

# *Is it possible to treat drug users with highly active antiretroviral therapies?*

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**A**t the end of 1999, there were approximately 130,000 people living with HIV in Argentina.<sup>1</sup> Since the beginning of the epidemic, there have been over 20,000 reported cases of AIDS. Of these, 40% are among injection drug users (IDUs). In males, 46% of total AIDS cases in Argentina are among IDUs.<sup>2</sup> Injection drug users constitute the largest proportion of HIV/AIDS patients in Argentina and caring for them is therefore central to everyday HIV clinical practice.

Many physicians, however, are hesitant to offer antiretroviral therapy to IDUs, fearing that drug users cannot adhere to demanding medication regimens. Indeed, many literature reviews and conference presentations suggest that active drug use is associated with poor adherence to antiretroviral therapy and recommend postponing the start of therapy until patients are enrolled in drug treatment or substitution programs. As a result, one of the populations most affected by HIV, drug users, has the poorest access to new therapies which have been proven to slow the progression of AIDS.

To what extent are current attitudes toward drug users based on medical evidence? Is it sound clinical practice to postpone antiretroviral therapy in drug users? Or is doing so propagating a belief that is based on misconception and “common sense” rather than thorough investigation? This review takes a fresh look at the growing body of literature about adherence to antiretroviral therapy, seeking to answer common questions and concerns about offering antiretrovirals to IDUs.

## **Is it possible to stop the progression of HIV in active drug users?**

Drug users are often poor and marginalized and therefore confront large barriers to medical care.<sup>3</sup> Often, they are less likely to receive highly active antiretroviral therapy (HAART), despite having lower CD4 counts and higher viral loads.<sup>4</sup> When engaged in stable primary care with an experienced physician and adequate support services, however, HIV+ injection drug users have clinical outcomes equal to those of HIV patients who do not use drugs.<sup>5</sup> When drug users take antiretroviral therapy, they enjoy the same clinical outcomes as homosexuals and non-drug using heterosexuals.<sup>6</sup>

## **Do drug users comply with Antiretroviral regimens?**

Adherence to highly active antiretroviral therapies is difficult and always of central clinical importance. Many clinicians feel that active drug use is an

absolute contraindication to starting antiretroviral therapy.

Data from countries around the world indicate, however, that active drug users do adhere to demanding HAART regimens:

- \* The EuroSIDA study, which included over 6000 European HIV patients from more than 50 medical centers, revealed that among patients who started HAART, there were no differences in CD4 or viral load responses to therapy between IDUs, homosexuals, and heterosexual non-IDUs. “Intravenous drug users were significantly less likely to start HAART, but among those who did, response to therapy was similar to that of other exposure groups.”<sup>7</sup>
- \* A sub-analysis of the EuroSIDA study, which included only patients who had baseline and follow-up viral load or CD4 counts, found no difference in response to therapy between IDUs and all other exposure groups. History of drug use did NOT independently predict treatment failure. “Despite our study including a relatively large percentage of intravenous drug users, who are believed to adhere worse when they are outside of drug substitution programs, no differences were found in virologic response depending on transmission category.”<sup>8</sup>
- \* In Switzerland, a study of 100 patients starting any form of antiretroviral therapy at a regional health clinic revealed that psychiatric history and history of drug use did NOT predict poor compliance.<sup>9</sup>
- \* In Spain, a prospective study of 133 patients, 71% of whom were IDUs, found that 58% achieved undetectable viral loads. Compliance rates were lower for IDUs, but only statistically significantly so at 6 months. In general, IDUs had only slightly lower compliance than non-IDUs and enjoyed similar clinical outcomes.<sup>10</sup>
- \* A second Swiss study of patients who were eligible to begin AZT therapy between 1989 and 1992 found that compliance was equal between IDUs and non-IDUs (81.3% vs. 83.2%).<sup>11</sup>
- \* In the United States, a study of 83 patients seen at the HIV clinic of a large public hospital found that on average, IDUs achieved 83% compliance with AZT therapy. A history of recent drug use did not predict poor compliance.<sup>12</sup>
- \* In the United States, a prospective study of 273 HIV patients, many of whom were injection drug users, found that although injection drug use was associated with treatment failure in bi-variate analysis, in multivariate analysis only high rates of missed clinic appointments predicted treatment failure. Thus, while drug use may contribute to higher rates of missing clinic appointments, drug users who are able to keep their appointments enjoy equal outcomes to other patients.<sup>13</sup>

