HELPING ADOLESCENTS WITH HIV ADHERE TO HAART

Acknowledgments

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Finally, the adolescents who struggle with this disease have been the inspiration for this monograph and for our work. Some of them have lost the battle with HIV, but many continue to fight. May this monograph help clinicians increase the number who will win.

Foreword

The purpose of this monograph is to enable clinicians to assist adolescents living with HIV to adhere to the complex regimens of highly active antiretroviral therapies (HAART). The monograph outlines a series of strategies and techniques with which clinicians can tailor antiretroviral regimens to teens' individual requirements, address the obstacles to adherence in their lives, provide them with opportunities to practice medicine-taking behaviors, and give them continuing support when they finally initiate HAART.

These interventions are presented with a sense of urgency because so many young lives are at stake. At the end of 1997 more than 26,000 youth from ages 13 to 24 had been diagnosed with AIDS. The 111,368 reported people with AIDS from ages 20 to 29 comprise 18 percent of the Nation's AIDS cases diagnosed through 1997 and, given the 10-year median time from HIV infection to AIDS diagnosis, most of them were probably infected while teenagers.[1] AIDS statistics are a poor indicator of the current status of the epidemic not only because they represent infections that probably occurred 10 years ago but also because disease progression to AIDS is now being slowed by the use of potent antiretroviral drugs,[2] reducing the number of HIV-positive individuals who develop AIDS. In addition, we know that transmission patterns change over the years. However, the HIV statistics currently available also provide a skewed picture of the epidemic. There are few population-based surveys, and other HIV surveys only represent the subgroup of individuals who have come forward to be tested. While large-scale samples, such as Job Corps applicants and people who seek voluntary HIV testing, tell us that there are indeed adolescents with HIV, they provide only minimum numbers. We think there is a much larger group of youth with HIV and that many adolescents who are HIV-positive have not sought testing and do not know their HIV status.

The demographics of large-scale convenience surveys (for example, applicants to the Job Corps, applicants to the military, and voluntary counseling and testing data) and numerous targeted surveys consistently indicate that HIV seroprevalence is higher among certain populations of youth than among the broader population of youth. Specifically, seroprevalence is higher among economically disadvantaged out-of-school youth;[3,4] African American and Latino youth,[3,5] especially among African American women;[6,7] teens in the rural South

and urban areas, especially in the Northeast;[8,5] homeless and runaway adolescents;[9] and young men who are gay or bisexual.[10]

Adolescents become infected with HIV through both sexual activity and injecting drug use, but they are more likely to have acquired HIV sexually. Drug use is an important factor in much of the sexual HIV transmission in teens; they may have engaged in high-risk sex related to crack use or exchanged sex for money or drugs.[11] In a sample of 50 adolescents receiving care at a New York City HIV clinic, 40 percent had used crack cocaine and 70 percent had engaged in survival sex. Of the girls, 82 percent acquired HIV through heterosexual activity and of the boys, 87 percent reported male-to-male sexual activity.[7] A growing group of adolescents living with HIV is those who were infected perinatally. The cohort of surviving children who were infected at birth in the first years of the HIV epidemic in the United States is now reaching its teens.[12] These young people share many of the same challenges in adhering to HAART as do their peers infected during adolescence.

Thus, statistics demonstrate that HIV experts must be prepared to care for an increasing number of adolescents with HIV in the coming years. Optimal care of adolescents with HIV includes early intervention with HAART. Given that the developmental issues of adolescence challenge the likelihood of successful adherence to HAART, that the social context of many adolescents with HIV is unsupportive of adherence, and that the medical consequences of nonadherence are extremely serious, it is important that adolescents receive assistance in adhering to HAART. Clinicians can improve the odds of youth succeeding by incorporating specific behavioral interventions into their practice and waiting to prescribe HAART to their adolescent clients until they have provided the appropriate preliminary groundwork.

The recommended interventions described here have been developed based on the experience of members of the Adolescent Medicine HIV/AIDS Research Network (AMHARN). They provide specialized HIV care to adolescents with HIV/AIDS in 15 programs throughout the United States. They have learned that with adolescents the impulse to intervene with HAART immediately should be tempered by the reality that teens face unique developmental challenges related to taking these medications. HAART can achieve nondetectable plasma levels of HIV; but, if it is taken sporadically, the virus can rapidly become resistant to the drugs, rendering them permanently ineffective.[13,14] With teens, early

initiation of HAART can result in treatment failure because they often are not yet developmentally or psychosocially ready to begin following the complex medical regimens of HAART. They are confronted with many life challenges that make adherence even more difficult for them than it is for adults.

For youth whose initial decision is not to begin HAART, and for youth who want to take HAART, it is possible to help them overcome barriers to adherence over time in the course of their clinical care. Behavioral interventions can move them toward being ready to begin HAART and can enhance their likelihood of success.

The Stages of Change paradigm developed by Prochaska and DiClemente[15] has been selected as the theoretical construct for the behavioral interventions implemented by the HIV experts of AMHARN. The application of this approach has not previously been studied with adolescent medicine-taking behaviors, but it is now being tested in adolescent AIDS programs across the country through Project TREAT (Treatment Regimens Enhancing Adherence in Teens). The TREAT program, which is based on the same principles of behavior change as the interventions in this monograph, includes an educational, an organizational, and a behavioral component. We encourage clinicians to use the behavioral interventions outlined in this monograph to improve adolescents' likelihood of success in taking HAART.

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1. Background: Creating The Context For Adherence

This monograph presents a series of behavioral interventions to help adolescents with HIV (defined here as young people from ages 13 to 24), overcome the multiple barriers to adherence that they face. Experts caring for adolescents with HIV recommend that this program of interventions be conducted before beginning adolescents on HAART, except under specific circumstances in which rapid initiation is critical or in which youth have demonstrated previous success in following complex medication regimens. The first circumstance for consideration of rapid initiation is in young women who are pregnant, when the likelihood of perinatal transmission can be greatly reduced by the use of zidovudine.[16] The second is in young people who have advanced HIV disease or a high viral load. The third is in acute seroconversion illness, when clinicians have the unique opportunity to intervene before HIV is well established in the body.[17,18] (See APPENDIX A and B for discussions of these clinical situations and the Selected Bibliography for resources for clinical care.)

1.1 Rationale for Early Intervention for Adolescents

Adolescents infected with HIV are a unique population who may obtain particular benefit from early intervention with antiretroviral medications. First, adolescents may have greater capacity than adults for immune reconstitution because of persistent thymic tissue, where CD4+ cells are processed. Second, those who were infected sexually or through injecting drug use are likely to be recently infected and therefore possibly to have less immune destruction from ongoing HIV infection compared to adults. Finally, adolescents who are naive to HAART are less likely to have resistant virus (although there have been documented cases of transmission of resistant virus). Although these factors are under study, and are therefore still theoretical, the argument for the potential benefit of HAART in adolescents with HIV infection is strong. It provides a compelling rationale for clinicians to address the especially challenging barriers to adherence for adolescents by working to enhance their ability to adhere to HAART.

The physical changes of puberty make some aspects of medical management of HIV in adolescents different from management in adults or children. Profound anatomic and physiologic changes are occurring that may affect drug distribution, metabolism, and excretion. During adolescence, sex hormones initiate processes of growth and sexual maturity. Gender-related changes in body

composition occur: girls develop higher proportions of fat; while boys develop higher proportions of bone and muscle mass. The effects of these changes on the pharmacokinetics and pharmacodynamics of drug therapies are not well understood,[19] but it is known that variables such as body composition and endocrine levels affect drug distribution, metabolism, and excretion.

The physiological changes of early adolescence are markedly different from those of late adolescence, so that metabolism of certain medications can vary considerably between a 13-year-old and 18-year-old. Until more is understood about the interrelationships between developmental age and appropriate drug dosage, clinicians must rely on general guidelines in prescribing medications to adolescents. Clinicians can use the drug dosage schedules based on Tanner staging of puberty, selecting pediatric doses for youth who are in Tanner stages I and II and adult doses for those in stages IV and V. They must also closely monitor those in stage III. In terms of the staging of HIV infection by CD4+ T-cell count, the adult normative values should be followed for adolescents until adolescent-specific data are available from the experts of the AMHARN to provide guidance in their treatment. Currently, the majority of the youth with HIV who are in treatment are in their late middle or late adolescence (17 years or older), and thus are in Tanner stage V.[17] (See the Selected Bibliography for resources on assessment and treatment of adolescents with HIV.)

1.2 Challenges of Adherence to HAART

Adherence, or compliance, as it has been termed until recently, can be defined as the extent to which a person's behavior conforms with a medical or health treatment plan.[20] Because people usually adhere to medical regimens less than perfectly, a common indicator of adherence is whether an individual has followed the medical regimen 80 percent of the time.[21] However, levels of adherence have been found to be much lower than that in specific patient populations. For example, in adults under treatment for chronic diseases such as hypertension, the average rate of compliance is 50 percent.[22] Moreover, up to 50 percent of patients under treatment for chronic conditions stop their medicines within 1 year and only 65 percent of those who continue their medicines are sufficiently compliant to achieve the therapeutic benefit.[20,23] Unfortunately, this level of adherence is inadequate and even dangerous for people taking HAART because inadequate dosing has been shown to promote viral resistance to the medications.[17]

Adolescents face the same barriers to adherence that challenge adults, as well as barriers related to achieving the developmental tasks of adolescence.[24] Adolescents living with HIV sometimes are challenged with additional psychosocial issues that affect their capacity for adherence.[25] (See TABLE 1-1 for barriers to adherence.)

The antiretroviral regimens themselves compound the problems of adherence for HIV-positive adolescents. Combination therapy is extremely complicated in terms of scheduling, proper dosing, drug interactions, and potential toxicities. Some drugs must be taken on an empty stomach, while others should be taken with food or specifically with a low-fat meal. Some must be taken at regular intervals around the clock. Certain drugs potentiate or inhibit the antiretroviral activity of other drugs. Treatment requires close monitoring and frequent medication adjustments related to drug resistance and patient toxicities. These factors make adherence to HAART difficult even for most mature adults. Many adolescents find these requirements unrealistic in the context of their lives.

1.3 Teens with Special Issues that Affect Adherence

Many adolescents living with HIV are faced with additional issues that can affect their adherence to medications.[26] Although some perinatally infected teens are asymptomatic, others have developmental delays that may affect their capacity for adherence. Because perinatally infected teens have been in treatment for many years, many have been exposed to a variety of antiretroviral drugs over the years and have few treatment options left, limiting the choice of regimens available to them.

A number of adolescents living with HIV also have parents living with the disease.[27] Some of them were infected perinatally, but others have become infected as teens through sexual activity or intravenous drug use, in neighborhoods where HIV is more common. Youth whose parents are HIV-infected may have experienced the trauma of caring for a parent and, perhaps, of watching that parent die of AIDS. They may have a profound mistrust of the antiretroviral drugs, associating them with the death or illness of a parent.

Many young women who are HIV-infected have children. The challenge of adherence for young mothers is often compounded by the fact that they are managing the needs of a family and do not prioritize to attend to their own health needs in relation to those of their children, especially if their chil-

TABLE 1-1. Barriers to Adherence

Barriers for the general patient population	◎ Complexity of medical regimen ◎ Lack of social support ◎ Adverse effects of treatment ◎ Distrust of health providers ◎ Lack of understanding about the medication ◎ Difficulty coming to terms with a life-threatening illness
Additional barriers for adolescents	The developmental capacities of adolescence can create barriers to adherence. **Early adolescence** ◎ Concrete, not yet abstract, thinking (undeveloped problem-solving skills) ◎ Preoccupation with self and questions about pubertal changes. **Middle adolescence** ◎ Need for acceptance from peers (desire not to appear different) ◎ Present-orientation (decreased ability to plan for future doses and future implications of disease) ◎ Busy, unstructured lives (difficulty remembering to take pills) **Late adolescence** ◎ Establishment of independence (the need to challenge authority figures and restructure regimens) ◎ Feelings of immortality (disbelief that HIV can hurt them)
Additional barriers for adolescents with HIV	◎ For most, fear of disclosure of their HIV status to family and friends ◎ For many, lack of adult or peer support to reinforce their adherence ◎ For youth establishing independence, the conflict between needing to challenge authority figures and needing to depend on adult providers for support in taking HAART ◎ For asymptomatic adolescents, difficulty accepting the implications of a serious illness when they still feel well ◎ For some who still think concretely, difficulty grasping the concept that there is a connection between strict adherence to HAART and prevention of disease progression ◎ For youth who live in the inner city, fear that they will die from violence, not AIDS ◎ For homeless and transient youth, lack of refrigeration or a place to store medicines and lack of a daily routine

dren are also HIV-infected.[16] Caring for a partner with HIV can also be a barrier to care-seeking and treatment adherence for young women.

Adolescents with HIV who are gay, lesbian, bisexual, or transgender may anticipate judgement from clinicians about their sexual orientation. It may be difficult for clinicians to get them into care or to establish the therapeutic alliance that underlies successful adherence.[28] (See Selected Bibliography for sources of information on sexual minority youth.)

Homeless adolescents with HIV include both youth who are living on the streets or in shelters and youth who are functionally homeless (i.e., they have no permanent place to live and stay with different relatives and friends from week to week). Both groups of young people may have difficulty managing adherence because they do not have a safe or regular place to store, much less refrigerate, their medications and have little structure in their lives.[29,30] (See Selected Bibliography for sources of information on homeless youth.)

For young people in the foster care and juvenile justice systems, adherence can be challenging for a number of reasons. They may have concerns about confidentiality in systems in which authorities must store and administer their medications or in which they share living quarters with other youth. If they are transferred from one facility to another, their medical care may be transferred to new providers without continuity or monitoring of their treatment regimens.

Adolescents who come from dysfunctional families may not have a structured routine or support for adherence at home. Moreover, youth who are suffering, or have suffered from physical or sexual abuse may have difficulty trusting adults and, thus, developing a therapeutic alliance with clinicians. Adolescents who have preexisting psychological or substance abuse problems may have behavior problems or cognitive deficits that threaten adherence.[29,31] (See Selected Bibliography for resources on drug use in adolescents with HIV.)

