



AIDS TREATMENT UPDATE

Take as prescribed

What does adherence research say about the challenges positive people face today?

BY WILL ANDERSON

Getting people to take their medications as prescribed has always been a problem for medicine. However brilliant the achievements of the modern medical machine, the complicated social world of individual lives always lurks outside the clinic door – a world which medicine would often like to ignore, but which won't go away. Adherence to medications brings these two worlds into conflict. However vehemently doctors implore their patients to comply with their instructions, adherence to these instructions is always beyond their control. Whether or not medications are taken, ignored, forgotten or thrown away depends on individual lives in all their difference and complexity.

Currently HIV clinics, care services and even HIV prevention organisations are all developing initiatives focussed on tackling the 'problem' of adherence to HAART. In these pioneering times, the question of who is best placed to address this problem remains open and all sorts of ideas for interventions are being generated. This enthusiasm to respond to the challenge presented by adherence to HAART seems well-founded, given the crucial role of adherence in the long-term success of antiretroviral therapy. But there is an irony in all this professional activity. For adherence to HAART is a challenge which, ultimately, people with HIV must tackle for themselves. The medications have to be taken, day in, day out, and only self-help in its most basic form will ensure this takes place. No-one else can take the pills for you.

Recent evidence suggests that most people with HIV are doing very well in coping with the demands of adherence to HAART. In a recent qualitative study of HAART, participants described their experiences of learning to live with the pills [1]. Their stories were characterised by the process of adjusting the routines

of their daily lives; integrating the treatment schedule meant making the pills as routine as everything else:

"It gives me a structure to the day. I have to get up, basically to feed the animals. Then I take my drugs and then I have to wait an hour before I can have breakfast. The midday one is the peculiar one because I've got to wait either an hour before food or two hours after food to take it. Then in the evening I end up having supper at 10 o'clock at night which gives me indigestion... So that's the regime and I have to carry that through, but it's not difficult – just very boring."

Other participants in the study described similar daily routines with varying degrees of acceptance, frustration and resentment. But they all shared a common commitment to taking the pills; to making whatever adjustments to life that were necessary. This was not always easy, but the alternative was far worse:

"Sometimes I feel tired of the drugs. But it's like food that when you don't eat, you die. You have to eat. I can't say that I can stop now."

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Any understanding of adherence (and non-adherence) to HAART must begin with this basic equation. People taking antiretroviral medications understand the choices they face. This was confirmed in Sigma's recent national study (see *AIDS Treatment Update 76*): almost all (97%) of those who were taking HAART agreed with the statement that 'HIV is still a very serious condition'. Furthermore, 94% said they knew that 'HIV can become resistant to treatments, especially if they are not taken properly' [2]. So not only is HIV still perceived to be very bad news, but the unusually harsh consequences of non-adherence are also widely understood.

This combination of incentives for adhering to HAART is unusual among treatments for chronic diseases. The general research literature on adherence to medications proposes that willingness to take treatment depends on assessment of the severity of the illness and susceptibility to it – if you do not think that your illness is very serious, or think that it will not affect you much, you are unlikely to take medications properly. People with HIV know where they stand on these issues.

Consequently, although rates of adherence average a meagre 50% in many other conditions [3], people with HIV miss a dose much more rarely – three quarters of those responding to Sigma's study had not missed a dose in the previous week, i.e. they were 100% adherent. Research into other conditions has also shown that many people adjust treatment regimens to fit in with the other demands of their lives, which may often be considered far more important than taking medications [4]. People with HIV understand they must do their best to adjust their lives to fit the treatment regimen, not the other way round.

The contrast with research into other illnesses draws attention to how comparatively well people with HIV are doing in adhering to their medications. This is contrary to the usual perspective, which starts with the assumption that perfect adherence to HAART is essential and then judges how poorly people with HIV are doing. But it is only by recognising how unusually good people with HIV are at sticking to their regimens, that non-adherence to HAART can be understood.

WHY ARE DOSES MISSED?

People with HIV do not usually miss doses because of a lack of motivation to take the treatments or because they choose to give greater priority to other things in their lives.

Although occasional 'drug holidays' for special reasons are not unknown, deliberate non-adherence is rare.

The reasons for non-adherence to HAART reported in recent studies suggest that doses are usually missed either because people forget or because of nausea or side-effects. Forgetfulness and failure to plan ahead are the main reasons for non-adherence. Forgetting happens for many reasons – being too busy, being distracted, being too involved in work or pleasure. It is also easy to forget the pills when going out or to find yourself away from home for longer than expected. Sleeping through a dose indicates another failure to plan ahead. Any kind of change, interruption or intrusion into individuals' established daily routines can undermine

“Although timers, alarms and other devices have their place, they should be tools within a larger endeavour.”

expectations, divert reminders and make it easier for doses to be missed.

