Abstract
Adherence is defined as the extent to which the patient follows the agreed treatment modality or intervention required. Adherence or attachment is the cornerstone of therapeutic success. There is a resulting decrease in viral load and elevation of CD4 with significant improvement in quality of life. Appropriate future management and other therapeutic strategies decreased resistance to antiretroviral therapy. Prospective studies in adults and children have shown that the risk of virological failure increases in proportion to the lower doses administered as well as to resistance. Evidence suggests that adherence problems occur frequently in children and adolescents. Multiple studies have reported a very low percentage (50%) in children. There are a variety of factors such as drug formulation, e.g., presentation, frequency of doses, child’s age, and characteristics of parents and children that have all been associated with adherence. This is changing, especially because adolescents do not want to be different from their peers. In clinical practice, the use of reminder systems such as paging devices and alarm clocks are accepted by some teenagers.

Key words: adherence, adhesion, HIV, child, adolescence.

We define adherence or adhesion as the extent to which the patient follows the treatment modality that has been granted, or the intervention required.1

Adherence to antiretroviral medications is essential for therapeutic success in patients infected with human immunodeficiency virus (HIV) and, therefore, for a better quality of life. It is also one of the most important factors for determining viral suppression from antiretroviral treatment (ARV).2-4 Lack of adherence can enhance virologic failure.

Prospective studies in adults and children have shown that the risk of virologic failure increased in proportion to the number of missed doses.2,5-7

Subtherapeutic doses of ARV drugs from lack of adherence stimulate the production of resistance, which may be to one or more of the drugs administered in the indicated regime. On the other hand, the production of cross-resistance has been linked to other ARV treatments of the same family, which compromises the effectiveness of the administered regime.

Suboptimal adherence has implications for limiting the future impact of ARV therapy in patients who have developed viral strains resistant to these medications, being of utmost importance because we have to remember that these treatments are initiated in childhood and adolescence and continue into adulthood in such a way that, if they demonstrate good adherence to treatment, they will be less likely to develop resistance and also other alternative treatments in adulthood, offering a very safe and effective treatment.

The evidence suggests that adherence problems occur frequently in children and adolescents. Multiple studies
have reported a range from very low percentage up to 50% in children. A variety of factors such as the medical formulation (pharmaceutical), dose frequency, child’s age and psychosocial characteristics of the parents and children have been associated with adherence.\textsuperscript{6,8,9}

These findings illustrate how difficult it is to maintain constant levels of adherence and, above all, the need to work with the parents and relatives who care for the children with integral education, support and supervision.

We discuss some factors associated with adherence in children and adolescents infected with HIV.

**Specific Points of Adherence in Children**
Adherence is a complex health behavior influenced by the prescribed medication regimen as in certain chronic diseases such as arterial hypertension, diabetes mellitus, etc.

Some patient characteristics and the limited availability of ARV treatments in the presentations for infants, such as suspensions, represent a major challenge to adherence.\textsuperscript{7,10}

Moreover, infants and preschool children are dependent on other people for administration of medications as well as for the monitoring of oral tolerance, adverse effects and the capacity for adherence to a regimen of several drugs. Before starting this regimen, the child needs assessment from medical personnel and their family environment as well as the capacity and willingness of the patient to take the medication.

Healthcare personnel or family members can assess the primary responsibility for school-age children or adolescents to take their medication by themselves according to their maturity level and before they reach maturity and are able to assume such responsibilities. There are many other barriers for adherence for HIV-infected children. For example, healthcare personnel or a family member can reveal the diagnosis of HIV infection to the child or teenager before they know about this and are not ready to assimilate this information, with a consequent impact on adherence.

Other specific problems may arise such as the reluctance of healthcare personnel to fill prescriptions in their communities or home situations as occurs in rural communities and small ranches. They must hide or relabel the new drugs in order to maintain confidentiality and secrecy of their disease at home or away from home, such as at school or their job.

The lack of social support and poor family supervision promote a tendency to skip doses, with their doses being very irregular especially when parents are away from home or when the child is in school.