Adolescents who participate in illegal activities, such as prostitution or drug dealing, may have real issues with judgmental providers and special concerns about confidentiality that affect their willingness to access care and their ability to trust their health providers.

1.4 Getting Youth into Care

For some adolescents with HIV, the first challenge in helping them succeed with HAART is attracting them into primary care. Often the most effec-

tive strategy for gaining their trust is to address their immediate needs, which may be as basic as food and shelter.[32] (See Selected Bibliography for resources for outreach and recruitment of adolescents into care.)

Some adolescents will test their providers by making and then breaking contact, then returning to see whether their providers will remain available to them. Engaging them by continuing to reach out and demonstrate nonjudgmental concern is a staff intensive, but often rewarding process. The essential message that this persistence conveys to adolescents is that their providers care about them and about what happens to them. Research regarding factors that contribute to adolescents accessing care indicates that a personal, respectful provider attitude is commonly the most important issue.[33,34]

A particular need for many youth is assurance of confidentiality because of the perceived risks of disclosure related to obtaining care. Teens may require rigorous proof that their confidentiality will be protected before they will engage with their health care providers. Statutes differ by state as to the conditions under which minors can receive health care without parental permission. At a minimum, youth can legally obtain care for sexually transmitted diseases (STDs) and pregnancy without parental permission. In some states, HIV is considered an STD; in others it is not.[35] Providers must know the local laws and work within the bounds of the law to best meet their clients' needs.

1.5 Foundation for Adherence: A Therapeutic Alliance

The therapeutic alliance between the clinician and the adolescent facilitates behavior change toward adherence. Although the concept of therapeutic alliance was developed in the field of psychotherapy,[36] it has been acknowledged as an important aspect of health provider relationships as well.[37,38]

"Therapeutic alliance is a process that emerges within a provider-client interaction in which both the client and the provider are (1) actively working toward the goal of developing client health behaviors chosen for consistency with the client's current health status and life style, (2) focusing on mutual negotiation to determine activities to be carried out toward that goal, and (3) using a supportive and equitable therapeutic relationship to facilitate that goal."[39]

According to some experts, the therapeutic alliance is a necessary precondition and—in fact, the key to the change process—with the outcome of the work a function of the strength of the alliance itself.[37,40,41]

There is a dynamic tension between adolescents' need to establish their independence and their inherent dependence on their clinicians, particularly when those clinicians offer them medicine as potent as HAART. Their need to establish independence sometimes creates the impulse to resist the development of a therapeutic relationship, an impulse that clinicians must work to overcome.[42] The role of clinicians is to support youth in their inevitable transition from childhood through adolescence to adulthood.

With adolescents, clinicians should begin working to establish the therapeutic alliance as soon as they reach out to engage youth in treatment. Given the volatility of adolescents' emotions, the therapeutic alliance must continually be renewed and renegotiated in order to maintain youth in treatment. By remaining empathic and nonjudgmental and by demonstrating concern, respect and caring for them, clinicians, despite being adults and authority figures, can maintain adolescents in treatment as they move through the stages of behavior change.

1.6 Components of Care for Successful Adherence

Successful treatment adherence in adolescents usually requires the support of a range of providers. Engaging adolescents and maintaining them in treatment requires commitment and is staff intensive. Meeting the needs of adolescents with psychosocial problems such as chemical dependency or homelessness is even more demanding. Adolescent HIV clinics usually integrate the work of a multidisciplinary staff, including physicians, nurse practitioners or physicians assistants, nurses, social workers, psychologists, health educators, pharmacists, case managers, and outreach workers. In addition, even a comprehensive adolescent HIV clinic requires a range of community services. The staff must develop reliable sources for referral and develop working relationships with those agencies.[43] (See Selected Bibliography for resources in developing comprehensive adolescent care services.)

The complexity of the problems faced by many adolescents with HIV requires coordination and communication among team members, whether they are all housed at a single site or they are at various locations. Adolescent HIV providers all use some mechanism to achieve effective, regular interdisciplinary communication.

2. Five Stages Of Behavior Change: Interventions To Support Adherence

Learning and adopting the new behaviors required for adherence to HAART can be thought of as a process of behavior change. The Transtheoretical or Stages of Change model for behavior change provides a dynamic set of interventions to assist adolescents in successfully adhering to HAART. This model, developed by James O. Prochaska and C.C. DiClemente,[15,44] has been used to study behavioral change and has demonstrated that there are certain processes that individuals tend to use to help themselves work through the developmental stages of behavioral change. According to the model, individuals move cyclically through a series of changes (see TABLE 2-1) as they adopt a new behavior. An individual's movement is rarely linear; usually the successful adoption of a new behavior happens after at least several cycles through the stages.

The Stages of Change theory of behavior change has been selected as the paradigm for interventions to support adolescent adherence to HAART because of its relevance to what we know about youth. The model uses behavioral interventions to assess and increase young people's readiness to begin HAART and then to support their successful maintenance on treatment. The model is dynamic and process-oriented, adapting well to the fluctuating nature of adolescent attitudes and behaviors. As a framework for assisting adolescents to adhere to HAART regimens, it can assist clinicians to avoid premature initiation of HAART and subsequent treatment failure.

With adolescents, the stages of behavior change are particularly fluid. Teens often do not move progressively through the stages from I to V; rather, they move back and forth among the stages. For example, they can move from the Action stage directly through the Relapse process back to the Preparation stage, where it is appropriate to provide additional support and problem-solving to attempt to resolve the issues that led to stopping their medicine. However, some teens will move even further back, to Contemplation or Precontemplation, where other interventions are needed for them to move forward again. The ultimate objective is to assist them to achieve stage V, Maintenance, and then to provide interventions to support their ongoing success.

At each stage of the behavior change process, specific interventions are helpful in guiding teens toward the next stage. Conversely, other interven-

tions are ineffective because they do not address the state of readiness related to that particular stage. The interventions used to assist teens to initiate and follow a medication regime must be appropriate for their particular stage of readiness.

TABLE 2-1. Stages of Behavior Change

Stage	Definition	Goal	Objectives
Precontemplation	Not thinking about starting HAART	To shift the decisional balance regarding taking HAART from negative to positive	**Assist youth to** ◎ Become aware of the HIV disease process and the potential value of HAART ◎ Understand their personal reluctance to taking HAART ◎ Consider the possibility of taking HAART
Contemplation	Thinking about starting HAART in the next 6 months	To complete the shift of decisional balance regarding taking HAART from negative to positive	**To enable adolescents to** ◎ Assess their psychosocial and behavioral readiness to begin HAART ◎ Enhance their self-esteem ◎ Overcome their misgivings about their ability to adhere to HAART
Preparation	Planning to begin HAART in next 30 days or has made a recent attempt to begin	To maximize readiness to initiate HAART	**To assist adolescents to** ◎ Overcome the barriers and strengthen the supports in their lives for adherence to HAART ◎ Enhance their capacity for adherence ◎ Build skills for taking medicines successfully
Action	Has been taking HAART for less than 6 months	To maintain successful adherence to HAART	**To assist teens to** ◎ Maintain the therapeutic alliance ◎ Continue to solicit the support they need in their lives to remain adherent ◎ Determine and monitor progress toward shared therapeutic goals
Maintenance	Has been taking HAART for 6 months or more	To continue to maintain successful adherence to HAART	**To continue to assist teens to** ◎ Maintain the therapeutic alliance ◎ Continue to solicit the support they need in their lives to remain adherent ◎ Determine and monitor progress toward shared therapeutic goals

When teens say, "I'm not ready to start taking HAART,"

our goal should not be to change their minds, our goal should be to help them *become* ready. That is what the behavioral interventions are designed to do.

In summary, the Transtheoretical or Stages of Change model of behavior change provides a theoretical framework for the application of a series of targeted behavioral interventions to assist adolescents with HIV to adhere to HAART.[45,46] Behavior change toward maintenance of consistent adherence to complex medical regimens occurs in repeated movement through a series of stages that includes Precontemplation, Contemplation, Preparation, Action, Maintenance, though not necessarily in that order, with the ultimate goal of stabilizing in the Maintenance stage.

3. Precontemplation Stage

Most teens who present with HIV infection have no intention of taking HAART in the foreseeable future. They are in the Precontemplation stage of behavior change. They may be unaware or unconvinced that HIV poses a threat to them personally, they may be overwhelmed about the prospects of treatment, or they may feel the disadvantages of treatment outweigh the benefits. They may be unwilling to consider the inconvenience or side effects, perhaps are discouraged regarding their ability to take the medicines successfully, or they may have decided against taking HAART based on stories they have heard about the negative experiences of others. Whatever the reasons, they are convinced that the negative aspects of taking HAART outweigh the positive.

The interventions of the Precontemplation stage are aimed at assisting adolescents to change their attitudes and beliefs about HIV, enabling them to consider taking HAART. While the interventions may precipitate a rapid change, in some cases the move from the Precontemplation to the Contemplation stage may take months or years and may require a precipitating event such as suffering from serious opportunistic infections or seeing friends become ill and die of AIDS. That said, providing youth with clear messages in a supportive and caring environment has the potential of breaking through the resistance that prevents them from taking the drugs that could prolong and enhance the quality of their lives.

3.1 Goal and Objectives

The goal of the Precontemplation stage is to shift the decisional balance regarding taking HAART from negative to positive. The objectives are to assist youth in the following:

- Becoming aware of the HIV disease process and the potential value of HAART,
- Understanding their personal reluctance to taking HAART, and
- Considering the possibility of taking HAART.

3.2 Interventions

The interventions for the Precontemplation stage can be integrated into activities designed for all youth who are living with HIV. Strategies for imple-

mentation of these interventions, which include group and individual activities, are described at the end of this section. Interventions should be selected from the group below to create a treatment plan to address the unique situation of each adolescent.

3.2.1 Provide Basic Information and Dispel Myths About HIV/AIDS and Its Treatment

The first intervention during the Precontemplation stage is to teach teens basic information about the HIV disease process and about how HIV is treated with HAART (see TABLE 3-1). Education, coupled with the second and third interventions (providing opportunities to relate to the experiences of peers living with HIV and to talk about their feelings about HIV), is designed to help them change their attitudes about HIV and HAART. This prepares them to consider taking HAART, thus moving them toward the next stages of behavior change. The information provided should convey the challenges of adherence while also making medicine-taking seem plausible within the adolescent perspective and lifestyle.

The impact of information can be enhanced by the way in which it is delivered. For example, adolescents are much more receptive to information provided by people whom they trust. A strategy to enhancing the impact of information is to convey it through stories (in videos, for example, or in talks by peer educators who describe their own experiences).

Dispelling myths and correcting inaccurate information is an important aspect of this intervention. Determining adolescents' levels of understanding and identifying incorrect knowledge requires sensitivity. Suggested strategies include those listed below:

- Asking direct questions (however, youth are often self-conscious about making mistakes or appearing foolish, so tact is critical if they do not know the answers or provide incorrect answers.);
- Asking what they have heard about HIV or HAART rather than asking what they themselves know about these topics; and
- Asking them to ask questions, which can then be answered correctly.

TABLE 3-1. Topics for the Precontemplation Stage

Information to convey, so that teens' decision whether to begin HAART is based on appropriate understanding of its benefits and limitations	◎ HIV transmission and the silent HIV disease process ◎ The impact of HIV on the immune system (it disables and kills CD4+ cells) ◎ How HAART interrupts the HIV cycle of reproduction ◎ Importance of adherence in preventing development of resistance to antiretrovirals ◎ Complexity of drug regimens
Myths to dispel and misinformation to correct	◎ The longer you take HAART, the more resistant HIV becomes ◎ The medicines will kill you ◎ If you take HAART, you are not infectious to others ◎ The side effects are intolerable

Clinicians should provide information in a manner that conveys acceptance of and respect for the teens' current decision about beginning HAART. It is critical to acknowledge that it is their decision whether and when to take the medicine. Being respectful of their decisions even when disagreeing with them is an important aspect of maintaining a supportive relationship.

3.2.2 Provide Opportunities For Adolescents to Relate to the Experiences of Peers Who Are Infected With HIV

Another intervention suitable for the Precontemplation stage is to provide opportunities for youth to develop empathic responses to other people living with HIV, especially their peers. This can be accomplished through educational sessions with HIV-positive speakers, support group sessions with other adolescents with HIV, and videotaped interviews with people living with HIV. Activities in which they hear the experiences of other young people with whom they can identify, and who have successfully taken HAART, are particularly valuable. The experience can assist them to develop more optimistic outlooks about their HIV disease. (See Internet sites for consumer-oriented treatment information under antiretroviral treatment in the Selected Bibliography for other resources that provide a hopeful perspective on treatment with HAART and HIV infection in general.) Given the importance of peer relationships in the lives of adolescents, input from peers who are taking HAART can be a powerful means for them to consider the possibility of taking HAART themselves and to begin to believe that they could overcome the obstacles of the complex regimens.

3.3.3 Provide Opportunities For Teens to Talk About How They Feel About Having HIV

Another intervention for the Precontemplation stage is to give youth opportunities to express their feelings about being infected with HIV. At this stage they need activities that enable them to share how they feel about being infected and to verbalize their fears and misgivings about beginning HAART. Self-exploration of these issues can occur both in support groups and in individual sessions with medical and mental health clinicians. As they process their responses to what they have learned and heard from others, adolescents may begin to consider new possibilities for themselves.

During this stage, some adolescents continue to believe that they are not infected or that HIV does not pose a threat to them. Although breaking through this attitude is a key element in assisting them to move to the next stages of behavior change, the denial may be a valuable coping mechanism and therefore must be replaced with equally strong supports for survival. Teens who avoid facing the fact that they are HIV-positive may begin to find it safe to acknowledge the reality of their infection and adopt health-seeking behaviors once the window of hope that "there is life after HIV" begins to open.

