

leprosy spectrum may also undergo overlapping type 1 and 2 reactions. Thus, the complexity of the clinical picture may make the distinction between these two types of reaction difficult (?). We had two such patients grouped in type 2 reaction in our series. Admittedly, these cases could not be differentiated by serum ferritin estimations.

So far as we know, until now there is no laboratory method except histology to gauge the severity of lepra reactions. Although the elevation of the serum ferritin level in lepra reactions is an indicator of nonspecific inflammatory processes, our preliminary data warrant a further in-depth study on the rise and fall of this acute phase reactant during lepra reaction.

—Kunal Saha, M.Sc., M.B.B.S., Ph.D.
K. N. Rao, Ph.D.
Avind Kashyap, M.Sc.

*Immunology Department
Vallabhbai Patel Chest Institute
Delhi 110007, India*

—V. N. Sehgal, M.D., F.N.A.Sc.
S. K. Agrawal, M.D.

*Department of Dermatology
and Medicine
Maulana Azad Medical College
New Delhi 110002, India*

Acknowledgment. The authors are grateful to the Indian Council of Medical Research, New Delhi, for financial assistance.

REFERENCES

1. BIRGEGARD, G., HALLGREN, R., KILLANDER, A. and STOMBERG, A. Serum ferritin during infection. *Scand. J. Haematol.* **21** (1978) 333–340.
2. BRYCESON, A. and PFALTZGRAFF, R. E. *Leprosy*. 2nd ed. Edinburgh: Churchill Livingstone, 1979, pp. 65–71.
3. CHAKRABARTY, A. K., KASHYAP, A., SEHGAL, V. N. and SAHA, K. Solubilization of preformed immune complexes in sera of patients with type 1 and 2 lepra reactions. *Int. J. Lepr.* **56** (1988) 559–565.
4. CONNOLLY, K. M., STACHER, V. J., LABRIE, T. and FLUNO, C. Modulation of acute phase response and *in vitro* measurement of interleukin-1 activity following administration of dexamethasone to adjuvant arthritic rats. *Immunopharmacology* **15** (1988) 133–142.
5. GUPTA, S., IMAM, A. and LICORISH, K. Serum ferritin in acquired immunodeficiency syndrome. *J. Clin. Lab. Immunol.* **20** (1986) 11–14.
6. Hoffbrand, A. V. and PETTIT, J. E. Iron deficiency and other hypochronic anemias. In: *Essential Haematology*. Oxford: Blackwell Scientific Publications, 1980, pp. 28–41.
7. JOPLING, W. H. *Handbook of Leprosy*. 2nd ed. London: William Heinemann Medical Books, 1978, pp. 66–74.
8. MANSON-BAHR, P. E. C. and APTED, F. I. C. *Manson's Tropical Diseases*. 18th ed. London: English Language Book Society, 1982, pp. 298–322.
9. RAO, K. N., SAHA, K. and CHAKRABARTY, A. K. Undernutrition and lepromatous leprosy. III. Micronutrients and their transport proteins. *Hum. Nutr. Clin. Nutr.* **41** (1987) 127–134.
10. RIDLEY, D. S. and JOPLING, W. H. Classification of leprosy according to immunity; a five-group system. *Int. J. Lepr.* **34** (1966) 255–273.
11. SAHA, K., BHATNAGAR, A., SHARMA, V. K. and CHAKRABARTY, A. K. Enzyme immunoassay of serum beta-2-microglobulin levels in various histological forms of leprosy with special reference to its elevation in type I and type II lepra reactions. *J. Clin. Microbiol.* **21** (1985) 658–661.
12. SAHA, K. and RAO, K. N. Undernutrition in lepromatous leprosy. Part V: Severe nutritional deficit in lepromatous patients co-infected with pulmonary tuberculosis. *Eur. J. Clin. Nutr.* **43** (1989) 117–128.
13. SAHA, K., RAO, K. N., SEHGAL, V. N., GADI, S., JAIN, V. K. and CHAKRABARTY, A. K. Radioimmunoassay of serum cortisol levels in leprosy patients with reference to type I and II reaction. *Lepr. Rev.* **56** (1985) 117–125.
14. VAN BRAKEL, W., KIST, P., NOBLE, S. and O'TOOLE, L. Relapse after multidrug therapy for leprosy: a preliminary report of 22 cases in West Nepal. *Lepr. Rev.* **60** (1989) 45–50.
15. WHO STUDY GROUP. Chemotherapy of leprosy for control programmes. Geneva: World Health Organization, 1982. Tech. Rep. Ser. 675.

