MATHEMATICAL MODELLING OF HIV - IMMUNE DYNAMICS

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Abstract

Human immunodeficiency virus type one (HIV-1) infection leads to CD4+ T cells depletion that will eventually lead to impairment of immune functions. The thesis first reviews the virological, biological and mathematical background necessary to model immune responses to HIV-1 infection and drug effects on HIV-1 disease. In this thesis, deterministic mathematical models for immune responses to HIV-1 infection, optimal control of highly active antiretroviral therapy (HAART) in HIV-1 infection and effects of chemotherapy on baseline HIV-1 disease parameters are constructed to understand the effects of both cytotoxic T lymphocytes (CTLs) and drugs. For the mathematical analysis, we applied concepts from dynamical systems, optimal control methods and epidemiology complemented by numerical simulations. Analysis of the basic model of immune responses to HIV-1 infection shows that CTLs' soluble antiviral factors contribute most to viral control during chronic infection. The optimal control model indicates that for highly toxic drugs, small dosage sizes and allowing drug holidays make a profound impact in improving the quality of life, reducing systemic costs and reducing economic costs of therapy. The analysis of the model that captures the dynamics of the immune system and two HIV-1 variants under antiretroviral therapy reveals that CD4+ T cell increases occur in two principal stages and that there is a dynamic equilibrium between viral load and CTL abundance in infected individuals during drug administration. The model also suggests that drug resistance is a major factor that makes complete disease eradication by therapy impossible.