Adolescent HIV clinics throughout the country include mental health professionals who specialize in adolescent care as part of the team who monitor and provide ongoing support to youth. If this is not possible, it is important to develop close collaboration with community mental health agencies that can provide this component of care.

3.3.3.1 Strategies for Implementing the Interventions of the Precontemplation Stage

Precontemplation interventions can be accomplished in a number of ways that complement each other. These interventions are listed below:

- Individual one-to-one sessions with clinicians;
- Group sessions with peers facilitated by clinicians; and
- Written and electronic educational materials, used individually, with clinicians, or in peer groups.

A combination of individual and group activities is optimal. Group activities provide reality checks by exposing youth to other infected and at-risk

teens, while individual sessions with clinicians enable adolescents to process what occurred in group and to have a safe, more private place to explore their own feelings and ideas.

Examples of individual and group activities facilitated by experts include the following:

- Educational group sessions with presentations by or videotapes of medical experts;
- Educational group sessions with an invited HIV-positive speaker who is taking or who has considered HAART;
- Support groups for adolescents with HIV infection in which they discuss their feelings and opinions;
- Individual sessions with psychologists, social workers, nurses, or physicians in which adolescents learn about HIV and discuss their feelings; and
- Individual sessions with trained peer counselors who can provide information about HIV and share their own experiences with HAART.

Support groups and educational sessions should be facilitated by experienced clinicians for a number of reasons: (1) to correct misinformation that teens may share in the group, (2) to maintain respect for all participants' feelings about their disease and decisions about treatment, and (3) to ensure that youth with intense psychosocial needs do not dominate the group and are referred to other more appropriate services to meet their needs.

Allowing group sessions to be light, with opportunities for socializing and eating, decreases the tension that can develop when discussing difficult topics. Having a mix of adolescents in various stages allows those who are in the Precontemplation and Contemplation stages to hear the experiences of those in Preparation, Action, and Maintenance stages. When there are insufficient adolescents to form a group, asking a teen at a more advanced stage to meet with a teen in a beginning stage can prove useful for both teens, although a clinician should always monitor the interactions for adverse emotional reactions on the part of either young person.

4. Contemplation Stage

Adolescents who are planning to begin HAART in the next 6 months are in the Contemplation stage. Usually they have reached the point of considering HAART but still have misgivings and/or serious barriers that constrain their likelihood of success. While they have become aware that the medicine may be of benefit to them, they are still not certain that the benefits outweigh the disadvantages of taking the medicine. They engage in information-seeking and reevaluate themselves and their abilities in light of what HAART will demand of them.

4.1 Goal and Objectives

In the Contemplation stage, the goal is to complete the shift of decisional balance regarding taking HAART from negative to positive. The objectives are to enable adolescents to take the following actions:

- Assess their psychosocial and behavioral readiness to begin HAART;
- Enhance their self-esteem; and
- Overcome their misgivings about their ability to adhere to HAART.

4.2 Interventions

During the Contemplation stage, interventions become more directly self-exploratory. Interventions achieve the objectives primarily through one-to-one counseling sessions with individual teens, supplemented with group sessions and the use of educational materials.

- **Assist teens in exploring their feelings about taking medicine, HAART in particular.**

  An important intervention during the Contemplation stage is to assist teens in exploring their feelings about taking medicine in general and HAART in particular. Youth should also continue to receive information about HAART, in small repetitive doses. Two excellent formats for these combined interventions are group and individual psychoeducational sessions with clinicians.

  One-to-one sessions reinforce the therapeutic alliance, the culmination of the process that began with engaging youth in care. As a nurse practitioner explained to one young woman, “Think of me as your best friend when it comes to these medicines. We’re going to

do this together." The time invested in this process is critical to the tone and trust needed for all subsequent stages of behavior change. During these counseling sessions, clinicians help youth to confront their personal feelings about HIV infection and its meaning in their lives. They become able to relate this to feelings about their overall health and to their previous experiences with illness and medications.

- **Provide opportunities for teens to identify their own strengths and weaknesses in relation to adherence to medicines.**

  During the Contemplation stage, clinicians help teens understand their own strengths and weaknesses in relation to adherence. TABLE 4-1, Medication Adherence Assessment, contains a number of questions that can guide the discussion. In fact, the Adherence Assessment tool is useful for structuring the next interventions of the Contemplation stage (which assist youth to assess their readiness to begin HAART) and for structuring some of the interventions of the Preparation stage (which assist youth to develop strategies to overcome barriers to adherence). The assessment questions are rarely used sequentially with clients. It is primarily a checklist for determining that clinicians have addressed all the issues related to adherence. However, it can be used to initiate concrete discussions about habits, experiences, and supports for taking HAART.

- **Assist adolescents to examine sources of support for, and barriers to, adherence in their lives.**

  An important intervention at this stage is to assist adolescents to examine barriers and supports in their social and physical environments in relation to their potential to adhere to HAART. Again, the Medication Adherence Assessment is a useful instrument for guiding discussion. Home visits can also provide a very informative assessment of the level of support available in the home environment. The intervention can be accomplished in individual or group discussions using exercises such as the following:

  - **A review of past history** or current experience with other medication regimens, such as PCP prophylaxis, including questions such as, What were the problems you had in taking the pills? Was there anyone who helped you remember to take them?
  - **A hypothetical walk through a typical day** in their lives, and then a second walk through that day adding a specific two- or three-times-a-day medicine regimen that includes refrigerat-

ed medicine, medicine to be taken on an empty stomach, etc. Questions could include the following: What activities do you do everyday? How does your weekend differ from your weekday? What activities do you do every weekend? Who is around, and do they know your HIV status? Where would you put your medicines when you go to (work, school, visit friends)?

TABLE 4-1. Medication Adherence Assessment

Factors That May Influence Decision to Take Medication

Client perception of health status	◎ What is the meaning of the HIV infection to the patient? ◎ What is his or her perception of his or her level of wellness and illness? ◎ What does taking medicine mean to the patient? ⊙ Does he or she believe medicine will help him or her? ⊙ What are his or her past experiences with medicines, including those taken by family members?
Social support network	◎ Who is the most significant person in the patient's life? ◎ Is this person aware of the patient's diagnosis? involved in the patient's care? ◎ With whom does the patient live? ◎ Who in the patient's home knows the diagnosis of the patient? ◎ Who doesn't know? ◎ What is the patient's relationship with the clinic team?
Living arrangements and financial situation	◎ Housing ⊙ Does the patient have stable housing? ⊙ Does the patient have a space he or she calls his or her own? ⊙ Does the patient have access to a refrigerator and a secure place to store his or her medications? ◎ Health insurance ⊙ Does the patient have health insurance that will pay for his or her medications?
Presence of psychopathology and problems with substance use	◎ Does the patient have an active psychiatric diagnosis (e.g., manic depressive disorder, poor impulse control, major depression, suicidality)? ◎ Is the patient an active substance user (e.g., marijuana, alcohol, crack, cocaine, heroin, Valium, Xanax)?
Developmental level	◎ What is the patient's developmental stage? ◎ What are the patient's developmental goals?

TABLE 4-1. Medication Adherence Assessment (continued)

Factors That May Influence Ability to Perform the Work of Taking Medications

Time orientation and organization	◎ Ability to remember recent past ◎ Ability to organize self toward immediate future ◎ Routine organization of activities of daily living both during the week and on the weekend ⊙ What time does the patient awake? ⊙ What does he or she do on awakening? ⊙ Meal schedule, etc. ◎ Future plans and goals
Physical abilities	◎ Visual acuity ◎ Reading ability ◎ Ability to open bottles ◎ Ability to take out correct number of pills ◎ Ability to take pills at the correct time of day ◎ Ability to put pills in mouth ◎ Ability to swallow pills ◎ Ability to follow directions ◎ Ability to prepare medications in advance
Ability to recognize and tolerate side effects	◎ Ability to distinguish between major and minor side effects ◎ Ability to tolerate discomforts of individual medications
Medical regime complexity	◎ Number of pills ◎ Number of doses ◎ Additional directions for dosing ◎ Mechanical actions necessary for preparation (e.g., crushing pills, mixing powder with liquid)

NOTE: This assessment was developed in 1998 by Alice Myerson, MSN, PNP of the Adolescent AIDS Program at the Montefiore Medical Center in New York.

A particularly significant barrier to adherence, and one that needs to be addressed by the end of the Contemplation stage, is lack of disclosure of HIV status to significant people. If teens are living with guardians (parents, foster parents, etc.) or sexual partners (husbands, boyfriends) to whom they have not disclosed, it is unlikely that they can successfully adhere to HAART.

Youth need to have active encouragement from supportive people in their everyday lives, such as parents or close friends, to meet the day-to-day challenges of adherence. These individuals can give them the emotional support of knowing they are not alone and give structured reminders to back up their own good intentions.

Youth should identify the persons whom they can ask to provide daily support in taking their medicines. In the next stage, Preparation, these individuals will begin to participate in the educational sessions the adolescents receive.

- **Provide opportunities for adolescents to conduct risk/benefit analyses in relation to their beginning HAART.**

  The next intervention is to assist teens in conducting risk/benefit analyses regarding HAART. This intervention usually occurs as an informal interactive process during one-on-one sessions with clinicians. Teens are encouraged to weigh the factors they have learned about their own strengths and weaknesses and the supports and barriers in their environment. This should be done in regard to time and energy, convenience, confidentiality, and other effects the regimen would have on their lives. An exercise that can structure and facilitate the process is making two lists, one of the advantages and one of the disadvantages of taking HAART.

- **Provide activities to enhance adolescents' self-esteem and to provide structure and purpose for their lives.**

  Another intervention is to provide teens with experiences aimed at building self-esteem, which can enhance adolescents' ability to take control of their own health, including taking medicines successfully. Interventions used by adolescent HIV clinics include activities that provide teens with an immediate sense of accomplishment, such as learning computer, parenting, or communications skills, and activities with long-term goals, such as making plans to complete high school or to obtain vocational training. One adolescent HIV clinic has developed a series of classes titled Life Directions, which enhances life skills and offers career planning (for information, contact Chris Ambrose, LSW, Children's Hospital of Philadelphia on the Internet at ambrose@email.chop.edu).

  An added advantage of encouraging teens to work or go back to school is that youth who have daily activities are the most likely to feel they can incorporate a medicine regimen into their lives. Encouraging youth to begin new activities can provide them with structure, give them a sense of self-worth, and provide reasons for them to look toward a real future for themselves.

  According to a provider: "Teens who have somewhere to go every day (school or work) are more likely to succeed in taking their

medicines regularly. We work with real basics, such as motivation to get out of bed. Help with self-esteem. Reminders that they **do** have choices."

- **Provide experiences aimed at enhancing teens' ability to take control of their health.**

  An intervention that has successfully enhanced teens' ability to take control of their own health is to train them to become consumer advocates and peer educators. The knowledge that they gain from this type of training, coupled with the self-confidence they develop as they begin to speak before groups and receive the esteem of their peers, enables some adolescents to have a much stronger belief that they can and should take control of their own health. Thus, programs that provide peer education to adolescents can help the peer educators themselves strengthen their capacity to adhere to HAART. (However, clients who become peer educators also need special support. When they become role models for adherence to HAART, they may face added emotional turmoil and guilt if they themselves fail to adhere.)

4.3 Making the Decision Whether to Initiate HAART

After completing the interventions for the Precontemplation and Contemplation stages, adolescents and clinicians jointly decide if the youth is ready to begin treatment and therefore to move on to the Preparation stage, where he or she will prepare to select and begin a HAART regimen. (See TABLE 4-2.) To move forward, adolescents should be concretely aware of the challenges of HAART, have a good idea of the problems they will encounter and the supports that exist in their lives, and possess a positive attitude about their ability to succeed with HAART.

In theory, adolescents who are below the age of majority are still dependents, and decisions should be made with their parents. In practice, however, adherence by adolescents will not occur without their full participation; it is critical that the processes of assessing their readiness and determining whether and when to initiate treatment focus on them, not their family members. Treatment decisions are most effectively made in frank, open discussions between providers and teens. If the family is available and involved, a family meeting can be a useful way to include others besides the youth in the decisionmaking and in the teaching.

On the provider side, treatment decisions are best made with the input and participation of the entire treatment team—people from various disciplines who are working with the adolescents. This provides the widest perspective on all the relevant factors, including not only physical condition and immune status, but also psychological strengths and weaknesses, social support systems, home environment, and beliefs and knowledge about HIV and HAART. The process of working toward consensus will also help refine the treatment plan.

TABLE 4-2. Factors to Consider in Deciding Whether to Initiate HAART

- Willingness of the individual to begin therapy
- Degree of existing immunodeficiency as determined by CD4+ T-cell count
- Risk for disease progression as determined by the level of plasma HIV RNA
- Potential benefits and risks of initiating therapy in asymptomatic persons
- Likelihood, after counseling and education, of adherence to the prescribed treatment

SOURCE: U.S. Department of Health and Human Services. (1998). Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. *Morbidity and Mortality Weekly Report,* 47(R-55):43-91.

Often the final decision is made after weighing a list of advantages against an equally long list of reasons a teen is not ready to begin HAART. For example, with youths who are somewhat motivated, but unsure about taking HAART, the question may arise as to whether the family issues that have already prevented them from disclosing their HIV status to their parents are sufficient to sabotage their adherence.

When youth are assessed as not ready to begin HAART, most providers in adolescent HIV clinics choose to follow the dictum, "First, do no harm." Given the long-term harm if HAART is not taken properly, they argue that it is best not to risk treatment failure by initiating HAART prematurely. Instead, they prefer to continue to expose teens to the behavioral interventions of the Precontemplation and Contemplation stages, hoping to assist them to progress toward being more likely to successfully adhere. Other providers, however, because of the expected clinical benefits of early intervention, feel they must push to begin treatment as early as possible despite the likelihood of nonadherence. This strategy has sometimes worked and sometimes failed.

