

Immunoglobulins in Leprosy¹

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The great variation in the clinical manifestations of leprosy is well recognized, and the role of host immunity to *Mycobacterium leprae* is believed to be involved. In addition, skin reactions to lepromin⁽⁵⁾ and 2,4-dinitrochlorobenzene⁽¹⁰⁾ indicate that the lepromatous form of leprosy is associated with a depression of delayed hypersensitivity, while other types of the disease have a normal incidence of sensitization. The humoral immune response studied by several investigators has also shown abnormalities. In particular, various results on the serum levels of immunoglobulins in leprosy patients have been observed in various reports^(1, 2, 5, 8, 9, 11).

The aim of this report is to compare the immunoglobulins in the lepromatous form (LF) and the nonlepromatous form (NLF) of leprosy against different types of control groups in an attempt to clarify the cause of previous contradictory results.

MATERIALS AND METHODS

Family study. Families were selected according to the criteria described by de Vries, *et al.*⁽³⁾ with some modifications. Not less than two affected and healthy siblings were included in each family. The latter had to be older than the youngest affected sibs, or at least ten years old if they were the youngest.

All patients were classified into two types of leprosy—LF, which included LL, BL, and BB, and NLF, consisting of BT and TT.

The 26 families included in this study consisted of 59 unaffected siblings (18 males and 41 females); 55 affected siblings (24 males and 31 females), 19 NLF and 36 LF

cases. Their ages in years ranged from 6–53, 6–44, and 3–48 for the unaffected, NLF, and LF cases, respectively. The duration of disease ranged from 1 month to 5 years for NLF and from 1–20 years for LF cases. All of the families were inhabitants of the northeastern provinces of Thailand.

Ninety-three unrelated, apparently healthy volunteers (42 males and 51 females, aged 6–69 years) from the northeastern provinces were used as normal controls for the family study.

Random study. A total of 102 random unrelated leprosy (RC) patients attending the Central Skin Clinic of the Leprosy Division, Department of Communicable Disease Control, Ministry of Public Health, Bangkok, were studied. There were 37 NLF and 65 LF patients, ranging in age from 10–60 and 15–65 years, respectively. The duration of the disease ranged from 1–30 years for NLF and from 5 months to 32 years for LF leprosy.

The controls for the random study consisted of 95 unrelated, apparently healthy laboratory staff, school children, volunteers, and blood donors of the Ramathibodi Hospital in Bangkok. There were 61 males and 34 females, ranging in age from 11–73 years.

The patients and the controls in both groups belonged to the same ethnic group. The diagnosis and classification of leprosy were based on the clinical and histopathological findings⁽⁷⁾. The immunoglobulins were determined by using the single radial immunodiffusion technique of Mancini.

RESULTS

The levels of IgG, IgA, and IgM in various durations of LF and NLF leprosy in RC patients and affected siblings from the provinces of northeastern Thailand are shown in Figures 1 and 2. The results are summarized in The Table.

DISCUSSION

There are many discrepancies in results of serum immunoglobulin levels in leprosy.

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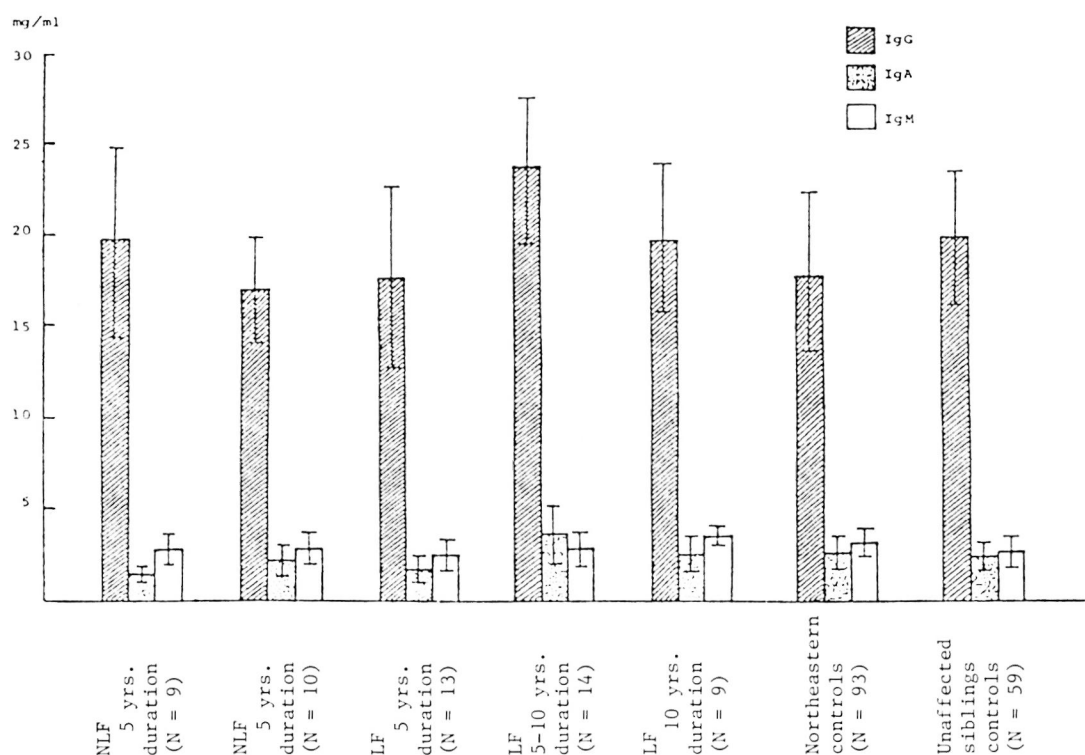


