CARVALHO, A. C. Tumor shedding and coagulation. Science **212** (1981) 923–924.

- EDWARDS, R. L. and RICKLES, F. R. On the origin of leukocyte procoagulant activity. Thromb. Res. 13 (1978) 307–308.
- GECZY, C. L. and HOPPER, K. E. A mechanism of migration inhibition in delayed-type hypersensitivity reactions. II. Lymphokines promote procoagulant activity of macrophages *in vitro*. J. Immunol. **126** (1981) 1059–1065.
- GECZY, C. L. and MEYER, P. A. Leukocyte procoagulant activity in man: an *in vitro* correlate of delayed-type hypersensitivity. J. Immunol. **128** (1982) 331-336.
- HAREGEWOIN, A., GODAL, T., MUSTAFA, A. S., BE-LEHU, A. and YEMANEBERHAN, T. T cell conditioned media reverse T cell unresponsiveness in lepromatous leprosy. Nature 303 (1983) 342–344.
- HORWITZ, M. A., LEVIS, W. R. and COHN, Z. A. Defective production of monocyte-activating cytokines in lepromatous leprosy. J. Exp. Med. 159 (1984) 666–678.
- NOGUIERA, N., KAPLAN, G., LEVY, E., SARNO, E., KUSHNER, P., GRANELLI-PIPERNO, A., VIEIRA, L., GOULD, V., LEVIS, W., STEINMAN, R., YIP, Y. and COHN, Z. Defective gamma interferon production in leprosy. Reversal with antigen and interleukin-2. J. Exp. Med. **158** (1983) 2165–2170.
- 9. PRYDZ, H. and ALLISON, A. C. Tissue thromboplastin activity of isolated human monocytes. Thromb. Haemost. **39** (1978) 582–591.
- PRYDZ, H., ALLISON, A. C. and SCHORLEMMER, H. U. Further link between complement activation and blood coagulation. Nature 270 (1977) 173– 174.
- PRYDZ, H., LYBERG, T., DETEIX, D. and ALLISON, A. C. *In vitro* stimulation of tissue thromboplastin (Factor III) activity in human monocytes by immune complexes and lectins. Thromb. Res. 15 (1979) 465–474.

- RICKLES, F. R., HARDIN, T. A., PITLICK, F. A., HOYER, M. E. and CONRAD, J. Tissue factor activity in lymphocyte cultures from normal individuals and patients with hemophilia. Am. J. Clin. Invest. 52 (1973) 1427–1434.
- RICKLES, F. R., LEVIN, J., HARDIN, J. A., BARR, C. F. and CONRAD, M. F. Tissue factor generation by human mononuclear cells: effects of endotoxin and dissociation of tissue factor generation from mitogenic response. J. Lab. Clin. Med. 89 (1977) 792–803.
- RIVERS, R. P., HATHAWAY, W. E. and WESTON, W. L. The endotoxin-induced coagulant activity of human monocytes. Br. J. Haematol. 30 (1975) 311– 316.
- ROTHBERGER, H., ZIMMERMAN, T. S., SPEIGEL-BERG, H. L. and VAUGHAN, J. H. Leukocyte procoagulant activity: enhancement of production *in vitro* by IgG and antigen-antibody complexes. J. Clin. Invest. **59** (1977) 549–557.
- SCHWARTZ, B. S., LEVY, G. A., FAIR, D. S. and EDGINGTON, T. S. Murine lymphoid procoagulant activity induced by bacterial lipopolysaccharide and immune complexes is a monocyte prothrombinase. J. Exp. Med. 155 (1982) 1464–1469.
- STACH, J. L., STROBEL, M., FUMOUX, F. and BACH, J. F. Defect in the generation of cytotoxic T cells in lepromatous leprosy. Clin. Exp. Immunol. 48 (1982) 633-640.
- VAN GINKEL, C. J. W., VAN AKEN, W. G., OH, J. I. H. and VREEKEN, J. Stimulation of monocyte procoagulant activity by adherence to different surfaces. Br. J. Haematol. 37 (1977) 35-45.
- WATSON, S., BULLOCK, W., NELSON, K., SCHAUF, V., GELBER, R. and JACOBSON, R. Interleukin-1 production by peripheral blood mononuclear cells from leprosy patients. Infect. Immun. 45 (1984) 787–789.

