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Granuloma Formation in Leishmaniasis: A Mathematical Model

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Abstract

Leishmaniasis is a disease caused by the *Leishmania* parasites. The two common forms of leishmaniasis are cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL). VL is the more severe of the two and, if untreated, may become fatal. The hallmark of VL is the formation of granuloma in the liver or the spleen. In this paper, we develop a mathematical model of the evolution of granuloma in the liver. The model is represented by a system of partial differential equations and it includes migration of cells from the adaptive immune system into the granuloma; the rate of the influx is determined by the strength of the immune response of the infected individual. It is shown that parasite load decreases as the strength of the immune system increases. Furthermore, the efficacy of a commonly used drug, which increases T cells proliferation, increases in an individual with stronger immune response. The model also provides an explanation why, in contrast to humans, mice recover naturally from VL in the liver.

1 Introduction

Leishmaniasis is a parasitic disease caused by infection with an obligate intra-cellular protozoa called *Leishmania*, the disease parasite [18, 89]. Infection occurs when a female sand fly bites a human and injects into his/her body the flagellated form of the *Leishmania* parasites, the promastigotes, which are endocytozed into phagocytic cells and quickly transform into amastigotes (non-flagellated *Leishmania*). The amastigotes then mature and disseminate into different parts of the body [7, 14, 15, 64, 88].

There are more than 20 species of the *Leishmania* parasite, and more than 30 different species of the parasite vector, the female sand fly. The two common forms of leishmaniasis are cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL), of which over 350 million people from all continents are at risk worldwide [4, 57, 88]. VL is the more severe, and sometimes fatal, form of the disease; it develops when the *Leishmania* parasites infect macrophages located in internal organs such as the bone-marrow, liver and spleen [14, 15, 18, 57, 64, 82, 88].

The primary symptoms of VL include abdominal pain, fever, shivering and weight loss. However, signs of bacterial co-infection such as pneumonia, diarrhea or tuberculosis may lead to death if they persist for several weeks without treatment [18, 88].

The hallmark of visceral leishmaniasis is the formation of granulomas in the liver or the spleen. Granulomas are inflammatory foci containing infected cells. They are formed as immune cells migrate towards the source of infection, surround the infected cells and try to kill or control them [2, 59]. In the process of surrounding the infected cells, granulomas