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Assessment of the Immune Deficit in Leprosy Patients and the Effect of Recombinant IL-2 *in Vitro*[1]

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Leprosy manifests as a clinical and immunologic spectrum, ranging from the localized, paucibacillary, immunologically competent tuberculoid (TT) form to the disseminated, bacilliferous, immunologically deficient lepromatous (LL) disease ([23, 31]). Several hypotheses have been suggested to explain the hyporesponsiveness of peripheral blood mononuclear cells (PBMC) from lepromatous patients, including humoral substances such as blocking antibodies ([25]), lymphocytotoxic antibodies ([33]), immune complexes ([4]), and mycobacterial phospholipids ([38]). Other work has demonstrated that cellular mechanisms are responsible for this unresponsiveness. Both macrophages ([32]) and T lymphocytes ([17]) from LL patients have been shown to have suppressor activity. Mehra, *et al.* ([16]) suggested that a population of T-suppressor cells are specifically induced by the terminal sugar of phenolic glycolipid-I (PGL-I), the *Mycobacterium leprae*-specific glycolipid. In addition, investigators have shown that the T-helper: T-suppressor cell ratio is low in LL patients, supporting a shift in regulation of the immune response toward suppression ([22, 39]). Recent evidence points to a lack of lymphokine production in cells from lepromatous patients ([9, 11, 14, 18, 21, 26]). These results suggest that LL patients lack a soluble lymphocyte product, such as interleukin-2 (IL-2), rather than lacking *M. leprae* reactive T lymphocytes. The mechanism causing the interleukin deficiency in these patients is unclear but may be related to the presence of T-suppressor cells, which have been shown in experimental systems to suppress IL-2 production ([29]).

The present study examined the *in vitro* response of PBMC from treated and untreated patients across the spectrum of leprosy, and compared them with three groups of control subjects: healthy household contacts (without signs or symptoms of leprosy); age, sex, and ethnically matched controls from the endemic area; and laboratory

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TABLE 1. *Patient classification.*

Patient	Sex	Age (yrs)	Clinical histologic diagnosis	Duration of treatment (wks)	Drugs[a]
1	M	22	LL	1	RFP; DDS; CFZ
2	M	25	LL	48	RFP; DDS; CFZ
3	F	42	LL	4	RFP; DDS; CFZ
4	M	24	LL	68	RFP; DDS
5	M	47	LL	0	Untreated
6	F	23	BL	52	RFP; DDS
7	M	31	BL	1	RFP; DDS
8	M	65	BT	1	RFP; DDS
9	F	17	BT	0	Untreated
10	F	22	TT	0	Untreated
11	M	27	TT	0	Untreated

[a] RFP = rifampin; DDS = dapsone; CFZ = clofazimine.

staff controls. Utilizing the lymphocyte proliferation assay, PBMC were cultured with sonicated *M. leprae,* Dharmendra lepromin, PGL-I, or PPD. Suppression of the proliferative response to concanavalin A (ConA) by these antigens was also assessed as described by Mehra, *et al.* ([16]). In addition, recombinant IL-2 (rIL-2) was added to designated cultures to determine if IL-2 could augment the antigen-specific unresponsiveness of BL/LL patients.

MATERIALS AND METHODS

Patients and control subjects. Blood was obtained from leprosy patients attending the Georgetown Hospital Public Health Clinic, Guyana, along with household contacts and unrelated age, sex and ethnically matched subjects. Whole-blood specimens were flown to Boston on the same day of bleeding. Two patients and their respective control subjects were from the Boston area. Leprosy patients were classified according to the clinical and histopathologic criteria described by Ridley and Jopling ([31]). Five lepromatous (LL), 2 borderline lepromatous (BL), 2 borderline tuberculoid (BT), and 2 tuberculoid (TT) patients were evaluated with 8 household members without signs or symptoms of disease (household subjects); 7 age, sex and ethnically matched individuals from the endemic area; and 8 volunteers from our laboratory staff (Table 1). LL and BL patients are grouped together in the presentation of the data, as are TT and BT patients.

Patients were either untreated or treated with dapsone and rifampin, with or without clofazimine, for 1–16 months at the time blood was drawn (Table 1).

Antigens and rIL-2. *M. leprae* extracted from the tissues of infected armadillos was sonicated for 15 min and used at final concentrations of 1–10 μg dry weight per ml. Dharmendra lepromin (National Institute of Leprosy Research, Tokyo, Japan), kindly donated by the late Dr. Charles C. Shepard (Centers for Disease Control, Atlanta, Georgia, U.S.A.), was extensively dialyzed against phosphate-buffered saline (PBS) and used at a final dilution of 1:10. PGL-I, the species-specific mycoside, a generous gift of Dr. Patrick J. Brennan (Colorado State University, Fort Collins, Colorado, U.S.A.), was incorporated into liposomes by Dr. Shirley W. Hunter (Colorado State University), and used at final concentrations of 0.05 μg/ml to 5.0 μg/ml. Liposomes were prepared as described by Six, *et al.* ([35]), by sonication of a mixture of 2.0 mg sphingomyelin, 0.73 mg cholesterol, 0.065 mg dicetylphosphate, and 0.23 mg PGL-I in 125 μl Tris buffer (pH 8.0) for 1 hr.

rIL-2 was generously supplied by Dr. Kirston Koths (Cetus Corporation, Emeryville, California, U.S.A.) and used at final concentrations of 1, 10, 100 and 500 U/ml. Purified protein derivative (PPD; Con-

naught Laboratories Ltd., Willowdale, Ontario, Canada) was used at a final concentration of 6.25 μg/ml for a peak proliferative response.