Frequently, it is the adolescents who decide they are not ready to begin HAART, and their providers attempt to change that decision. This is a time when clinicians need reminders that ultimately the decision belongs to the

youth. Listed below are some recommended strategies for providers in this situation:

- Remember that adolescence is a time of flux: Consider that a youth's decisions, no matter how adamant, may be temporary and subject to change;
- Respect youth's positions and accept their current decisions, but continue to address the barriers to adherence through supportive, not coercive, interventions; and,
- Be aware that it may take a dramatic wake-up call, such as an opportunistic infection, or the death of a friend to AIDS, to convince an adolescent to begin treatment.

5. Preparation Stage

Adolescents in the third stage of behavior change, Preparation, have reached the point of seriously considering taking HAART and plan to start within the next month. The decisional balance has shifted for them, and they feel the advantages outweigh the disadvantages of HAART. They have gained insight into the challenges of adherence and are ready to address them. They have examined their past experiences and are ready to set goals and priorities. During Preparation, youth cement the therapeutic alliance as they work with clinicians to achieve their goals.

While the Preparation stage may seem arduous, the experience of the clinicians at the AMHARN adolescent HIV clinics supports the value of these interventions. These experts have learned, sometimes through tragic trial and error, that "it doesn't work any other way." They have seen many adolescents become resistant to the most potent medicines before they were able to incorporate the routines of medicine-taking into their lives. They recommend that clinicians take the time required to implement the interventions of the Preparation stage. Doing so can maximize the likelihood of success on the first try when administering these powerful and expensive medications to adolescents.

5.1 Goal and Objectives

The goal of the Preparation stage is to maximize readiness to initiate HAART. The objectives are to assist adolescents to do the following:

- Overcome the barriers and strengthen the supports in their lives for adherence to HAART;
- Enhance their capacity for adherence; and
- Build skills for taking medicines successfully.

5.2 Interventions

The interventions of the Preparation stage involve intense collaboration between clinicians and teens in examining and perfecting adherence strategies and in practicing medicine-taking skills. Much of the work is in one-to-one clinical sessions, backed up by continued supportive activities with other teens. Clinicians determine which of the following interventions are appropriate

for each adolescent, and then tailor their approach to meet the needs of each individual adolescent.

- **Select regimens appropriate to teens' needs.**

  Once a clinician has determined potential regimens, the next step is to select in conjunction with the adolescent which regimen is most appropriate for that individual. Youth should be provided with the opportunity to become familiar with the drugs and consider whether the specific medicines are feasible for them. Not only do teens have individual requirements for what is acceptable in terms of taste, schedule, size and number of pills, they also have a need to feel in control of what is happening to them. Offering options, or at least asking whether the recommended regimen is acceptable, can avert the use and subsequent failure of a powerful regimen that a particular teen finds personally impossible. In short, adolescents should be consulted in making the final decision about what drug regimen is best suited for their lifestyles.

  Incorporating pill-taking into an established lifestyle is difficult. Manipulating medication schedules to fit adolescents' social and physical environments is more successful than adjusting teens' lives to accommodate their medicine-taking. Some experts feel that twice-a-day regimens have the best potential for success with adolescents, who can then take them at home, before they leave in the morning and after they return in the evening.

  Some examples of typical considerations are shown below:

  - Planning how they will manage to take medicines without being seen by people to whom they have chosen not to disclose (schoolmates, work colleagues, or family members);
  - Scheduling pill-taking to coincide with regular activities such as eating breakfast or brushing teeth; and
  - Rejecting a regimen with medicine(s) that must be refrigerated if no refrigeration is available to the youth for the midday dose when she or he is at school.

- **Provide opportunities for adolescents to become familiar with the medicines.**

  The next intervention is to provide opportunities for teens to become familiar with the selected regimen. Clinicians can use a

variety of strategies, some of which are listed in TABLE 5-1, Becoming Familiar with the Drugs.

TABLE 5-1. Becoming Familiar with the Drugs

Activity	Advice
Tasting and swallowing the pills	Let them taste the powders (says one clinician, "I won't prescribe DDI unless they taste it first"). Have them try it with chocolate syrup to mask the flavor. Let them swallow vitamins equivalent to the sizes of each pill. You may discover a pill is too big for the youth to swallow.
Handling and pre-pouring the pills	Have them count out the various pills in the regimen to see how many are taken, how many times a day; show them how to fill a 7-day medicine box. Give them a change purse with a day's supply that they can always carry with them: many young people are impulsive and should expect to change their plans suddenly. (Suggest to sexually active youth, "It's like carrying condoms—you always need to be ready.")
Scheduling	Work the timing of pill-taking into regular activities of the day, such as brushing their teeth or taking a shower. It's important not to arrange the day around the pill-taking. The medicines should be "deemotionalized" and should not rule their lives. BID regimens are strongly preferred.
Providing choices	Optimal regimens should be selected by the health care team. Then the youth and health care team decide which regimen to use. Some youth may require a regimen that is not the clinical first choice, but is acceptable in terms of size, number of pills, or number of doses per day.
Being creative in setting up individualized systems	Different people have different issues. Concrete thinkers need mechanical systems they can learn by rote. Impulsive youth need regimens that minimize the number of doses and require minimal preplanning and coordination with food.
Providing teaching materials	Provide them with diagrams or pictures of the regimens.

Ample time should be set aside to review the regimens, to practice setting out the pills, and to observe that the youth correctly understand the regimens they are to take. Clinicians should know the pills by sight in order to be able to discuss them graphically with the youth, who may or may not learn the names. During this process, opportunities should be provided for the youth to discuss their misgivings and fears and to ask all their questions regarding treatment.

Many adolescent HIV clinicians find it useful to arrange a series of teaching sessions with the medications at hand: at least two ses-

sions in which the adolescent and clinician can complete the activities listed in TABLE 5-1. This time can also be used to introduce information about the dosing requirements and possible side effects, as well as to show teens how to fill the 7-day medicine container.

One of the challenges facing clinicians as they instruct adolescents about medicines is to make certain the youth understand the instructions correctly. In order to avoid misinterpretation it is important to write down the doses explicitly, and, better yet, to draw pictures of the pills. One young man interpreted "Take three in the morning" to mean, "Take one pill at 3 a.m.," and returned to the clinic a month later having been seriously under-medicated. TABLE 5-2, Sample Worksheet for Weekly HAART Regimen, is a chart that can be used to write out or diagram the dosing schedule and that allows for different times on different days such as on weekends. Some pharmaceutical companies have developed teaching tools such as charts with stickers representing the various antiretroviral drugs to be placed in spaces for the time of day at which doses are to be taken.

In some adolescent clinics, adolescents fill their prescriptions at private pharmacies and return to the clinic for instruction and practice sessions. In other situations, adolescents fill their prescriptions and a nurse makes home visits for instruction and practice, providing the appropriate containers at that time. In one clinic, all the practice sessions occur in the clinic using drug samples, and the adolescent has an opportunity to consider several alternatives, even tasting the liquid medicine, before deciding on an acceptable regimen and receiving the first prescription. Whatever the scenario, a vital element in all cases is to have the adolescent wait to take the medicines until the clinician and adolescent agree that he or she is ready.

- **Assist adolescents to strengthen reinforcement for adherence among their family and friend support systems.**

  An important intervention during the Preparation stage is to assist adolescents to strengthen the reinforcement they receive from their family and friends. If possible, youth should identify a specific individual who can attend practice sessions, learn about the medicines with them, and then agree to remind them to take their medicine. They need a person who can provide them with day-to-day support and in whom they can confide information about their

TABLE 5-2. Sample Worksheet for Weekly HAART Regimen

Name of drug, dose, and number of pills	Times of day to take the medicine						
	MON	TUES	WED	THURS	FRI	SAT	SUN
	[write time of each dose]						

Special instructions: [food, water, other medicines]

progress. For youth who do not have such a person, a member of the clinical staff may offer to be that person and can ask the youth to call and check in by telephone.

A home visit by a provider can sometimes assist adolescents in reinforcing helping relationships they may have at home. For example, a visiting social worker might negotiate a pact between a teen and a grandparent who takes heart medicine to talk to each other every night before bedtime and remind each other to take his or her medicines.

Maintaining the continued reinforcement of peer support is also useful during this stage, particularly to remind youth that others can and do integrate HAART into their lives. Peer support groups or social activities with other HIV-positive young people are the best mechanisms to provide interaction with teens successfully taking HAART. However, presentations or videotaped interviews with people discussing their experiences with HAART can also be useful.

- **Structure mechanisms for teens to practice medicine-taking behaviors at home.**

  After adolescents have selected their drug regimens, enlisted support persons, addressed environmental barriers, and strengthened environmental supports, they need to practice the behaviors required to take the medicine in as realistic a setting as possible. The best way to do this is by going through a week-long trial run using proxies for the actual medicines. Simulated drug-taking often identifies additional barriers that are better addressed before rather than after the actual medication regimen has begun.

  For a simulated regimen, proxies such as vitamins or different colored jelly beans are used to represent the various pills in the regimen. The numbers of pills in the trial run must equal the number of pills in the proposed HAART regimen. Instructions for the surrogate regimen should be the same as the instructions for the antiretrovirals (e.g., dosing times, fluid and food requirements, and refrigeration requirements) and should be clearly communicated to the youth, both verbally and in writing. (See TABLE 5-2 for a sample medication table, which allows for times to be varied according to the activities of each specific day of the week.) They then fill a pill container with a week's supply and follow the prescribed regimen for an entire week.

Advice from an HIV-positive girl. **I find the doses I have to take during the day are the hardest to manage: when I'm away from home, either at school or hanging out with friends. My HIV status is my own private business and I have the right to control who knows and who doesn't. You need to have a plan developed ahead of time so you don't give away your HIV status without meaning to. Having a story ready works best for me. I carry my medicines in a Tylenol bottle and say I have a headache. I know somebody who says he has asthma and has to take medicine to help him breathe.**

When they return to clinic a week later, they review their experiences (successes and difficulties they encountered). Were the frequency and particular dose times okay? Did they bear total responsibility or did someone provide reminders or other support? The purpose of the debriefing is to reevaluate the youths' environment and skills using their experience from the week of practice. The next step is to plan strategies to overcome the barriers to successful adherence they have identified. On the other hand, if the trial run was completely unsuccessful, perhaps the selected regimen was ill-advised and should be replaced with another. Alternatively, the youth may need more time at an earlier stage of behavioral intervention. Some youth become discouraged after an unsuccessful rehearsal and begin weighing the negative aspects of medication-taking more heavily than the positive aspects. Such a situation demands the utmost in caring and nonjudgmental support from clinicians, with calm reassurance that "this happens all the time; I will be here for you; we will work this out."

Making Home Visits. **Some adolescent HIV clinicians have found home visiting to be critical in supporting adherence to HAART. During the Preparation stage, a home visit may be useful to do the following:**

- **Assess the home environment, including familial supports and barriers;**
- **Reinforce helping relationships;**
- **Teach the family the importance of adherence to HAART and/or teach the actual medicine regime; and**
- **Check that the medicines and dosages on the labels are correct and that the correct medicines have been dispensed (for adolescents who have not brought their medicines to clinic).**

Using Physical Devices. **Three physical devices have been developed or adapted to assist patients in taking medication:**

- **Multichambered plastic medicine boxes, with slots for four doses of pills a day for 7 days, are usually easy to obtain from drug stores. Some clinics purchase them in bulk in order to have them available when clients come to clinic; others depend on home health agencies to provide them to clients;**
- **Timers, either attached to medicine containers or sold separately, help teens to remember when to take their doses, especially during the day when they are busy and apt to forget;**
- **Small containers can be used for a day's supply of pills when out in the community.**

5.3 Outcomes of the Preparation Stage

The youth should have the following materials before progressing to the Action stage (initiating the regimen):

- A table listing the daily doses of the regimen, in words, diagrams, or both (see TABLE 5-2);
- Medicine containers appropriate to their individual needs (for example, a compartmentalized box that holds a week's supply of medicine; a box with a timer for a day's supply); and
- A supply of the medicine that has been checked by a clinician for accuracy.

A home assessment may reveal much that would not otherwise have been picked up in the clinic. For example, an adolescent with a supportive family had filled his or her prescription, had reviewed his or her medicines, had practiced pouring a week's supply in the clinic, and was about to start on his or her treatment regimen. However, a home visit showed that the household was more disruptive than the staff had thought. Staff then reconsidered with him or her whether he or she needed more supports in place before beginning the regimen.

Sometimes home visits are not possible (for example, in order to maintain a teen's confidentiality in a group home). Other situations can be arranged, such as having them come into clinic with their pills or meeting them in a coffee shop near their homes. One young person's family knew he or she was on HAART, but he or she was too embarrassed to have a nurse visit his home and refused a home visit. Instead, that person agreed to meet the staff person at a nearby diner with his or her bag of pills.

6. Action And Maintenance Stages

Adolescents begin the Action stage of behavior change as soon as they begin taking the actual medicines. When they have continued successfully on HAART for 6 months, they have reached the Maintenance stage of behavior change. In these stages, youth do modify their behavior, change their experiences, and continue to manipulate their environments to overcome problems that arise. They have the necessary skills to maintain the behavior and are aware of the pitfalls that can undermine continued effective action. They develop strategies to prevent lapses from becoming complete relapses. During these stages the likelihood of either internal or external factors precipitating a "drug holiday" always exists. Adolescents continue to need supportive interventions.

6.1 Goal and Objectives

The goal of the Action and Maintenance stages is to maintain successful adherence to HAART. The objectives are to assist teens to do the following:

- Maintain the therapeutic alliance;
- Continue to solicit the support they need in their lives to remain adherent; and
- Determine and monitor progress toward shared therapeutic goals.

6.2 Interventions

The interventions of the Action and Maintenance stages provide encouragement and support to adolescents taking HAART while closely monitoring their adherence and the effectiveness of their treatment. Clinicians must continue to actively engage adolescents during these stages.

- **Maintain regular contact with adolescents,** even between clinic appointments.

