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Serologic Responses to *Mycobacterium leprae*-specific Phenolic Glycolipid-I Antigen in Sooty Mangabey Monkeys with Experimental Leprosy[1]

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The mangabey monkey model offers a unique opportunity to follow immune responses in leprosy over the course of the infection in a host similar to man and to make comparisons with autologous control data. Importantly, the model makes it possible to study immune parameters immediately following the initial infection with *Mycobacterium leprae*. Similar data are difficult to obtain for leprosy in humans because of the unknown mode of infection and the long incubation period.

Since 1980, we have studied over 30 sooty mangabey monkeys (*Cercocebus atys*) inoculated with *M. leprae* ([18]). We describe here the antibody responses in a group of eight sooty mangabeys to phenolic glycolipid-I (PGL-I), a specific *M. leprae* antigen ([5]).

We inoculated the monkeys with varying doses of *M. leprae* and obtained sera from each animal before and at defined intervals after infection with *M. leprae*. Analysis of sequential sera over a 35-month period permitted correlations with the clinical course of the infection. Significantly, observations were made early, prior to the appearance of disease symptoms, and thereafter. The responses of the animals to infection with *M. leprae* varied. Some mangabeys failed to develop disease; others developed severe lepromatous (LL) leprosy; still others developed milder neuritic forms of the disease. Comparable longitudinal studies in human leprosy patients have not been reported and, indeed, are not readily feasible.

MATERIALS AND METHODS

Animals. Eight sooty mangabeys were obtained from the breeding colony at the Yerkes Regional Primate Research Center (YRPRC), Atlanta, Georgia, U.S.A. These animals, provided by Dr. Harold McClure, were all males born in 1980. After holding for 90 days in quarantine, serum samples were obtained and stored at −70°C. The monkeys were anesthetized with ketamine HCl for examinations and interventions.

***M. leprae* inoculations.** On 14 July 1983, the inoculum was aseptically obtained from a male mangabey monkey (A022) experimentally infected in March 1980 ([18]). The *M. leprae* used to inoculate A022 was isolated from mangabey A015, the first known monkey with naturally acquired leprosy. Newly formed, nonulcerated skin lesions were surgically removed from A022 and placed on ice. The tissue was minced, homogenized in phosphate buffered saline (PBS) in a Tenbroek homogenizer, passed through gauze, and centrifuged at low speed. Aliquots were removed for bacterial counts and determination of the morphological index (MI) ([17]). The suspension contained 6.9 × 10^9 acid-fast bacteria (AFB) per ml with a MI of 10%. We inoculated each of the eight adolescent, male mangabeys (D171–D178) with a total of 7 ml of this suspension or with serial, 10-fold dilutions thereof: 3 ml intravenously (i.v.) via the saphenous vein, and 4 ml intradermally (i.d.) by injecting approximately 0.5 ml at each of eight sites [the dorsum of the left (L) forearm, the L lateral calf, the L and right ear tips, the tip of the nose, the L eyebrow, the L upper

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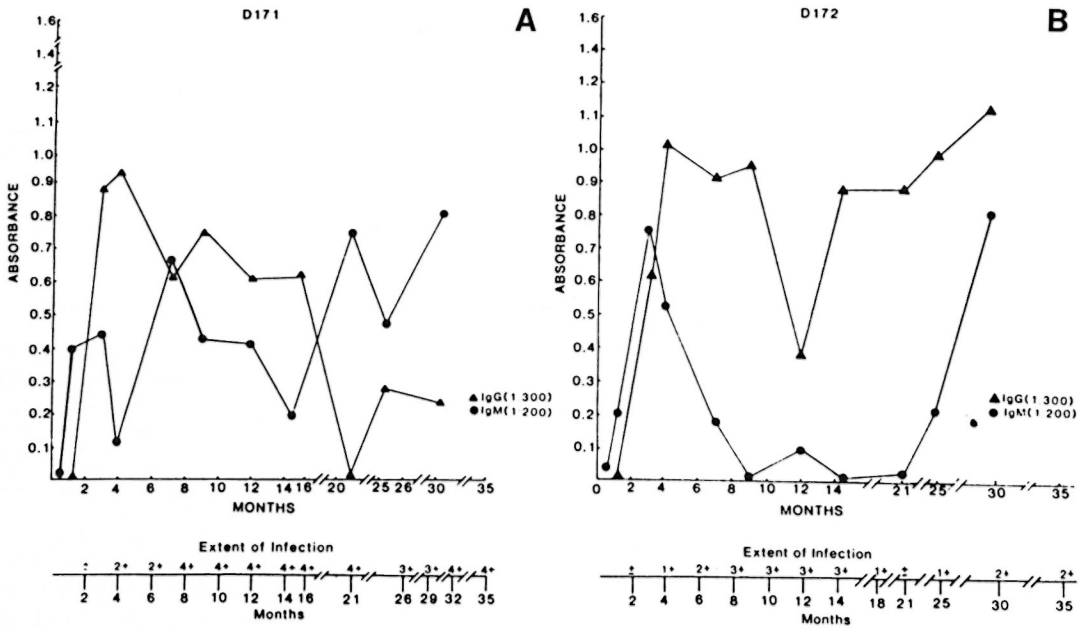