The minutiae of anyone's daily life are unique: the unpredictability of life works itself differently into every personal story. This is why it is impossible to predict who will or will not be adherent. The attempts of dozens of recent studies to identify characteristics of people who are more likely to be non-adherent have largely failed to produce any clear results – only poor mental health is consistently associated with lower adherence. There is too much going on in any individual's life for any one aspect of that life to be generally predictive of non-adherence. For example, although a study of women's experience of HAART has drawn attention to the particular strategies that women with children may employ to maintain adherence [5], in general women are no more or less likely to be non-adherent than men [2,6]. Even

EDITOR'S NOTE

This special issue of *AIDS Treatment Update* focuses on adherence to anti-HIV treatments – the business of taking every pill exactly as prescribed; an essential part of successful therapy. In planning this issue we were interested to find out the nature of the problem, whether we know what works, and how this is reflected in the current practice of some of the major treatment centres, and those who commission their services.

This month's Factsheet offers practical tips to help adherence. An earlier Factsheet (number 9, November 1996) explained *Compliance*, another word for adherence, and is available from NAM.

such basic things as the numbers of medications, doses and pills people take have no consistent association with adherence.

QUALITY OF LIFE & ADHERENCE

At this point a distinction needs to be made between people's success in adhering to HAART and their experience of taking HAART. These are very different things, requiring different kinds of interventions. Someone who finds taking medications every day extremely difficult and frustrating may nonetheless be perfectly adherent. Similarly, someone who finds that the pills barely interfere with daily life may miss doses often. Although Sigma's recent study found no associations between adherence and the numbers of medications and pills people were taking, those who had more complicated regimens were more likely to report finding HAART difficult to take [2]. People may need support to cope with taking the treatments, especially at the outset when fluctuating blood levels of the drugs may cause side-effects, but this may be unrelated to their commitment and ability to take the pills on time.

DESIGNING INTERVENTIONS

What, then, can be done to help improve adherence to HAART? Above all, non-adherence is likely to be a problem, to a greater or lesser degree, for everyone taking HAART. The attempt to identify a 'needy' minority is futile as it is impossible to predict who will be non-adherent – it is the changing circumstances of people's lives which lead to non-adherence, not who they are. There is only a clear case for special targeting of people who are depressed or who have existing difficulties coping with everyday life. In general, interventions should be designed for everyone taking HAART.

There are clearly a couple of basic things which underscore the commitment of people with HIV to taking HAART: their appreciation of the seriousness of HIV and their understanding of the consequences of non-adherence. It seems unlikely that most people with HIV need to be reminded of what the disease could do to them. But education about why adherence is important is vital – in the Sigma survey, the minority who did not know about the dangers of resistance and cross-resistance were much more likely to have been non-adherent [2]. The need here is for education – people should not simply be told that adherence is important, but must understand the reasons why this is so.

Even with total commitment to taking the medications, people still miss doses. Good intentions are not enough. Interventions

should therefore focus on helping people to overcome unintentional non-adherence. This requires planning ahead and anticipating all the myriad of changes and unexpected events that can make up anyone's life. Adherence strategies should aim not only to integrate the treatment routine into existing routines, but also to anticipate disruptions in these routines, however minor – going to bed at the wrong time, waking up in the wrong place, finding the wrong food in the fridge. Such interventions may not be complicated, but nor are they straightforward; they must be pursued systematically. Although timers, alarms and other devices have their place, they should be tools within a larger endeavour.

A RANGE OF CONTRIBUTIONS

Helping people plan for adherence should be a staple task of clinical practice. This may be better carried out by professionals such as clinical psychologists (or at least with their support) than left solely to doctors. Clinical psychologists, trained in the business of thinking and doing ('cognitive-behavioural' interventions) have plenty to offer. Systematic monitoring of adherence should be central to regular clinical monitoring and should include careful review of the reasons for any non-adherence and fine-tuning of personal adherence strategies.

The pharmaceutical companies must strive to make their products as palatable as possible as nausea before or after taking medications remains far too common a reason for non-adherence. Chronic side-effects must also be minimised. Simpler regimens will principally lead to improvements in quality of life, and this is reason enough for their development to be pursued. However, though the numbers of medications and pills taken may have little bearing on adherence, dietary restrictions undoubtedly increase non-adherence and can severely complicate people's lives [7].

Outside the clinic, it is up to every individual to knuckle down, with or without immediate support in the daily business of remembering – i.e. from partners, family or pets (see quote above). Support from social and voluntary services will be important for some in coping with life taking HAART, especially in the early stages. This support should be focussed (as it has always been) on improving quality of life, embracing a sensitivity to adherence management where appropriate.

People with HIV are doing well – remarkably well – in adhering to HAART. No doubt there is much more that can be done. But it is always going to be the people who are taking the drugs who end up doing most of it.

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Seeing the full picture

How might working with a clinical psychologist help with adherence?

BY BARBARA HEDGE

Clinical psychologists have been involved in the care of people with HIV disease since the start of the epidemic. My own work on adherence dates back to the pre-combination therapy era when many people were referred to clinical psychologists for support with their fears of losing their sight to CMV eye disease.