  A critical intervention in the Action and Maintenance stages is to maintain regular contact with adolescents. Teens should be scheduled to return to clinic every few days to 2 weeks, depending on the clinician's level of concern about adherence. Once it is certain that the regimens are being taken correctly, monthly visits are appropriate for most teens, with longer intervals only in exceptional cases. Scheduling consecutive appointments with two or more

providers (physician, social worker, etc.) can reduce the number of trips required. If possible, an outreach worker, social worker, or home care nurse should make home visits periodically to reassess the situation. Home visits can provide important information regarding not only the family situation, but the medicines; for example, they are an opportunity to check when the prescriptions were last filled and how many are left in the bottle.

In addition to formal health care visits, other contact is needed to provide teens with support on an interim basis. Agreed-upon mechanisms for checking in every week or 2 will prevent small problems from becoming large ones that begin to erode the youth's resolve and belief in self-capacity for adherence. Telephone calls, drop-in home visits, birthday cards, and invitations to support groups and clinic activities are all ways to actively reach out to adolescents and let them know that their health providers care how they are doing.

According to teens themselves, one of the most important factors in motivating them to take their medicines is whether they feel their providers are concerned.[33] This is expressed not only in their clinician's manner during consultations, but also in consistent contact, direct questions regarding teens' adherence, and respectful problem-solving when they lapse.

A clinician describes one clinic's process: "We begin with an intensive 2-week start-up that includes home visits. We have found that the best predictor of long-term adherence is initial adherence. In assessing a teen's adherence, we give her permission to admit that it hasn't worked. We ask, "how many times have you missed?" rather than "Have you missed any doses?" We ask, "How many times did you take your pills yesterday and the day before?" rather than "Have you been taking your pills regularly since the last time I saw you?"

- **Encourage teens to continue to solicit support from friends and family for taking HAART.**

  An ongoing intervention of the Action and Maintenance stages is to encourage adolescents to continue to solicit support from friends and family for taking HAART. In addition to regular contact with their providers during these stages, they also need activities to ensure peer support and continued reinforcement. Continued clinic-based peer activities such as educational sessions, support groups,

and social events help teens to maintain a sense of belonging and counteract the sense of isolation they may experience because only a few people know their HIV status.

For some adolescents, it may be appropriate to encourage additional social involvement by inviting them to participate in consumer advocacy activities, such as Consumer Advisory Boards, in educating other teens about HIV, as speakers in workshops, or as peer counselors for HIV-infected adolescents in earlier stages of behavior change. Although this level of activity might be an additional pressure for some teens, for others it can be an opportunity to become more empowered and to increase self-esteem, thus contributing to successful adherence.

- **Enlist the collaboration of adolescents in monitoring their progress.**

  Close monitoring of adherence and clinical progress is an essential intervention with adolescents. It is important to develop a collaborative process for this so teens do not feel that monitoring is a one-way process, with the clinician checking up on them. Specific strategies and techniques can be used to sensitively and respectfully monitor the accuracy and consistency of pill-taking. Some suggestions are included in TABLE 6-1, Strategies for Monitoring and Supervising Pill-taking.

TABLE 6-1. Strategies for Monitoring and Supervising Pill-taking

ACTIVITY	ADVICE
Recall of pill-taking	Adolescents should be asked about their adherence in a nonthreatening way that acknowledges the possibility or probability of missed doses. The time frame with the shortest period of recall is the best to ask about: "How many times did you take your pills in the last 3 days?" is better than "Have you taken your pills every day for the past 2 weeks?"
Demonstration	Adolescents should be asked to demonstrate what pills are taken each day, when, and under what conditions (on an empty stomach, etc.) to assess whether they remember and still understand the regimen.
Pill counts	Whether youth bring their medicines into the clinic or a home care nurse visits them in the home, the number of pills left in the bottle should be counted to determine whether the correct number has been taken so far. Counting the empty spaces in the medicine box can also gauge the accuracy of pill-taking.

Checking on refills	Various methods can determine whether their prescriptions have been refilled: call to remind them to contact the pharmacy; arrange for the youth's support person to call and check; with the youth's permission, have the pharmacy report to the clinic if the prescription is not refilled.
Praise for success	Adolescents need to be praised for their efforts and for each of the successes they have achieved. It is good to enumerate the problems they have managed to overcome and to identify each achievement individually.
Correction of mistakes	When mistakes regarding the regimen are identified, they need to be corrected matter of factly and clearly. However, at the same time, the adolescents' self-esteem must be supported through assurances that mistakes are commonplace and acknowledgment that the regimen is difficult to follow.
Identification and addressing of barriers to adherence	Youth should continue to be asked what barriers they have encountered in taking their pills. Ample time should be allowed to discuss the problems and to identify solutions.

- **Assist adolescents to develop strategies for resolving lapses.**

  When youth have successfully reached the Maintenance stage, it is time to give praise, but not to lessen vigilance. An effective intervention that acknowledges the very real possibility of adolescents taking "drug holidays" is to assist them to develop strategies for resolving lapses. (A lapse is a temporary interruption of medicine that may not require stopping a selected regimen, whereas a relapse is a complete cessation in taking medicines that requires both changing regimens and going back to an earlier stage of behavior change.) Adolescence is a time of turmoil and upheaval, and many events can occur in young peoples' lives that disrupt consistent medicine-taking. Moreover, it is developmentally normal for teens to experience drastic shifts in their perspectives, beliefs, and goals. According to one seasoned physician, "For teens, changing their minds is as natural as 2-year olds having temper tantrums." Clinicians should anticipate that the upheavals will occur and encourage their young clients to seek their assistance when experiencing untoward events or shifts in priority. This may result in short breaks in medicine-taking that can be reversed rather than in cessation of the regimens.

  Clinicians should expect adolescents to move between the stages of behavior change. For example, during the Preparation stage, as the process of taking medication becomes more concrete to teens, they

may become overwhelmed or decide that it will be too much trouble, and move back to the Precontemplation stage.

Mitigation of guilt is as important as provision of praise. Youth require assurance that failure to take the medicines does not mean that they are bad or failures as persons. In assessing the reasons for the relapse, an up-beat attitude is needed to sustain their motivation to continue rather than to give up. ("Let's look at what else we can try" rather than "The regimen you just stopped was the best one, and now there are no good options left for you.") The key is to stress successes and to diminish failures.

7. The Process of Relapse

At some point during treatment, it is common for youth to stop adhering to HAART, which puts them in Relapse behavior. When this happens, sensitive and tactful responses are critical in order to mitigate the serious medical consequences while alleviating guilt and anxiety. The clinician's role is to assist them to transition back to an earlier stage of change as smoothly as possible and to initiate the interventions for that stage. They can then begin progressing forward through the stages again with the objective of once more becoming able to successfully initiate and adhere to a HAART regimen.

Because relapses increase the probability of drug resistance and future treatment failures, they are particularly discouraging events for youth. The frequency of relapse among teens is such that the idea of a relapse event is introduced in the Action and Maintenance stages in order to prepare them for the possibility and to stress the importance of contacting the clinical team for help in restarting.

Relapse is observed so frequently that it can be viewed as an expected part of the process through which teens ultimately achieve successful adherence.

A provider gave this advice: "We must be patient with the kids. We need to push, but we also must be forgiving. They want so much to not disappoint us. It's so awful for them when they fail. We have to figure out how to validate them no matter what they do."

7.1 Goal and Objectives

The goal of interventions during a relapse is to mitigate the extremely serious consequences of the interruption of treatment. The objectives are to assist adolescents to take the following actions:

- Restore self-efficacy; and
- Renew the effort to successfully begin HAART.

7.2 Interventions

Clinicians should move through the Relapse interventions as quickly as possible without causing alarm. Becoming settled in another stage of behavior change and establishing new therapeutic goals can contribute much toward

assisting the teen in reestablishing a sense of security and optimism after having relapsed from adherence.

- **Dispel guilt and restore self-esteem.**

  The first and most immediate Relapse intervention is to work with teens to dispel guilt and restore self-esteem by assuring them that relapse is a common occurrence and that nearly everyone has problems adhering to HAART. A careful balance of clinical concern and personal sensitivity is demanded. Clinicians should help youth understand the seriousness of nonadherence and its consequences, while conveying that what is being asked would be exceedingly difficult for anyone. It is useful to stress that we all learn more from our failures than our successes and to recast the event as a learning experience.

- **Work with adolescents to assess the cause of the relapse.**

  The next intervention is to work with adolescents to examine the circumstances that contributed to the relapse. It is important not to reflexively instruct the youth to restart the medication. Together, the clinician and the teen must identify whatever changed the decisional balance from "pro" to "con" and caused the youth to abandon the regimen.

  Clinicians should explain that they want to help youth to understand what happened in order to address the factors that made adherence difficult. This team approach helps to convey the message that they do not have to struggle with this challenging task alone, that they are being supported and that their providers do not intend to give up on them. For some teens, an exercise such as keeping a diary related to pill-taking for 3 days may help them to concretely identify the constraints that caused the relapse. For others, the constraint may be obvious and need no exploration, for example, a change in daily routine caused by getting a new boyfriend or dropping out of school.

- **Assist adolescents to determine the current stage of behavior change.**

  Clinicians then assist adolescents to determine their current stage of behavior; clinician and teen work together to establish new and appropriate therapeutic goals. The youth can then begin to progress again through the stages.

The factor causing the relapse may turn out to be side effects or a scheduling problem, and the youth may simply need his or her regimen or schedule adjusted to reinitiate therapy. However, sometimes it is a life circumstance that is much more serious or complex. If an adolescent is anxious to try again, he or she may be able to transition back to the Preparation stage, where he or she practices the skills related to medication-taking. On the other hand, if the adolescent has decided that his or her lifestyle does not support taking HAART, perhaps clinicians should consider using the interventions for the Precontemplation stage to again assist the youth to move forward. If this is the case, clinicians may be the ones requiring reassurance, in order to resolve their sense of urgency for the youth to restart HAART immediately. They can remind themselves that during adolescence everything is in flux. A decision made today is for today, and tomorrow's decision will very likely be different.

- **Work out a mutually agreed-upon plan to facilitate renewed progress forward.**

  The final intervention during the Relapse stage is for clinicians and the youth to work out a mutually agreed-upon plan to facilitate renewed progress. They should review the interventions that were helpful the first time around and discuss ways to use those interventions again. The therapeutic alliance is even more important now in assisting youth to overcome the obstacles that caused the relapse. The fact that their clinicians have maintained confidence in them and continue to support them assures adolescents that they will not be abandoned, whatever the outcome.

  That said, we also know that many adolescents will be unable to follow the HAART protocol, despite intense preparation and support. Some will never start treatment; others will fail treatment as a result of nonadherence. However, we must underscore their successes, maintaining optimism no matter how many times adolescents relapse. Their next try may be the breakthrough.

8. Recommendations For Assisting With Adherence To HAART

This series of behavioral interventions is presented because adolescents with HIV are much more likely to succeed in adhering to HAART if they have appropriate assistance. Adolescents living with HIV face a series of challenging barriers related to taking HAART. To begin with, they share with adults the potentially stigmatizing diagnosis of HIV and the inherent complexities of the HAART regimens. As teenagers, they tend to feel immortal and want to establish their independence, feelings that compete with the demands of medication adherence. Many adolescents with HIV have additional circumstances, such as homelessness, addiction, motherhood, or struggles with sexual identity that complicate their life situations and can sometimes make adherence to HAART nearly impossible. Therefore, clinicians require many tools besides the prescription pad to effectively treat HIV-infected youth. These include the ability to establish therapeutic alliances and to work collaboratively with youth, a team of clinical and community-based providers and services and the time to teach, support, and encourage adolescents as they struggle with the barriers to adherence in their lives.

The following keys to assisting adolescents with HIV to adhere to HAART are recommended:

- Taking the time to guide adolescents through the interventions of the Stages of Change process;
- Initiating HAART only when they are psychosocially ready; and
- Providing ongoing maintenance and support.

Even then, the vagaries of the adolescent psyche will limit the success rate we are able to achieve in maintaining adolescents on HAART. However grim the prospects may appear, the reality is that adolescents have an energy and a resilience that may very well tip the scales in their favor. Clinicians have the responsibility to give them the chance to overcome the odds and win the battle with HIV no matter how many tries it takes.

References

1. U.S. Department of Health and Human Services. *HIV/AIDS Surveillance Report: U.S. HIV and AIDS cases reported through December 1997.* Year-end edition 9(2). (GPO 1998-637-090/60239). Washington, DC: U.S. Government Printing Office.

2. Detels R, Munoz A, McFarlane G, et al. (1998). Effectiveness of potent antiretroviral therapy on time to AIDS and death in men with known HIV infection duration. *Journal of the American Medical Association,* 280:1497-1503.

3. Conway GA, Epstein MR, Hayman CR, et al. (1998). Trends in HIV prevalence among disadvantaged youth. *Journal of the American Medical Association,* 269:2887-2889.

4. Valleroy LA, MacKellar DA, Karon JM, Janssen RS, and Hayman CR. (1998). HIV infection in disadvantaged out-of-school youth: Prevalence for U.S. Job Corps entrants, 1990 through 1996. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology,* 19:67-73.

5. St Louis ME, Conway GA, Hayman CR, Miller C, Peterson LR, and Dondero TJ. (1991). HIV infection in disadvantaged adolescents. *Journal of the American Medical Association,* 266:2387-2391.

6. Rogers AS, Futterman D, Levin L, and D'Angelo L. (1996). A profile of human immunodeficiency virus-infected adolescents receiving health care services at selected sites in the United States. *Journal of Adolescent Health,* 19:401-408.

7. Futterman D, Hein K, Reuben N, Dell R, and Shaffer N. (1993). HIV-infected adolescents: The first 50 patients in a New York City program. *Pediatrics,* 91:730-735.

8. Burke DS, Brundage JF, Goldenbaum M, et al. (1990). Human immunodeficiency virus infections in teenagers. *Journal of the American Medical Association,* 263:2074-2077.

9. Pfeifer RW, and Oliver J. (1997). A study of HIV seroprevalence in a group of homeless youth in Hollywood, California. *Journal of Adolescent Health,* 20:339-342.

