ABSTRACT.  
Objective. To acquire a deeper understanding of factors that influence adherence to highly active antiretroviral therapy (HAART) in a pediatric population.

Methods. We performed a qualitative study of adherence in children who receive HAART in a Belgian pediatriac acquired immune deficiency syndrome referral center. Eleven primary caregivers were interviewed to assess their child’s adherence and influencing factors. The interview guidelines were based on the development of an extensive literature review. Adherence to treatment was assessed using caregivers’ self-report and laboratory results. Content analysis for common items was performed, and statements of adherent and less-adherent patients were compared.

Results. Three main factors influenced adherence. Adherent patients were found to internalize the medical information to a stronger extent than less-adherent patients. Adherent patients showed stronger motivation to stick to the medical regimen on the basis of personal cost-benefit analyses, ie, perceived benefits outweighed the costs or difficulties experienced. Adherent patients developed greater problem-solving capacities, ie, ways to deal with practical complications of medication intake. The interviews revealed a fourth, more dynamic component: knowledge, motivation, and capacities evolved in a progressive way, related to individual stages of coping with human immunodeficiency virus (HIV).

Conclusions. The data suggest that coping with HIV and the process of establishing good adherence may be interrelated. Caregivers who accept the disease may be more likely to internalize the received information and thus develop a stronger motivation to fight for the child’s life. Problem-solving skills sustain this adherence, and medication becomes a priority in the adherent caregivers’ daily lives. On the contrary, less-adherent caregivers may be situated at less advanced stages of the coping process. Thus, tailor-made approaches adapted to the individual HIV-related coping strategies need to be developed to improve adherence in children and caregivers. Pediatrics 2004;114:e591–e597. URL: www.pediatrics.org/cgi/doi/10.1542/peds.2004-0085; HIV/AIDS, antiretroviral treatment, adherence/compliance, pediatric, qualitative study.

ABBREVIATIONS. HIV, human immunodeficiency virus; HAART, highly active antiretroviral therapy; AIDS, acquired immune deficiency syndrome.

The introduction of antiretroviral therapy has turned human immunodeficiency virus (HIV) into a chronic, noncurable disease. Highly active antiretroviral therapy (HAART) causes viral suppression and favors immunologic reconstitution, which decreases opportunistic infections, the development of acquired immune deficiency syndrome (AIDS), and mortality.1–3

Nevertheless, achieving and sustaining the required high level of adherence to a treatment regimen to control the disease remains a challenge. Drapeau and Melais4 defined adherence as “the extent to which an individual chooses behaviors that coincide with a clinical prescription achieved through negotiation between the health professional and the patient.” In the case of HAART, this suggests introducing multiple, strictly timed doses of several drugs, some with a bad taste, into daily life. Moreover, adherence of >95% seems necessary to achieve viral suppression and to avoid development of viral resistance.5,6

For HIV-positive children, sustaining adherence is even more challenging. First, medication-related factors such as volume, taste, diet prescriptions, intake of pills, strict timing of doses, and side effects are difficult to overcome for children.7,8 Second, young children depend on caregivers to adhere to medication regimens.1,2 That the caregiver is often also HIV positive can complicate the psychosocial conditions and influence the ability to adhere to the treatment.6,9 Third, issues such as disclosure, privacy, and caregiver’s feeling of guilt about vertical HIV transmission may increase the possibility of nonadherence.1,2,9,10

The aim of this qualitative study was to understand adherence behavior in a pediatric population, as reported by caregivers. The focus was on the identification of factors that promote and inhibit good adherence and on comparing them in adherent and less-adherent patients.