FIG. 1. Levels of immunoglobulins in NLF and LF leprosy siblings (family study).

The results obtained in LF leprosy have been more consistent than those obtained in NLF leprosy. Results in LF include increases in serum IgG^(1, 2, 5, 8, 9, 11), IgA^(2, 8, 9, 11), IgM^(1, 2, 5, 8, 11), IgD^(2, 8, 9), and IgE^(6, 8), but serum IgA was found to be normal by Lim and Fusaro⁽⁵⁾. The present study agreed with these others by showing increased serum IgG, IgA, and IgM in LF from central Thailand in the random study. The family study demonstrated a discrepancy in the results obtained from the northeastern part of Thailand, in which only IgG and IgA were found to be significantly increased in LF among those having the disease for 5–10 years, and the increase of IgM only in those with >10 years' duration of the disease.

The random study in LF from central Thailand displayed clearly the effect of treatment upon serum immunoglobulin levels. Serum IgG, IgA, and IgM decreased gradually after prolonged treatment, and these changes were most notable in IgM. These findings were not duplicated among the northeastern part of the family study. Bullock, *et al.*⁽²⁾ found that serum IgM in LF

decreased significantly after treatment, while serum IgA increased insignificantly after treatment. Currently, there are only the present study and that of Bullock, *et al.*⁽²⁾ that tried to correlate serum immunoglobulin levels with treatment, and both studies obtained the same results, showing decreased serum IgM after treatment. IgM antibody response is most likely to be present when a stimulating antigen remains in the host. Adequate chemotherapy will decrease the antigen load which may result in a decrease in the serum IgM. Why this consequence was not observed in the northeastern part of the family study is quite difficult to explain with the information presently available.

There has been more controversy in the results of serum immunoglobulins in NLF leprosy. Increased levels observed by other investigators include IgG and IgA^(5, 8, 9) and IgM and IgD^(8, 9). Serum IgG, IgA, and IgM in NLF were found to be normal by Bullock, *et al.*⁽²⁾ and Youngchaiyud⁽¹¹⁾, while Lim and Fusaro⁽⁵⁾ found serum IgM to be normal in NLF. Our findings among

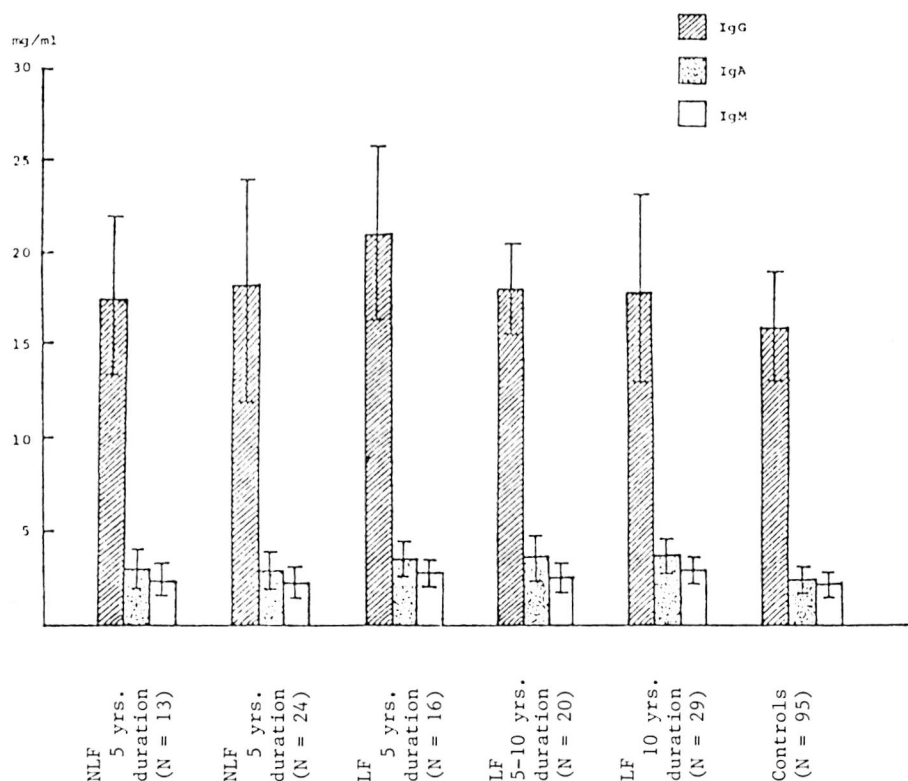


Fig. 2. Levels of immunoglobulins in random NLF and LF leprosy (random study).

