Correspondence


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There are no paradoxes of adherence and drug resistance to HIV antiretroviral therapy

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Sir,

The recent leading article by Bangsberg et al.1 is misleading in that it could lead readers to believe that there is increased resistance to highly active antiretroviral (ARV) therapy (HAART) with increased levels of adherence. In fact the authors make the case for increased resistance with increased adherence in ‘...cohort of individuals treated with either sequential monotherapy or earlier, less potent three-drug regiments...’ This is precisely why the current modality of treatment is HAART. High levels of adherence to HAART are required in order to achieve adequate and sustained viral suppression and minimize the risk of resistance. To suggest otherwise is to muddy the waters and undermine efforts at achieving the unprecedented levels of compliance required for successful roll out of HAART.

Inadequate viral suppression (from using monotherapy or poorly selected combinations of ARVs) results in resistance. This is not paradoxical and would be predicted from our current knowledge of how resistance develops. The authors make an excellent case for careful selection of the ARV combinations to make up HAART. However, the article does mislead in that it could be read to suggest that lower levels of adherence with a properly chosen HAART regimen may be acceptable, or even desirable.

References


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Reply

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Sir,

Dr Green suggests that our claim that antiretroviral drug resistance often occurs in highly adherent patients on highly active antiretroviral therapy (HAART) is misleading. We agree that this point may be confusing and indeed focus on this very ‘paradox’ in our leading article.

HAART became available in 1996 with the introduction of protease inhibitor therapy used in combination with two nucleoside analogues. Our data, obtained in a systematic sample of low-income individuals on HAART, indicate that half of all drug resistance occurred among individuals taking >92% of their medication and a quarter of all drug resistance occurred in individuals taking >92% of their medication.1 In a subsequent mathematical model using these empirical estimates, we determined that resistance to early protease inhibitor therapy was most common at 87% adherence.2 These data are consistent with those of several other groups and suggest that early HAART was not active enough to prevent resistance, even in the face of good adherence.3–8 The paradox is that we spent much of the late 1990s debating the public health wisdom of providing therapy to marginalized populations in the interest of preventing drug resistance, whereas the epidemiological evidence suggests that the burden of drug resistance fell on those who took most of their medication.

The relationship between adherence and resistance is clearly evolving and is different now from when HAART first became available. Today, high levels of adherence to maximally effective therapy (e.g. two nucleoside analogues and either a non-nucleoside reverse transcriptase inhibitor or a dual protease inhibitor) in a treatment-naive patient invariably results in durable viral suppression and no clear evolution of drug resistance. There may, however, be important differences in the risk of resistance at low levels of adherence between non-nucleoside reverse transcriptase inhibitors and dual protease inhibitors. Specifically, low levels of adherence may preferentially select