METHODS

This study was performed using semistructured interviews of primary caregivers—the administrators of drugs—of HIV-positive children who received HAART. The information that they report should provide broader insights on the problems faced...
with medication intake and adherence and help generate new hypotheses.11

Interviews were conducted from September to November 2002. All caregivers interviewed had their children followed by a multidisciplinary care team at the AIDS referral center of the Middelheim Hospital (Antwerp, Belgium). In addition, 2 adolescents were interviewed directly, as they were considered to be responsible for their own medication intake. Social nurses and psychologists, part of the multidisciplinary care team, approached caregivers and adolescent patients to obtain verbal informed consent for study participation. Patients were informed about the study goals and the procedure. Confidentiality was guaranteed. When patients consented, the interviewer (a pediatrician who was not part of the care team) was presented to them, and an appointment for an interview was made. In this sense, the study participants were subject to preselection by the multidisciplinary care team, ie, caregivers who experienced severe psychosocial or emotional distress during the study period were not approached.

Interviews were conducted in the interviewee’s preferred language (Dutch, French, or English). On average, an interview took ~60 minutes. The number of interviews was determined by content saturation. Demographic information on patients was obtained through analysis of patient records.

We reviewed literature on adherence to HAART to develop the major topics and categories of questions.2,6,7,10,12–31 The interview guidelines (Table 1) contained 4 broad topics: self-report of adherence, factors that influence adherence, assistance in the child’s medication intake, and personal perspectives.

The level of adherence was assessed by self-report (the primary caregiver) and confirmed by the laboratory results of viral load and CD4 counts in the preceding year. When in the last 3 days no missed doses were reported, no problems with adherence were reported over the last year, and the laboratory results confirmed this picture, the child was classified as adherent. Children were classified as less adherent when caregivers reported having missed a dose in the last 3 days or having regularly missed a dose over the last year. In addition, laboratory results over the last year had to confirm this picture.

Recordings were transcribed and analyzed for content manually and partly with the qualitative analysis software package NUD*IST (QSR International Pty Ltd, Doncaster, Australia). Transcripts were repeatedly scrutinized for common items, which formed the basis of categorization in a framework.32 During analysis, text units were identified and the data were grouped into 3 main categories: knowledge, motivation, and capacity to adhere. The statements of adherent and less-adherent patients were compared to identify the influence of these categories. This revealed a fourth component: the process of becoming adherent. Data therefore were rescrutinized for the role of this last aspect in each of the major categories. Researchers with different backgrounds provided input to the analysis to increase its validity.

RESULTS

Eleven caregivers of the 18 children who were followed at the referral center for antiretroviral treatment were interviewed. Three of the 18 caregivers were not approached by the care-providing team to participate in the study because the team considered that the interview would be too distressing for them given their current psychosocial family situation. Three had no appointment during the study period, and 1 refused. Of the 11 caregivers interviewed, 3 reported recurrent problems with adherence; their children thus were labeled less adherent (Table 2). There was a strong correlation between the self-report reflecting adherence and an increasing or stable CD4 and decreasing or undetectable viral load.

All children received 2 daily dosed combination therapies. Eight were on triple therapy, and 3 were on quadruple therapy (Table 3). Patient’s statements were classified as elements of knowledge, capacity, motivation, and the process of becoming adherent.

Knowledge of the Disease and Its Treatment

All caregivers had received information about the natural HIV progression and understood the effect of treatment. However, the comparison of adherent and less-adherent patients revealed a difference in the manner in which information had been internalized. Caregivers of adherent children had integrated this information into their own health beliefs. They rephrased it in their own words, emphasizing the necessity of adherence to medication: “In my understanding, the disease is inhibited somewhere, so that it can’t expand anymore. It stays somewhere in a corner. But, if you don’t take the medication, it can invade the whole body.”

Viral resistance as a consequence of suboptimal adherence was mentioned by only 4 caregivers; 3 of them were adherent: “If you start this treatment, you have to continue. You may not forget, otherwise the viral load and CD4 change and make you sick again. But also, the medicine may not work anymore, because the virus becomes resistant.”

Less-adherent patients seemed to consider this information as an external matter. When talking about the effect of treatment, they referred explicitly to the medical team as the information source, as if they were not completely convinced: “If they tell me that I have to take, I take. I suppose it’s OK, otherwise they would not prescribe it.”