The administration of CMV prophylaxis was complicated and time consuming. It required central venous access and took over an hour to administer, three or more times a week. We investigated adherence and found it to be high (approximately 80%), with people carrying out the main tasks but cutting corners when they thought they could, e.g. on cleaning the central line access. Those who had good 'emotional support' were more adherent than those who did not. The availability of 'practical support' did not affect levels of adherence.

Although it is very important to provide people with the information necessary for them to take medications appropriately, information on its own is not sufficient to increase adherence behaviours. Similarly, mechanical aids such as beepers, timers and pill boxes may help but leave many of the reasons for non-adherence unaddressed.

"WHAT DO I HAVE TO GAIN?"

I see some individuals who had been ill for some time with HIV-related diseases when combination therapy was introduced. They have lost their partner and many friends to AIDS, given up work some time ago, cleared up their affairs and are ready to die. Combination therapy may have returned some good health but it cannot return the life and the people that have been lost. It is difficult for anyone to return to work or to reconstruct a social life after a period of absence of maybe five years or more. Having come to terms with the end of life approaching it's sometimes too much for an individual to face this reconstruction again, particularly as it may not be successful.

LOW MOTIVATION

Low mood and depression prevent people from assessing the situation realistically. All the negative aspects are noted and few of the positive aspects. There are cognitive, behavioural and pharmacological ways of treating low mood which are very successful,

i.e. to increase adherence we often need to address the cause, not the adherence directly.

PERCEIVED LOW VULNERABILITY

Regular CD4 counts and viral loads can be both incentives and disincentives to adherence. Good results can act as reinforcers for the behaviours which led to them. If a person has taken pills as required and then has a good set of results, then these are likely to encourage further pill taking according to instructions. However, if a person has made a number of errors in medication taking, e.g. not always observed dietary restrictions, taken some late or not at all, and then has a good set of test results, reinforcement for a continuation of such behaviours is given. The person re-evaluates the messages given by health workers into "I can take a few cuts in the requirements and still be OK". Thus the level of adherence aspired to is reduced, and the actual level of adherence achieved might be lower still. Similar decreases in adherence can result from messages given by health professionals that indicate that less than perfect adherence is satisfactory.

LOW SELF-EFFICACY

When people think or fear they cannot do a task they may not try, or may give up at the first failure – this has confirmed their fears. For people who have little faith in themselves (low self-efficacy) the message that antiretrovirals are difficult to take may deter them from seriously trying. Spending time analysing their actual abilities and weaknesses can allow attention to be paid to teaching skills which will assist them in adhering to medication regimens. (There's no point in giving information about what to do if they don't think they can do it, or teaching skills they already have).

HIGH COSTS

The regimen which seems best therapeutically for a person may have high costs. If these are too high relative to the perceived advantages the person will not adhere. Patients are often very thankful to their physicians and do not want to upset them or seem churlish. Physicians who wheedle or coax patients to take medications are likely to get an

NOTE

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agreement, but then low adherence as the patient has no motivation to comply. If an honest relationship can be forged between patient and physician, with the patient understanding that what they do is for themselves, not for the physician, and that the decision is theirs, then negotiation can take place to ensure that the patient receives the best regimen that they are willing to take. As a clinical psychologist I would aim to increase individuals' assertiveness skills so that they feel able to negotiate with physicians or to decide to change physicians if they were not satisfied. (Luckily the latter is rarely needed).

OFFERING SUPPORT

A study I am currently analysing suggests that about 15% of people on antiretrovirals are excellent adherers, a further 15% are very poor and there is great variation amongst the rest. For these 70% the most frequent reasons given for not adhering are forgetting and being unable to cope with taking pills in an unforeseen situation. This suggests that increasing skills in remembering and planning for difficult events are probably the most useful techniques for increasing adherence.

I frequently address these issues with individuals experiencing difficulties in individual sessions. I have also run (and will run more) groups for people who need some support. The times when drugs are not taken as recommended are analysed, possible options are considered and a plan is devised to minimise the chance of the same difficulty occurring again. Using a group approach has several advantages:

- ♦ they can see that they are not the only one finding the pill taking difficult and that other reasonable (not mad or bad) people have similar problems
- ♦ when looking for options for how to deal with difficulties the group is invited to give suggestions, which capitalises on the ideas of everyone and shows that there is value in their own ideas
- ♦ HIV takes so much away from people that it is important that health workers do not take away more by assisting more

than is necessary. This sort of approach, facilitating the best ideas from people with HIV is more likely to lead to empowerment and higher self-esteem which itself increases adherence.

In reality all humans are fallible and it is normal to make mistakes. The problem comes when after one or two mistakes people see themselves as failures, as unable to keep control and so give up trying to adhere. The model 'relapse prevention' encourages people to not despair if they make a mistake. It does not say it is OK, but it says that one mistake is not the end of the world. The important thing is to ensure that it does not happen again. Once again the aim is to empower people to look after themselves, not to see themselves as failures, mad or bad.