NLF (of ≥ 5 years' duration) from central Thailand in the random study showed only significantly increased IgG and IgA, results which were identical to those of Lim and Fusaro. Our findings, that serum immunoglobulin levels in NLF were less affected

when compared with LF, agreed well with those of other workers. One outstanding result was found among the northeastern affected siblings in the family study, namely, that serum IgA in NLF was significantly decreased in early cases and increased after

THE TABLE. Significant changes of serum IgG, IgA, and IgM in leprosy.^a

Type	Lepromatous form (LF)		Nonlepromatous form (NLF)	
	Random study	Family study	Random study	Family study
IgG	↑ in all durations $p < 0.0005$	↑ in 5-10 years $p1, 2 < 0.0005$	↑ slightly in <5 years ↑ in ≥ 5 years $p < 0.025$	↓ in ≥ 5 years $p1 < 0.025$
IgA	↑ in all durations $p < 0.0005$	↓ in <5 years $p1 < 0.0005, p2 < 0.025$ ↑ in 5-10 years $p1 < 0.025, p2 < 0.005$	↑ in all durations $p < 0.01$	↓ in <5 years $p1, 2 < 0.0005$ ↓ slightly in ≥ 5 years
IgM	↑ in <5 years $p < 0.0005$	↓ in <5 years $p1 < 0.01$ ↑ in >10 years $p1 < 0.05, p2 < 0.0005$		↓ in ≥ 5 years $p1 < 0.05$

^a p = p value vs central normal control, in random study, Student's *t* test.

p1 = p value vs northeastern controls, in family study, Student's *t* test.

p2 = p value vs unaffected siblings, in family study, Student's *t* test.

prolonged treatment. Youngchaiyud also observed an insignificant decrease in serum IgA in early NLF (¹¹).

The present study demonstrated differences in serum immunoglobulin levels in the two populations, i.e., the central and northeastern parts of Thailand. The northeasterners are well recognized as heavily affected by malnutrition, opisthorchiasis, and other parasitoses, all of which influence serum immunoglobulin levels. The serum immunoglobulin levels are also influenced by how early the leprosy is diagnosed and treated. The present study has clearly demonstrated that serum levels of immunoglobulins, especially IgM in LF of RC patients and IgA in NLF of northeastern affected siblings, change after treatment. This study also shows clearly the need for proper selection of normal controls in order to obtain a meaningful interpretation. Controls from different regions in the same country, and even from two populations in the same region, were shown to be entirely different and, thus, may give rise to quite different interpretations of the same results in leprosy patients.

SUMMARY

Serum immunoglobulins were estimated by the single radial immunodiffusion technique and the results were compared among various groups of leprosy patients. Most of the serum immunoglobulin classes are increased in lepromatous leprosy patients. Controls from different regions in Thailand and even from two populations in the same region show different results. This can lead to different interpretations of results in leprosy patients and may explain apparent discrepancies in earlier studies of serum immunoglobulins in leprosy.

RESUMEN

Usando la inmunodifusión radial simple se cuantificaron y compararon los niveles de las inmunoglobulinas séricas en varios grupos de pacientes con lepra. La mayoría de las clases de inmunoglobulinas estuvieron aumentadas en los pacientes lepromatosos. Los controles de diferentes regiones de Tailandia y aún los de dos poblaciones de la misma región, mostraron diferentes resultados. Esto puede conducir a diferentes interpretaciones de los resultados en los pacientes con lepra a la vez que puede ayudar a explicar las aparentes discrepancias en estudios anteriores sobre las inmunoglobulinas séricas en la lepra.

RÉSUMÉ

On a procédé à une détermination des immunoglobulines du sérum, en utilisant une technique d'immunodiffusion radiale unique. Les résultats ont été comparés dans divers groupes de malades de la lèpre. La plupart des classes d'immunoglobulines du sérum se sont révélées augmentées dans la lèpre lépromateuse. Des témoins provenant de différents régions de Thaïlande, ainsi que des témoins appartenant à deux populations de la même région, ont présenté des valeurs différentes. Ces observations peuvent mener à diverses interprétations des résultats obtenus chez des malades de la lèpre. Elles pourraient expliquer les discordances apparentes relevées dans des études antérieures quant aux taux d'immunoglobulines du sérum dans la lèpre.

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