ISSUE 15 1999

The Birchgrove

THE BIRCHGROVE GROUP, P.O. BOX 9, ABERTILLERY, WALES NP13 1YD. TEL: 01222 520045

Knowing when to stop.

New research prompts warning to people on treatment:

Don't try this at home

One of the questions most frequently asked at NAM Information Forums and Treatment Workshops is "When can I stop combination therapy?"

Until very recently the established wisdom was that combination therapy, like a puppy, is for life. However, some researchers are now suggesting that stopping treatment in controlled circumstances may not always be harmful. In fact, it may hold the key to long-term control of HIV without the need for continuous therapy.

At last month's 6th Conference on Retroviruses and Opportunistic Infections in Chicago, Dr Franco Lori of the US-Italian research body RIGHi; presented further information about 'the Berlin patient', a man who received treatment with ddI, hydroxyurea and indinavir just after becoming infected. The man interrupted treatment twice due to other medical conditions (with a slight viral load rebound the first time), and eventually stopped altogether. When he finally stopped, his viral load was undetectable and has remained so ever since.

At the Geneva AIDS conference last July, Lori reported that no replication-competent HIV could be isolated from the lymph nodes of the patient, but further tests have revealed very small amounts. However, no viral load rebound has occurred after two years off treatment, and strong anti-HIV immune responses have been detected. Dr Lori believes that these responses may have been stimulated by a period of brief and not too high viral rebound, and have remained strong enough to control residual HIV replication when therapy was stopped altogether.

To test his theory, Dr Lori has investigated this treatment model using ddI, hydroxyurea and PMPA (a nucleoside analogue like adefovir) to treat SIV infection in three macaque monkeys. After several treatment interruptions during which viral load rebounded, the monkeys are now off treatment again, and so far, have gone for over one hundred days without any viral load rebound. Dr Lori's team also reported on three people who started treatment on ddI, hydroxyurea and either d4T or a protease inhibitor with viral loads ranging from 1 6,000 copies to 720,000 copies. All started treatment within one year of infection. Rather than having missed doses or taken what are commonly called 'drug holidays', these people followed a structured treatment pattern of three weeks on treatment, an interruption until viral load rebounded above 5,000 copies, three months on treatment, another one week interruption, and a further three months on treatment before another interruption. At each treatment interruption the time it took for viral load to rebound grew longer, leading the researchers to suggest that the immune system may be playing a role in controlling HIV

Four people treated with AZT / 3TC and ritonavir soon after infection were studied by the Aaron Diamond Centre in New York. Researchers reported that two of the men, who had interruptions in therapy due to poor adherence, had undetectable viral load for 21 and 1 4 months respectively after stopping therapy completely. On the other hand, two men who stopped therapy abruptly after similar breaks in treatment had viral load rebounds within three to four months. Long- term

continued on page 1

When to Stop

Continued from Front Page

undetectability and the speed of viral rebound was associated with the strength of H IV-specific cytotoxic T-lymphocyte (C D8) responses, which may have been stimulated by brief bursts of viraemia.

These studies have all looked at people or monkeys infected with HIV (or SIV) for less than one year who began treatment very soon after infection. Similar experiences in people who began treatment later have not been reported, and appear unlikely given the progressive loss of immune function seen in people with longer-term infection. In fact Dr Lori himself conjectured after a recent speech about his work given in London, that the preservation of HIV-specific immunity might be dependent on starting treatment during the short 'window period' before seroconversion.

"This is experimental data which is of interest but should not lead any individual to change therapy for the moment", said Lori.

WHAT'S HAPPENING IN PRACTICE?

In other cases where people have stopped anti retroviral therapy and stayed off it for some weeks or months, viral load comes back. There has been speculation that part of the reason for this rebound is the disappearance of HIV-specific immune responses. Paradoxically, if HIV suppression is 'too successful', the HIV proteins which the immune system needs to encounter in order to programme an HIV-specific immune response may be removed. Immunologists at the Chelsea and Westminster Hospital and elsewhere are working on a variety of projects to see what HAART does to HIV-specific immunity, and how it can be assisted with substances like interleukin-2, interleukin-1 2 and a therapeutic vaccine called Remune.