FIG. 1. Longitudinal antibody responses (IgG, ▲; IgM, ●) to PGL-I (upper portion) and clinical staging (−, ±, and 1+ to 4+) of leprosy (lower portion) in mangabeys D171 (**A**) and D172 (**B**) before and at intervals after inoculation with 4.8×10^{10} *M. leprae*. (See Methods section for explanation of the staging system.)

lip, and the dorsum of the L wrist]. Mangabeys D171 and D172 received a total of 4.8×10^{10} AFB; D173 and D174, 4.8×10^{9} AFB; D175 and D176, 4.8×10^{8} AFB; and D177 and D178, 4.8×10^{7} AFB.

The mangabeys were housed individually. Serum samples were obtained and periodic clinical findings recorded. Nasal smears were taken by calcium alginate swabs at each examination and stained for AFB by the Ziehl-Neelsen method. Periodic biopsy specimens were observed by routine histopathologic procedures and stained by the hematoxylin-eosin and Fite-Faraco methods.

Clinical evaluations. The entire body surface was examined with special attention to the inoculation sites, and cooler areas of the body (e.g., tail and scrotum) for disseminated disease. Blood and serum samples were taken for clinical evaluations and antibody determinations.

Clinical status was staged as follows: −, no disease; ±, small (<2 mm), nonulcerated areas of abnormal pigmentation and/or infiltration at dermal inoculation sites; 1+, well-stained AFB in nasal secretions or in a biopsy specimen (Bx) or other sample of a dermal lesion or >2 mm lesions at multiple inoculation sites; 2+, solidly staining AFB in nasal secretions and other lesions at dermal inoculation sites; 3+, lesions at uninoculated dermal sites (usually with positive nasal secretions); and 4+, ulceration or enlargement (>1 cm) of or increases in numbers of disseminated dermal lesions or combinations of these characteristics. All histopathologic classifications of leprosy are according to the Ridley and Jopling system ([15]).

ELISAs. *M. leprae*-specific PGL-I antigen was purified from human *M. leprae* obtained from armadillo tissues using published methods ([7]). The ELISA methods used were those of Cho, *et al.*, with minor modifications ([3]). Purified PGL-I (40 μg/ml) was suspended in 0.2 M carbonate buffer at pH 9.2. Fifty μl (2 μg) of PGL-I or carbonate buffer alone were added to the wells of flat-bottomed, 96-well plates (Immulon I; Dynatech Laboratories, Inc., Chantilly, Virginia, U.S.A.), which were incubated overnight at 4°C. The plates were then washed three times using 200 μl of 1% bovine serum albumin (BSA) in 10^{-3} M phosphate-buffered saline (PBS), pH 7.2, allowing 7 min incu-

