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## SIMILARITIES BETWEEN IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS) IN AIDS AND LEPROSY REVERSAL REACTION

The adoption of highly active antiretroviral therapy (HAART) in aids has prolonged the survival and improved the general health status of patients. These good results are related to suppression of viral replication and recovery of CD4 in threshold levels allowing suspension of primary and secondary prophylactic treatment for opportunistic pathogens. Nevertheless, some of the patients submitted to HAART (10 to 25%) started to show episodes of paradoxical deterioration in their clinical status, many times severe, based on inflammatory reactions to certain opportunistic infectious agent in their usual site or in other less habitual locations. These episodes, known as immune reconstitution inflammatory syndrome (IRIS), develop days or months after the beginning of HAART, ranging from minimal to fatal progression.

Similar occurrences have been found in leprosy from the pre-sulphone era until the multidrugtherapy (MDT). These occurrences are typical of the borderline group during or even after end of treatment. They are characterized by episodes of multiple granulomatous cutaneous lesions, appearing after the regressive process (reversal reaction). These lesions show variable intensity, and frequently are accompanied by neurites (also variable), which represent the most common cause of neurological damage in leprosy. During sulphone monotherapy reversal reaction episodes were observed not only on skin and nerves, but extended to lymph nodes, mucous membranes, synovial membranes and viscera, justifying death in some cases. Some of these have been reported in previous issues of this journal.

The immune reconstitution in aids is clearly verified by the decreased viral load, high CD4 levels and control of opportunistic infections. In borderline leprosy there are variable levels of cellular immunity, therefore, in the absence of specific treatment there will always be bacillary replication. Over time, this increases the bacillary

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load which can alone justify changes in the granuloma, in the morphology, extension and spread of dermatological and neurological lesions. On the other hand, it is believed that the components of the cell wall of bacilli (phenolic glycolipid and lipoarabinomannan) suppress the cellular immunity and amplify the downgrading of non-treated borderline patients. Specific treatment leads to death and fragmentation of bacilli. The speed of resolution of granulomatous lesions depends on individual immune response. In reversal reaction episodes, granulomas are more tuberculoid compared with initial biopsy suggesting immune reconstitution, which has been corroborated by finding of increased blood or *in situ* Th1 cytokines (IL2, IFN $\gamma$  e TNF $\alpha$ ).

Two question remain in both diseases, aids and leprosy:

1. Are reactivations during treatment related to antigens associated with ongoing infection or recognition of persisting antigens associated with previous infection after prophylactic treatment of aids or MDT treatment for leprosy?
2. Since a small percentage of individuals treated present such reactional episodes, should we think about a triggering factor?

Opromolla suggested that all reactivation episodes in leprosy were related to host response to replication of persisting bacilli. In biopsies of cutaneous lesions during reversal reaction we don't find viable bacilli. In the same sense, however, Darier, in the 50<sup>th</sup> edition of the Compendium "Precis de Dermatologia" (1947), suggested that late

cutaneous and extracutaneous syphilis manifestations were indeed an allergic phenomena, because treponemas were not identified in lesions. Nowadays, at least in the cutaneous manifestations, named now late secondary syphilis, treponemas are still not identified, however, lesions disappear quickly with use of penicillin.