Tuberculosis infection is acquired through inhalation of aerosolized infectious particles containing *Mycobacterium tuberculosis*, which can reach the alveoli in the distal airways. Macrophages and dendritic cells (DCs), the first host cells targeted by invading bacilli, are the key mediators of innate immunity to *M. tuberculosis*. In the course of infection, additional macrophages and resident DCs are recruited to the site of infection. Mature DCs relocate to the lymph nodes where they produce inflammatory cytokines and there is development of adaptive immune response which includes helper (CD4+) T-cells, cytotoxic (CD8+) T-cells, γδ T-cells and the production of interferon γ (IFNγ) and tumour necrosis factor α (TNFα), both key cytokines in immunity to tuberculosis. The host immune responses sufficiently contain the infection in about 90 per cent of the HIV-negative individuals, without achieving sterilization, and only about 10 per cent of the infected individuals progress to disease. The progression of primary infection to disease is slow in humans taking a few weeks to several years. Chemotherapeutic treatment of clinical disease does not always lead to sterilization.

Dormant tubercle bacilli can remain alive within the human host for decades and the bacillary reactivation is kept in check by the host immune response. It has been shown that many cases of tuberculosis result from reactivation of latent infection, at least in countries with low or moderate tuberculosis endemicity. Since it is only a small proportion of infected individuals who develop clinical disease, the risk of becoming infected with *M. tuberculosis* would be different from the risk of progression to active disease, either as progression of primary infection to primary progressive disease or reactivation of latent infection. The rising incidence of tuberculosis over the last two decades has increased the need to define host factors that control resistance to the development of active tuberculosis. Worldwide malnutrition and starvation are major causes of immunosuppression and increased susceptibility to tuberculosis. Several different aspects of malnutrition can be held responsible for the immunosuppression, and recently leptin has been described as a possible link between nutrition and immune status. Leptin, a 16-kDa non-glycosylated polypeptide protein is produced mainly by the adipocytes, and the circulating concentrations are proportional to fat mass. By virtue of its structural similarity to the type I cytokine superfamily, and the expression of its functional receptor in all cell types of innate and adaptive immunity, leptin is shown to modulate the immune response and favour a Th1 response while inhibiting the secretion of Th2 cytokines. Leptin signaling has been shown to promote the maturation of DCs, activation of monocytes, macrophages and natural killer cells. In the absence of leptin signaling, DCs display a Th2-biased cytokine profile, and altered Th1:Th2 cytokine balance is associated with a corresponding change in the immuno-stimulatory capacity on T cells. Furthermore, leptin is shown to promote the survival of DCs, T and B lymphocytes by suppressing Fas-mediated apoptosis, which may result from its induction of anti-apoptotic proteins and downregulation of pro-apoptotic proteins. Recently it has also been shown that leptin can act as a negative signal for the proliferation of Foxp3+ regulatory T cells. Regulatory T cells have been shown to suppress Th1 immune responses. Thus reduced leptin concentrations by virtue of impairment of Th1 cell-mediated immunity may present a risk factor for development of tuberculosis. Indeed it has been shown that leptin-deficient mice are more susceptible to *M. tuberculosis* than wild-type mice, suggesting that leptin contributes to protection against tuberculosis. Similarly low serum leptin level associated with reduced body fat or nutritional deprivation is shown to be a direct cause of secondary immunodeficiency and increased susceptibility to infection.
In this issue Prabha et al. have studied the role of leptin in tuberculous pleuritis by measuring the leptin and cytokine levels in serum and pleural fluid by ELISA. There are hardly any studies on the role of leptin in immunity during extrapulmonary tuberculosis infection and this study is a good contribution towards understanding of the complex immune mechanisms during M. tuberculosis infection. Authors have found that despite higher Th1 cytokine levels in the pleural fluids, the leptin levels were significantly lower in tuberculous pleuritis as compared to the non-tuberculous subjects. No significant correlation was found between the levels of IFN-γ, TNF-α, IL-12, IL4, and CD4+ cells and leptin levels in the tuberculous pleuritis patients. Their results concord with a similar study done by Celik et al., and also confirms their previous study with similar observations at the systemic level in HIV patients with tuberculosis infection. In line, studies done in patients with pulmonary tuberculosis also report low serum leptin levels and lack of significant correlation between serum pro-inflammatory cytokines and leptin levels. On the other hand, some studies have reported a conflicting data with elevated serum leptin levels in tuberculosis patients. Prabha et al. conclude that leptin might not have any role in immunity against M. tuberculosis, particularly at the site of infection. However this conclusion is not fully supported by the data presented in the paper. We do not know the duration of low leptin concentration in these patients, or whether low leptin concentration preceded the development of active disease or is the consequence of the disease process. Low serum levels of leptin associated with active tuberculosis rather support the concept that probably low leptin concentrations contribute to the increased susceptibility of the progression of infection to disease.

It has long been observed that thin people are more prone to develop tuberculosis. It has also been suggested that patients with low leptin levels recover from active tuberculosis with increased sequela. There are several questions which must be answered to clarify the role of leptin in immunity to tuberculosis, for example; do low leptin levels present a risk factor for the progression of infection to disease? Secondly, is there any influence of leptin levels on the severity/pathogenesis of active disease? Since re-activation of latent infection is associated with a shift in the immune response from Th1 towards Th2 pattern, it can be hypothesized that low leptin levels eventually lead to re-activation of latent infection. Further studies are needed to see whether leptin plays any role in the prevention of reactivation of latent infection. If a causative relationship between leptin and immune function in tuberculosis is established, there are exciting novel possibilities of using leptin-based therapeutic tools. Until now, the only clinical use of leptin has been for a few cases of genetically leptin-deficient individuals where it reversed some immune dysregulation and in obese patients to reduce food intake. Leptin administration could be used to stimulate the immune system during immune suppression and tuberculosis as an adjunct to chemotherapy. In conclusion, further studies are needed to understand the crosstalk between immune system and leptin and the role of leptin in tuberculosis immunity.

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MUSTAFA: DOES LEPTIN HAVE A ROLE IN IMMUNITY TO TUBERCULOSIS? 693


