technology, may provide the most important clue for diagnosis of CSD, particularly for atypical cases.

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**References**


**Knowledge of and Adherence to Antiretroviral Therapy**

Sir—Miller et al. [1] constructed a medication knowledge score (MKS) based on antiretroviral drug name, number of pills per dose, and dosing schedule to assess knowledge about antiretroviral therapy (ART) among a cohort of 128 HIV-infected patients. Pictures of the medications were also provided to the patients, but knowledge of pill appearance was apparently not included in the MKS. Miller and colleagues stated in the abstract that “poor medication knowledge 8 weeks after regimen initiation was associated with lower adherence and with a lower level of literacy in a multivariate model (P = .03)” [1, p. 514]. Adherence was prospectively and objectively assessed by a combination of methods, including use of Medication Event Monitoring System electronic bottle caps. This study provided several insights into the dynamics of patients’ knowledge of medications and stressed the importance of assessing patients’ understanding of ART dosing in clinical practice. I would like, however, to discuss some potential problems in their article.

Careful reading of the Results section shows that (1) MKS at week 8 was significantly associated with adherence during weeks 0–8 (P = .05), (2) MKS at week 8 was significantly associated with adherence during weeks 8–48 (P = .05), and (3) in the multivariable analysis, low literacy level (P = .03) and not using a device to complete the study (P = .01) independently predicted low MKS; however, no information was given regarding the association of these latter factors with adherence. It is important to clarify whether the association between low MKS and poor adherence remained statistically significant after adjusting for literacy level, because low education level was found to be an independent risk factor for poor adherence in this cohort [2], in contrast with other studies [3].

In their introduction, Miller and colleagues suggest that “poor adherence to antiretroviral therapy is associated with the development of drug-resistant HIV strains” [1, p. 514]. Results of the study [4] chosen by Miller et al. [1] to support their hypothesis did not convince me. Genotypic mutations conferring resistance to protease inhibitors (PIs) were, in fact, more frequently observed in adherent than in nonadherent patients. Are Miller et al. [1] aware of any evidence of the link between low adherence and resistance to PIs?

In the Discussion section, Miller et al. [1] stated that their findings were consistent with those of other investigators who measured the association between medication knowledge and adherence using subjective reports. In fact, an Italian study group [5] previously investigated this issue and reported no association between knowing the names (P = .11) or dosing (P = .57) of ART agents and having detectable levels of PI, a drug adherence surrogate that is not subjective.

In my opinion, a patient who is able to recognize their medications on a board that displays several pills but who does not know the names because of a poor literacy level demonstrates at least equal, if not more, treatment knowledge than does a patient who knows the medication names but who does not know what they look like after several weeks of taking them daily. Clinicians tend to overestimate the impact of socioeconomic factors on adherence [3, 6]. Thus, asking patients only for the drug names may add to clinicians’ confusion regarding therapy adherence among their patients.

Finally, I suggest an alternative conclusion that does not confuse level of literacy and medication knowledge: because low levels of literacy strongly influenced the MKS, the addition of existing tools based on pill appearance [7] may be an interesting approach to finding the most effective way to assess patients’ medication knowledge and requires additional study.

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Reply

Sir—We appreciate the interest of Parienti [1] in our investigation [2] of the associations between medication knowledge and antiretroviral therapy adherence. The “pictures of medications” described in our article were color photographs of each antiretroviral and/or actual pills mounted to a cardboard placard. Data on all commercially available antiretroviral doses and formulations were presented to patients. Thus, our method of assessing knowledge was more comprehensive than simply asking for drug names, because it gave patients a choice of multiple methods to identify their medications.

In response to issues raised by Parienti [1], we should note that our findings of an association between low education level and suboptimal adherence are not unique [3, 4]. Associations between suboptimal adherence and poor knowledge of beneficial health-related behavior have been reported elsewhere [5, 6].

Parienti [1] notes that we did not discuss the association between mean knowledge score and adherence after adjusting for patient literacy level. In our model that predicted adherence [7], literacy level was not associated with adherence \( P = .88 \). Thus, we think adding data on the level of literacy to the model of knowledge that predicted adherence would be unlikely to change the results. Regardless of findings from additional modeling, the association between poor medication knowledge and worse therapy adherence on a bivariable level suggests that surveying patients about medication dosing would help identify patients at risk for adherence problems. Knowledge deficiencies detected in this manner would be amenable to interventions that may enhance antiretroviral activity.

Parienti [1] also notes that improved adherence may not be associated with decreased likelihood of the emergence of drug-resistant virus. Although it is widely asserted that suboptimal adherence is associated with development of antiretroviral resistance [8], there are limited data on this relationship. We are aware of the investigation cited by Parienti [1], which found an association between increased adherence and increased incidence of drug resistance. These findings are highly intriguing and deserve further exploration and confirmation using other patient populations and methods. However, there are several important limitations to that investigation. First, resistance could only be detected in those patients whose virus loads were high enough to perform genotypic analysis; drug resistance associated with lower virus levels may have been missed. Second, the analysis focused on a subpopulation of patients who did not respond to their regimens, which is not the population at risk for protease inhibitor resistance. Third, the investigation looked at mutations associated with drug resistance in the protease gene. Barriers to resistance to reverse-transcriptase inhibitors may be different than those of protease inhibitors. In a clinical trial that included patients treated with a nevirapine-containing triple drug regimen, of the 6 patients receiving this treatment who developed nevirapine resistance, 5 (83%) reported nonadherence [9]. This proportion was higher than the overall proportion of patients in this study arm who reported nonadherence to nevirapine. At this time, it is premature to conclude that increased adherence is associated with higher likelihood of acquiring antiretroviral resistance.

In summary, there remain challenges to identifying and improving suboptimal adherence. We believe that our investigation adds to these efforts and highlights a relatively simple way to identify patients at risk for poor adherence and to institute rapid interventions to correct dosing misunderstandings.

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