LONG-TERM PROBLEMS

In reality, as time goes on and people take medications for increasing lengths of time all the factors which affect adherence are likely to vary, e.g. reinforcement of test results, perceptions of risk and changing priorities. In all chronic illnesses, adherence is poor especially when people are well. Adherence patterns in HIV disease are unlikely to be any different, so we might expect that as medication becomes more efficacious and people take it for longer that adherence will decrease. If the real issues, i.e. setting up services to build skills, address depression and low self-efficacy are not tackled now – both clinically and through detailed research – we can expect increased problems in the future.

My hope is that the importance of the behavioural sciences might be more appreciated in the clinical setting as well as in the field of HIV prevention. In some areas, resources are being withdrawn from the mental health field to pay for HIV medications. If attention is not paid to adherence then even the best medications will fail. Now we need a truly multidisciplinary approach to treatment, utilising the skills of the behavioural scientists such as clinical psychologists as well as those of the physicians and pharmaceutical industry.

HOW MUCH ADHERENCE IS ENOUGH?

At a meeting of AIDS scientists earlier this year, researchers from Nebraska presented findings from their study of adherence in people taking protease inhibitors. The relationship between missed doses and keeping viral load at undetectable levels was startling. Of sixteen people who took at least 95% of their doses, fifteen had undetectable viral load. This figure was just three for a group of 16 who took less than 70% of their doses. At lower rates of adherence the likelihood of sustaining viral load below 400 copies fell sharply, and the greatest improvements in CD4 counts were also linked with the best adherence. (Swindells S et al. 6th Conference on Retroviruses & Opportunistic Infections, Chicago, abstract 92, 1999).

Learning from experts

Could this Australian doctor-led model be transferred to the UK?

INTERVIEW BY MEGAN NICHOLSON

Australian HIV GP Cassie Workman expects 100% adherence to drug regimens from her patients. For her part, she seeks to match drugs to people, not vice versa.

AIDS Treatment Update: What are the core elements of your approach to adherence?

Cassie Workman: It's primarily about patient education and, secondly, about individualising treatments to patients.

We usually spend around two or three hours thinking up a combination. We try to get people to work out what they're like over a period of time, versus what people would like to think they are really like. We go through a large amount of questions about their lifestyle. Get them to keep a chart – the earliest that they get up, the latest that they get up, the latest they go to bed, the earliest they go to bed – that sort of thing. And then what time they eat and what sort of stuff they eat.

We then try and match a combination. Sometimes there isn't a perfect option for people, but at least it's about patients feeling like they are in control.

ATU: What type of education work do you do?

CW: Giving [patients] a really clear idea of what the drugs should do. We get people back and do a viral load two weeks after they have started. People can see that their viral loads have dropped dramatically.

ATU: How did you develop this approach?

CW: It was taken from what people did well. I'm constantly amazed when I look at adherence studies which focus on people who can't take drugs. What we did here was talk to [those] who took drugs really really well and used their experience to get other people to take drugs well.

ATU: So you've identified the problem – what do you do?

CW: It's usually a specific set of circumstances and what we do is try to come up with some way of solving that particular set of circumstances. Whether it's that they leave a dose somewhere else or sometimes people just run out of their drugs.

In all these situations when patients find themselves without drugs, it's a crisis. About

once a week, we have to find drugs for somebody overseas. About twice or three times a week we have someone drop in and pick up a drug dose

ATU: How do you know this approach works?

CW: There have been a couple of studies from the States that suggested that you could look at viral load as a quasi study of compliance. What we had in the practice was an incredibly high rate of below detection. We'd see about 90% of patients being below detection on their first regimen. That then continues; we don't see that drop out over time.

ATU: Do people weary of treatment?

CW: I think you have to reinforce it. The vast majority of our patients have CD4 counts that continue to rise. We still ring people up when they get a higher T cell count than they've ever previously had.

ATU: Do you find people coming to you wanting to stop their drug treatment?

CW: There are a number of very interesting studies that have been done on stop-start. Unfortunately, we haven't managed to get it through to patients and other doctors that this is only about seroconverter patients. They were not chronically infected patients. You can show people the results from the studies done on chronically infected people which show that virus doubles incredibly quickly, CD4 counts drop off incredibly quickly.

Partly what people need is simply to be able to express a whole lot of that. Some doctors think it means they're after permission to stop, and I think that's crap. What they are after is some ability to actually express all of that and I think that is totally reasonable.

At the same time, we've got patients who are going to stop taking their drugs. Fine but monitor it. Do a viral load a month after you stop and let's see where it is. And a number who have done that, talk about that as actually being quite empowering. They now know why they are taking the drugs.

ATU: Any weaknesses in this approach?

CW: It's time-based, so I think that's one of the real failings of it. It's certainly not individually cost-effective.

SUPPORT MODELS

Over the next few pages health care workers actively involved in supporting adherence are interviewed. Limited space prevents us from mentioning the many other similar projects. In common with Cassie Workman's approach, Brighton's Royal Sussex County Hospital offer early viral load testing after two weeks. Their pharmacist-led clinic was formed over two years ago in response to adherence problems. Recent innovations include the availability of a short stay at respite centre, the Sussex Beacon for people beginning treatments. St Thomas' Hospital in London will shortly begin a controlled study to assess the value of a continuing programme of adherence support delivered by a specialist nurse.