***In vitro* lymphocyte cultures.** PBMC were isolated from heparinized blood 12–15 hr after bleeding by density gradient centrifugation over Lymphocyte Separation Medium (Litton Bionetics, Charleston, South Carolina, U.S.A.). PBMC were cultured in round-bottom microculture plates with RPMI 1640 containing 10% pooled human AB serum (MA Bioproducts, Walkersville, Maryland, U.S.A.), 2 mM L-glutamine, 10 mM Hepes buffer, 100 IU penicillin per ml, and 100 μg streptomycin per ml.

Cultures designated for studies of antigen-induced proliferation received 20 μl of one of the three leprosy antigen preparations (sonicated *M. leprae,* lepromin, or PGL-I) or PPD, and unstimulated cultures received 20 μl of culture medium. Various concentrations of rIL-2, ranging from 1–500 U/ml, were also added to cultures with and without antigen in a checkerboard design. All cultures were plated in triplicate. Five-day cultures were pulsed with 1 μCi tritiated thymidine (^{3}H-TdR; 6.7 Ci/mmol; New England Nuclear, Boston, Massachusetts, U.S.A.) and harvested 18 hr later. ^{3}H-TdR incorporation was determined as counts per minute (cpm) by liquid scintillation counting, and the difference between cpm of antigen-stimulated cultures and cpm of unstimulated cultures (Δcpm) was calculated for PBMC with and without rIL-2. Stimulation indices for various added factors were calculated as the ratio of Δcpm of cultures in the presence of a factor and Δcpm of cultures in the absence of the same factor. Data were analyzed by analysis of variance.

Cultures designated for determination of antigen-induced suppression of ConA-induced proliferation received 20 μl ConA (Miles Laboratories Inc., Elkhart, Indiana, U.S.A.) for a final concentration of 2.5 μg/ml (a dose which produced suboptimal stimulation under our experimental conditions). One of the three antigen preparations or medium only was then added to triplicate wells. Following 2 days of culture, cells were pulsed with 1 μCi ^{3}H-TdR, harvested 18 hr later, and ^{3}H-TdR incorporation determined. The percent suppression was determined as previously described by Mehra, *et al.* ([17]) according to the following formula and greater than 20% suppression was considered significant:

$$\% \text{ Suppression} = 100 - \left(\frac{\text{cpm antigen + ConA}}{\text{cpm ConA alone}}\right) \times 100$$

RESULTS

Response of PBMC to mycobacterial antigens. PBMC proliferation in response to *M. leprae,* lepromin, and PGL-I liposomes is shown in Figure 1. TT/BT patients and the three groups of control subjects demonstrated proliferation to *M. leprae* (Fig. 1A) and lepromin (Fig. 1B). The LL/BL PBMC proliferative response was, however, significantly lower than that of the TT/BT patients and control groups ($p < 0.005$).

PGL-I liposomes (Fig. 1C) did not elicit proliferation in the majority of PBMC tested. A range of 0.05–5 μg/ml was tested on selected patients and controls, and no proliferation was evident. In parallel, liposomes without PGL-I were cultured with PBMC, and in most cases the apparent stimulation or suppression in certain individuals was caused by the liposomes rather than the PGL-I (data not shown).

The response to PPD was similar to that seen for lepromin and *M. leprae*; proliferation was poor in 6 of the 7 LL/BL patients compared to TT/BT patients and subjects from the three control groups (Fig. 2).

Effect of rIL-2 on PBMC. In an attempt to augment the poor mycobacterial antigen response seen in LL/BL patients, cultures of PBMC with and without antigen were supplemented with varying concentrations of rIL-2 (1–500 U/ml). Table 2 illustrates the response of PBMC from patients and controls to lepromin in the absence or presence of rIL-2 (0–10 U/ml depicted). There was a consistent dose-dependent increase in proliferation to rIL-2 in the presence of lepromin in patients as well as in the control groups. However, the stimulation indices for LL/BL patients were generally high because of their initial low response to antigen