Capacity to Follow the Medication Regimen

Our data revealed that the ability to be adherent depended on 3 components: the necessary cognitive

<table>
<thead>
<tr>
<th>TABLE 1. Interview Guidelines</th>
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<tbody>
<tr>
<td>Adherence to treatment</td>
</tr>
<tr>
<td>Knowledge of medication scheme: (1) description of drug, (2) prescribed doses per day, and (3) prescribed number of pills/milliliters of syrup per dose</td>
</tr>
<tr>
<td>Self-report of adherence last 3 days</td>
</tr>
<tr>
<td>Self-report of missed doses</td>
</tr>
<tr>
<td>Factors that influence adherence</td>
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<tr>
<td>Personal history of adherence</td>
</tr>
<tr>
<td>Perceived obstacles and facilitators to adherence</td>
</tr>
<tr>
<td>Perceived capacity to take medication every day</td>
</tr>
<tr>
<td>Perceptions of the disease, the treatment, and the importance of adherence</td>
</tr>
<tr>
<td>Stigma</td>
</tr>
<tr>
<td>Acceptance of diagnosis</td>
</tr>
<tr>
<td>Quality of the mother-child relationship</td>
</tr>
<tr>
<td>Assistance for intake of child’s medication</td>
</tr>
<tr>
<td>Description of people assisting with intake of child’s medication</td>
</tr>
<tr>
<td>Unexpected help</td>
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<tr>
<td>Situations in which nobody could help</td>
</tr>
<tr>
<td>Personal perspectives</td>
</tr>
<tr>
<td>Attitudes toward life and the future</td>
</tr>
<tr>
<td>Advice for improving the services of the multidisciplinary team</td>
</tr>
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</table>
Skills to Follow a Medication Scheme

All caregivers were introduced to devices to help them follow the medication scheme (alarm watch, pillbox). In the adherent group, these were successfully appropriated: “In the beginning they gave us a written scheme. We looked at it, but I think we often forgot a dose, because you can’t see what you do. With that pillbox, you can see it.”

In less-adherent patients, these aids did not seem to work very effectively: “When I hear the alarm, that helps remind me to take the medications; I think, ‘I’ll take it in a while,’ and then sometimes I forget.”

Weekends and holidays posed additional challenges. Adherent patients overcame these with greater ease: “During the weekend, I set the alarm for 8 o’clock. I get up, give her the pills, and she continues sleeping.”

Less-adherent patients did not seem to cope as well: “Sometimes during the holidays, I forget. When I wake up then, I see it is much too late. I still take them, but it is too late.”

Self-Efficacy

Adherent patients clearly perceived themselves as able to adhere. They mentioned drug intake as a routine, well integrated into their daily activities: “Everything goes perfectly. It is a routine. There is really no problem.” They stressed that the monitoring of laboratory results confirmed their ability and motivated them to continue.

On the contrary, 2 less-adherent patients still perceived adherence as a difficult task: “It is very difficult to take in time, every day again,” and, “Sometimes I take, sometimes I forget, sometimes I say ‘no.’ Sometimes I’m so tired of taking.”

Problem Solving

Apart from skills and self-efficacy, caregivers need to be able to solve new emerging problems.

Coping With Child’s Resistance

Almost all caregivers mentioned a history of opposition from their child as a result of bad taste and side effects. Adherent patients demonstrated creativity in solving such problems: “I tried to give him nice tasting things, to promise him a reward. I tried many ways. Sometimes he accepted, sometimes he refused and then I had to force him.” Caregivers of less-adherent patients did not mention any such strategies: “It was always a fight to make him take the medication.”