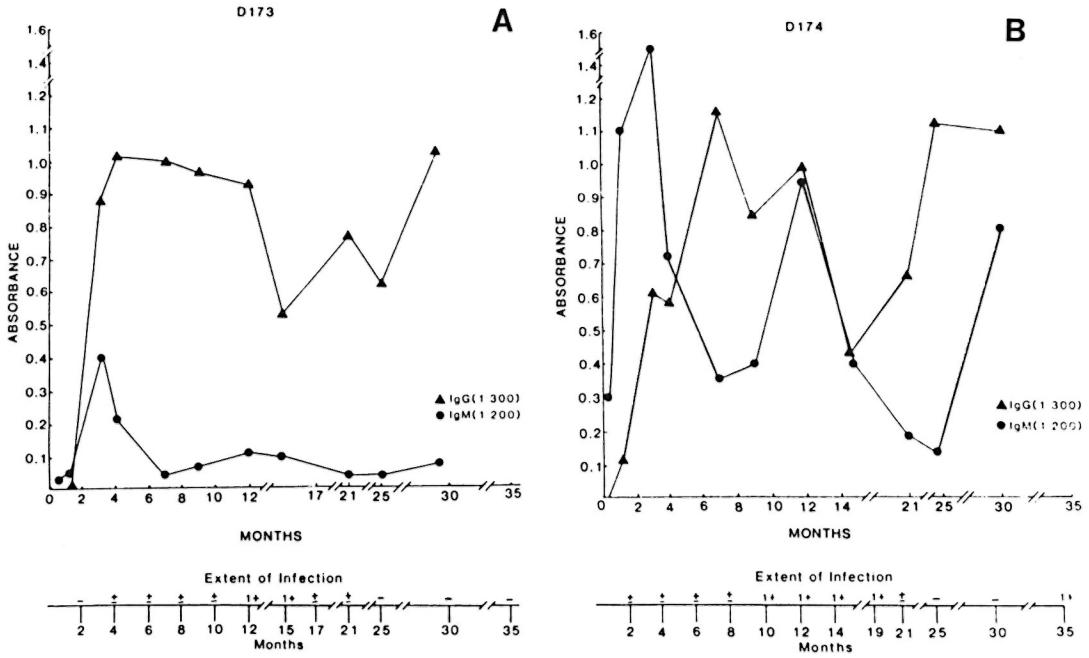

FIG. 2. Antibody responses to PGL-I and clinical staging in mangabeys D173 (**A**) and D174 (**B**) inoculated with 4.8×10^9 *M. leprae*. (See Fig. 1 for details.)

bation per wash. One hundred μl of 1% BSA-PBS was then added and incubated at room temperature for 1 hr. The plates were again washed three times, as before, and 50 μl of diluted sera added to each experimental well followed by 45 min incubation at room temperature. Optimal antibody dilutions were determined by prior titrations. The dilutions chosen for assay, based on these titrations, were 1:100 for IgM and 1:300 for IgG. Each sample was assayed in duplicate with duplicate control wells containing serum but lacking PGL-I antigen.

Excess serum was then removed by washing three times with 200 μl of 1% BSA-PBS. Fifty μl of peroxidase-labeled anti-human IgG or IgM antibody was then added to each well at the predetermined optimal dilution (1:1000 for IgG and 1:2000 for IgM). The enzyme-linked (ELISA) reagents were affinity purified anti-human Fc fragment γ- or μ-chain specific (Cooper Biomedical, Malvern, Pennsylvania, U.S.A.). The ELISA antibody was incubated for 45 min at room temperature, and the plates again washed three times with BSA-PBS. Fifty μl of *o*-phenylene-diamine (Sigma Chemical Co., St. Louis, Missouri, U.S.A.) at 80 mg/ml in 0.1 M acetate buffer, pH 5.5, containing 0.2% H_2O_2, was added to each well. The plates were incubated at room temperature for 10 min and 5 N HCl (50 μl/well) added. The optical density (OD) at 490 nm was determined for each well using an ELISA reader (MR-700; Dynatech Laboratories, Inc., Alexandria, Virginia, U.S.A.). The final OD reported herein represents the OD of wells containing PGL-I antigen minus that in control wells that lacked PGL-I antigen but contained all other components.

RESULTS

There was usually a good correlation between the dose of *M. leprae* inoculated and the onset of symptoms and initial severity of the lesions (Figs. 1–4, lower portions). Mangabey D171 (Fig. 1A, lower portion), which received the highest dose of *M. leprae* (4.8×10^{10}), developed severe LL-type leprosy with dissemination to the nasal mucosa by 5 months postinoculation; the disease continued to progress, and required treatment at 38 months. Mangabey D172 which also received the highest dose developed severe, disseminated LL leprosy within a 9-month period, but by 18 months the dis-