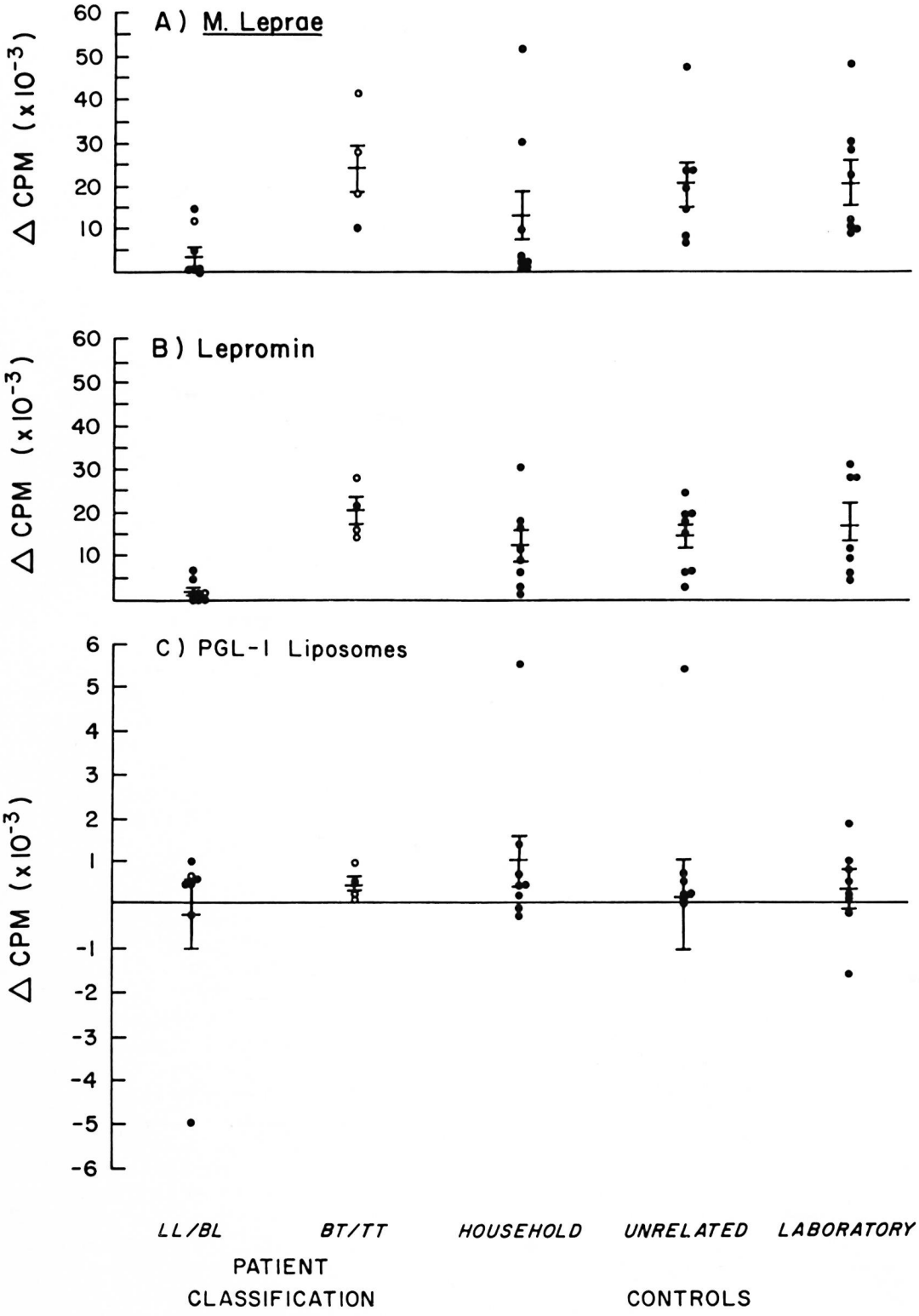

FIG. 1. Proliferative response of PBMC from patients across the leprosy spectrum and from control subjects to A) sonicated *M. leprae* (1 μg/ml), B) Dharmendra lepromin (1:10), or C) PGL-I delivered in liposomes (0.5