Disclosure to Child

In some cases, disclosure of HIV status was a necessary step to overcome the child’s opposition. When children did not feel sick, they did not understand why they had to take the medication. Therefore, caregivers gradually explained to their children that they had to take the medication to prevent the onset of illness, but they preferred not to mention HIV until the child would understand the meaning: “He knows that he has to take his pills, but he

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adherent</th>
<th>Less Adherent</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of children</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Gender of child</td>
<td>5 girls, 3 boys</td>
<td>1 girl, 2 boys</td>
</tr>
<tr>
<td>Mean age of child, y (range)</td>
<td>8.5 (0.25–17.25)</td>
<td>13 (6.70–18.75)</td>
</tr>
</tbody>
</table>

**TABLE 2. Characteristics of the Caregivers and Their Children**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adherent</th>
<th>Less Adherent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regimens</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 NRTIs + 1 NNRTI</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>2 NRTIs + 1 PI</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2 NRTIs + 1 boosted PI</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>2 NRTIs + 1 NNRTI + 1 PI</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>2 NRTIs + 1 NNRTI + 1 boosted PI</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

**TABLE 3. Characteristics of the Medication**

<table>
<thead>
<tr>
<th>Characteristic of Medication</th>
<th>Adherent</th>
<th>Less Adherent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean duration of therapy, y (range)</td>
<td>4 (0.25–7.10)</td>
<td>5 (3.30–6.25)</td>
</tr>
<tr>
<td>&gt;3 antiretroviral medications</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>2 doses/d</td>
<td>8</td>
<td>3</td>
</tr>
</tbody>
</table>

NRTI indicates nucleoside reverse transcriptase inhibitors; NNRTI, nonnucleoside reverse transcriptase inhibitors; PI, protease inhibitors.
doesn't know why. He only knows that he will become ill when he doesn’t take them. The child is too young to understand; he would possibly start talking about it at school.”

Adherent caregivers mentioned that the child usually became more cooperative after disclosure. The child felt responsible and helped to remind the caregiver about the medication: “Now, she understands and it has become a routine. She can forget her schoolbag, but not her syrup, ‘Mum, we have to go to school and I didn’t get my syrup yet,’ she says.”

Among the less-adherent caregivers, 2 of 3 children were informed of their HIV status at 11 and 14 years and were still struggling with their diagnosis years later. This clearly did not enhance their cooperation: “Before knowing his status, he sometimes refused his medication. He told me that he was cured, that he didn’t feel pain anymore. He said that he didn’t have to go to the hospital anymore. Once the team revealed the disease to him, he behaved very difficult. He didn’t want to do anything anymore.”

**Coping With Stigma**

The stigma attached to HIV hampered the systematic intake for all interviewees. Calling it “the disease of shame,” they wished to keep the child’s condition secret.

In the less-adherent group, this was an important reason for not taking the medication or taking it too late: “When I am with somebody else, I think, ‘How will I do?’ When I get back home, then I take, but it is too late.”

Adherent caregivers had many ways to avoid this problem. They mentioned adapting the intake of medication to their social activities. Some had meticulously planned their intakes at times when they did not expect visitors: “I give her the medication at 6 o’clock in the morning, because I don’t like to give medications when there are people.” Others found ways to take medication very discreetly when people were around, eg, by giving the child an excuse to leave the room or pretending the medications were vitamins. Others even decided to restrict or avoid social contacts that made adherence difficult: “I can’t let her stay overnight at friends, because of the medication.”

Although dealing with HIV openly would free caregivers from having to hide the medication, disclosing HIV status to others was not common. One caregiver was open about her child’s HIV status. Four caregivers disclosed to 1 particular person, from whom they expected to receive empathy and support. The remaining 6 caregivers kept the disease secret. Only 1 of 3 less-adherent patients disclosed the diagnosis to the family and school.

The inability to disclose HIV status led to social and emotional isolation. As such, the psychosocial team had a very important support role: “I tell my problems to the doctor, because I have nobody to tell. When I’m distressed, I tell him and then I feel better.”

**Motivation to be Adherent**

Willingness to adhere depended on 3 factors: the acceptance of HIV diagnosis, the emotional quality of the mother-child relationship, and the recognition of future prospects. When learning about the child’s initial HIV diagnosis, all caregivers described similar phases of the HIV-related coping process: an initial response of denial, followed by anger, depression, and a deep sense of grief. Finally, facing the reality of HIV/AIDS, adherent caregivers accepted the disease within their own system of beliefs and values: “You have to learn to live with it. Everybody has a problem, well, that’s my problem.”

