The Role of Cell-to-Cell Transmission in HIV Infection: Insights From a Mathematical Modeling Approach, Year 2

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HIV infection remains a global public health challenge. While current drug treatments effectively suppress HIV viral loads below the detection level, complete eradication of the virus remains elusive. HIV latent infection is a significant obstacle to viral eradication. Many HIV patients also experienced transient viral loads above the detection limit, known as “viral blips,” even after maintaining well-controlled viral loads for an extended period. The mechanisms underlying the establishment of HIV latency and the emergence of HIV blips remain unclear. Building upon the published model and results from Year 1, our study investigates the role of cell-to-cell transmission in the generation of HIV latency and blips. We conducted a comprehensive mathematical analysis of model equilibria and their stability, utilizing the basic reproduction number — a critical threshold widely used in epidemiology to determine if a disease will expand or die out. Computer simulations, employing the best-fitting parameters of the model to experimental data, demonstrate that cell-to-cell transmission primarily contributes to latent infection before therapy. However, after therapy, the proliferation of latently infected cells becomes the major factor in HIV latency and persistence. Furthermore, our study reveals that random activation of latently infected cells can generate viral blips in patients undergoing therapy. These findings have crucial implications for understanding HIV latent infection and persistence, providing valuable guidance for the development of more effective treatment strategies to control or even eradicate the virus.