

## CORRESPONDENCE

*This department is for the publication of informal communications that are of interest because they are informative and stimulating, and for the discussion of controversial matters.*

### Hypergammaglobulinemia, Secondary Macroglobulinemia and Paraproteinemia in Leprosy

TO THE EDITOR:

Bonomo and co-workers (Hypergammaglobulinemia, secondary macroglobulinemia and paraproteinemia in leprosy. *Internat. J. Leprosy* 37 (1969) 280-288) reported immunoglobulin changes in patients with leprosy. They incorrectly interpreted a previous report (Lim, S.D. and Fusaro, R.M., *Leprosy*. IV. The quantitation of immune globulins (IgG, IgA, and IgM) in leprosy sera. *Internat. J. Leprosy* 36 (1968) 144-153). Bonomo *et al.* incorrectly stated that the quantitative immunoglobulin method used in the later publication was immunoelectrophoretic. The method was the quantitative immunodiffusion method of Ouchterlony.

Bonomo *et al.* reported immunoglobulin changes in the sera of 306 leprosy patients. They do not state whether the patients were receiving any treatment. This simple fact is of major importance as systemic treatment of leprosy will change the clinical manifestations and course of the disease. In all probability, the concentrations of serum immunoglobulins will be altered. This is apparent in their data. The low and high concentrations of the serum Ig are more variable than normal concentrations, a finding often noted in any treated group when compared to normal or control groups. It is almost impossible to draw any conclusions about serum Ig concentrations in such a heterogeneously treated group of leprosy patients.

The report (*Internat. J. Leprosy* 36 (1968) 144-153) very carefully stated that patients were untreated (216 patients). In addition, the controls were done on normal Koreans who were matched by age and sex against the leprosy patients in order to have comparable groups. Bonomo *et al.* tell us nothing about their controls (normal

group). The following questions about their normal controls are important: (1) Are controls age and sex matched with leprosy group? (2) What are nationalities of the control group? Quantitative data? (3) Did the normal sera come from the same geographic locale as the patients? (4) Were the normal values reported by you, done by you at the same time as the tests on the leprosy sera?

In addition, Bonomo *et al.* should give us more information about their reported serum Ig concentrations. Beside knowing the mean and range, it would be helpful to know the standard deviation and standard error.

The most critical analysis of serum immunoglobulins in leprosy patients still appears to be the earlier publication in the *International Journal of Leprosy* 36 (1968) 144-153). The following inadvertent errors in the early publications (*Internat. J. Leprosy* 36 (1968) 144-153, *Leprosy* IV. and *Internat. J. Leprosy* 36 (1968) 154-161, *Leprosy* V) should be noted: (1) *Leprosy* IV, (a) Table 8, IgA, All patients, Mean 247 correct to 274, (b) Table 9, IgA, L type,  $261 \pm 9^a$  correct to  $261 \pm 9$  and (c) Table 13, age 20-39, All patients  $297 \pm 6$  correct to  $279 \pm 6$ , and (2) *Leprosy* V, Table 4, IgM,  $20 \pm S.E.$ , 56 correct to 6.

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## TO THE EDITOR:

I would like to emphasize that we did not intend to implicate any particular publication in considering the limits of the immunoelectrophoretic semiquantitative determinations. We were not able, however, to estimate the significance of Drs. Lim and Fusaro's immunoelectrophoretic analyses, from the figures given in their paper (Lim, S.D. and Fusaro, R. M., *Leprosy* IV. The quantitation of immune globulins (IgG, IgA, and IgM) in leprosy sera. *Internat. J. Leprósy* 36 (1968) 144-153).

The major purpose of our investigation was the detection of peculiar serum protein abnormalities such as paraproteinemia in its various forms, as hypo-gammaglobulinemia, dys-gammaglobulinemia and macroglobulinemia. This was clearly indicated in our paper title, "Hypergammaglobulinemia, secondary macroglobulinemia, and paraproteinemia in leprosy."

Several serum protein methods (agar and immunoelectrophoresis, analytical ultracentrifugation, and quantitative immunoglobulins determinations) were employed to detect abnormalities which are obviously missed by quantitative estimations alone, even when the most reliable methods, like those employed by Dr. Fusaro, are used.

Another criticism by Dr. Fusaro concerns the possible effect of treatment of our patients on our results. This appears a favorite point of his since he raised it also for a paper (*Ann. Int. Med.* 72 (1970) 602) by Dr. Sheagren and associates. Dr. Sheagren and associates have offered an adequate reply. They noted that the population differences between the two reports differ in many more respects than the presence or absence of therapy. They wrote, "Regional differences may be much more important. For example, our patients were free of parasitic disease, whereas such are common in

Korea, as is well known, parasitic infestations in themselves may increase levels of serum immunoglobulins. . . . Serial studies in several areas could clarify the issue."

In addition, it should be remarked that the most conspicuous levels of immunoglobulins were found in our lepromatous patients which usually are treated more heavily than other categories of patients. On the whole our quantitative results appear similar to those of Drs. Lim and Fusaro (Tables 9 and 10 of their work), whose data were quoted in our work. In advance of the publication of their paper I was g'ad to let Dr. Fusaro know, at his request, the preliminary published (Bonomo L. and Dammacco, F., *Protein Changes and Immunity in Some Chronic Infectious Diseases. Proceedings of the International Symposium on Gammopathies, Infections, Cancer and Immunity. Carlo Erba Foundation Milan 1968*), results of our investigations. So it seems somewhat surprising to us that Dr. Fusaro did not mention at all, not even for criticism, our results in his paper. We did not consider the statistical evaluation of our data because we were aware that our data did not lend itself to such procedures, and, above all, it was beyond the scope of our investigation. Our main purpose was the estimation of the general trend of hyperglobulinemia in leprosy and the detection of unusual serum protein patterns in leprosy rather than pure quantitative studies.

By this approach new fascinating features were detected that can be added to the different immunologic aspects of leprosy previously described by us and other distinguished authors.

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