Interleukin-2 Receptors in the Sera of Leprosy Patients

TO THE EDITOR:

A variety of immunological changes occur in borderline tuberculoid leprosy progressing toward the lepromatous pole (⁴). A

particular deficit in the number and functions of T cells has been seen in step-ladder fashion from the tuberculoid to the lepromatous end. On the other hand, B-cell ac-

tivity is generally noted to be elevated as we shift from the tuberculoid to the lepromatous pole (12). B cells are activated by antigens of *Mycobacterium leprae* with accompanying hypergammaglobulinemia associated with the appearance of autoantibodies also to a variety of tissue components (14). It has been suggested that a portion of the autoantibodies bind to the T-helper-cell population (3). Apart from interleukin-1 (IL-1), interleukin-2 (IL-2) plays an important role in the generation of T- and B-cell immune reactions (8). As a result of antigenic stimulation of T lymphocytes, IL-2 is produced and receptors for lymphokines are also expressed (2). IL-2 is also necessary for the sustained long-term growth of T cells and for the generation of cytotoxic T-cell responses (16). Rubin, *et al.* (9) demonstrated the accumulation of soluble IL-2 receptors (IL-2R) in the culture supernatant when human T lymphocytes were stimulated *in vitro* with mitogen, antigen or anti-T3 antibody. The same group of workers (10) reported elevated levels of circulating IL-2R in patients with T-cell leukemias. The quantification of IL-2R in the sera of leprosy patients could therefore be a useful indicator of T-cell-mediated responses, and hence was carried out in the present study.

Patients. Eighty-eight patients registered in the Leprosy Clinic of Nehru Hospital attached to the Postgraduate Institute of Medical Education and Research, Chandigarh, India, were studied. They included 21 patients with lepromatous leprosy (LL), 6 with LL undergoing erythema nodosum leprosum (ENL), 28 with borderline lepromatous (BL), 28 with borderline tuberculoid (BT), and 5 with tuberculoid (TT) leprosy. Five ml samples of venous blood were drawn from each patient. The sera were separated and stored at -70°C until the assay was carried out. Samples similarly drawn and stored were obtained from eight healthy controls.

IL-2R assay. The quantification of IL-2R levels in the serum samples was done in duplicate using the cell-free Interleukin-2 Receptor Test Kit (T Cell Sciences, Inc., Cambridge, U.K.).

The range of IL-2R in healthy individuals was 190–690 units/ml with an average of 395 units/ml (S.E.M. 59.7). A significant elevation ($p < 0.001$) of IL-2R was seen in

THE TABLE. *Interleukin-2 receptor serum levels.*

Subjects	No. studied	Range (units/ml)	Mean \pm S.E.M.
Controls	8	190–690	395 \pm 59
LL without ENL	21	500–1600	1112 \pm 71
LL with ENL	6	670–1030	960 \pm 80
BL	28	340–1600	1063 \pm 68
BT	28	160–1520	1026 \pm 59
TT	5	690–1480	1102 \pm 71

all of the leprosy patients, regardless of the clinical type of the disease (The Table).

Discussion. Normal resting T and B lymphocytes display very few IL-2 receptors on their surface. Antigenic stimulation results in their division and expression on the cell's plasma membrane. A form of the IL-2R protein which is 10 kDa smaller than the usual 65 kDa membrane-bound IL-2 is also released into the surrounding tissue fluid, the significance of which is not yet known but is also detectable by the system used.

Elevated levels of soluble IL-2R have been shown in a number of pathological conditions (10), in certain autoimmune diseases (1), and in viral infections, the classical example being the acquired immunodeficiency syndrome (11). However, few studies are available regarding the levels of soluble IL-2R in leprosy. Tung, *et al.* (13) reported significantly higher levels of IL-2R in patients of the multibacillary type while paucibacillary patients had significantly lower levels compared to the controls, possibly suggesting that the potential for development of delayed-type hypersensitivity responses to *M. leprae* antigens as such is insufficient to elicit more IL-2 receptors in the serum. Modlin, *et al.* (7) have found equal numbers of IL-2R-bearing cells in tuberculoid and lepromatous lesions, but Longley, *et al.* (5) found decreased numbers of IL-2R cells in lepromatous lesions.

The responsiveness of B cells to IL-2 can also be induced by appropriate activation. Tsudo, *et al.* (15) reported that human B cells stimulated with *Staphylococcus aureus* (Cowan strain I) for 3 days proliferated in response to affinity-purified IL-2. Activated B cells were shown to express IL-2 on their surface and anti-IL-2R blocked the proliferative response to IL-2. Other workers have confirmed this for both murine (17) and human (6) activated B cells.

In the present study, elevated levels of soluble IL-2R were seen in all types of leprosy. The increase observed in the IL-2 receptors in the sera of leprosy patients could be due to several reasons: a) antibodies might be generated against IL-2R which bind to the specific receptors and the complexes are extruded into the circulation by the activated cells; b) IL-2 produced by *M. leprae*-activated T cells might be structurally defective and unable to attach to the IL-2R and thereby enters the circulation; c) IL-2R are produced by cells other than OKT4+, especially B cells which are known to increase in lepromatous leprosy⁽¹²⁾. Studies conducted on these lines would probably give some insight into the immune reaction against *M. leprae*.

—Nirmal Kumar Ganguly, M.D., F.A.M.S.
Chetana Vaishnavi, Ph.D.