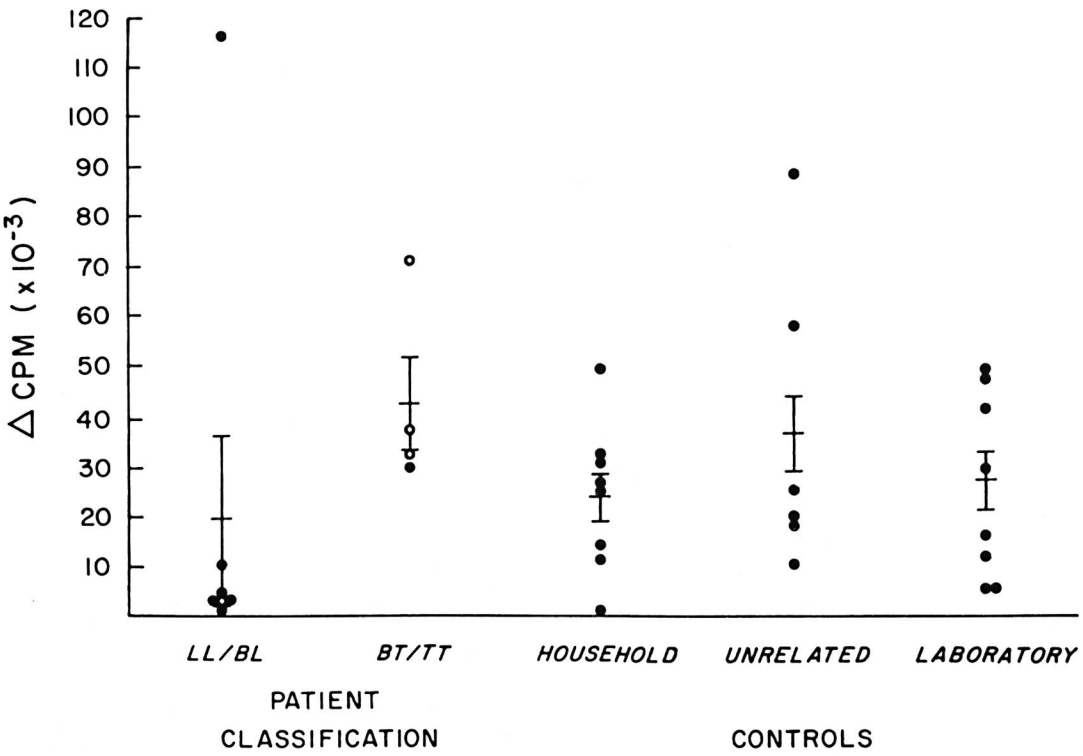

FIG. 2. Proliferative response of PBMC from leprosy patients and control subjects to PPD at a final concentration of 6.25 μg/ml. ^{3}H-TdR incorporation was measured during the last 18 hr of a 6-day culture. Untreated patients = O; treated patients or controls = ●; bars represent mean Δcpm ± S.E.M. for each group.

alone. Similar results were seen when rIL-2 was added to cultures with *M. leprae* (data not shown).

The response of patients and control subjects was increased in the presence of rIL-2 alone, and proliferation of PBMC from LL/BL patients when cultured with lepromin and rIL-2 was similar to that seen in BT/TT patients and controls (Fig. 3).

Response of PBMC to ConA in presence of mycobacterial antigens. Figure 4 depicts the PBMC response from leprosy patients across the spectrum of the disease and control subjects stimulated to proliferate with ConA in the presence of *M. leprae* (Fig. 4A), lepromin (Fig. 4B) or PGL-I delivered in liposomes (Fig. 4C). There were no consistent differences in ConA-induced proliferation between LL/BL patients, TT/BT patients and control subjects when PBMC were cultured with the three antigen preparations.

DISCUSSION

This study was designed to evaluate the effect of IL-2 *in vitro* on the immunologic unresponsiveness of patients across the spectrum of leprosy. Previous studies have shown conflicting data about the effect of IL-2 on responses of lymphocytes from leprosy patients. This study sought to compare patients with three carefully selected healthy control groups: household contacts without signs or symptoms of leprosy; age, sex, ethnically matched subjects living in the endemic area but not having known contact with patients; and laboratory staff members (three of whom handled mycobacterial re-

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μg/ml; note the different cpm scale for PGL-I). Cells were cultured for 6 days with each antigen and incorporation of ^{3}H-TdR was measured during the last 18 hr of culture. Untreated patients = O; treated patients or control subjects = ●; bars represent mean Δcpm ± S.E.M. for each group.

