Reply to Ganesan et al

To the Editor—We read with interest the recent study by Ganesan et al [1] that highlighted the increasing research in chronic immune activation and a potential strategy to modulate its impact in individuals infected with human immunodeficiency virus (HIV). Chronic immune activation remains of particular concern as it predicts HIV disease progression independently of viral load and has been associated with suboptimal immune reconstitution despite highly active antiretroviral therapy (HAART) [2, 3].

Many processes likely contribute to this heightened immune activation state described with HIV infection [4]; however, the impact of tobacco smoking, which is highly prevalent in the HIV-infected population, on immune activation should also be considered [5]. The significant impact of tobacco smoking in terms of morbidity and mortality are well described in populations regardless of HIV status [6, 7]. Data on the immunological impact of tobacco smoking in the HIV-infected population, however, are limited. Tobacco smoking has been associated with a poorer immunologic response (hazard ratio [HR] = 0.85) in a study of >900 HIV-infected women who initiated HAART [8]. A higher risk of immunologic failure (HR = 1.52), viral rebound (HR = 1.39), death (HR = 1.53), and AIDS (HR = 1.36) was also reported [8]. Another study reported a positive dose response between packs smoked per day and CD4+ T-cell counts observed for HIV-negative smokers, but this was considerably attenuated in HIV-infected smokers [9]. In a subgroup analysis from the latter study, HIV seroconverters who smoked before becoming infected with HIV had faster declines in CD4+ T-cell counts than those who were nonsmokers prior to diagnosis [9].

We have published data on differences in markers of T-cell maturation and activation between HIV-infected individuals with optimal versus suboptimal CD4+ T-cell recovery despite long-term viral suppression on HAART; these methods are described elsewhere [3]. Using these data, we have now evaluated the impact of those persons’ tobacco-smoking status on levels of T-cell activation to illuminate this important topic.

Percentages of activated CD4+ and CD8+ T lymphocytes were determined in current tobacco smokers (n = 15) (CD8+ data from 1 current/ever smoker not available) and noncurrent smokers (n = 32) with HIV RNA <50 copies/mL for >2 years. There were no significant differences in sex, age, CD4+ T-cell count, or HIV load in current smokers versus noncurrent smokers. However, there was a significantly higher percentage of CD8+ HLA-DR+ T lymphocytes (2.25 vs 0.96; P = .005) as well as CD4+ HLA-DR+ T lymphocytes (2.55 vs 1.16; P = .017) in the current smokers versus noncurrent smokers, respectively. There was also a significantly higher percentage of CD8+ HLA-DR+ T lymphocytes (1.96 vs 0.92; P = .004) and CD4+ HLA-DR+ T lymphocytes (2.34 vs 1.06; P = .006) when analyzing ever smokers (n = 20) (CD8+ data from 1 current/ever smoker not available) versus never smokers (n = 27). Furthermore, there was a trend to a higher percentage of...
CD8+ CD38+ HLA-DR+ T lymphocytes (1.63 vs 0.96; \( P = .06 \)) in the current smokers versus noncurrent smokers. Both the current and ever smokers had a significantly lower percentage of CD4+ CD38+ T lymphocytes compared with nonsmokers.

These data are intriguing but limited, because they are derived from a small group of HIV-infected individuals with long-term viral suppression on HAART. Given the findings of Ganesan et al [1], who demonstrated significant reductions in percentages of CD4+ HLA-DR+ and CD8+ HLA-DR+ T lymphocytes with atorvastatin therapy, the impact of tobacco smoking on prevalent T-lymphocyte activation requires further evaluation, with the ultimate goal to determine whether smoking cessation can reduce T-lymphocyte activation. This would be an excellent cost-effective intervention.

The triple impact of HIV infection, tobacco smoking, and elevated levels of immune activation remains of concern, especially because the HIV-infected population is aging in the era of HAART. Tobacco smoking should be considered as a potential modifier in future research protocols, and changes in activated T lymphocytes with smoking cessation warrant further study. While assessing the immune effects of tobacco smoking on HIV-infected individuals, it is vitally important to develop best practices to safely and effectively help HIV-infected smokers quit. Data on immune activation may serve as an additional impetus for patients and their care providers.

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**References**