Getting a good start

Delivering adherence support to the UK's biggest clinical cohort

INTERVIEW BY ANNA POPPA

The Kobler Centre at London's Chelsea and Westminster Hospital is one of the largest and best known HIV treatment centres in the UK. Over the years, one of the things it's become best known for is a relatively interventionist approach to the use of anti-HIV treatment. Now a pilot project begun several months ago ensures that everyone who decides to begin anti-HIV drugs pays a visit to the START Clinic.

Kobler Centre patients are referred to the START Clinic once they've made a firm decision to begin treatment (in discussion with the doctor they see regularly), and have considered and selected a particular drug combination. Their visit to the START Clinic is intended to support these decisions, providing information about how the drugs need to be taken and how to fit them into a daily routine. It also provides an opportunity to reverse earlier decisions, though in practice this happens rarely.

Over a whole morning at the Kobler Centre, visitors to the clinic have the opportunity to discuss their new treatment regimen with a nurse, a pharmacist, a dietician, a doctor and a health advisor. There's plenty of time to discuss dietary requirements, possible interactions with other drugs, electronic reminders, drug storage, potential side-effects, and whatever emotional issues might have been raised by the process of considering starting treatment.

Dr John Walsh has been involved in setting up the START Clinic and discussed its development with *AIDS Treatment Update*:

AIDS Treatment Update: What have been the key factors in the development of this clinic?

John Walsh: Initially it came about following a large multidisciplinary meeting at the clinic where a need for such a service was identified. This was not seen as something occurring in isolation, but as part of a range of services to aid adherence among our clinic attenders including work with people whose combination is failing, work with those experiencing side-effects to treatment, input from clinical psychologists and new initiatives by THT in the community.

There was no patient involvement at the start, as we wanted to get some sort of service going ASAP. However it has always been managed in a rather organic fashion, and since its inception we have regularly sampled the views of patients and clinicians in an

informal manner. This has resulted in a number of changes to the service. The number of investigations performed is being greatly reduced, patients will not have to come to the clinic fasted and they will be given specific appointment times with the pharmacist and myself to reduce waiting. In order to reduce information overload, visits to the dietician and health advisor will be on an as required basis, and all consultations will occur in a private clinic room.

ATU: How are you measuring its success in terms of improving rates of adherence?

JW: Proving that this improves adherence would involve a form of controlled trial, which is beyond our scope. At present we are focussing on finding ways of following up people who have attended the clinic who might have specific problems, to ensure these have been resolved.

ATU: What kind of support with adherence is being offered to people who've been on therapy since before the START Clinic began?

JW: For the last month I have been running a new clinic for people whose first combination is failing in order to ensure that they get the best out of the next one. Once our specialist nurse is in place (which we hope will be very soon) s/he will run a weekly self-referral clinic for people with adherence problems who have not yet failed (which I'm sure you would agree is more sensible than waiting until failure occurs). The aim will be either to address problems within the clinic or to act as a clearing house to direct patients to other services, such as a psychologist or a social worker.

ATU: What single change is needed to improve rates of adherence amongst people with HIV?

JW: There are as many reasons for non-adherence as there are patients on therapy. I think the most important change must be for healthcare workers to take it more seriously as an issue, and not simply pay it lip service. It needs to be a central consideration in how we plan our services and talk to patients. We need to build trust with our patients so that they are not scared or ashamed to admit the difficulties they are running into.

Doctor I've stopped the pills

Report from a counsellor-based model of adherence support

INTERVIEW BY KEITH ALCORN

Counsellors or health advisers in HIV clinics have an important role to play in adherence support, in the view of Riva Miller, Head of the HIV Counselling Team at the Royal Free Hospital, London. In a pilot study, her team is looking at the effect of a single counselling intervention on adherence, viral load, CD4 count and quality of life. The intervention is designed to encourage people to examine their beliefs about a range of issues that may affect adherence. "If you address dreaded issues early, you can sometimes – not always – pre-empt problems", says Riva.

KEY QUESTIONS

Counsellors focus on questions designed to get people to think about the personal impact of taking pills every day, such as:

- ◆ What is your understanding of HIV treatment and the effects it might have?
- ◆ What is the best outcome you can imagine, and what is the worst?
- ◆ What do you think it will be like to take pills every day?
- ◆ How will your routine differ at the weekend and what effect might this have on pill taking?
- ◆ What effect might pill taking have on your current and future relationships?
- ◆ Who would you tell if you stopped taking the pills for any reason?

Answers are assessed by getting the patient to score the severity of the problem so that these scores can be correlated with adherence, viral load, CD4 count and quality of life reports.

However, giving the correct answers is not the point of the process, says Riva Miller. "Asking the question is as important as the

answer to the question. It encourages people to think about things in ways they might not have done previously, and allows them to examine their beliefs about treatment and what is possible for them with someone who is an outsider to the clinical relationship." The approach is similar to the one used with repeat HIV testers at the clinic, and focusses on problem-solving.