Department of
Experimental Medicine

—Surrinder Kaur, M.D., F.A.M.S.
Nalini Agnihotri, M.Sc.
Bhushan Kumar, M.D., M.N.A.M.S.

Department of Dermatology
Postgraduate Institute of
Medical Education and Research
Chandigarh 160012, India

REFERENCES

- BURMESTER, G. R., JAHN, B., GRAMATZKI, M. and KALDEN, J. R. Analysis of rheumatoid synovial T cells expressing the receptor for interleukin-2 (IL-2) and/or the Ia antigen: different phenotypic expression as compared to *in vitro* activated T cells. Abstract in Scand. J. Rheumatol. **12** Suppl. 49 (1983) 31.
- CANTRELL, D. A. and SMITH, K. A. The interleukin-2 T cell system: a new cell growth model. Science **224** (1984) 1312–1316.
- DORSETT, B., CRONIN, W., CHUMA, V. and IOACHIM, H. L. Anti-lymphocyte antibodies in patients with the acquired immune deficiency syndrome. Am. J. Med. **78** (1985) 621–626.
- GODAL, T., MYKLESTAD, B., SAMUEL, D. R. and MYRVANG, B. Characterisation of the cellular immune defect in lepromatous leprosy; a specific lack of circulating *M. leprae* reactive lymphocytes. Clin. Exp. Immunol. **9** (1971) 821–831.
- LONGLEY, B. J., HAREGEWOIN, A., DE BEAUMOUNT, W., SMITH, K. A. and GODAL, T. Lepromin stimulates interleukin-2 production and interleukin-2 receptor expression *in situ* in lepromatous leprosy patients. Lepr. Rev. **57** Suppl. 1 (1986) 189–198.
- MINGARI, M. C., GEROSA, F., CARRA, G., ACCOLLA, R. S., MORETTA, A., ZUBLER, R. H., WALDMANN, T. A. and MORETTA, L. Human interleukin-2 promotes proliferation of activated B cells via surface receptors similar to those of activated T cells. Nature **312** (1984) 641–643.
- MODLIN, R. L., HOFMAN, F. M., HOROWITZ, D. A., HUSMANN, L. A., GILLIS, S., TAYLOR, C. R. and REA, T. H. *In situ* identification of cells in human leprosy granulomas with monoclonal antibodies to interleukin 2 and its receptor. J. Immunol. **132** (1984) 3085–3090.
- ROBB, R. J. Interleukin-2: the molecule and its function. Immunol. Today **5** (1984) 203–209.
- RUBIN, L. A., KURMAN, C. C., FRITZ, M. E., BIDDISON, W. F., BOUTIN, B., YARCHOAN, R. and NELSON, D. Soluble interleukin-2 receptors are released from activated human lymphoid cells *in vitro*. J. Immunol. **135** (1985) 3172–3177.
- RUBIN, L. A., KURMAN, C. C., FRITZ, M. E., YARCHOAN, R. and NELSON, D. L. Identification and characterisation of a released form of interleukin-2 receptor. In: *Leukocytes and Host Defense*. Oppenheim, J. J. and Jacobs, D. M., eds. New York: Allen R. Liss, Inc., 1986, pp. 95–102.
- SETHI, K. K. and NAHER, H. Elevated titers of cell-free interleukin-2 receptor in serum and cerebrospinal fluid specimens of patients with acquired immunodeficiency syndrome. Immunol. Lett. **13** (1986) 179–184.
- SHARMA, S., GANGULY, N. K., KUMAR, B., KAUR, S. and CHAKRAVARTI, R. N. T and B lymphocytes and blastogenesis in leprosy. Lepr. India **51** (1979) 194–202.
- TUNG, K. S. K., UMLAND, E., MATZNER, P., NELSON, K., SCHAUF, V., RUBIN, L., WAGNER, D., SCOLLARD, D., VITHAYASAI, P., VITHAYASAI, V., WOROBEC, S., SMITH, T. and SURIYANAND, V. Soluble serum interleukin 2 receptor levels in leprosy patients. Clin. Exp. Immunol. **69** (1987) 10–15.
- TURK, J. L. and BRYCESON, A. D. M. Immunological phenomena in leprosy and related diseases. Adv. Immunol. **13** (1971) 209–266.
- TSUDO, M., UCHIYAMA, T. and UCHINO, H. Expression of Tac antigen on activated normal B cells. J. Exp. Med. **160** (1984) 612–617.
- WAGNER, H., HARDT, C., HEEG, K., RÖLLINGHOFF, M. and PFIZENMAIER, K. T-cell-derived helper factor allows *in vivo* induction of cytotoxic T cells in *nu/nu* mice. Nature **284** (1980) 278–280.
- ZUBLER, R. H., LOWENTHAL, J. W., ESERD, E., HASHIMOTO, N., DEVOS, R. and MACDONALD, H. R. Activated B cells express receptors for and proliferate response to pulse interleukin-2. J. Exp. Med. **160** (1984) 1170.