

The impact of latent herpesvirus infections on the mobilization of recent thymic emigrants and extrathymic T-cells in response to acute aerobic exercise in man

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**Abstract**

T-cells typically mature in the thymus gland, which eventually succumbs to age-related atrophy, resulting in a decreased naïve T-cell repertoire in middle to later years. Aged individuals and those with persistently reactivating herpesvirus infections have an increased reliance on the extrathymic maturation of T-cells due to the shrinking effects that age and latent viral infection has on the naïve T-cell repertoire. Acute bouts of aerobic exercise are known to mobilize T-cells that exhibit both a naïve and late-stage differentiation phenotype into the blood compartment; however, it is not known if recent thymic emigrants (RTE) or extrathymic T-cells contribute to the lymphocytosis associated with exercise. **PURPOSE:** To examine the impact of latent cytomegalovirus (CMV) and Epstein-Barr virus (EBV) infection on the mobilization of RTE and extrathymic T-cells in response to acute exercise. **METHODS:** Otherwise healthy CMV or EBV seropositive (CMV+ or EBV+) and CMV or EBV seronegative (CMV- or EBV-) males (age 23-35y) completed a 30-min cycling protocol at 85% of maximum power. Lymphocytes isolated from whole blood before, immediately after, and one hour after exercise were surface stained with monoclonal antibodies to identify phenotypes of RTE (CD103+/CD62L-) and extrathymic T-cells believed to mature in the liver (CD3+/CD25-/CD122+) and the epithelium of the small intestine (CD3+/CD4-/CD8-; TCR $\gamma\delta$ +/CD8 $\alpha\alpha$ +; CD3-/CD2+/CD7+). Cell populations were analyzed by flow cytometry and antibodies against CMV and EBV were determined in serum by ELISA. **RESULTS:** Preliminary analyses show that the proportion of RTE among the total CD3+/CD4+ or CD3+/CD8+ T-cell subsets did not change immediately after exercise, but was elevated above baseline 1h later due to the preferential egress of late stage differentiated T-cells. Neither CMV nor EBV status influenced the proportions of RTE in blood in response to exercise. T-cells mainly found in intestinal mucosa (i.e. CD3+/CD4-/CD8- and CD3-/CD2+/CD7+) were found to increase in blood immediately after exercise; an effect that appeared to be more pronounced in EBV but not CMV-infected subjects. **CONCLUSION:** An acute bout of aerobic exercise elicits the mobilization of T-cells exhibiting phenotype characteristics of extrathymically matured T-cells, suggesting that extrathymic T-cell mobilization contributes to the lymphocytosis associated with acute exercise. This effect appears to be amplified in subjects carrying a latent EBV but not CMV infection. Future research should attempt to establish the impact of long-term exercise and latent herpesvirus infections on the frequency of RTE and extrathymic T-cells in the aged, as this could have significant implications for age-associated immune dysfunction.