At the Royal Free, 38 patients were referred to counsellors during a three month pilot study. "In several cases we have told doctors that prescription may be inappropriate because the patients' beliefs about therapy were predictive of non-adherence. In one case a patient had said yes to the doctor but told us that he had thrown AZT away in the past, whilst in another case the patient was convinced that the drugs would kill her."

However, more subtle patterns of non-adherence, such as the occasional missed dose, cannot be predicted from a preliminary interview, which is why it is useful to allow people to review where the problems might arise for themselves.

"In several cases people told us that they anticipated no problems, until we got to the question about relationships, and in particular, future relationships. This made people stop and think. We are trying to deal with problems before they arise, rather than at the stage when people come in and say, doctor, I've stopped the pills."

The process also challenges the beliefs of professionals. "We found with several patients who lead very chaotic lives that pill taking introduced structure, and the individuals said that this was good, and had been one of the benefits of going on therapy. I don't make assumptions that it will always be bad."

NEW FROM NAM: APRIL 1999 HIV & AIDS TREATMENTS DIRECTORY

NAM's acclaimed HIV & AIDS Treatments Directory is a comprehensive guide to all aspects of HIV treatment. This new fully revised edition contains a wealth of information on the latest thinking on all aspects of HIV treatment including:

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Children and adherence

Families and children affected by HIV face particular challenges

INTERVIEW BY ROBERT FIELDHOUSE

Though the number of HIV-infected children across Europe is low, in the UK they tend to be concentrated in the Greater London area. Naturally, many of these children are from families who are also affected by HIV. The experience of therapy as positive or negative by one member of the family can often influence other family members' feelings about starting therapy.

Non adherence rates in chronic childhood illnesses range from 20-80%. The highest rates are in adolescents. *AIDS Treatment Update* spoke to three members of the Family HIV Service based at St Mary's Hospital, London, to find out what measures have been introduced to help positive children to be more adherent to therapy. They were Stephen Head, a clinical nurse specialist; Jo White, a specialist health advisor; and Dr Hermione Lyall, a paediatric HIV clinician.

The vast majority of children treated at St Mary's are from African families, many of whom are concurrently dealing with complex and often stressful issues around immigration, housing, welfare as well as coping with the language barrier.

AIDS Treatment Update: How many children are currently being cared for at St Mary's?

St Mary's: We have ninety-five HIV-infected children. Sixty-three of those are on combination therapy. 75% are on triple therapy, 7% on quadruple therapy and 18% are on dual therapy.

ATU: What medications are being used?

SM: We're using all of the nucleoside analogues. AZT, ddI, d4T, 3TC, ddC and abacavir are all available as liquid formulations. We don't use ddC very often and *Combivir* tends to be used predominantly in children over twelve, as it is only available in tablet form. However it certainly makes for a simpler regimen. Both nevirapine and efavirenz are being used here in children. We've found nevirapine a wonderful drug for adherence. Twenty-one children are currently using it and only one had to be stopped due to a rash. Efavirenz can make kids feel 'spaced out'. Ritonavir, indinavir, saquinavir and nelfinavir are also currently being used.

ATU: Are there problems specifically associated with children taking therapy?

SM: Definitely. Different age groups come with their own problems and concerns. With any child under five it is highly likely that they will spit the medication out, so parents are often very confused as to whether they are able to get adequate levels of a drug into their child. With this age group it is impossible to reason with them about the need to take their medication – they might not yet have developed health beliefs but they are sure enough when something doesn't taste right!

Many of the liquid formulations are renowned for tasting foul, tablets and powder are often very chalky. We've found ddI to be more popular with children as it can be given with *Malox* (an antacid) which gives it a cherry or mint flavour.

We've found the 5 to 11 age group the easiest to work with. By this age you can involve them in the negotiation around the responsibility of taking their medication and we've found this to increase the likelihood that they will be adherent. We offer positive reinforcement to all of our children taking therapy when they do achieve the goals that are set for them. We reward them with a toy from our treasure trove.

Once children reach their teenage years, they can become very resentful of having to take medication and find it increasingly difficult to adhere. Adolescence is a time associated with beginning to take control of one's life and therapy can really interrupt this process. Often people in authority are not particularly effective as educators to teenagers – more peer support is needed and this is often very difficult because the children really only get to meet up with one another here at the hospital. We are also acutely aware of the desire of many families to maintain absolute levels of confidentiality, and this often prevents many families from making contact with other affected families.

Most children are notorious for having poor appetites and so it's not particularly helpful to put them on therapies which require them to eat substantial meals. Indeed we've looked at ways of separating medicines from food since we believe we may exacerbate an already fragile relationship to food. Nelfinavir seems to be more popular from a taste point of view but it is very chalky and the sheer amount of the powder formulation that you have to mix into food is startling.

Most children are on combinations that are dosed twice daily so this cuts out many

potential problems associated with taking medication whilst at school. Often school is the most constant thing in a child's life and we have recognised a need to keep some areas of a child's life completely free from the complications of HIV. Keeping drugs out of school makes clear sense.

ATU: How have you developed services here to address the needs of children?

