de la lèpre est commune et qu'elle est en relation avec le type de lèpre présenté par le malade index. Le fait que l'on ait pu détecter des anticorps PGL-I_{SA} chez un tiers des personnes n'ayant aucune exposition domiciliaire connue à la lèpre, souligne la nécessité de toujours inclure dans les études menées chez les contacts de lèpre des sujets témoins comparables et originaires de la même régioin endémique.

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