10. Katz MH, McFarland W, Guillin V, et al. (1998). Continuing high prevalence of HIV and risk behaviors among young men who have sex with men: The Young Men's Survey in the San Francisco Bay Area in 1992 to 1993 and in 1994 to 1995. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology,* 19:178-181.

11. Heffernan R, Chaisson MA, and Sackoff JE. (1996). HIV risk behaviors among adolescents at a sexually transmitted disease clinic in New York City. *Journal of Adolescent Health,* 18:429-434.

12. Kuhn L, Thomas PA, Singh T, and Tsai W. (1998). Long-term survival of children with human immunodeficiency virus infection in New York City: Estimates from population-based surveillance data. *American Journal of Epidemiology,* 147:846-854.

13. Mellors, JW, Kingsley, LA, Rinaldo, CR, et al. (1995). Quantitation of HIV-1 RNA predicts outcome after seroconversion. *Annals of Internal Medicine,* 122:573-579.

14. Mellors, JW, Munoz A, Giorgi, JV, et al. (1997). Plasma viral load and CD4 lymphocytes as prognostic markers of HIV infection. *Annals of Internal Medicine,* 126:946-954.

15. Prochaska JO, and DiClemente CC. (1983). Stages and processes of self change of smoking: Toward an integrative model of change. *Journal of Consulting and Clinical Psychology,* 51:390-395.

16. U.S. Department of Health and Human Services. (1998). Public Health Service Task Force Recommendations for the Use of Antiretroviral Drugs in Pregnant Women Infected with HIV-1 for Maternal Health and for Reducing Perinatal HIV-1 Transmission in the United States. *Morbidity and Mortality Weekly Report,* 47(RR-2):1-30.

17. U.S. Department of Health and Human Services. (1998). Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. *Morbidity and Mortality Weekly Report,* 47(R-55):43-91.

18. Schacker T, Collier A, Hughes J, et al. (1996). Clinical and epidemiologic features of primary HIV infection. *Annals of Internal Medicine,* 125:257-264.

19. Hein K. (1994). Introduction to the special issue on pharmacokinetics and pharmacodynamics in adolescents. *Journal of Adolescent Health,* 15:612-627.

20. Besch CL. (1995). Compliance in clinical trials. *AIDS,* 9:1-10.

21. Haynes RB, McKibbon KA, and Kanani R. (1996). Systematic review of randomized trials of interventions to assist patients to follow prescriptions for medications. *Lancet,* 348:383-386.

22. Samet JH, Libman H, Steger KA, et al. (1992). Compliance with Zidovudine therapy in patients infected with HIV Type 1: A cross-sectional study in a municipal hospital clinic. *American Journal of Medicine,* 92:495-502.

23. Sackett, DL, and Snow, JS. (1997). The magnitude of compliance and non-compliance. In *Compliance in Health Care.* Haynes RB, Taylor DW, Sackett DL, (Eds.). Baltimore, MD: Johns Hopkins University Press.

24. Ladebauche P. (1997). Managing asthma: A growth and development approach. *Pediatric Nursing,* 23:37-44.

25. Smart RG, and Ogborne AC. (1994). Street youth in substance abuse treatment: Characteristics and treatment compliance. *Adolescence,* 29:733-745.

26. Hein K, Dell R, Futterman D, Rotheram-Borus, MJ, and Shaffer N. (1995). Comparison of HIV+ and HIV-adolescents: Risk factors and psychosocial determinants. *Pediatrics,* 95:96-104.

27. Chabon B, Hoffman N, Hershey B, Futterman D. (1997, March). High prevalence of HIV among parents of HIV positive youth. Presented at the annual research meeting of the Society of Adolescent Medicine, San Francisco, CA.

28. Ryan C, and Futterman D. (1998). *Lesbian & gay youth: Care and counseling.* New York: Columbia University Press.

29. Morey MA, and Friedman LS. (1993). Health care needs of homeless adolescents. *Current Opinions in Pediatrics,* 5:395-399.

30. Clatts MC, Davis WR, Sotheran JL, and Atillasoy A. (1998). Correlates and distribution of HIV risk behaviors among homeless youths in New York City: Implications for prevention and policy. *Child Welfare,* 77:195-207.

31. Martinez TE, Gleghorn A, Marx R, Clements K, Boman M, and Katz MH. (1998). Psychosocial histories, social environment, and HIV risk behaviors of injection and noninjection drug using homeless youths. *Journal of Psychoactive Drugs,* 30:1-10.

32. Farrow JA, (Ed.), Deisher RW, Brown R, Kulig JW, and Kipke MD. (1992). Position paper on the health and health needs of homeless and runaway youth. *Journal of Adolescent Health,* 13:717-726.

33. Rogers AS, Futterman D, Henry-Reid L, and Moreno V. (1998, March). The REACH Project Community Advisory Board for the Adolescent Medicine HIV/AIDS Research Network. HIV Counseling and Testing: Youth Report What will Work. Presented at the annual meeting of the Society for Adolescent Medicine 1998, Atlanta, GA.

34. Rawitscher LA, Saitz R, and Friedman LS. (1995). Adolescents' preferences regarding HIV-Related Physician Counseling and HIV testing. *Pediatrics,* 96:52-58.

35. English A. (1992). Expanding access to HIV services for adolescents: Legal and ethical issues. In DiClemente RJ, (Ed.). *Adolescents and AIDS: A generation in jeopardy.* Newbury Park, CA: Sage.

36. Horvath AO, and Luborsky, L. (1993). The role of the therapeutic alliance in psychotherapy. *Journal of Consulting and Clinical Psychology,* 61:561-573.

37. Bordin ES. (1979). The generalizability of the psychoanalytic concept of the working alliance. *Psychotherapy Theory, Research and Practice,* 16:252-260.

38. Skyler JS. (1997). Tactics for Type I diabetes. *Current Therapies for Diabetes,* 26:647-657.

39. Madden BP. (1990). The hybrid model for concept development: Its value for the study of therapeutic alliance. *Advances in Nursing Science,* 12:75-87.

40. Tichenor V, and Hill CE. (1989). A comparison of six measures of working alliance. *Psychotherapy: Research and Practice,* 26:195-199.

41. Horvath AO, and Symonds BD. (1991). Relation between working alliance and outcome in psychotherapy: A meta-analysis. *Journal of Counseling Psychology,* 38:139-149.

42. Godenne GD. (1995). Forming a therapeutic alliance with teenagers. *Adolescent Psychiatry,* 20:289-298.

43. Tenner A, Feudo R, and Woods ER. (1998). Shared experiences: Three programs serving HIV-positive youths. *Child Welfare,* LXXVII:222-250.

44. Prochaska JO, and Velicer WF. (1988). Measuring processes of change: Applications to the cessation of smoking. *Journal of Consulting and Clinical Psychology,* 56:520-528.

45. Fava JL, Velicer WF, and Prochaska, JO. (1995). Applying the Transtheoretical model to a representative sample of smokers. *Addictive Behaviors,* 20:189-203.

46. Velicer WF, Fava JL, Prochaska JO, Abrams DB, Emmons KM, and Pierce JP. (1995). Distribution of smokers by stage in three representative samples. *Preventive Medicine,* 24:401-411.

Selected Bibliography

General HIV Medical Care

Bartlett, J.G. (1998). *1998-1999 Guide to Medical Care of Patients with HIV Infection*. Eighth edition. Baltimore, MD: Williams & Wilkins.

Also accessible on the Internet as *Medical management of HIV.* (1998). http://www.hopkins-aids.edu/publications/index_pub.html.

Cohen, P.T., Sande, M.A., and Volberding, P.A. (1994). *The AIDS Knowledge Base.* Waltham MA: Massachusetts Medical Society.

Also accessible on the Internet as *The AIDS Knowledge Base.* (1997 edition). http://hivinsite.ucsf.edu/medical.

Antiretroviral Treatment

U.S. Department of Health and Human Services. (1998). Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. *Morbidity and Mortality Weekly Report.* 47(R-55):43-91.*

U.S. Department of Health and Human Services. (1998). Report of the NIH Panel to Define Principles of Therapy of HIV Infection. Morbidity and *Mortality Weekly Report.* 47(R-55):43-91.*

Internet sites for updates on treatment information:

American Medical Association
(http://www.ama-assn.org/special/hiv/treatmnt/treatmnt.htm)

Johns Hopkins University
(http://www.hopkins-aids.edu/publications/index_pub.html)

University of California at San Francisco
(http://hivinsite.ucsf.edu/medical/ and http://arvdb.ucsf.edu/)

Internet sites for consumer-oriented treatment information:

Critical Path (http://www.critpath.org/)

Project Inform (http://www.projinf.org/pub/pip_index.html)

The Body (http://www.thebody.com/)

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* These documents can be ordered through the National AIDS Clearinghouse (1-800-458-5231) or can be downloaded from the Internet (http://www.hivatis.org/trtgdlns.html).

Gay Men's Health Crisis Treatment Issues
(http://www.gmhc.org/aidslib/ti/ti.html)

Accessing Clinical Trials

AIDS Clinical Trials Information Service: 1-800-874-2572.

Online Guide to HIV Clinical Trials in the United States:
http://hivinsite.ucsf.edu.tsearch

Antiretroviral Treatment of HIV-infected Pregnant Women

U.S. Department of Health and Human Services. (1998). Public Health Service Task Force Recommendations for the Use of Antiretroviral Drugs in Pregnant Women Infected with HIV-1 for Maternal Health and for Reducing Perinatal HIV-1 Transmission in the United States. *Morbidity and Mortality Weekly Report.* 47(RR-2):1-30.*

Treatment and Care of Adolescents with HIV Infection

Chabon B, and Futterman D. (1995). HIV Infection in adolescents: Prevention and treatment. *International Pediatrics.* 10:311-320.

Futterman D, Hoffman N, and Hein K. (1998). AIDS and HIV infection. In Friedman S, Fisher M, and Schonberg SK (Eds.). *Comprehensive Adolescent Health Care*, Second Edition. St. Louis, MO: Mosby.

Futterman D, Hoffman N, and Chabon, B. (In press). Treating adolescents with HIV infection, Parts I and II. *AIDS Clinical Care.*

Comprehensive Adolescent HIV Program Development

Kunins H, Hein K, Futterman D, Tapley E, and Elliot A. (1993). A guide to adolescent HIV/AIDS program development. *Journal of Adolescent Health,* special supplement, pp 1-168.

National Significance Program. (1998). Special projects of national significance program: Ten models of adolescent HIV care. *Journal of Adolescent Health,* special supplement, 23(2):1-131.

Tenner A, Feudo R, and Woods ER. (1998). Shared experiences: Three programs serving HIV-positive youths. *Child Welfare.* LXXVII:222-250.

---

* These documents can be ordered through the National AIDS Clearinghouse (1-800-458-5231) or can be downloaded from the Internet (http://www.hivatis.org/trtgdlns.html).

Outreach: Getting Youth into Care

Dilorenzo TA, Abramo DM, Hein K, Clare GS, Dell R, and Shaffer N. (1993). The evaluation of targeted outreach in an adolescent HIV/AIDS program. *Journal of Adolescent Health*. 13:301-306.

The Therapeutic Alliance

Coupey SM. (1997). Interviewing adolescents. *Pediatric Clinics of North America*. 44:1349-1364.

Sexual Minority Youth

Ryan C, and Futterman D. (1998). *Lesbian & Gay Youth: Care and Counseling*. New York: Columbia University Press.

Drug Use in Adolescents with HIV

Martinez TE, Gleghorn A, Marx R, Clements K, Boman M, and Katz MH. (1998). Psychosocial histories, social environment, and HIV risk behaviors of injection and noninjection drug using homeless youths. *Journal of Psychoactive Drugs*. 30:1-10.

Morse EV, Morse PM, Burchfield KE, and Zeanah PD. Behavioral factors affecting HIV prevention for adolescent and young adult IDUs. *Journal of the Association of Nurses in AIDS Care*. 9:77-90.

Homelessness in Adolescents with HIV

Bangsberg D, Tulsky JP, Hecht FM, and Moss AR. (1997). Protease inhibitors in the homeless (commentary). *Journal of the American Medical Association*. 278:63-65.

Clatts MC, Davis WR, Sotheran JL, and Atillasoy A. (1998). Correlates and distribution of HIV risk behaviors among homeless youths in New York City: implications for prevention and policy. *Child Welfare*. 77:195-207.

Farrow JA, (Ed.), Deisher RW, Brown R, Kulig JW, and Kipke MD. (1992). Position paper on the health and health needs of homeless and runaway youth. *Journal of Adolescent Health*. 13:717-726.

Morey MA, and Friedman LS. (1993). Health care needs of homeless adolescents. *Current Opinions in Pediatrics*. 5:395-399.

APPENDIX A. Summary Of The Principles Of HAART

TABLE A-1. Summary Of The Principles Of Therapy Of HIV Infection

- HIV replication results in immune system damage and progression to AIDS. HIV infection is always harmful. Regular, periodic measurement of HIV RNA levels (viral load measurements)
  - Determines the risk for HIV disease progression; and
  - Guides decisions to initiate and change antiretroviral treatment regimens (HAART). Measurement of CD4+ T-cell counts monitors the extent of immune dysfunction.
- Treatment decisions are individualized based on both viral load levels and CD4+ T-cell counts.
- The goal of HAART is maximum achievable suppression of HIV replication to below the levels of detection by sensitive viral load assays. The most effective means of maximizing suppression of HIV replication is through treatment with simultaneous initiation of combinations of antiretroviral drugs that
  - The patient has not received before; and,
  - That are not cross-resistant with drugs the patient has received.
- Each antiretroviral drug used in combination therapy should always be used according to optimum schedules and dosages.
- Any changes in therapy reduce future treatment options because the number of drugs is limited and cross-resistance occurs.
- Women should receive optimal antiretroviral therapy regardless of pregnancy status.
- These principles apply to HIV-infected children, adolescents, and adults, although the treatment of HIV-infected children involves unique pharmacologic, virologic, and immunologic considerations.
- Persons identified during acute primary HIV infection should also be treated with combination antiretroviral therapy to achieve viral load levels below detectable levels with sensitive plasma HIV RNA assays.
- HIV-infected persons should be considered infectious even with undetectable viral load levels, and should be counseled to avoid sexual or drug-use behaviors that would transmit HIV or other infectious pathogens.