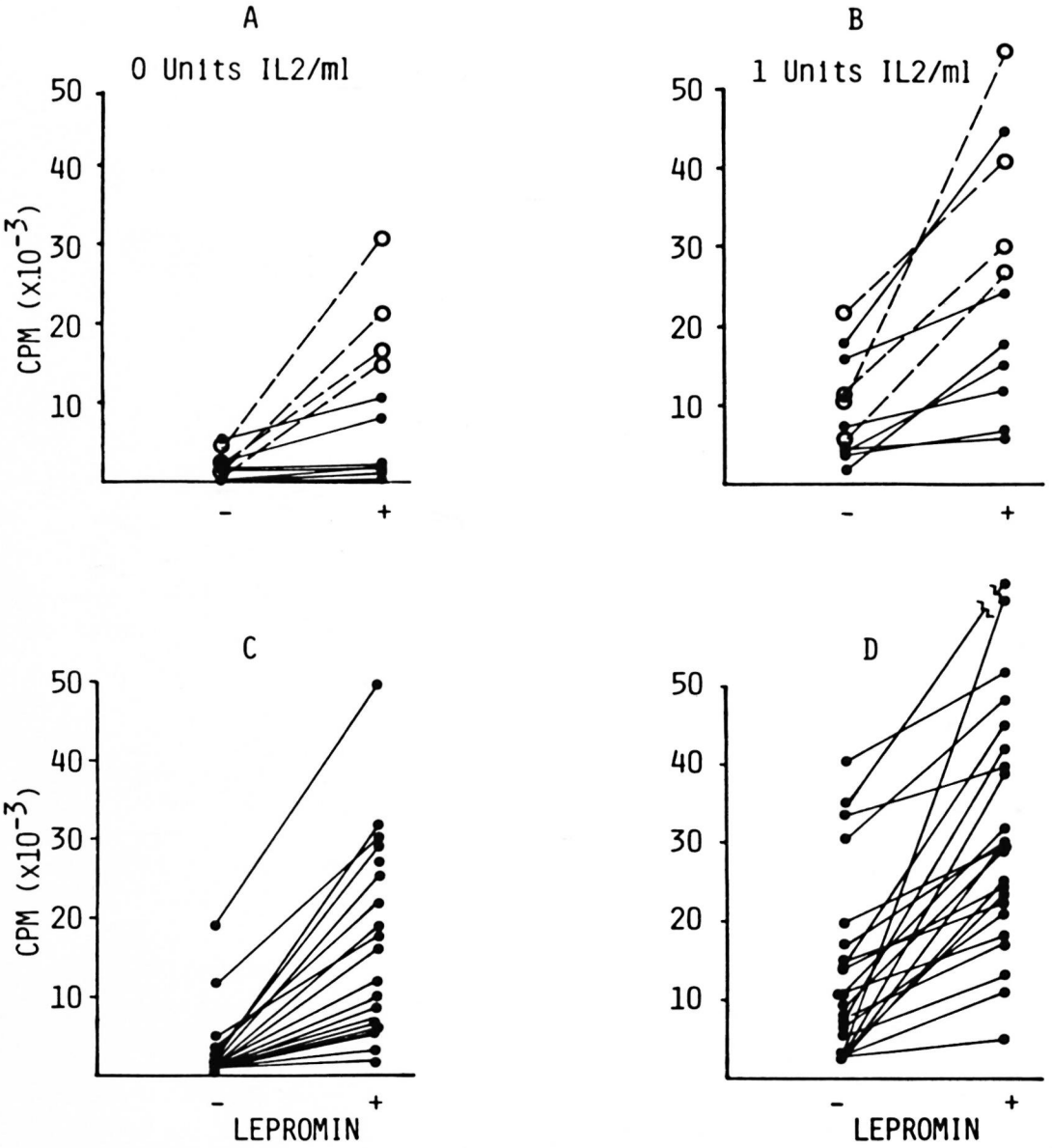

FIG. 3. Proliferative response in the presence and absence of lepromin and rIL-2. Results are expressed as mean Δcpm for triplicate cultures for: **A** and **B**, LL/BL patients = ●; **A** and **B**, BT/TT patients = ○; **C** and **D**, household contacts, age, sex ethnically matched controls, laboratory staff controls = ●. **A** and **C** represent addition of no IL-2; **B** and **D** represent the addition of 1 unit IL-2 per ml.

agents but whose response was not significantly different from the others). It is apparent on reviewing the literature that few studies have included testing control subjects in parallel with patients ([3]).

As previously reported by other investigators ([1, 2, 6, 8, 30, 36, 37]), our data demonstrated that the proliferative response of PBMC from lepromatous patients to *M. leprae* and *M. leprae* derivatives was minimal compared to the response seen in most healthy contacts and tuberculoid patients. The same pattern of response in patients and control subjects was observed when PBMC were cultured with Dharmendra lepromin but, interestingly, not when the *M. leprae*-spe-

cific glycolipid, PGL-I (incorporated in liposomes), was added to cultures.

PGL-I is of great interest since this unique *M. leprae* antigen may contain epitopes important in modulating the immune response in leprosy patients. In a series of studies, Brennan and associates ([7, 12, 13]) have demonstrated that the antigenic properties of this glycosylphenolic phthiocerol diester reside in the terminal 3,6-di-*O*-methylglucose. Although antibodies to PGL-I have been identified in leprosy patients ([40]) our studies demonstrated that this carbohydrate determinant, when delivered in liposomes *in vitro,* does not elicit a proliferative response in either patients or contacts who had strong responses to complex mixtures of *M. leprae* antigens. Recently, Brett, *et al.* ([5]) demonstrated that PGL-I did not stimulate a proliferative response *in vitro* or a delayed-type hypersensitivity response *in vivo* in mice immunized with *M. leprae.*

Our results indicate that rIL-2 seemingly reversed the immunological nonresponsiveness in LL patients. However, this was not an antigen-specific proliferative stimulation, since rIL-2 enhanced ^{3}H-TdR uptake by PBMC from all patients and controls whether in the presence or absence of mycobacterial antigens. It is therefore impossible to accord to IL-2 a preferential augmentation of the *M. leprae*- or lepromin-induced response in lepromatous lymphocytes. Lower doses of IL-2 (0.001–0.1 U/ml) were tested on selected patients and controls, but these concentrations had little mitogenic effect and did not correct the deficient antigen-specific response in cells from LL patients (data not shown). Haregewoin, *et al.* ([9]) initially demonstrated that the *M. leprae*-specific unresponsiveness could be corrected with T-cell-conditioned medium which contains a variety of different lymphokines, including IL-2. Since these experiments, they ([10]) as well as others ([3, 14, 21, 24, 34]) have shown that IL-2 from various sources may improve ^{3}H-TdR uptake of stimulated PBMC from some LL patients in the presence of *M. leprae* antigens, but the responses were variable or not specific for *M. leprae.*