It may be assumed that feelings of guilt about vertical HIV transmission influence adherence: “I feel guilty, but fortunately she is in good health. I feel that I have to maximize my love; giving medication is protecting her against the illness.”

Adherent caregivers became convinced that medication created new possibilities. As a result, they set new goals for themselves. These perspectives reinforced their efforts to be adherent. Adherent caregivers often mentioned personal experiences that convinced them of the potential of the drugs: “I know that I have to give the medication to my child, that I have to be strict. This is my own will, because my husband died of AIDS.”

They felt anxious about their child’s health and future and perceived medication as a weapon to protect him or her against illness and death: “I realize that I have the power to postpone the death of my child thanks to the medication.”

As a result, they tried to enjoy life with their child as much as possible and made plans for the future: “In Africa, having HIV meant dying very soon. Here it’s different with the medication. I will start to study and become somebody.”

Patients made their personal analysis of perceived benefits and costs of taking medication. Adherent patients perceived that advantages outweighed perceived inconveniences: “I prefer the heavy triple therapy to the suffering caused by the disease.”

On the contrary, less-adherent individuals seemed not to have completed all stages of the coping process. They did not deny having the disease but struggled more about the painful reality of HIV/AIDS: “I wonder why I always have to take medicines, why am I alone, why do I have HIV.”

Their future perspectives seemed to be less clear. Some caregivers did enjoy life but rather by living from one day to the other. The future would confront them with the painful reality of their disease: “I don’t like to think about the future, because of the disease. I know I’ll become ill,” and, “I am waiting for death to come, or the, the . . . thing.”

**The Process of Becoming Adherent**

All interviewees reported an evolution in their knowledge, capacities, and motivation to achieve adherence. However, the stage of evolution differed in adherent and less-adherent caregivers. Regarding knowledge, the pace of evolution in internalizing the information provided by the care team, was differ-
ent. Regarding practical problems, all patients faced difficulties with adherence at the beginning of the treatment. The adherent caregivers prioritized the medication and progressively overcame all practical obstacles, learned to integrate the medication into their daily life, and were creative in finding solutions for newly occurring problems. Thus, pill taking became a routine, something they did without thinking: “In the beginning, we used an alarm to help remind us when to take. Now it’s a routine.” Adolescents mentioned a difficult transition period when they became responsible for the intake of their medication. They had to learn to organize their day around the medication and often forgot to take them.

An important difference in motivation between adherent and less-adherent caregivers was linked to the coping process and its progress. Adherent caregivers, in particular adherent adolescents, clearly had reached the stage of acceptance more often and had set new goals: “You forget because you have other things to do, the children are waiting for you to take care. I had to accept.”

DISCUSSION

Our study was limited by the heterogeneity of the studied population that was recruited from 1 referral center. We included infants and adolescents, which might introduce a difference in the relative importance of the factors that influence adherence. However, we think that this sample provides a realistic picture of the diversity of children followed in an AIDS referral center. This might increase the external validity of our findings. Another obvious limitation was the small number of less-adherent patients. It thus may be difficult to forge conclusions for factors that inhibit adherence behavior. Therefore, we scrutinized the results for recurrent differences between adherent and less-adherent patients.

Our findings confirmed that knowledge, capacity, and motivation are important determinants of adherence behavior. Caregivers had to become convinced of the importance of adherence (knowledge), of their ability to achieve it (capacity), and of their willingness to administer the medications to the child (motivation). These 3 determinants had to be permanently and concomitantly present during the whole therapy to make medication a priority in daily life.

Our study revealed important differences between adherent and less-adherent caregivers for these 3 factors and, more precise, in their evolution. Regarding knowledge, adherent patients were strongly convinced of the necessity of medication and transformed adherence into a personal objective. On the contrary, less-adherent patients still perceived the medicinal control of the disease as imposed on them by the care team. Our findings on differences in internalization thus are in line with other studies showing that patients with an internal locus of control achieved better adherence than those with an external locus of control.33

Regarding the capacity to integrate medication in daily life, adherent caregivers developed an array of solutions to practical problems and stigma. Less-adherent caregivers still perceived these problems as a daily burden. This corresponds with Reddington’s pediatric study,7 which stated that the main difference between adherent and nonadherent caregivers was the feeling of inability to adhere (capacity).