SOURCE: Adapted from U.S. Department of Health and Human Services Report of the NIH Panel to Define Principles of Therapy of HIV Infection. (1998). *Morbidity and Mortality Weekly Report.* 47(R-55), 1-43.

APPENDIX B. Medical Treatment With HAART*

B.1 Medical Readiness to Begin Treatment

B.1.1 Measurement of Viral Load (Plasma HIV RNA Level)

Viral load testing is the essential measurement on which decisions to initiate or change antiretroviral therapies are based. Viral load is measured at diagnosis of HIV infection and every 3 to 4 months in untreated patients, then immediately before treatment and 4 to 8 weeks after therapy begins.

Plasma HIV RNA testing is not recommended during or within 4 weeks after the following:

- Treatment of any intercurrent infection,
- Resolution of symptomatic illness, and
- Immunization.

Viral load is positively associated with disease progression: the higher the initial viral load the greater the likelihood that HIV disease will progress quickly to full-blown AIDS.[2,3] A viral load of less than 40 copies/ml is required in most cases to maintain long-term suppression of viral replication.

B.1.2 Medical Indications for HAART

Treatment with HAART has been shown to arrest the decline of CD4+ cell count and extend the time to development of AIDS and time to death.[4] Issues regarding HAART therapy differ by stage of illness and will be discussed below.

- Acute HIV infection,
- Asymptomatic HIV disease,
- Symptomatic HIV disease, and
- Advanced HIV disease (any condition meeting the 1993 Centers for Disease Control and Prevention definition of AIDS).

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* The following guidelines are taken largely from the Guidelines for the Use of Antiretroviral Agents in HIV-infected Adults and Adolescents.

B.1.3 Assessment for HAART in Adolescents with Acute HIV Infection

Adolescents who have had a recent exposure to HIV and exhibit the symptoms of an acute, flu-like syndrome should be assessed for acute, or primary, HIV infection, which is considered an ideal time to initiate HAART.

The tests required for a final determination of acute HIV infection are listed below:

- Negative or indeterminate HIV antibody test, and
- Positive qualitative or quantitative PCR testing.

B.1.4 Assessment for HAART in Adolescents with Asymptomatic HIV Disease

Although expert opinion varies regarding the correct time to initiate treatment in asymptomatic adults, for asymptomatic adolescents there are additional compelling reasons to begin treatment early. First, adolescents are more likely to be newly infected (i.e., they may enter care closer to the time of their sexual or drug using debut and thus be closer to the time of their infection) so that the efficacy of HAART will be reinforced by a more intact immune system. In addition, there is preliminary evidence in the cohort being studied by the clinicians in AMHARN that adolescents may have a greater capacity than adults for immune reconstitution because of persistent thymic tissue. Finally, because teens may be early in the infection process they may harbor fewer resistant viruses, further facilitating treatment efficacy.

Most clinicians try to start adolescents on HAART as early as possible in the disease process, regardless of CD4+ T-cell count or level of viremia, while some prefer to wait until there is some indication of immune dysfunction. (See TABLE B-1 for some of the risks and benefits of early initiation of HAART in asymptomatic adults with HIV.)

TABLE B-1. Risks and Benefits of Early Initiation of HAART in Asymptomatic Patients with HIV

Potential Benefits

- Control of viral replication and mutation, reduction of viral burden;
- Prevention of progressive immunodeficiency;
- Potential maintenance or reconstitution of a normal immune system;
- Delayed progression to AIDS and prolongation of life;
- Decreased risk of selection of resistant virus; and
- Decreased risk of drug toxicity.

Potential Risks

- Reduction in quality of life from adverse drug effects and inconvenience of current maximally suppressive regimens;
- Earlier development of drug resistance;
- Limitation in future choices of antiretroviral agents because of development of resistance;
- Unknown long term toxicity of antiretroviral drugs; and,
- Unknown duration of effectiveness of current antiretroviral therapies.

SOURCE: U.S. Department of Health and Human Services. (1998). Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. *Morbidity and Mortality Weekly Report,* 47(R-55):43-91.

B.1.5 Assessment for HAART in Young Women with HIV Who Are Pregnant

Young women who present during pregnancy should have their immune status assessed in the same way as other adolescents. The treatment goals are to maintain the health of the mother-to-be and to block perinatal transmission. Pregnancy should not preclude the use of optimal combination therapy for the health of the mother-to-be. As of 1998 zidovudine (ZDV) was the only antiretroviral drug demonstrated conclusively to reduce perinatal HIV infection, but combination therapies are under investigation and are increasingly being used during pregnancy.[5] Updated information should be obtained regarding appropriate treatment for pregnant adolescents.

For young women who are not yet on combination therapy, a HAART regimen with a specific antiretroviral agent (to date, just ZDV) proven to reduce perinatal transmission is recommended. For young women whose health permits, the regimen should be initiated after the first trimester to try to decrease any potential teratogenic effects of the medication.

Young women who become pregnant while receiving combination therapy should be continued on these regimens regardless of the pregnancy, after receiving counseling concerning current knowledge regarding antiretrovirals dur-

ing pregnancy. If the regimen does not include an antiretroviral shown to reduce perinatal transmission, such an agent should be added to the regimen.

B.1.6 Assessment for HAART in Adolescents with Symptomatic or Advanced HIV Disease

Assessment of adolescents who present with symptomatic or advanced HIV disease includes immune function, renal function, hepatic function, hematologic system function, and presence of gastrointestinal disorders such as malabsorption that could potentiate drug toxicity. Assessment of immune function is complicated in advanced HIV disease because plasma HIV RNA should not be tested during or within 4 weeks after successful treatment of any intercurrent infection or resolution of symptomatic illness.

All adolescents with symptomatic HIV infection or AIDS defining conditions should receive maximally suppressive regimens of HAART. However, the issues of overlapping drug toxicities and drug interactions are compounded by the increased number of drugs required in advanced-stage HIV disease. Moreover, preexisting wasting and anorexia, liver disease, or bone marrow suppression may complicate the therapies that are safe or effective with certain youth.

The initiation of HAART may be postponed in advanced-stage disease because of clinical considerations related to treatment of an acute illness (such as drug toxicity, ability to adhere to treatment regimens, drug interactions, and laboratory abnormalities). However, once patients are being maintained on an antiretroviral regimen they should not have the therapy discontinued during an acute opportunistic infection (OI) or malignancy, except in cases of drug toxicity, intolerance, or drug interactions.

B.2 Selecting the Appropriate Antiretroviral Regimen

B.2.1 Drugs Used in the HAART Treatment

To date, three families of antiretroviral drugs have been developed:

- Nucleoside reverse transcriptase inhibitors (NRTIs);
- Nonnucleoside reverse transcriptase inhibitors (NNRTIs); and
- Protease inhibitors (PIs).

Using combinations of drugs from at least two of these categories, including at least one PI, ensures that at least two steps in the HIV replication process are arrested, greatly reducing the possibility of successful HIV replication. After reviewing the information below, see APPENDIX C for suggested sample regimens for adolescents.

Ongoing clinical trials are examining new antiretroviral drugs and various combinations of drugs. These trials are continually introducing new possibilities to the list of treatment regimens. The information in the monograph is current as of November 1998. To find more updated information, refer to Internet resources listed in the Selected Bibliography.

B.2.2 Recommended Antiretroviral Combinations for Treatment-Naive Adolescents

For adolescents with HIV with no previous antiretroviral treatment (i.e., "treatment-naive"), the keys to antiretroviral therapy are two-fold:

- To treat with a maximally suppressive regimen that achieves undetectable viral plasma RNA levels using a viral load assay sensitive to 40 copies/ml, and
- To keep the regimen as simple and straightforward as possible in order to enhance adherence.

B.2.3 Considerations When Selecting a Regimen

For adolescents, a simple regimen is one that has few pills, small pills, few and flexible dosing times per day, and no dietary or intake requirements or restrictions. Simplification of the regimen, however, does not mean that undertreatment is acceptable. Rather, the regimen should be selected with

some attention to the lifestyle constraints of adolescents that could deter adherence. The goal is to aggressively treat youth who are interested and willing to take HAART using regimens that they can successfully adhere to.

When choosing a regimen for initiation of therapy, consideration should be given to the nature of the resistance that may develop to that particular agent. Certain antiretrovirals may become ineffective after a single point mutation, whereas others require several mutations before becoming resistant. 3TC (Epivir) and nevirapine (Viramune) are two agents that require only one point mutation in the virus to lead to significant resistance. For this reason, they should only be used in maximally suppressive regimens using at least three agents. In addition, it appears that there may be more cross-resistance with all of the PIs than first realized. Therefore, they should also only be used in maximally suppressive regimens, (i.e., only used with at least two other agents).

Use of antiretroviral agents as monotherapy is contraindicated, except when no other options exist or during pregnancy to reduce perinatal transmission if the mother refuses other antiretroviral therapy.

The only exceptions besides nevirapine to the principle that all antiretroviral drugs should be started simultaneously at full dose are the following: dose escalation regimens are recommended for ritonavir and in some cases, ritonavir plus saquinavir.

Particular attention should be paid to drug interactions between the PIs and other agents, as these are extensive and often require dose modification or substitution of various drugs. Toxicity assessment should occur at least twice during the first month of therapy and every 3 months thereafter. In particular, two NRTI combinations that are not recommended are listed below:

- **ZDV plus d4T.** This combination has not been studied and should not be used together since they represent the same nucleoside analogue.
- **ddI plus ddC.** This combination should not be used because of the similarity of their side effects (peripheral neuropathy and pancreatitis).

B.2.4 Treating Adolescents on Two-Drug Combination Therapy

Youth who are presently on double combination therapy and doing well should have their regimens changed at the discretion of the clinician and patient based on both CD4+ T-cell count and plasma RNA levels and the youth's willingness and ability to comply with the increased complexity of the regimen. Some may choose to switch to triple therapy, while others may select to wait until there is evidence of increasing viral replication. The risk of the former is the earlier development of resistance to the newly introduced PI, while the risk of the latter is the development of resistance to the nucleoside analogues being used.

B.3 Medical Treatment with HAART

B.3.1 Monitoring during HAART

When initiating treatment in asymptomatic adolescents, CD4+ T-cell counts and plasma HIV RNA levels should be performed on two occasions for accuracy and consistency of measurement. However, with advanced HIV disease, HAART should be initiated after the first viral load measurement to prevent delay in treatment. Because of differences among commercially available tests, confirmatory tests should be measured by the same laboratory using the same technique to ensure consistent results.

The speed of viral load decline and movement toward undetectable are affected by the baseline CD4+ T-cell count, initial viral load, potency of the regimen, level of adherence, prior exposure to HAART, and the presence of OIs. However, viral load should decrease by at least 1.0 $\log^{10}$ within 1 month, (less change may merely reflect daily changes in viral load dynamics). The viral load should generally be below detectable levels (<40 RNA copies/ml plasma) within 3 to 4 months, although in some cases it may take longer, especially if the viral load is particularly high. If not, the clinician should reassess patient adherence, rule out malabsorption, consider repeat RNA testing to document lack of response, and/or consider a change in drug regimen.

Viral load values may be affected by intercurrent infection and by vaccinations. Therefore, these and other clinical factors must be taken into account when measuring antiretroviral treatment effect. Clinical complications and sequential changes in CD4+ T-cell count may complement the viral load test in evaluating a response to treatment.

After adolescents have been on HAART successfully for 6 months and have undetectable viral loads using a viral assay sensitive to below 40 copies/ml plasma, they require monitoring at least every 3 months of the following:

- Viral load,
- Immune status (CD4+ T-cell counts and ratios), and
- Clinical status.

A substantial decrease in CD4+ T-cell count is a decrease of more than 30 percent from the initial baseline value for absolute CD4+ T-cell counts and a decrease of greater than 3 percent from the initial baseline value for percentages of cells.[1] In the event of discordance between trends in viral load and CD4+ T-cell count, treatment decisions become more complicated and clinical consultation is warranted.

Assays to determine genotypic resistance are commercially available; however, these have not undergone field testing to demonstrate clinical utility. They are not approved by the Food and Drug Administration and are only recommended for clinical use by clinicians trained in their use, in situations in which they are deemed necessary to make decisions on optimal HAART choices.

B.3.2 Interruption of Antiretroviral Therapy

Antiretroviral therapy may have to be interrupted for many unavoidable reasons, including intolerable side effects, drug interactions, first trimester of pregnancy when the mother so elects, and unavailability of a prescribed drug. Because potential development of drug resistance during interruption of treatment is of great concern, when any antiretroviral medication must be discontinued for an extended time, clinicians recommend that all antiretroviral agents be stopped simultaneously, rather than continuing one or two agents. This theoretically minimizes the emergence of resistant viral strains.

Initiation of HAART is often associated with some degree of recovery of immune function, which, in some adolescents with advanced-stage HIV disease with subclinical OIs, may result in new immunologic responses to the OI pathogen, causing new symptoms in association with the heightened immunologic and/or inflammatory response. This should not be interpreted as a failure

of HAART, and these newly presenting OIs should be treated appropriately while maintaining the antiretroviral regimen. Viral load measurement is helpful in clarifying this association.

B.3.3 Changing a Failing Regimen

The decision to change regimens should take into consideration a number of complex factors:

- Recent clinical history and physical examination;
- Plasma HIV RNA levels measured on two separate occasions;
- Absolute CD4+ T-cell count and changes in counts;
- Remaining treatment options in terms of potency, potential resistance patterns from prior antiretroviral therapies, and potential for adherence/tolerance;
- Assessment of adherence to medications; and
- Preparation of the youth for the implications of the new regimen (side effects, drug interactions, dietary requirements, etc.).