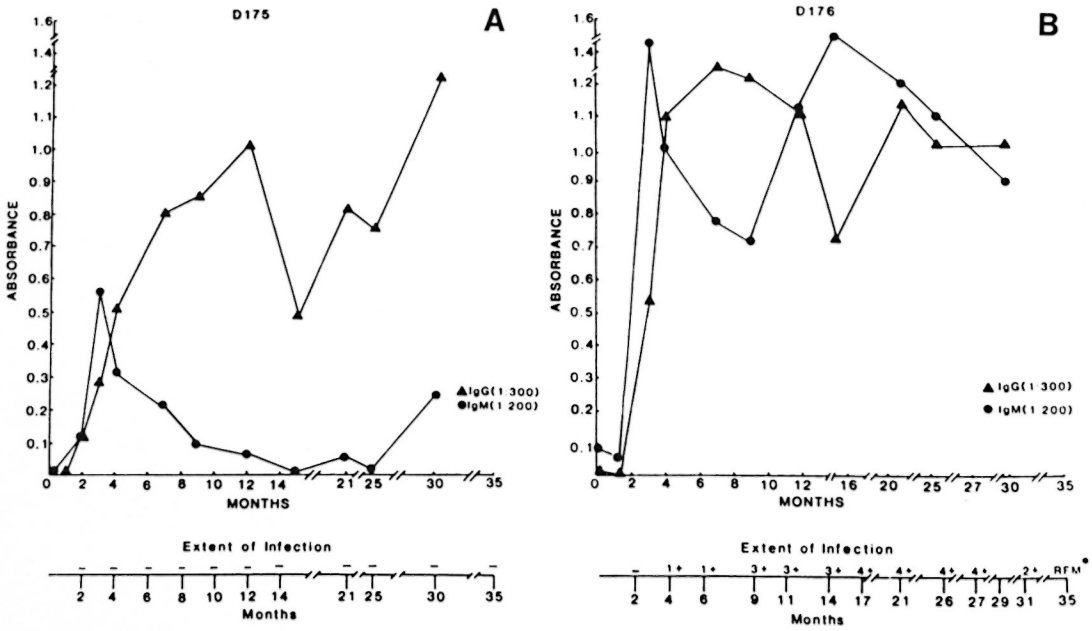

FIG. 3. Antibody responses to PGL-I and staging in mangabeys D175 (**A**) and D176 (**B**) inoculated with 4.8 × 10^8 *M. leprae*. (See Fig. 1 for details. RFM* in **B** indicates that mangabey D176 was treated with rifampin, beginning at month 27, and had shown a dramatic positive response by month 35.)

ease began a spontaneous regression which was sustained until reactivation, with continued progression between months 26 and 29 postinoculation (Fig. 1B, lower portion).

D173 and D174 (Figs. 2A and B) both received a 1:10 dilution of inoculum (4.8 × 10^9 AFB). D173 developed limited lesions at the inoculation sites on the ears, nose and calf by 5 months with slow progression until 14 months when sustained spontaneous regression began, culminating in complete remission by 25 months postinoculation. Mangabey D174 behaved similarly, but with a recurrence of disease 35 months postinoculation (Fig. 2B).

D175 and D176 both received a 1:100 dilution of inoculum (4.8 × 10^8 AFB). D175 (Fig. 3A) has not developed leprosy at 50 months postinoculation. In contrast, mangabey D176 developed severe, disseminated LL leprosy within 9 months, with continued progression requiring chemotherapy by 35 months (Fig. 3B, lower portion). Disease progression in D176 was much more rapid than in any of the other mangabeys in the study. D177 and D178 (Figs. 4A and B) received a 1:1000 dilution of *M. leprae* (4.8 × 10^7). D177 showed the first AFB-positive dermal lesion (subpolar LL leprosy) at 26 months with dissemination requiring chemotherapy by 42 months postinoculation (Fig. 4A). D178 had no significant lesion until enlargement of a nerve in the outer left ankle was noticed at 35 months (Fig. 4B). A biopsy from the site at that time showed indeterminate leprosy ([15]) which has persisted (50 months postinoculation) in D178 in the absence of any dermal lesions.

The upper portions of Figures 1–4 show the anti-PGL-I IgG and IgM antibody responses in each mangabey corresponding to clinical changes. In each of the eight mangabeys, there was an initial IgM response that peaked within 3 months postinoculation. This was followed by a decline that was sustained in the animal with regressive disease (D172) and in those with little or no evidence of sustained clinical disease (D173, D175, D177, and D178) (Figs. 1–4). The rising IgM titer observed in D172 and D177 approximately 30 months postinoculation coincided with a reactivation of leprosy in D172 and the first appearance of lesions and AFB in the nasal secretions of D177 (Figs. 1B and 4A). In mangabeys with immediate and sustained, progressive leprosy (D171,