SM: Each child who begins therapy is given a treatment diary. Within the treatment diary the child or their parent records information of the planning meeting which is used to discuss the child's current clinical situation, details of drugs used in the past or currently being used. From this information an action plan is developed and recorded for later reference. Getting children started on medication is easy. It's maintaining them which is difficult.

We have developed leaflets about all of the drugs, which are more child-centred. We provide each child with wall charts or diaries and coloured stickers to monitor each time they have taken their medication appropriately. Colour coding the drug containers often helps children, particularly those for whom English is not their first language, to distinguish between the drugs.

It is vitally important to remember that therapy is for life. This is why we put such a huge emphasis on a long pre-consultation before starting therapy. More and more we are finding ourselves holding back beginning therapy until we're convinced it's the right time for that child and that their family is in a position to give them adequate support.

ATU: When is the appropriate time?

SM: Preparation is the most important thing. We look at the impact of therapy on the whole

family. There are many issues which will contribute to adherence which may require intervention from agencies other than the hospital – many of the children come from families where stigma and confidentiality are big issues, let alone the big social issues – immigration and housing.

A stable home life can often be a major factor in deciding whether a child can stick to their treatments or not. Increasingly we are using the community team, which consists of social workers and health visitors to provide ongoing support to children beginning therapy. They do house calls to check that the child and the family are coping with their therapy and are able to refer the child or their family to appropriate agencies who can offer additional support.

If more than one family member has to start therapy then we tend not to start them all at the same time. Instead we would make a programme to decide when it is best to start each individual member.

ATU: What does the future hold?

SM: There are so few positive children in this country that we need multinational studies to answer the questions to all kinds of potential problems that we are concerned about: long-term toxicity and side-effects of the drugs, how to maintain ongoing adherence right throughout childhood and into adulthood.

We need drug companies to work together to produce more concentrated versions of the drugs so as to cut down on the number and size of the pills and we need better tasting liquid formulations.

The bottom line is that current combinations are too difficult for children to take. We not only want to be able to improve children's health but also maintain and improve their quality of life.

NEWS IN BRIEF

New UK Guidelines

The British HIV Association has published a discussion draft of its 1999 guidelines on the use of anti-HIV treatments. The full document can be downloaded from the joint BHIVA/NAM website at <http://www.aidsmap.com>.

A final consensus statement should be available by July and may differ from the key points highlighted here:

- ◆ The recommendation that treatment should begin at CD4 below 350 or viral load above 55,000 copies. This is a change to the 1998 guidelines which

proposed a viral load level "associated with risk of disease progression".

- ◆ Treatment during acute seroconversion is also recommended, preferably through participation in a clinical trial.
- ◆ Last year's guidelines suggested therapy should begin with two nucleoside analogues plus either an NNRTI (at viral load levels below 50,000 copies), or a protease inhibitor (at any viral load level, but particularly at high viral loads). The 1999 guidelines propose that an NNRTI-based regimen has clear advantages as first line therapy, whilst acknowledging

the absence of clinical trials proving their effectiveness in terms of reduced illness or death. Protease inhibitor-based combinations are seen as less attractive because of problems with adherence, side-effects and variation in absorption. (This issue was reviewed in Which Drugs First? in *AIDS Treatment Update* 76).

- ♦ Resistance tests may help decision making, particularly if changing therapy.

US guidelines

American treatment guidelines from the National Institute of Health have also been updated recently. They propose that treatment should be offered to anyone with a CD4 count below 500 or viral load above 20,000 copies. First-line therapy should be two nucleoside analogues plus either a protease inhibitor, or the NNRTI efavirenz. Read these guidelines (and US guidelines on treating children with HIV) on the web at <http://www.hivatis.org>.

Delavirdine & lipids

The NNRTI delavirdine has not been associated with increased levels of fats (lipids) in the blood in people new to treatment who took the drug within five large international trials. This was the finding of research presented by Professor Brian Gazzard of London's Chelsea and Westminster Hospital at the recent Nutrition in HIV Infection conference in Cannes (abstract O2).

However, people taking delavirdine were significantly more likely to have cholesterol increases if they had previous experience of anti-HIV treatment (although the total number with such increases was small in each study). Triglycerides and glucose did not rise significantly in any study group.

Increases in cholesterol, triglycerides and glucose have been common in people taking protease inhibitors. It is suspected that these changes may be linked to changes in body fat distribution, also known as the lipodystrophy syndrome, which appears to affect around 50% of people who receive protease inhibitor treatment for more than 18 months.

Steroids & wasting

A small American study has reported that the use of the anabolic steroid, oxandrolone, results in significant increases in lean body mass, weight and strength. 24 men with HIV-associated weight loss were treated with weekly testosterone injections (given at a relatively low dose of 100mg) whilst undergoing an eight week weight training programme. Half also received oxandrolone (20mg/day), which was allocated at random.

Whilst both groups benefited from the treatment they received, those in the oxandrolone group fared best. Two people on oxandrolone experienced liver toxicities, which led one to stop treatment. Others reported mood swings (in both groups) and anxiety (5 in the oxandrolone group). Increased libido was reported by 2 in each group. This study was reported in the April 14th issue of *JAMA*, and the full text is available at <http://www.ama-assn.org/special/hiv>.