Failure can occur for a variety of reasons:

- Initial viral resistance to one or more agents,
- Altered absorption or metabolism of the drug,
- Multidrug pharmacokinetics that adversely affect therapeutic drug levels, and
- Poor adherence by the adolescent.

Adolescents should be considered for changing therapies for the following reasons:

- They are receiving incompletely suppressive antiretroviral therapy with single or double nucleoside therapy and with detectable or undetectable plasma viral load;
- They have been on potent combination therapy, including a PI; and their viremia was initially suppressed to undetectable levels but it has again become detectable; and

- They have been on potent combination therapy, including a PI; and their viremia was never suppressed to below detectable limits.

Specific criteria for changing a regimen include the following:

- The virologic response is less than a 1.0 $\log^{10}$ decrease in plasma HIV RNA in 1 to 2 months of therapy and the viral load is not under the limit of detection (less than 40 copies of HIV RNA per ml) after 3 to 4 months;
- The viral load remains detectable (above 40 copies of HIV RNA per ml) after 4 to 6 months of therapy (however, the degree of initial decrease in plasma HIV RNA and the overall trend in decreasing viremia should be considered. For example, a person with 1,000,000 viral copies per ml prior to therapy who stabilizes after 6 months of therapy at a detectable level of HIV RNA that is below 10,000 copies per ml may not warrant immediate change in therapy);
- Virus is detected repeatedly after initial suppression to undetectable levels, suggesting the development of resistance. (However, the degree of viral increase should be considered; a small increase in viral load may warrant monitoring, but will likely require a change in regimen);
- A reproducible threefold or greater increase occurs from the nadir of plasma HIV RNA that is not attributable to intercurrent infection, vaccination, or test methodology;
- Undetectable viremia has been achieved with double nucleoside therapy. (Most people on double nucleoside therapy who do not modify the regimen to include at least one PI eventually experience treatment failure);
- CD4+ T-cell counts, measured on at least two separate occasions, persistently decline; and
- Clinical deterioration occurs (however, a person with advanced HIV disease when antiretroviral treatment was initiated may get a new OI after a good antiretroviral therapy response, in which case the OI may not necessarily reflect treatment failure).

The lack of numerous treatment options may cause clinicians to be more conservative in deciding whether to change therapies. Consideration of alternative options should include potency of the substituted regimen, and probability of tolerance of, or adherence to, the alternative regimen.

Partial suppression of virus is superior to no suppression of virus. Some clinicians and their patients have decided to suspend treatment to preserve future options or because a sustained antiviral effect cannot be achieved.

When possible, youth who require a change in an antiretroviral regimen but have no treatment options using currently approved drugs should be referred for consideration for an appropriate clinical trial. (See resources in Selected Bibliography.)

B.3.4 Therapeutic Options when Changing Antiretroviral Therapy

Different actions are required depending on why therapy needs to be changed. These actions include the following:

- **For drug intolerance or drug toxicity,** substitute one or more alternative drugs of the same potency and from the same class as the agent suspected to be causing the toxicity;
- **For treatment failure on an appropriate regimen** (two NRTIs and one PI or NNRTI), change the regimen entirely to drugs that have not been taken previously. At least two and preferably three new drugs must be used (typically two new NRTIs and one new PI or NNRTI, two PIs with one or two new NRTIs, or one new PI and one new NNRTI); and
- **For an inappropriate regimen but satisfactory viral load,** (e.g., two NRTIs or monotherapy), either (1) continue treatment with careful monitoring of viral load or (2) add appropriate drugs to the regimen. Most experts would recommend the latter option.

The decision to change treatment and design a new treatment regimen should be made with consultation from a clinician experienced in the use of HAART.

Changing only one medication is essentially using monotherapy for the resistant strain of HIV. In this situation, although there may be an initial

effect of the agent, it is often only transient with subsequent resistance and viral replication.

Dose modifications may be necessary to account for drug interactions using combinations of PIs or a PI and an NNRTI. Some adolescents will have few options because of previous antiretroviral use, toxicity, or intolerance. In the clinically stable patient with detectable viremia with no optimal change in treatment possible, it may be prudent to delay changing therapy until newer, more potent agents become available.

APPENDIX B References

1. U.S. Department of Health and Human Services. (1998). Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. *Morbidity and Mortality Weekly Report,* 47(R-55):43-91.

2. Mellors, JW, Kingsley, LA, Rinaldo, CR, et al. (1995). Quantitation of HIV-1 RNA predicts outcome after seroconversion. *Annals of Internal Medicine,* 122, 573-579.

3. Mellors, JW, Munoz A, Giorgi, JV, et al. (1997). Plasma viral load and CD4 lymphocytes as prognostic markers of HIV infection. *Annals of Internal Medicine,* 126, 946-954.

4. Detels R, Munoz A, McFarlane G, et al. (1998). Effectiveness of potent antiretroviral therapy on time to AIDS and death in men with known HIV infection duration. *Journal of the American Medical Association,* 280, 1497-1503.

5. U.S. Department of Health and Human Services. Public Health Service Task Force Recommendations for the Use of Antiretroviral Drugs in Pregnant Women Infected with HIV-1 for Maternal Health and for Reducing Perinatal HIV-1 Transmission in the United States. (1998). *Morbidity and Mortality Weekly Report,* 47(RR-2), 1-30.

APPENDIX C. Sample HAART Regimens*

For adolescents, a simple regimen is one that has few pills, small pills, few and flexible dosing times per day, and no dietary or intake requirements or restrictions. Simplification of the regimen, however, does not mean that undertreatment is acceptable. Rather, the regimen should be selected with some attention to the lifestyle constraints of adolescents that could deter adherence. The goal is to aggressively treat youth who are interested and willing to take HAART using regimens that they can successfully adhere to.

With this goal in mind, two sample regimens are suggested here that provide drug combinations with fairly simple dosing schedules (i.e., with the fewest number of pills and number of doses required during a 24-hour period of time.) Some clinicians may select other three-drug combinations based on discussions with the adolescents, previous treatment histories, or potential drug interactions with other medications.

No one regimen is appropriate for all adolescents. Both of these recommended regimens employ a three-drug combination, which is the standard for the initiation of all antiretroviral medications. However, it is important to note that the recommendations are not based on the results of adolescent-specific clinical trials. The recommendations were selected based on data primarily from clinical trials in adults.

C.1 Regimen #1

According to the U.S. Department of Health and Human Services (DHHS) guidelines for HAART, using an NNRTI, nevirapine, rather than a PI in combination with two NRTIs, does not achieve the goal of suppressing viremia to below detectable levels as consistently as does combination treatment with a PI and should be used only if more potent treatment is not possible. However, some experts consider that data are insufficient to choose between a three-drug regimen containing a PI and one containing nevirapine in the treatment-naive individual.† Many adolescent HIV experts elect to use two NRTIs

* These regimens are current as of November 1998. Clinical trials and drug approvals by the Food and Drug Administration will continue to change treatment regimens. Clinicians should refer to the latest information sources to obtain the most up-to-date treatment recommendations. (See the Selected Bibliography for continually updated Internet sites on HIV treatment.)

† U.S. Department of Health and Human Services. (1998). Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. *Morbidity and Mortality Weekly Report*, 47(R-55), 43-91.

with a nonnucleoside such as nevirapine because it is a PI-sparing regimen. If it is uncertain whether youth will be adherent, starting with nevirapine preserves the most potent combinations, those with protease inhibitors, for a time in the future when youth have become more capable of adhering. This regimen

TABLE C-1. Regimen #1: Nevirapine, d4T and ddI (PI-sparing regimen)

Drug	Daily dose	Requirements	Sample times
nevirapine (Viramune®)	200 mg QD (One 200 mg tablet) x 14 days, then 200 mg Q 12 hrs	None	8 am 8 pm
stavudine, d4T (Zerit®)	40 mg Q 12 hrs (One 40 mg capsule) for > 60 kg	None	8 am 8 pm
didanosine, ddI (Videx®)	200 mg Q 12 hrs for > 60 mg	Must be taken on an empty stomach (1 hr before or 2 hrs after meals)	8 am 8 pm
TOTAL	7 pills, then 8 pills		8 am 8 pm

TABLE C-2. Regimen #1: Side Effects and Drug Interactions

Drug	Side Effects	Drug Interactions
nevirapine (Viramune®)	Severe rash (dose escalation reduces the likelihood of severe rash, the most frequent side effect), fever, increased transaminase levels	Monitor if used with rifampin, rifabutin, oral contraceptives, protease inhibitors, triazolam and midazolam
stavudine, d4T (Zerit®)	Peripheral neuropathy, mild elevation of transaminases	
didanosine, ddI (Videx®)	Pancreatitis, diarrhea, peripheral neuropathy, nausea, headaches, insomnia, increased uric acid levels	ketoconazole, dapsone (administer at least 2 hrs before or after ddI)

is not advised when a teen has a high viral load or advanced disease because a three-drug combination with nevirapine is probably not sufficient in this case.

C.2 Regimen #2

This regimen is more effective than Regimen #1 because it includes a protease inhibitor and two NRTIs. It is easier to take because it uses a two-drug combination in one pill, Combivir®, which decreases the number of pills administered in 1 day. Another advantage is that it uses ZDV, the only drug to date that has been demonstrated to reduce perinatal transmission. Thus, it can be used both for maternal and fetal health in pregnant adolescents. (See APPENDIX C for a discussion of antiretroviral treatment in pregnant young women.) Because adherence may not be achieved with the first regimen given to an adolescent, Regimen #2 may be reserved for teens with advanced disease or those who are more likely to adhere.

TABLE C-3. Regimen #2: ZDV, 3TC, and nelfinavir

Drug	Daily Dose	Requirements	Sample Regimen
zidovudine (ZDV) + lamivudine (3TC) (Combivir®)	one capsule Q 12 hrs (300 mg ZDV and 150 mg 3TC)	None	8 am 8 pm
nelfinavir (Viracept®)	**Dosage #1** 750 mg Q 8 hrs (Three 250 mg tabs) **Dosage #2** 1250 mg Q 12 hrs (Five 250 mg tabs)	Take with food or light snack (non-acidic)	**Schedule #1** 7 am 3 pm 11 pm **Schedule #2** 8 am 8 pm
TOTAL	**Dosage #1** 11 pills **Dosage #2** 12 pills		**Schedule #1** 7 am 3 pm 11 pm **Schedule #2** 8 am 8 pm

TABLE C-4. Regimen #2: Side Effects and Drug Interactions

Drug	Side Effects	Drug Interactions
zidovudine (ZDV) + lamivudine (3TC) (Combivir®)	anemia, leukopenia, neutropenia, nausea, muscle weakness, headaches, malaise and fatigue, neuropathy, diarrhea, hair loss	
nelfinavir (Viracept®)	diarrhea, hyperglycemia, nausea, flatulence, rash	contraindicated with terfenedine, astemizole, cisapride, triazolam, or midazolam; levels reduced by rifampin, rifabutin; reduces level of oral contraceptives

APPENDIX D. Contacts For The Adolescent Medicine HIV/AIDS Research Network (AMHARN)

Northeastern Region

Adolescent AIDS Program/Risk Evaluation Program (REP)
Montefiore Medical Center, Bronx, New York
Referrals: 718-882-0023
PI: Dr. Donna Futterman: 718-882-0322

Adolescent Health Center
Mount Sinai Medical Center, New York, New York
Referrals: 212-423-2887
PI: Dr. Linda Levin

Health and Education Alternatives for Teenagers (H.E.A.T.)
Kings County Hospital
State University of New York at Brooklyn, Brooklyn, New York
Referrals: 718-467-4446
PI: Dr. Jeffrey Birnbaum

Adolescent Clinic
University of Medicine and Dentistry of New Jersey, Newark, New Jersey
Referrals: 973-972-5106 or 973-5098
PI: Dr. Paulette Stanford: 973-972-0361

Mid-Atlantic Region

Adolescent Clinic
University of Maryland, Baltimore, Maryland
Referrals: 410-328-3196 or 410-328-TEEN
PI: Dr. Ligia Peralta: 410-328-6495

Burgess Clinic
Children's Hospital National Medical Center, Washington, DC
Referrals: 202-884-5389
PI: Dr. Lawrence D'Angelo: 202-884-3068

The Adolescent HIV Initiative
Children's Hospital of Philadelphia, Philadelphia, Pennsylvania
Referrals: 215-590-3626 or 215-590-1468
PI: Dr. Bret Rudy

Midwestern Region

Division of Adolescent Medicine
Adolescent and Young Adult Clinic (AYAC)
Cook County Hospital, Chicago, Illinois
Referrals: 312-633-7438
PI: Dr. Lisa Henry-Reid

South/Southeastern Region

Adolescent Health Center
Children's Hospital, Birmingham, Alabama
Referrals: 205-939-9345
PI: Dr. Marsha Sturdevant: 205-934-5262

Adolescent Care Team
Tulane Medical Center, New Orleans, Louisiana
Referrals: 504-988-6805
PI: Dr. Sue Ellen Abdalian: 504-586-3881

Grady Pediatric Infectious Disease Clinic/Adolescent Program
Emory University, Atlanta, Georgia
Referrals: 404-616-9811 or 404-616-9790
PI: Dr. Mary Sawyer 404-616-6388

St. Jude Children's Research Hospital
Memphis, Tennessee
Referrals: 901-495-3486
PI: Dr. Patricia Flynn

Special Adolescent Clinic (SAC)
University of Miami/Jackson Memorial Medical Center, Miami, Florida
Referrals: 305-243-3442
PI: Dr. Lawrence Friedman: 305-243-5880

Children's Diagnostic and Treatment Center
Fort Lauderdale, Florida
Referrals: 954-728-8080, Ext 1059
PI: Dr. Ana Puga

Western Region

Risk Reduction Program
Children's Hospital of Los Angeles, Los Angeles, California
Referrals: 323-669-2390 (Stephanie Lee, MSW)
PI: Dr. Marvin Belzer: 323-669-2390