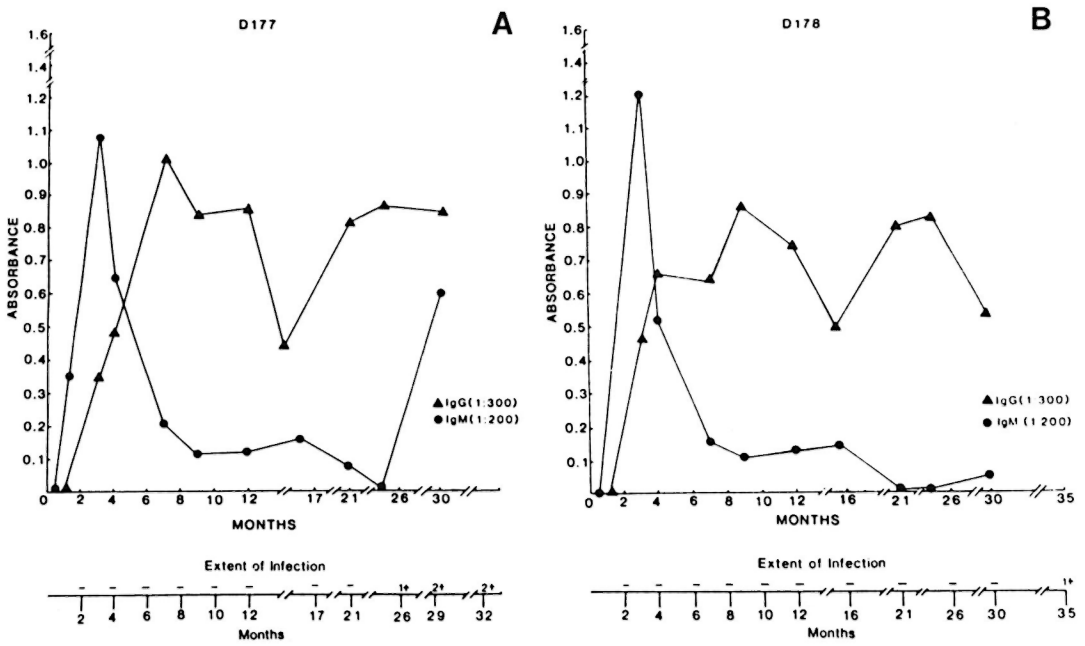

FIG. 4. Antibody responses to PGL-I and staging in mangabeys D177 (**A**) and D178 (**B**) inoculated with 4.8 × 10^7 *M. leprae*. (See Fig. 1 for details.)

D174, and D176), the initial IgM antibody peak was followed by a second or third substantial anti-PGL-I IgM antibody peak (Figs. 1–3).

Rising anti-PGL-I IgG antibody titers were observed in all of the animals within 3 months after *M. leprae* inoculation, and remained elevated in all but one animal, except for significant decreases that preceded or/and corresponded to periods of clinical progression of leprosy symptoms (Figs. 1–4, lower portions): D172, months 10–15; D173, months 17–25; D174, months 9–20; D176, months 12–25; and D177, months 12–21. The remaining monkey (D171), which developed severe, sustained, progressive LL leprosy that required treatment 38 months after inoculation, tended to have lower levels of anti-PGL-I IgG, with sustained significant titers of IgM, over the course of these studies.

After the serologic studies were completed, the clinical condition of the eight mangabeys continued to change. To date, 50 months postinoculation, both of the highest-dose recipients (D171 and D172) developed leprosy, but differences in the patterns of progression and outcome were noted (Figs. 1A and B). The disease in D171 progressed rapidly until rifampin treatment was started 38 months postinoculation. A dramatic positive response to the drug was observed. The lesions have healed and AFB have disappeared from the nasal secretions. The initial LL leprosy in D172 regressed, but AFB reappeared in nasal secretions during year 2 with neuropathic changes (rotational deformity of the foot) 35 months after infection. A skin-biopsy specimen of the tail revealed indeterminate leprosy at that time, and the clinical status remains unchanged 50 months postinoculation.

Both recipients of the 1:10 dilution of inoculum, D173 and D174, developed lesions at the dermal inoculation sites within 5 months after inoculation. These healed spontaneously by month 26 (Fig. 2). Mangabey D173 remains asymptomatic to date; whereas disseminated LL lesions appeared on the tail of D174 with AFB-positive nasal secretions during month 36, and those symptoms have persisted in D174 (50 months postinoculation).

