

## **BORDERLINE LEPROSY: *IN SITU* AND CYTOKINE PROFILE IN SUPERNATANT OF MONONUCLEAR CELL CULTURE**

**Thesis:** J. Venturini submitted this dissertation for his Masters in Tropical Diseases at Botucatu Medical School, São Paulo State University, UNESP, Botucatu, São Paulo State, Brazil, 2008.

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**ABSTRACT:** In order to contribute to a better understanding of cytokine participation in borderline leprosy, in the present study we determined – by *in vitro* and *in situ* examinations – the production of these cytokine mediation in non-treated borderline tuberculoid (BT) patients and borderline lepromatous (BL) patients. Seven non-treated BT patients, 12 non-treated BL patients, besides 19 healthy individuals (control group), were evaluated. Peripheral blood mononuclear cells (PBMC) were stimulated or not with specific-*M. leprae* stimulus (whole and sonicated *M. leprae* antigens) and a non-specific stimulus. After 48 hours, supernatant was collected for TNF-alpha, IFN-gamma, IL-10 and TGF-beta1 cytokine determination by ELISA. Biopsies from cutaneous lesions were submitted to histological analysis and hematoxylin-eosin and Fite-Faraco stainings; the sections then underwent iNOS, IL-10 and TGF-beta1 *in situ* detection by immunohistochemistry. Cytokine quantification in PBMC supernatants from patients showed that BT patients produced higher levels of IFN-gamma. Compared to healthy individuals, both borderline patient groups produced lower levels of TGF-beta1 while BL patients generated lower IL-10 levels. The *in situ* iNOS expression was higher in BT patients compared to BL individuals. On the other hand, TGF-beta1 cytokine revealed a higher proportion of immunostained cells in BL patients. There was no significant difference in IL-10 level between BT and BL patients. Regarding cutaneous lesions, in BL patients there was a negative correlation between TGF-beta1 tissue expression and IL-10. Independently of the clinical form, we observed a positive correlation between TGF-beta1 and bacterial index as well as a negative correlation between the TGF-beta1 tissue expression and iNOS. The results even showed a positive correlation between iNOS tissue expression and production of IFN-gamma by PBMC stimulated with *M. leprae* antigens. Taken together, the histopathological and immunological observations reinforce the notion of immunological instability in borderline leprosy patients and indicating the participation of mixed cytokines profiles in these individuals, specifically a Th1 profile in BT patients and Th2 profile in BL patients, with a possible participation of T-regulatory lymphocytes.

**KEY WORDS:** leprosy, borderline leprosy, cytokine, immunohistochemistry, peripheral blood mononuclear cells, immunopathology.

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