Oropharyngeal Candida Colonization and Human Immunodeficiency Virus Type 1 Infection

To the Editor—Gottfredsson et al. [1], in a cross-sectional study of oropharyngeal Candida colonization in 83 patients with human immunodeficiency virus type 1 (HIV-1) infection, reported that only plasma HIV-1 load was predictive of Candida load; neither CD4 lymphocyte level nor use of antiretroviral therapy was associated with colonization [1]. They hypothesized that high levels of HIV-1 may suppress local mucosal immune responses, thereby permitting increased Candida colonization, and speculated that control of HIV-1 replication may restore local immune function. Their findings certainly are consistent with these possibilities. However, there are at least 2 alternative explanations that might account for the interesting findings.

Cross-sectional studies do not provide information about causality for any associations found. However, even if high levels of HIV-1 do cause increased Candida colonization, suppressed local mucosal immunity is not the only possible mechanism that might explain such an occurrence. It was recently shown in vitro that HIV-1 glycoproteins may promote the virulence of Candida albicans [2]. Thus, increased local HIV-1 replication might have a direct effect on increased Candida colonization, without necessarily requiring the presence of defects in local immune function. Furthermore, such a mechanism need not imply disassociation of HIV-1 effects on local mucosal immunity from those on CD4 lymphocyte counts, as would be suggested by a better correlation of Candida colonization with HIV-1 effects on local immune function than with effects on CD4 lymphocyte counts.

In addition, patient self-report is known to overestimate adherence to prescribed medications [3], especially for regimens requiring multiple doses daily [4]. Preliminary observations of HIV-infected current and former drug users in the Bronx, New York, showed that medication adherence assessed by electronic monitoring was significantly correlated with HIV load but that self-reported adherence was not [5]. HIV-1 load is inversely correlated with actual use of effective highly active protease inhibitor–containing antiretroviral regimens. Even though oropharyngeal Candida colonization was not independently associated with the reported use of protease inhibitors, its association with HIV-1 load suggests that there may well have been less use of protease inhibitors in colonized patients. Since protease inhibitors have antifungal activity [6], it is possible that the actual use of protease inhibitors, better reflected by low HIV-1 load than by self-reported adherence, had a direct effect on reducing oropharyngeal Candida colonization. It would be of interest to know if the independent association of Candida colonization with HIV-1 load was seen in the subgroup of patients known not to have received either current or recent protease inhibitor therapy.

Until longitudinal studies are available and actual rather than reported use of chemotherapeutic agents with antifungal activity can be accurately measured and controlled for in analyses, it may be premature to conclude that HIV-1 load has a direct effect on local mucosal immunity, which promotes oropharyngeal Candida colonization.

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References


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Reply

To the Editor—We thank Klein et al. [1] for their cogent response to our work [2] in which we reported that, among various clinical parameters in a cohort of human immunodeficiency virus (HIV)–infected patients, plasma HIV RNA levels had the most significant association with oropharyngeal Candida colonization. As Klein et al. point out, this association could be the result of 3 possibilities: HIV affecting mucosal