Although the patient population we tested was small, we felt that they were clinically and histologically well defined. We saw no reason to continue testing large numbers of subjects when we found that rIL-2 did not clearly correct the antigen-specific unresponsiveness in LL patients and since a nonspecific stimulation of IL-2 was seen in lymphocytes from the control subjects. It is questionable whether T lymphocytes are induced to divide in the presence of IL-2 alone. The augmented proliferation noted with IL-2 alone in this study suggests that expres-

TABLE 2. *Proliferative response to lepromin in the presence or absence of recombinant IL-2 (rIL-2).*

		rIL-2 (U/ml)		
		0	1	10
		cpm	cpm (SI)	cpm (SI)
		Patients		
1	LL	8,739[a]	24,048 (3)	ND
2	LL	997	6,371 (6)	38,477 (39)
3	LL	614	7,462 (12)	16,599 (27)
4	LL	1,115	12,217 (11)	28,483 (26)
5	LL	828	14,961 (18)	45,935 (56)
6	BL	1,290	17,702 (14)	51,865 (40)
7	BL	11,745	45,533 (2)	117,162 (10)
8	BT	21,943	41,863 (2)	ND
9	BT	16,900	27,393 (3)	46,595 (3)
10	TT	15,059	29,636 (2)	57,008 (4)
11	TT	31,670	54,052 (2)	76,887 (2)
		Controls[b]		
HC		50,004	102,860 (2)	ND
HC		19,336	28,954 (2)	ND
HC		8,858	25,717 (3)	46,812 (5)
HC		7,139	28,904 (4)	60,221 (8)
HC		3,043	17,617 (6)	59,584 (20)
HC		16,984	32,141 (2)	67,042 (4)
HC		1,115	12,217 (11)	28,483 (26)
HC		2,214	5,943 (3)	35,576 (16)
AC		30,248	52,581 (2)	ND
AC		22,157	40,868 (1)	ND
AC		7,123	13,490 (2)	31,815 (5)
AC		16,374	24,750 (2)	51,411 (3)
AC		6,023	11,560 (2)	20,604 (3)
AC		25,584	39,363 (2)	78,193 (3)
AC		7,380	18,857 (3)	34,488 (5)
LC		19,304	24,845 (1)	47,839 (3)
LC		7,155	22,578 (3)	65,823 (9)
LC		10,728	30,919 (3)	98,634 (9)
LC		27,770	61,612 (2)	198,838 (7)
LC		32,187	42,927 (1)	110,926 (3)
LC		6,952	29,828 (1)	49,659 (2)
LC		17,467	48,781 (3)	115,486 (7)
LC		30,189	45,502 (2)	86,556 (3)

[a] Results are expressed as mean cpm of triplicate cultures. Numbers in parentheses represent the stimulation indices (cpm with rIL-2/cpm without rIL-2).

[b] HC = household control; AC = age-, sex-, ethnically matched control; LC = laboratory control.