One of the 1:100-diluted *M. leprae* recipients, D175, failed to develop any significant sign of leprosy except for early, tran-

sient nodules at the inoculation sites on the free margins of the ears (Fig. 3A). At present (50 months), this animal is completely free of any sign of leprosy. The second 1:100 *M. leprae* recipient, D176, developed LL leprosy within 5 months which disseminated by 9 months after inoculation. The disease in D176 became life-threatening by 26 months after infection (Fig. 3B). Rifampin therapy led to complete remission.

The two recipients of the 1:1000 dilution of inoculum, D177 and D178, developed leprosy slowly (Figs. 4A and B). Lesions classified as subpolar lepromatous leprosy (LLs) first appeared at the inoculation sites on the ears of D177 during month 26. The lesions in this animal remained confined to inoculation sites on the ears and nose, but became greatly enlarged and ulcerated. The animal lost weight, became severely anemic, and required rifampin therapy at month 42. Its response to antibiotic therapy has been slower than that of most other treated mangabeys, but has led to overall clinical improvement. Mangabey D178 appeared to have enlarged nerves in the left lateral ankle region at month 35. A skin biopsy from that region showed indeterminate leprosy which persists at month 50.

DISCUSSION

The onset of disease symptoms tended to parallel the size of the inoculum, but the ultimate course of the disease appears to depend upon individual host susceptibility. Over a 4-year period, by chance one mangabey of each pair in the titration experiment developed severe LL-type leprosy (D171, D174, D176, and D177). Three animals (D171, D176, and D177) required treatment. Moreover, the severity of the disease in D176 was out of proportion to the relatively small inoculum it received. One mangabey in each pair in the titration study either failed to develop significant leprosy (D173 and D175), developed severe LL leprosy followed by a period of spontaneous reversal and subsequent reexacerbation (D172), or showed delayed onset (47 months postinoculation) of indeterminate leprosy (D178). The basis for the variation in susceptibility to leprosy infection among the monkeys is not known. It is possible that immune mechanisms may be partially involved, because normal mangabeys can give either positive or negative lepromin skin tests (Gormus, *et al.*, manuscript in preparation) and *in vitro* blastogenic responses to *M. leprae* antigens ([14]). The mangabeys in this titration study were not skin tested prior to *M. leprae* inoculation to avoid the implications of a possible microvaccination effect. The animals were born in the breeding colony at the YRPRC in Atlanta, and have had no known exposure to leprosy. Thereafter, if individual variations are based on differences in immune status, it would appear that "natural," or genetically controlled immunity or immunity to cross-reacting antigens might influence susceptibility.

The antibody response patterns to PGL-I antigen varied between the eight mangabeys studied, especially the IgM responses. Three of the four animals that ultimately developed severe LL leprosy produced initial anti-PGL-I IgM peaks in excess of 1.0 OD unit and the fourth (D171) produced a sustained IgM titer, usually in excess of 0.4 OD units, over the first 18 months postinoculation. Of the remaining four mangabeys, one animal (D178) with sustained indeterminate leprosy gave an initial IgM peak in excess of 1.0 OD unit; another (D172) that presently has indeterminate leprosy gave an initial IgM anti-PGL-I peak greater than 0.7 OD units and showed a second rise in IgM titer corresponding to a period of clinical exacerbation (after month 21); and two mangabeys (D173 and D175) which have shown little or no evidence of disease gave relatively low IgM anti-PGL-I peaks which diminished and remained low over the course of study.

The IgG anti-PGL-I responses were uniformly high throughout our study in 7 of the 8 animals, except for occasional significant decreases that usually preceded and/or corresponded to periods of clinical progression of leprosy symptoms.

From the correlations described, there is a relationship between the type and level of anti-PGL-I antibody that arises after *M. leprae* exposure and the severity of the leprosy that develops. The data suggest that the best prognostic combination is high IgG and low IgM anti-PGL-I titers. Initial IgM titers in excess of 1.0 OD unit and/or rising or sustained IgM titers, especially together with low or decreasing IgG levels, appear

to precede and/or correspond to periods of progressive disease. The data do not reveal a definite cause-effect relationship between antibody isotype and the susceptibility to leprosy, or the severity of the disease. The results, however, do suggest that such a cause-effect mechanism could exist, and future studies are needed to investigate that possibility. It is accepted that effective anti-*M. leprae* immunity depends on a functioning T-cell response to *M. leprae* antigens ([5]); humoral immunity is thought to play a less important role. The present data suggest, however, that some interaction between the two compartments may take place by undefined mechanisms and the serological profile to PGL-I antigen may be useful in predicting T-cell responsiveness to *M. leprae.*