**Points of Adherence Specific to Adolescents**
Adolescents infected with HIV also face challenges in adherence.\textsuperscript{6,11,12} Several studies have identified the “burden” for them to continue with these medications since infancy and, thus, express their lifestyle, a situation favoring them to not want to carry their medications with them.\textsuperscript{6,11}

Denial and fear of HIV infection are common especially among young people newly diagnosed; this may lead to a refusal to initiate or continue ARV therapy.

Mistrust of medical treatment, misinformation about HIV, lack of knowledge about the medications, lack of availability and efficacy of ARV treatment can all be barriers to adherence among adolescents because they are concerned and are not convinced of their treatment and thus do not have proper monitoring of their ARV therapy.

It is common for infected adolescents to experience challenges such as taking complex medication regimens and a constant medical care routine.

However, adolescents may have long histories of poor adherence. Regardless of the mode of acquisition of the HIV infection, infected adolescents may have very low self-esteem, which leads to depression, chaotic lifestyles, drug addictions and, as concomitant phenomena, mental illnesses and poor adaptation to social environment for their disease due to a lack of family and social support.

Depression, alcohol or drug abuse, lack of school attendance, and the stage of advanced HIV disease are correlated with non-adherence.\textsuperscript{12}

Adherence to complex regimens is an important problem, with a tendency to change, particularly when adolescents do not want to be different from their
peers.\textsuperscript{13,14}

In clinical practice, some adolescents accept the use of reminder systems such as paging devices and alarm clocks. Small and discreet pillboxes are another alternative, providing an organized and useful method for treatment adherence.\textsuperscript{15}

**Evaluation of Adherence and Supervision**
The process of sensitization of adherence and evaluation should begin before initiation of therapy and, with each clinic visit, routine monitoring of adherence should be incorporated.

A comprehensive assessment should be instituted for all children for the initiation of ARV treatment or when changing it.

Evaluations at each visit should include all healthcare personnel involved—physician, nurse and social worker. Behavioral tests were conducted by psychologists about factors that may affect adherence both to a child and to an adolescent and their family. These tests will help identify individual needs for intervention.

Sensitization of adherence should focus on the commitment to establish a dialogue and to sharing in the responsibility of taking the medicine. Specific questions should be used to obtain information on previous experiences, as well as the concerns, interests and treatment expectations.

Adherence is difficult to accurately assess. Evaluation methods have shown different results, and each intervention has its limitations.\textsuperscript{15}

Healthcare personnel often overestimate adherence. Regular supervision is the key to early identification of problems and can reinforce the importance of taking the prescribed medicine.

Viral load response to a new regimen is often the most accurate indication of adherence, but this may be far less valuable in children with histories of long treatment and multiresistance to the virus.

Other measures include the quantitative report of missing doses reported by healthcare personnel, family, children and adolescents (highlighting recently omitted doses during a period of 3 days or a week), descriptions of medication regimens, and reports of obstacles to their administration. It is recommended to ask questions about stress, pill storage and their daily agenda.\textsuperscript{6,9,15}

Verification of the exchange of drugs at the pharmacy and accounts of pills can identify issues not apparent with adherence.\textsuperscript{16}

Electronic monitoring devices such as medication monitoring systems (MEMS) record the opening of medication bottles by a computer chip on the top of the bottle.\textsuperscript{17} They have been shown to be useful tools for measuring adherence with some patients.\textsuperscript{16,18}

Unscheduled visits (unexpected) to the home may play an important role in the assessment of adherence and in some cases can confirm the suspected non-adherence. It can also confirm the non-adherence when dramatic clinical responses occur and by the laboratory during ARV therapy during hospitalization or when adjusting supervised treatment.\textsuperscript{19-21}

Preliminary studies suggest that the determination of plasma concentrations and supervision aimed at medication intake may be useful methods for identifying non-adherence.\textsuperscript{22} It is important for clinicians to recognize that lack of adherence is a common problem and that it may be difficult for patients to admit that they are not taking their medication.

Furthermore, it appears that adherence can change over time. An adolescent who at the beginning of treatment was able to adhere strictly may, over time, abandon complete adherence.