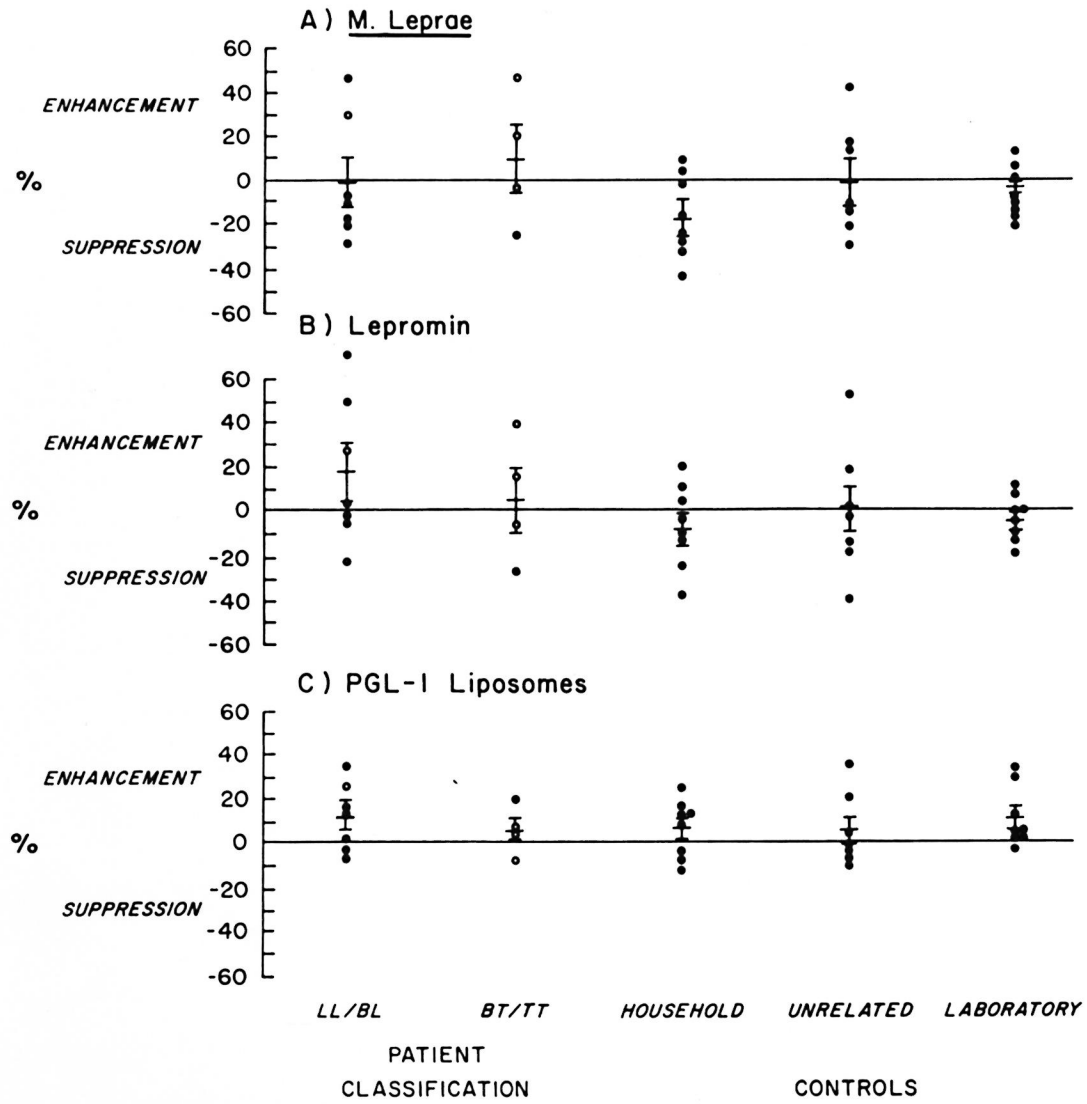

FIG. 4. Response of PBMC from leprosy patients and control subjects to 2.5 μg ConA/ml in the presence of: **A)** = sonicated *M. leprae* (1 μg/ml); **B)** = Dharmendra lepromin (1:10); or **C)** PGL-I in liposomes (0.5 μg/ml). ^{3}H-TdR incorporation was measured during the last 18 hr of a 3-day culture. Each circle represents the response of an individual subject assayed in triplicate; bars represent mean percent enhancement or suppression ± S.E.M. in each group; ○ = untreated patients; ● = treated patients and control subjects.

sion of IL-2 receptors on lymphocytes had been induced by some other prior stimulus *in vivo* or *in vitro*.

We were unable to reproduce the intriguing findings of Mehra, *et al.* ([17]), that lepromin and PGL-I could induce suppression of the ConA response of lymphocytes from some LL patients, even though rigorous attempts were made to duplicate the experimental conditions, including the use of the same source and lot of lepromin and liposomes containing PGL-I, culture medium supplemented with 10% human AB serum, addition of mycobacterial antigens 20 min before addition of ConA, suboptimal doses of ConA (2.5 μg/ml) and comparison of round- versus flat-bottomed microculture plates ([16, 17]). Recently, however, investigators employing T-cell lines and clones from patients have demonstrated *M. leprae*-specific suppression *in vitro* ([19, 20, 28, 34]).

Inconsistent results underline the inade-

quacy of methods that have been used to document the antigen-specific immunologic unresponsiveness in LL patients. Differences in mycobacterial antigen preparation, type and dose of mitogen employed, culture medium supplements (e.g., source and lot of serum), time in culture, patient populations, and their treatment status are a few of the many experimental variables which could account for the conflicting data. In view of subtle differences in methods and laboratory conditions and the difficulty experienced by several reputable laboratories in reproducing previous *in vitro* observations, it is clearly important that more consistent methods be developed to evaluate the immunological defect in lepromatous leprosy. Investigators have routinely employed peripheral blood as the source of lymphoid cells to study mechanisms of unresponsiveness, in spite of the fact that the majority of bacilli are found in the skin and not the blood. Modlin, *et al.* ([18]) and Longley, *et al.* ([15]) have demonstrated differences in T-lymphocyte subset patterns in granulomas of tuberculoid and lepromatous patients. Clearly, alterations in the microenvironment may have substantial effects on the local immune response and further efforts to examine the function of lymphocytes in the skin, rather than in the blood, as has been recently reported by Modlin and colleagues ([19, 20]), may provide more reliable clues about the mechanism of unresponsiveness in lepromatous patients.

SUMMARY

Although the mechanism of immunologic unresponsiveness in lepromatous leprosy remains unknown, it has been shown that interleukin-2 (IL-2) production is defective in these patients. Peripheral blood mononuclear cells (PBMC) were isolated from treated (<16 months) and untreated leprosy patients as well as household contacts; age, sex, ethnically matched control subjects; and laboratory staff. PBMC were cultured for 6 days with sonicated *Mycobacterium leprae* (1–10 μg/ml), Dharmendra lepromin (1:10), or phenolic glycolipid-I (PGL-I) (0.05–5.0 μg/ml) in medium supplemented with various concentrations of recombinant IL-2 (rIL-2) or cultured for 3 days with one of the three mycobacterial antigens in the presence of concanavalin A (ConA). TT/BT patients and household control subjects had a robust response to *M. leprae* and lepromin, but were unresponsive to PGL-I delivered in liposomes. PBMC from LL patients did not respond to any of the three antigen preparations. rIL-2 induced proliferation of PBMC both in leprosy patients and control subjects regardless of the presence or absence of the three leprosy antigen preparations. This antigen nonspecific augmentation of proliferation by the wide range of doses of rIL-2 employed makes difficult the interpretation of the enhanced thymidine incorporation noted when rIL-2 is added in the presence of antigen to cultures of lymphocytes from LL patients. Our studies are at variance with reports that leprosy antigens, specifically PGL-I, induce immunological suppression, in that mycobacterial antigens did not cause significant suppression of the ConA-induced proliferations of PBMC from patients.

