

Leishmaniasis is a neglected--though widely distributed--tropical disease caused by protozoan parasites of the genus *Leishmania*. Methotrexate (MTX), an antagonist of folic acid, blocks the synthesis of purines and pyrimidines. Commonly used to treat autoimmune diseases, its precise mechanism of action remains unknown, although it has been described to reduce the inflammation associated with these diseases. It also reduces the multiplication of lymphocytes, and thus has a direct effect on immune system function. It might, therefore, influence the development of an adequate immune response to *Leishmania* infection. However, the murine model of *L. infantum* infection allows the study of the immune response and of the mechanisms affecting protection against/susceptibility towards the development of VL. This immune response is organ-specific; the infection is usually cleared from the liver in the first few weeks, but it becomes chronic in the spleen and bone marrow. The present work characterises the parasite load developed in, and immune response to, *L. infantum*-induced VL in C57BL/6 mice that, prior to and during infection, received immunosuppressant treatment with MPDN, anti-TNF antibodies, or MTX. However, an increase in cases of VL has also been detected among recipients of solid organ transplants and patients receiving immunosuppressants to treat autoimmune diseases such as rheumatoid arthritis, lupus erythematosus and inflammatory bowel disease. After their bonding to the target molecule, the multiplication of amastigotes in infected macrophages is favoured, increasing the chances of developing clinical leishmaniasis--an outcome confirmed in animal models lacking the gene . for TNF