**What Behavioral and Social Factors Influence Compliance to HIV therapy?**

A variety of behavioral and social factors influence patients' adherence to HIV therapy. It is important to understand these factors, as identifying and addressing them before initiating HAART can

improve compliance.

It is also important to realize that many of these factors co-exist with drug use. Thus, the common experience that “drug users do not adhere to therapy” may ignore the confounding effects of poverty, domestic abuse, psychiatric illness, and poor doctor patient communication that characterize many drug users’ lives.<sup>14</sup>

In the United States, a bi-variate, retrospective analysis of African-American HIV patients found five factors to be associated with poor compliance: age, homelessness, number of drug injections in the previous 30 days, trading sex for drugs, and the perception that AIDS is no longer a serious disease due to the development of new antiretroviral medications.<sup>15</sup> None of these factors was an individual predictor. The nexus of all five risk factors suggests that an interaction of complex social and behavioral influences impacts treatment adherence. Identifying one risk factor, like active drug use, and using it to predict treatment failure will not provide accurate clinical guidance.

1. Poor clinician-patient relationship
  2. Active mental illness, in particular depression
  3. Lack of patient education and inability of patients to identify their medications
  4. Lack of reliable access to primary medical care or medication<sup>17</sup>
  5. Domestic violence and discrimination<sup>18</sup>
  6. Medication side effects may also cause poor adherence. More recently, fear of or the experience of metabolic and morphologic side effects of HAART has been associated with poor adherence.<sup>19</sup>
- Factors that are related to poor adherence include<sup>16</sup>**

1. Availability of emotional and practical life supports
  2. The ability of patients to fit their medications into their daily routine
  3. The understanding that poor adherence leads to resistance
  4. The recognition that taking all medication doses is important
  5. Feeling comfortable taking medications in front of other people
  6. Optimal viral suppression<sup>21</sup>
- Predictors of good adherence include<sup>20</sup>**

Although patient self report is a weak predictor of adherence, a patient prediction of poor adherence is a strong predictor of poor adherence and should be taken seriously.<sup>22</sup>

Physician estimation of patient compliance is a poor predictor.<sup>23</sup>

**What specific techniques have been used to increase IDU’s compliance with chronic medical therapies?**

Addressing systematic barriers to care can greatly improve IDU’s adherence to chronic medication regimens like HAART. Specially designed programs, which take into account the needs of vulnerable populations, can often improve adherence to medication.<sup>24</sup> In particular, the incorporation of adherence interventions into convenient primary care settings, the training and deployment of peer educators, pharmacists, nurses, and other health care personnel in

adherence interventions, and the monitoring of clinician and patient performance regarding adherence are beneficial.<sup>25</sup>

In the United States, for example, flexible clinic hours, accessible clinicians, and cash or food voucher incentives led to homeless patients achieving 74% adherence to once daily INH, and to 56% taking potent antiretroviral therapy with adherence of 75% to 85%.<sup>26</sup> Similarly, in New York, a famous study reported only 11% adherence with once daily INH therapy at the Harlem Hospital.<sup>27</sup> Following the initiation of on-site and home-visit supervised therapy, compliance rose to 91%.<sup>28</sup>

### **Are there drug-drug interactions between antiretroviral therapies and recreational drugs?**

There currently are no published clinical studies of HAART in patients who use cocaine. There are basic science studies which look at the effects of cocaine on the cytochrome p450 system, but the

final clinical implications are not clear.<sup>29</sup> Toxicologists at the Hospital Fernandez report never seeing an acute interaction between cocaine and antiretroviral medications.<sup>30</sup> Similarly, toxicologists at the Bellevue hospital in New York City, which offers care to a large number of injection drug users, report never seeing an acute complication of antiretroviral therapy in active cocaine users.<sup>31</sup> Thus, while data are scarce, there is no absolute contraindication to HAART in cocaine using patients.