Adefovir access

In early May, Gilead Sciences Inc announced that their experimental anti-HIV drug adefovir was to be made available through the French government compulsory expanded access arrangement. But other European countries will have to wait until the programme has been approved in each country, which means that it is unlikely that the drug will be available in the UK before the end of June.

Adefovir is a nucleotide analogue, a drug which stops the activity of HIV's reverse transcriptase enzyme in a slightly different way from the nucleoside analogue drugs such as AZT and 3TC. Adefovir is also active against HIV which is already resistant to AZT and 3TC, so it may be an attractive 'salvage' option (see *AIDS Treatment Update* 72).

Gilead say the drug will be made available to adults who have failed treatment with at least two nucleoside analogues and one protease inhibitor regardless of their viral load or CD4 count. The company advises that another new antiretroviral agent should be added at the same time. Doctors who wish to enquire about the scheme on behalf of a patient should call the European office of Quintiles on 00 33 3 88 77 45 98.

An adefovir intensification study is due to begin recruiting at centres in the UK shortly. The ADHAART study (Gilead Protocol 415) is a blinded, placebo-controlled trial which will investigate the effects of adding adefovir to the treatment of people with viral load between 50 and 400 copies, who have been on stable HAART for at least 16 weeks. Full details are on <http://www.aidsmap.com> in the Clinical Trials section.

Viagra warning

Viagra producers Pfizer have warned that people taking the drug alongside protease inhibitors should decrease the *Viagra* dosage to 25mg in order to limit the risk of potentially dangerous drug interactions. Only one 25mg dose should be taken within a 48-hour period. This safety warning also applies to people taking the antibiotic erythromycin, or anti-fungals ketoconazole or itraconazole.

ADVISORY PANEL

We are pleased to welcome Dr Barry Peters to NAM's Medical Advisory Panel, which comments on *AIDS Treatment Update*'s content prior to publication. Barry is Senior Lecturer and Head of the Academic Department of Genitourinary Medicine at St Thomas' Hospital, London.

NOTICEBOARD

New services

TAIC (Treatments, Advice, Information and Support) is a new service for gay and bisexual men which is being piloted in the Edinburgh area. Information, a telephone helpline, support groups and counselling are all part of this new project from Gay Men's Health and SOLAS which aims to offer practical and emotional support to both HIV-positive and untested men. For more details call Gay Men's Health on 0131 558 9444 or SOLAS on 0131 661 0982.

In London, the Terrence Higgins Trust are currently seeking HIV Treatment Buddies – volunteers who can give support to people starting or having difficulties with their therapy. You need not be on treatment yourself and training and support will be provided. Contact the THT Volunteer Office on 0171 831 0330 for details.

THT have also announced a new Treatment Support Group for people new to combination therapy. The group begins on June 10th and runs for six weeks. For information about joining call the Counselling Team on 0171 831 0330.

Body Positive in London will be offering courses on managing treatments for people

currently on combination therapy. There will also be one-off evening sessions for people about to start taking treatments. Both will begin September. Contact Robert Fieldhouse at BP on 0171 287 8010 for details.

NAM forums

June's forum, 'Treating Primary HIV Infection', is on Monday, June 21st and the guest speaker is Dr Sabine Kinloch of the Royal Free Hospital, London. Sabine will discuss the potential benefits of being tested for HIV very soon after being at risk. People who discover they are HIV-positive in this early period could take treatments to protect immunity which is lost as HIV progresses.

On July 26th, Dr Graeme Moyle from London's Chelsea & Westminster Hospital will speak on 'Fat Changes and Lipodystrophy', presenting the latest information from the First International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV to be held in San Diego in late June.

The venue for both meetings is the Palms Room, 4th Floor, University of London Union, Malet Street, London WC1. Admission is free and the forums run from 7pm to 9pm. A sign language interpreter is available.

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ANY QUESTIONS?

The following national agencies, all based in London, offer one-to-one advice and information about treatment options, in person or over the telephone:

◆ AIDS Treatment Project

Phoneline: 0645 470047
Monday & Wednesday, 6pm - 9pm
All calls charged at local rates.

◆ Body Positive

Treatment Advice: Tue, Wed & Fri 2pm - 7pm
Call Adam, Jo or Robert on 0171 287 8010 to make an appointment.

◆ The Terrence Higgins Trust

Helpline: 0171 242 1010 Daily 12noon - 10pm
Treatment Support: Call Sarah Porch on 0171 831 0330 for an appointment.

NAM recommends readers to seek treatment advice from more than one source, and to discuss all your decisions with your doctor.

The publishers have taken all such care as they consider reasonable in preparing this newsletter. But they will not be held responsible for any inaccuracies or mis-statements of fact contained herein. Inclusion in this newsletter of information on any drug or clinical trial in no way represents an endorsement of that drug or trial. This newsletter should always be used in conjunction with professional medical advice.

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