RESUMEN

Aunque el mecanismo de la anergia inmunológica en la lepra lepromatosa permanece desconocido, se ha demonstrado que la producción de IL-2 es defectuosa en estos pacientes. Se realizó un estudio en el que se aislaron células mononucleares de la sangre periférica (CMSP) de pacientes tratados (menos de 16 meses) y de pacientes no tratados, asi como de contactos convivientes apareados por edad, sexo y orígen étnico. También se incluyeron como controles al personal del laboratorio. Las CMSP se cultivaron por 6 días con sonicados de *Mycobacterium leprae* (1–10 μg/ml), con lepromina de Dharmendra (1:10), o con glicolípido fenólico-I (GLP-I) (0.05–0.5 μg/ml), en medio suplementado con varias concentraciones de IL-2 recombinante (IL-2r) o se cultivaron por 3 días con uno de los 3 antígenos micobacterianos en presencia de concanavalina A (ConA). Los pacientes TT/BT y los contactos convivientes sanos mostraron una fuerte respuesta al *M. leprae* y a la lepromina, pero no respondieron al GLP-I incluido en liposomas. Las CMSP de los pacientes LL no respondieron a ninguno de los 3 antígenos. La IL-2r indujo proliferación de las CMSP tanto en los pacientes con lepra como en los controles, independientemente de la ausencia o presencia de las 3 preparaciones antigénicas. Este incremento de la proliferación inducido inespecificamente por la amplia gamma de dosis de IL-2 usada, dificulta la interpretación del incremento en la incorporación de timidina cuando la IL-2 se adiciona en presencia de antígeno a los cultivos de linfocitos de los pacientes LL. Nuestros estudios difieren de otros donde se indica que los antígenos del *M. leprae*, especificamente el

GLP-I, induce supresión inmunológica, ya que en nuestro caso, los antígenos micobacterianos no causaron ninguna supresión significativa de la proliferación de las CMSP de los pacientes inducida por ConA.

RÉSUMÉ

Le mécanisme de l'immunodéficience dans la lèpre lépromateuse demeure inconnu. On a cependant démontré que la production de l'interleukine-2 (IL-2) est anormale chez ces malades. On a isolé des cellules mononucléaires (PBMC) du sang périphérique de malades atteints de lèpre traités pendant moins de 16 mois, et d'autres qui n'avaient pas été traités. On a procédé au même prélèvement chez des contacts domiciliaires, chez des sujets témoins assortis pour l'âge, le sexe et le groupe ethnique, et chez des employés du laboratoire. Les cellules mononucléaires ont été cultivées pendant 6 jours en présence d'un sonicat de *Mycobacterium leprae* (1–10 μg/ml), de lépromine de Dharmendra (1:10), ou du glycolipide phénolique-I (PGL-I) (0,05–5,0 μg/ml), dans un milieu de culture auquel on avait ajouté diverses concentrations d'interleukine-2 obtenues par recombinaison (rIL-2); une autre méthode a consisté à mettre en culture, pendant 3 jours, ces cellules avec un des trois antigènes mycobactériens, en présence de concanavaline A (ConA). Les malades atteints des formes TT ou BT de lèpre, de même que les sujets témoins qui étaient contacts domiciliaires, ont présenté une réponse marquée à *M. leprae* et à la lépromine; ils ne répondaient cependant pas au PGL-I administré dans des liposomes. Lès cellules mononucléaires de malades atteints de la forme LL n'ont répondu à aucune des trois préparations antigéniques. L'interleukine-2 recombinée a entraîné une prolifération des cellules mononucléaires, tant chez les malades de lèpre que chez les individus témoins, et ceci sans égard pour la présence ou pour l'absence des trois préparations d'antigènes de la lèpre. Cette prolifération accrue, non spécifique quant à l'antigène, obtenue avec une gamme de doses étendues de rIL-2, rend difficile l'interprétation de l'augmentation qui a été notée dans l'incorporation de la thymidine lorsque le rIL-2 est ajouté en présence d'antigènes à des cultures de lymphocytes récoltées chez des malades LL. Ces études ne sont pas en accord avec d'autres rapports qui relatent que les antigènes de la lèpre, et particulièrement le PGL-I, induit une suppression immunologique, car ici les antigènes mycobactériens n'ont pas entraîné de suppression significative de la prolifération induite par la ConA dans des cultures de cellules mononucléaires provenant de malades.

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