Motivation seemed to result from a personal cost-benefit analysis. The complex therapy with its side effects, the burden on daily life, and the social limitations as a result of social stigma weighed on the negative side of the balance. The possibility to postpone the onset of illness, i.e., to fight for the child’s life and future, weighed on the positive side. In the case of adherence, the perception of advantages of medication outweighed the disadvantages. This cost-benefit analysis is in line with the findings of Donovan’s qualitative study exploring adherence to rheumatoid arthritis medication in adults.34

In conclusion, the interviews of caregivers revealed the same 3 determinants as those proposed by Fisher and Fisher for effective interventions in their Information-Motivation-Behavioral Skills model.35–37 In addition, our results suggested a dynamic dimension in the adhering process. Knowledge, capacities, and motivation developed progressively, related to the stage of coping. Indeed, most caregivers mentioned an initial response of denial, followed by anger, then bargaining, depression, and finally a deep sense of grief. This process corresponds with the 5 stages of mourning identified by Kübler-Ross.38

Our findings suggest that once the disease was accepted, the caregiver internalized the presented information (knowledge) and engaged in the fight for the life and future of the child through good adherence to the medication (motivation). The medication became a focal point in their life. To sustain their behavior, they developed skills to integrate the medication into their daily life and finally achieved a routine (capacity). Thus, caregivers were capable of solving new problems related to side effects, social stigma, or change in daily routine. Less-adherent caregivers were situated at less advanced stages of this coping process and thus were found to be struggling with the treatment. Hence, the stage of the coping progress is crucial.

CONCLUSIONS

From these findings we can draw some conclusions on effective intervention strategies to improve adherence. First, the care team should work continually and concomitantly on all 3 factors: knowledge, capacity, and motivation. This is in line with a meta-analysis of adherence concluding that “comprehensive interventions combining cognitive, behavioral and affective (motivational) components were more effective than single-focus interventions.”39

Second, it is crucial to take the evolutionary nature of the caregiver’s and the child’s coping process into account. Because of the great number of obstacles to adherence, it may be worthwhile for the care-providing team to consider nonadherence as the default setting, i.e., the starting point at the beginning of treatment. The care team should tailor its approach to the individual progress of grief and acceptance.
Regarding the knowledge component, as initial denial disturbed the internalization of information, it is recommended that the care-providing team repeat the information when the caregiver makes progress in his or her coping process. Making the caregiver a partner in treatment decisions should prevent him or her from considering the information an external matter. Regarding capacity, the care-providing team should not only advise on practical problems but also empower the problem-solving capacity of caregivers to encourage it to evolve. The care-providing team has to know whether the caregiver has an autonomous or a dependent type of personality. To enhance their self-efficacy, caregivers should be allowed to express their fears and uncertainties during consultations. It is important to provide positive reinforcement, e.g., through laboratory results. The periods of well-being can be used to fortify the relationship between the care-providing team and the caregiver, so that support can be given during stressful times.

It has been pointed out that HIV is a special case in the investigation of adherence in that a much higher level of adherence is required than with most other chronic diseases. However, the factors that were found to contribute effectively to adherence—knowledge, motivation, and capacity—and their evolution over time can be seen as universally affecting the process of establishing adherence. Improving knowledge among (pediatric) patients, motivating them to participate in the treatment, and improving their skills to cope with the disease in general and adherence in particular may be worthwhile strategies for other chronic diseases. Although the persisting stigma associated with living with HIV negatively affects adherence, it is likely that adherence outcomes with treatment for other chronic disease may even be better when adopting strategies based on the principles of improving knowledge, motivation, and capacity building among patients.

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Integrating Adherence to Highly Active Antiretroviral Therapy Into Children's Daily Lives: A Qualitative Study
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Pediatrics 2004;114;e591
DOI: 10.1542/peds.2004-0085

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