The attitude of not severely judging and having a trusting relationship promotes open communication and facilitates supervision. It is often helpful to ask older children and adolescents about the missed dose and problems that arise from taking them. There may be significant discrepancies between reports from the parents to those from the child. Therefore, clinical judgment is needed to interpret adherence information obtained from multiple sources.\textsuperscript{23}

**Strategies to Improve and Support Adherence**
Intensive monitoring is required, especially during the first critical months after initiating treatment. Patients should be seen frequently to assess adherence and identify the need for strategies to improve and support adherence. Strategies include development of goals in treatment plans for all patient’s needs, integrating...
medications into daily life routines (for example, use administration of medications with daily activities such as tooth brushing) as well as multifaceted approaches such as the regimen related to the system of education, behavior, and support directed to the children and families. 24-26

Although requiring intensive labor, there are programs designed for the administration of highly active antiretroviral therapy under direct observation of adults, whether in a clinic or at home, which have proven successful in the U.S. and worldwide, as well as in environments with limited economic resources. 27-30

**Strategies Related with the Regimen**

Highly active ARV regimens often require the administration of a large number of pills or flavored liquid medication in multiple daily doses, each with potential side effects and drug interactions.

To the extent possible, regimens should be simplified with respect to the number of pills or volume of liquid medication prescribed and also the frequency of therapy, while minimizing medicinal interactions and side effects.

When adherence is a problem, we need to address issues related to the medication such as side effects, observed improvement, etc.

If a regimen is too complex, it can be simplified. For example, when the number of pills is large, one or more drugs can be modified to produce a therapy that contains fewer pills. When adherence is related to the poor taste of a liquid or crushed tablet, it helps to mask the taste with a small amount of flavored syrup or food. This is only applicable if the medication does not have a contraindication to the administration of food or the child may be taught to swallow pills to overcome the aversion to the medicine. 31

**The Child or Family Relations with the Strategies**

The main approach taken by the clinical team to promote compliance with medication in children is to educate families about adherence, and this must begin before ARV therapy has been initiated or changed. It should include a discussion of the objectives of the therapy, the reasons for the priority commitment and concrete plans to support and maintain adherence to the medication for the children. We must explain to them and try to help them understand that the first ARV regimen has the best chance of long-term success.

The adherence of the caretaker and the education strategies should include providing information and adherence tools (visual and written material), a daily program to illustrate the times and doses of medications, demonstration of the use of syringes, medication cups, etc. A variety of behavioral tools can be used to integrate the child’s daily routine for taking medication in HIV-infected patients.

The use of behavior modification techniques, especially the application of positive reinforcement and the use of small incentives to make the medications acceptable, can be effective tools for promoting adherence. 32-34

The availability of mental health services and treatment of mental health disorders may also facilitate adherence to complex ARV regimens.

For children who are at risk of disease progression and when rejection of the medication is serious such as with constant vomiting, or they simply do not want to take them, placement of a gastrostomy tube may be considered. 35

Home interventions by nursing personnel may also be beneficial when adequate resources are available. 36

We have applied the direct observation of the ARV treatment in adults with promising results 27-30, 37 and adopted this approach in some programs for pediatric HIV, utilizing the services of home nursing along with day-to-day administration of medications at the clinic.

Healthcare personnel are related to the strategies to improve adherence through their relationships with the families. Healthcare personnel should initiate this process of interrelation with the family early in the course of treatment when the doctor has agreed with the treatment plan.

Fostering a relationship of trust and open participation in communication are especially important. The characteristics that are associated with better adherence in adult patients are consistency, providing clear information, answering questions, technical skills and commitment for monitoring. There are several resources for HIV available to help healthcare personnel become
disseminators of knowledge of adherence, of the factors that affect it and the strategies to support and improve it in children, teenagers and adults.

In conclusion, it is important for healthcare personnel to sensitize the family before treatment, during treatment, and whenever making a change in ARV treatment in regard to the importance of knowing the strategies to promote adherence. A rebellious adolescent who suspends or reduces the dosage of medications he/she has taken since childhood influences suboptimal doses and favors the emergence of resistant strains, leading to immunological and therapeutic failure. Therefore, the multidisciplinary team who cares for these patients such as a nurse, psychologist, social worker, responsible physician, etc. have an obligation to promote adherence in each consult with diverse strategies according to the patient, patient’s age, whether or not there are involved family members, to the presentations of the products, their cost, psycho-social conditions, etc. This conduct of awareness of adherence should be continued.

References

16. AIDS Institute, New York State Department of Health.