Most published reports indicate that the predominant anti-PGL-I response in most human leprosy patients is of the IgM type ([1, 2, 4, 9, 16, 19]). Schwerer, *et al.,* reported that anti-PGL-I IgM levels correlated with disease classification, increasing from the tuberculoid toward the lepromatous pole of the disease spectrum ([16]). Levis, *et al.,* observed a similar association between IgM anti-PGL-I levels and the disease spectrum with a positive linear correlation between the bacterial index (BI) and anti-PGL-I IgM levels ([9]). Patients with erythema nodosum leprosum (ENL) had lower levels of anti-PGL-I IgM than non-ENL patients with similar BIs. The latter group also reported that in LL and borderline lepromatous (BL) leprosy patients who had upgraded, there were high levels of anti-PGL-I IgG ([9]). The observations of Levis, *et al.* led to the suggestion that high anti-PGL-I IgM levels reflect bacillary persistence and that anti-PGL-I IgM is involved in the pathogenesis of ENL ([9]).

The IgM data reported herein are consistent with those of Schwerer, *et al.,* and Levis, *et al.,* in that our monkeys showed elevated anti-PGL-I IgM levels when the disease was advancing, i.e., when there was a presumed increase in the BI and decreasing IgM levels during periods of spontaneous regression. Our observation of high IgG anti-PGL-I titers in each of the animals, usually at OD values higher than the IgM anti-PGL-I levels, differs from that reported by Schwerer, *et al.* ([16]), Levis, *et al.* ([9]), or by other investigators ([2, 4, 19]). Our observations cannot necessarily be expected to duplicate those of other groups studying human leprosy patients, however, because we studied the early events after leprosy infection in the absence of any form of treatment. Most patients are studied after the appearance of clinical symptoms with no opportunity being afforded for prior study during preclinical incubation. If our suggestion that IgM anti-PGL-I correlates with susceptibility to leprosy is correct, then one would expect that patients who develop LL leprosy would have predominantly IgM anti-PGL-I antibody late in the disease after the appearance of symptoms. Also, in the human studies the vast majority of patients had been treated with various drugs for variable periods after diagnosis of infections that had been incubating for varying unknown periods of time in different patients ([2, 4, 9, 16, 19]). It is not unlikely that the antibody profile early in the infection might differ significantly from patterns observed years later and after treatment. In this regard, Brett, *et al.,* observed significant levels of anti-PGL-I IgG in 31 of 33 LL patients studied (17 of whom were untreated) with a large decrease in the anti-PGL-I IgG levels after long-term treatment ([1]).

It is also possible that our results in sooty mangabey monkeys differ from the data from humans because the manifestations of leprosy may be different between monkeys and humans. This question cannot be answered easily at present, but findings in prospective longitudinal studies of anti-PGL-I antibody levels in contacts who develop disease while under observation may resolve this issue. Mangabeys probably do not differ strikingly from humans because of their close phylogenetic relationship. All reagents tested that recognize components of the human immune system crossreact with mangabeys ([6, 10–14]). It is important to determine if humans are similar to monkeys in the anti-PGL-I IgG vs IgM responses early in the infection, since our data in mangabeys suggest the possibility that elevated anti-PGL-I IgM responses could possibly be involved in the induction of the leprosy-specific immunosuppression that is observed in LL patients. It is not yet known whether the immunosuppression is a cause or a result of the disease.

Levis, *et al.*, and others have suggested that there may be a block in the switching from IgM to IgG anti-PGL-I production in human LL patients ([8,9]). The data from monkeys suggest that IgM to IgG switching, in fact, may not be impaired, but that the high IgM to IgG anti-PGL-I ratios observed in most human leprosy patients may result secondarily as a consequence of other unknown mechanisms in longstanding LL leprosy. We will continue to monitor our treated and untreated sooty mangabeys longitudinally to assess temporal changes in IgM-IgG anti-PGL-I ratios.

SUMMARY

Four pairs of sooty mangabey monkeys (*Cercocebus atys*) were inoculated with serial, 10-fold dilutions of *Mycobacterium leprae*. The highest-dose pair received 4.8×10^{10} *M. leprae*. Serum samples were obtained and clinical signs of leprosy were recorded at intervals of 35 months. Longitudinal serum samples were assayed by an ELISA method for the presence of IgG and IgM antibodies to the *M. leprae*-specific phenolic glycolipid-I (PGL-I) antigen.