### **Cocaine**

There are known interactions between opiate drugs and antiretroviral treatments. Most of the data come from published studies of HAART in methadone patients in the United States and Europe. The best documented interaction is between nevirapine and methadone. Nevirapine is known to reduce the level of methadone in the blood. Patients who do not increase their dose of methadone when taking nevirapine experience withdrawal symptoms that are corrected when the methadone dose is increased or nevirapine is stopped.<sup>32</sup> Opiate drugs can also decrease the level of antiretroviral agents in the blood, necessitating increased doses of HIV medicines. The complete listing of interactions is beyond the scope of this summary. If you care for patients who use opiate drugs, refer to the excellent review:

### **Opiates**

Gourevitch MN, Friedland GH. Interactions between Methadone and Medications Used to Treat HIV Infection: A Review. *Mount Sinai Journal of Medicine*; 2000;67(5 & 6)429-436.

There is limited available data about the interaction of marijuana and antiretroviral therapy. Some studies have found a statistically insignificant decrease in the concentration of HIV medications in patients who smoke marijuana, but none have found a clinical impact.<sup>33</sup> Two studies that randomized patients to dose controlled THC cigarettes, dronabinol (THC) capsules, or placebo found no clinical interactions.<sup>34</sup>

### **Marijuana**

There has been at least one reported, nearly fatal interaction between antiretroviral therapies and ecstasy (MDMA) in a patient who was taking ritonavir and saquinavir. It is generally recommended that patients who are taking antiretroviral medication avoid using ecstasy.<sup>35</sup>

### **Ecstasy**

## What are the Current International Recommendations Regarding HAART for IDUs?

International bodies including the United States Department of Health and Human Services, International AIDS Society-USA Panel, British HIV Association, Brazilian Ministry of Health, and the

Spanish AIDS Study Group emphasize the complicated nature of the social factors that influence treatment compliance. All recommend working closely with *all* patients eligible for therapy and emphasize that it is impossible to isolate any single social factor which will lead to non-compliance.<sup>36</sup>

“..[N]o individual patient should automatically be excluded from consideration for antiretroviral therapy simply because he or she exhibits a behavior or other characteristic judged by some to lend itself to nonadherence. Rather, the likelihood of patient adherence to a complex drug regimen should be discussed and determined by the individual patient and clinician before therapy is initiated.”

United States Department of Health and Human Services, Panel on Clinical Practices for Treatment of HIV Infection. Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents.

## Conclusions

Despite a great deal of evidence suggesting that many IDUs are able to adhere to demanding antiretroviral regimens, many clinicians remain hesitant to prescribe HAART to active drug users. In part, this tendency is likely due to misconceptions and stereotypes about drug users. Past experiences suggesting that “drug users cannot adhere to antiretrovirals” may fail to take into account the complex relationship between drug use, poverty, homelessness, domestic violence, and psychiatric illness that affect many substance users’ lives. An evidence based approach suggests:

- Many drug users are able to adhere to demanding antiretroviral therapies.
- HIV positive drug users who are enrolled in continuous treatment with a qualified health professional enjoy clinical outcomes equal to other HIV positive patients.
- Social, behavioral, and clinical factors all influence adherence to medication.
- It is impossible to isolate any single factor as a definite predictor of non-adherence.
- Specially designed programs, which seek to address common barriers to adherence in vulnerable populations, are very successful in delivering new HIV medications to previously underserved communities.
- International health organizations stress the importance of considering the entirety of a patient’s medical and social context in making decisions about HAART.

Adherence to highly potent antiretroviral therapy is critical. Unfortunately, it is often very difficult to achieve. Above all, clinicians must be committed to working with patients to overcome difficulties rather than avoid the problem by simply refusing to offer treatment. If injection drug users are systematically excluded from HAART regimens, the medical community will be failing the very population that is most effected by HIV/AIDS.

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