Acute SIV Infection Results in Selective Depletion of Proliferating CD4+ T Cells in Neonatal Rhesus Macaques.

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Infants infected with human immunodeficiency virus (HIV) usually have a more severe course of disease and persistently higher viral loads than HIV-infected adults. However, the underlying pathogenesis of this exacerbation remains obscure. Here we examined and compared the rate of CD4+ and CD8+ T cell turnover in intestinal and systemic lymphoid tissues of neonatal and adult rhesus macaques, and of normal and age-matched simian immunodeficiency virus (SIV) infected neonatal rhesus macaques. The results demonstrate that infant primates have a much greater rate of CD4+ T cell proliferation and maturation than adult macaques, and that these proliferating, recently "activated" CD4+ T cells are selectively infected in intestinal and other lymphoid tissues of neonatal macaques, resulting in essentially a selective depletion of proliferating CD4+ T cells in acute infection. This depletion is accompanied by a marked increase in CD8+ T cell activation and production, particularly in the intestinal tract, indicative of inflammation. The data indicate intestinal CD4+ T cells of infant primates have a markedly accelerated rate of proliferation and maturation resulting in an expanded and apparently continual supply of optimal target cells (activated memory CD4+ T cells), which may explain the sustained “peak” viremia characteristic of pediatric HIV infection. In addition, the data suggest that the neonatal intestine may be a major source of CD4+ T cell precursors (a primary lymphoid tissue?) and possibly the major reservoir for persistent viral replication and persistence in HIV-infected infants. We hypothesize that eventual failure of CD4+ T cell turnover in intestinal tissues may indicate a worse prognosis for HIV infected infants.

This work was supported by NIH grants AI062410, AI084793, and RR000164.