In general, the onset of disease symptoms paralleled the number of *M. leprae* inoculated, but the ultimate course of disease depended upon individual animal susceptibility. Both IgG and IgM anti-PGL-I isotypes were observed in variable levels and patterns, related to the disease stage, among the eight mangabeys.

The data suggest that high IgG and low IgM anti-PGL-I levels correlated with less severe disease; whereas initial high IgM titers and/or rising or sustained high IgM titers, especially together with low IgG anti-PGL-I titers, preceded or corresponded to periods of progressive leprosy.

The results show that IgG and IgM anti-PGL-I antibodies can be present in significant titers among mangabeys early after infection with *M. leprae*. It appears likely that the relative levels of these anti-PGL-I isotypes may be correlated with the susceptibility of individual animals to the development of lepromatous leprosy.

RESUMEN

Cuatro pares de monos mangabey tiznados (*Cercocebus atys*) se inocularon con diferentes cantidades de *Mycobacterium leprae*. La dosis más alta fue de 4.8×10^{10} *M. leprae*. A diferentes intervalos de tiempo, durante 35 meses, se tomaron muestras de suero y se registraron los signos clínicos desarrollados. Las muestras de suero se estudiaron por un método inmunoenzimático (ELISA) para buscar la presencia de anticuerpos IgG e IgM contra el glicolípido fenólico-I (GLF-I) del *M. leprae*.

En general, la aparición de los síntomas de la enfermedad fue paralela al número de *M. leprae* inoculados pero el curso final de la enfermedad dependió de la susceptibilidad individual del animal. Se encontraron anticuerpos anti-GLF-I de ambos isotipos (en niveles y patrones variables dependiendo de la etapa de la enfermedad) en los ocho monos mangabey.

Los datos sugieren que los niveles elevados de IgG y bajos de IgM (anti-GLF-I) correlacionaron con una enfermedad menos severa y que los títulos de IgM anti-GLF-I inicialmente altos, o crecientes, o sostenidos elevados, especialmente junto con títulos bajos de IgG anti-GLF-I, precedieron o correspondieron a periodos de lepra progresiva.

Los resultados muestran que los anticuerpos anti-GLF-I, IgG e IgM, pueden encontrarse a títulos significantes entre los monos mangabey en las etapas tempranas de la infección con *M. leprae*. Es probable que los niveles relativos de estos isotipos anti-GLF-I estén relacionados con la susceptibilidad de los animales individuales al desarrollo de la lepra lepromatosa.

RÉSUMÉ

Quatres paires de singes mangabey (*Cercocebus atys*) ont été inoculés en série par des dilutions de *Mycobacterium leprae*, dont la concentration diminuait par un facteur 10. La paire ayant reçu la dose la plus élevée a été inoculée ainsi par $4,8 \times 10^{10}$ *M. leprae*. Des échantillons de sérum ont été recueillis et les signes cliniques de la lèpre ont été recherchés périodiquement pendant 35 mois. Des échantillons de sérum ont été testés par une méthode ELISA, en vue de déceler la présence d'anticorps IgG et IgM à l'antigène PGL-L spécique pour *M. leprae*.

En général, l'apparition de symptômes de la maladie correspondait au nombre de *M. leprae* inoculés. Toutefois, l'évolution ultérieure de la maladie a dépendu de la susceptibilité individuelle des animaux. On a observé, à des niveaux variables, et selon des profils divers, des isotypes IgG et IgM contre PGL-L. Ceci, chez les 8 singes étudiés, était en relation avec le développement de la maladie.

Ces données suggèrent que des taux élevés d'IgG contre PGL-L, et des taux bas d'IgM contre le même antigène, étaient en corrélation avec une affection moins grave. Par contre, des taux initiaux élevés d'IgM, de même qu'une augmentation ou le maintien à des valeurs élevées de ces taux précédaient ou correspondaient à des périodes progressives de la maladie, particulièrement lorsque ils étaient accompagnés de titres faibles IgG contre PGL-L.

Ces résultats montrent que les anticorps IgG et IgM contre PGL-L, peuvent être présents à des taux signi-

ficatifs chez les singes mangabey fort précocement après l'infection par *M. leprae*. Il semble dès lors très vraisemblable que les taux relatifs de ces isotypes anti-PGL-L peuvent être en relation avec la susceptiblité individuelle des animaux au développement de la lèpre lépromateuse.

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