A Preliminary Report on a Study of Serum Alpha-1-Antitrypsin and Immunoglobulin Levels in Lepromatous Leprosy

SEYHAN I. ÇELIKOĞLU, FAHİR M. GÖKSEL,
TURKAN SAYLAN AND SUNAY HAZNEDAR

*Department of Internal Medicine, Medical Clinic of Cerrahpasa Medical
Faculty and Clinic of Dermatology of Istanbul Medical Faculty,
University of Istanbul, Turkey*

and

JUDITH D. GOLDBERG

*Department of Biostatistics, Mount Sinai School of Medicine of
The City University of New York, New York, U.S.A.*

Introduction

While it is known that alpha-1-antitrypsin deficiency is associated with hereditary pulmonary emphysema (Laurell, 1963), respiratory distress syndrome in premature infants (Evans *et al.*, 1970), and juvenile liver cirrhosis (Sharp, 1971), its concentration in serum is considerably increased under various other physiologic and pathologic conditions (Ganrot and Bjerre, 1967; Kueppers, 1968, 1972; Schultze and Heremans, 1966; Cleve and Behrend, 1966).

Young *et al.* (1973) reported that alpha-1-antitrypsin levels, measured by the trypsin inhibitory capacity method, were increased in patients with untreated active sarcoidosis when compared with patients with inactive sarcoidosis and with age-sex matched healthy controls. Since the etiology of sarcoidosis is, at present, unknown, it would be of interest to assay these globulins in a chronic granulomatous disease of known etiology.

Human leprosy provides such an example. This disease is caused by a very slowly developing bacterial infection in which the antigenic load of the bacterial population cannot be rapidly decreased even by vigorous chemotherapy and antibiotic treatment. Therefore, human lepromatous leprosy affords an opportunity for the study of the effect of continuous antigenic stimulation on alpha-1-antitrypsin levels. In addition, immunoglobulin levels can be examined.

Materials and Methods

Sera from 34 hospitalized patients under treatment for lepromatous leprosy were obtained. These patients had been examined clinically and radiographically and smears of nasal or skin scrapings were positive for acid-fast bacilli in all subjects. Thirty normal controls donated sera for study. The patient and control groups were comparable with respect to age (mean ages are 46 for cases, 48 for controls) and sex (approximately 10% of each group are female). All patients and controls were Caucasians of Turkish origin. No patient was in a "reactional" state at the time of blood sampling.

Sera were separated and frozen within 24 h and stored at -20°C until assay. Quantitation of IgG, IgA, IgM and alpha-1-antitrypsin globulins was performed with Behringwerke* agar diffusion plates containing specific antisera (Mancini *et al.*, 1963) and antigen reference standards. Precipitin ring diameters were measured to the nearest 0.1 mm using an immunodiffusion reader.

Results

The mean levels of IgG, IgM, IgA and alpha-1-antitrypsin were all elevated among the leprosy patients compared with the normal controls (see Table 1). An examination of the correlation coefficients among these immunoglobulins and alpha-1-antitrypsin in the 2 groups showed higher correlations in the patient group.

These differences in correlation structure in the patients and controls suggested the possibility of some heterogeneity among leprosy cases. Three patients identified from plots of the data appeared to differ from the remaining patients.†

When these 3 patients were removed, the variables were uncorrelated among both the cases and controls. Therefore, these variables could be treated as independent variables.

Comparison of the mean levels of these variables, normals and the cases with the outlets removed indicated that the levels of the 3 immunoglobulins and alpha-1-antitrypsin were significantly elevated among the cases. The *t* values‡ for

* Farbwerke Hoechst AG, 6230 Frankfurt (Main) 80, Behring Department.

† These leprosy patients and their levels are:

Patient	IgG	IgM	IgA	Alpha-1- antitrypsin
Nr. 4-M.S.	5760	226	570	1000
Nr. 11-B.L.	3600	586	570	1400
Nr. 28-K.E.	1220	120	266	240

‡ While the variances are significantly larger (except IgM) among the leprosy cases, the more conservative statistical approaches did not affect the results (cf. G. W. Snedecor and W. G. Cochran (1967), *Statistical Methods*, 6th ed. Iowa State University Press, Ames, Iowa, pp. 114-118).

the differences between the leprosy patients and controls are:

	<i>t</i>	d.f.	<i>P</i> -level
IgG	5.92	59	< 0.001
IgM	4.11	59	< 0.001
IgA	4.89	59	< 0.001
Alpha-1-antitrypsin	6.05	59	< 0.001

TABLE 1

Serum immunoglobulins and alpha-1-antitrypsin levels in Turkish patients with lepromatous leprosy and normal controls

Group	IgG	IgM	IgA	Alpha-1-antitrypsin
A. Normal controls (<i>n</i> = 30)				
Mean (mg %)	1671.3	164.0	248.7	400.3
S.D.	477.6	82.8	81.6	82.5
Correlation with alpha-1-antitrypsin	0.156	0.151	-0.003	1.000
B. Leprosy patients (<i>n</i> = 34)				
Mean (mg %)	2982.9	270.8	395.0	610.3
S.D.	1184.2	122.6	137.7	219.0
Correlation with alpha-1-antitrypsin	0.304	0.270	0.439	1.000
C. Leprosy patients (<i>n</i> = 31) outliers removed				
Mean (mg %)	2930.3	267.0	387.9	584.2
S.D.	1080.0	111.2	134.9	147.1
Correlation with alpha-1-antitrypsin	0.087	-0.030	0.223	1.000

Discussion and Summary

The quantitative assay of alpha-1-antitrypsin and immunoglobulins in this study demonstrates that levels of IgG, IgA, IgM and alpha-1-antitrypsin are all elevated in the sera of patients with leprosy when compared with normal controls. In addition, these immunoglobulins are uncorrelated with alpha-1-antitrypsin in either leprosy patients or in normal controls.

Thus, the independence of immunoglobulin classes which has been observed in normal individuals (Allan Smith *et al.*) appears to be unchanged in leprosy even though chronic antigenic stimulation by *M. leprae* results in marked changes in concentration in all of the immunoglobulin classes.

References

- Allan Smith, M., McClellan, B. and Butterworth, M. (1967). Evidence for the independence of human immunoglobulin class levels. *Immunology* **13**, 483.
- Cleve, H. and Behrend, T. (1966). Quantitative immunological determination of alpha-1-acid glycoprotein and alpha-1-antitrypsin in sera of patients with rheumatoid arthritis. *Z. Rheumaforsch.* **25**, 278.
- Evans, H. E., Levi, M. and Mandi, I. (1970). Serum enzyme inhibitor concentrations in the respiratory distress syndrome. *Am. Rev. resp. Dis.* **101**, 359-363.
- Ganrot, P. O. and Bjerre, B. (1967). Alpha-1-antitrypsin and alpha-2-macroglobulin concentration in serum during pregnancy. *Acta obstet. gynecol. scand.* **46**, 126.

- Kueppers, F. (1972). The major proteinase inhibitor in rabbit serum, in pulmonary emphysema and proteolysis. (Ed. C. Mittman). p. 355. New York: Academic Press.
- Kueppers, F. (1968). Genetically determined differences in the response of alpha-1-antitrypsin levels in human serum to typhoid vaccine. *Humangenetik* **6**, 207.
- Laurell, C. B. and Eriksson, S. (1963). Alpha-1-globulin pattern in serum in alpha-1-antitrypsin deficiency. *Scand. J. clin. Lab. Invest.* **15**, 132-140.
- Lim, S. D. and Fusaro, R. M. (1968). Leprosy: IV. The quantitation of immunoglobulins (IgG, IgA and IgM) in leprosy sera. *Int. J. Lepr.* **36**, 144.
- Mancini, G., Vaerman, J. P., Carbonara, A. O. and Heremans, J. F. (1963). In *XI Colloquium on Protides of the Biological Fluids* (Ed. H. Peeters), p. 370. Amsterdam: Elsevier Publishing Company.
- Schultze, H. E. and Heremans, J. F. (1966). Molecular biology of human proteins with special reference to plasma proteins, p. 354. Amsterdam: Elsevier Publishing Company.
- Sharp, H. L. (1971). Alpha-1-antitrypsin deficiency. *Hosp. Pract.* **6**, 83-96.
- Sheagren, J. N., Block, J. B., Trautman, J. R. and Wolff, S. M. (1969). Immunologic reactivity in patients with leprosy. *Ann. intern. Med.* **70**, 295.
- Young, C., Jr. et al. (1973). Alpha-1-antitrypsin levels in sarcoidosis: Relationship to disease activity. *Chest* **64**, 39.