## Trial of Cimetidine in Lepromatous Leprosy—A Futile Attempt

## TO THE EDITOR:

Cimetidine is primarily an  $H_2$  histamine receptor antagonist, and is mainly used in the management of peptic ulcer. In the recent past there have been a number of reports suggesting an immunomodulatory property of this compound (<sup>1, 6, 9</sup>). Brown, *et al.* (<sup>3</sup>) have recently tried cimetidine in active as well as inactive cases of lepromatous leprosy (LL) and have observed no significant immunostimulation or leprosyrelated reactions. In our center, we have studied the immunostimulatory effect of oral zinc in LL and found it a nonspecific immunostimulant since it failed to generate specific sensitization in LLp (<sup>8</sup>). In the present study, cimetidine was used to suppress the suppressor T cells in order to enhance the immunostimulatory effect of oral zinc in LL.

Eight fresh cases of LL (6 LLs and 2 LLp) were treated with rifampin, 600 mg; dapsone, 100 mg; zinc sulfate, 220 mg; and cimetidine, 1200 mg (400 mg tid) per day for 3 months. At the end of the third month, there were no significant changes in the clinical charting, bacterial index, or histology. No leprosy-related reactions were seen during cimetidine therapy. These cases were followed up for 2 years, but did not show any significant differences compared with other modes of therapy (8). Only one case suffered from ENL reaction. The low incidence of ENL could also be because of simultaneous use of oral zinc in these patients  $(^{7, 8}).$ 

An earlier report by Daman and Rosenberg (4) observed the development of unresponsiveness to DNCB in patients with alopecia areata which was reversed by oral cimetidine therapy. This situation differs from the specific unresponsiveness seen in leprosy by the fact that in leprosy there is persistence of antigen. Another reason for the failure of cimetidine in leprosy could be that cimetidine is only effective in preventing the development of suppressor cells when it is given before the induction of suppressor cells (5). It has also been shown that cimetidine has no influence on suppressor activity of macrophages (2). Apart from these factors, the influence of the dose of cimetidine has also been highlighted by Jin, et al. (5); they have found 50 mg/kg body weight the most appropriate dose for counteracting generation of suppressor cells. In our study as well as the study by Brown, et al.  $(^{3})$  the dose of cimetidine was low as compared to that of Jin, et al. (5).

Before establishing the role of cimetidine, more understanding of the mechanisms of sensitization and unresponsiveness in leprosy is required. -Narender K. Mathur, M.D., F.C.A.I. *Professor and Head* 

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## REFERENCES

- 1. AVELLA, J., BINDER, H. J., MADSEN, J. F. and AS-KENOSE, P. W. Effect of histamine  $H_2$  receptor antagonists on delayed hypersensitivity. Lancet 1 (1978) 624-626.
- BENNETT, J., ZLOTY, P. and MCKNEALLY, M. Cimetidine blocks the development of tumor induced suppressor T-cell activity. J. Int. Immunopharmacol. 4 (1982) 280.
- BROWN, A. E., NELSON, K. E., MAKONKAWKEYOON, S., VITHAYASAI, V., SCOLLARD, D. M. and BULLOCK, W. E. A study of the immunological effects of cimetidine in patients with lepromatous leprosy. Int. J. Lepr. 52 (1985) 559–564.
- DAMAN, L. A. and ROSENBERG, E. W. Acquired tolerance to dinitrochlorobenzene reversed by cimetidine. Lancet 2 (1977) 1087.
- JIN, Z., KUMAR, A., CLEVELAND, R. P., MURRAY, D. L. and KAUFMAN, D. B. Inhibition of suppressor cell function by cimetidine in a murine model. Clin. Immunol. Immunopathol. 38 (1986) 350–356.
- JORIZZO, J. L., SAMS, W. M., JEGASOTHY, B. V. and OLANSKY, A. J. Cimetidine as an immunomodulator. Chronic mucocutaneous candidiasis as a model. Ann. Intern. Med. 92 (1980) 192–195.
- MATHUR, N. K., BUMB, R. A. and MANGAL, H. N. Oral zinc in recurrent erythema nodosum leprosum reaction. Lepr. India 55 (1983) 547–552.
- MATHUR, N. K., BUMB, R. A., MANGAL, H. N. and SHARMA, M. L. Oral zinc as an adjunct to dapsone in lepromatous leprosy. Int. J. Lepr. 52 (1984) 331– 338.
- ROCKLI, R. E. and BEER, D. J. Histamine and immunodulation. Adv. Intern. Med. 28 (1983) 225– 251.