However, researchers disagree about the extent to which HIV-specific T-cell responses matter. Although long-term non-progressors usually have very good HIV-specific immune responses, it is still unclear whether these are the essential mechanisms responsible for their non-progression. Their absence may be a marker of some other immune deficiency which ideally, critics argue, should be measured directly.

Long-term non-progressors are very rare. The usual response to HIV infection is for the virus to overwhelm the immune system in the first weeks of infection and delete the very cells that would normally play a key role in controlling a viral infection - cytotoxic T-cells. Researchers such as Dr Lori argue that if HIV is successfully controlled by HAART, replication can be shut down leaving a small amount of HIV-specific immune cells ready to respond next time the virus gets out of hand.

DANGEROUS AND MISLEADING

In the US and Europe activists and clinicians are concerned that these new findings represent a dangerous signal to people with HIV that it may be OK, in fact even beneficial, to take short drug holidays. Professor Tony Pinching of St Bart's Hospital, London, cautioned: "The research studies being described are just that - research in progress. There is no clear indication as to whether or in what circumstances they are generalisable. Great care is needed pending further data". Recent research at the Royal Free Hospital, London, due to be published shortly will show that in people who have low CD4 counts and high viral load before commencing therapy, an interruption of drug treatment leads to a high viral load rebound and a failure to regain viral control after resuming treatment Even in people who start therapy during primary infection, and who stop after one year, the response may not be good. Eight patients in the Spanish EARTH study with viral load below 20 copies after one year's therapy discontinued treatment with d4T/3TC/ritonavir. Three out of eight experienced a viral load rebound to at least half a log above their viral load level when they first started treatment, and every patient had detectable viral load within two to three weeks of stopping treatment. However, all eight saw their viral load back below 20 copies within a few weeks of resuming the d4T/3TC/ritonavir regimen.

HAART after a long period of undetectable viral load may be problematic because it could 'reset the clock' of viral clearance. Long-term protease inhibitor treatment is associated with a significant clearance of cells actively producing HIV. Stopping therapy could allow a burst of viral replication to establish new reservoirs of infected cells, rather than improving immune control of existing low levels of HIV production. This view is criticised by some as speculative however. Given that proponents of the viral eradication hypothesis now estimate that HAART must be taken for 26 years before the virus may be removed from all body compartments, a short break in treatment represents only a small proportion of this time. Short interruptions in treatment might also encourage the development of resistance. Some drugs pass through the body more quickly than others. For example, the time taken for half the dose of efavirenz to be eliminated from the body (called the half-life)

QUEST STUDY

This study is designed to assess if treatment (with Combivir, abacavir and omprenovir) early in the course of primary infection or recent seroconversion can lead to durable viral suppression after the drugs are stopped. The trial will also compare continuation

When to Stop

cont from P 1

on three drugs versus four after an initial four drug induction period. Trial sites are in Belfast, Brighton, London and Manchester. Absorption for Efavirenz is around 15 hours, nevaripine around 30. People who stop taking either of these drugs will therefore still have active quantities of drug in their blood for several days after. If stopped at the same time as other drugs with much shorter half-lives, the slowly diminishing levels of efavirenz or nevirapine act as effective monotherapies. This is a risky strategy - it is well established from early research on NNRTIs that they are particularly vulnerable to the rapid emergence of resistance when taken alone.

However, a number of recent studies have shown that it is quite possible to have a viral load rebound without evidence of resistance to all the drugs being taken. In the Spanish Earth study (referred to above), there was no sign that resistance to 3TC, (which appears rapidly when the drug is taken in the presence of ongoing viral replication), emerged as a consequence of stopping treatment. If you already have drug resistance, especially to a protease inhibitor, and you have run out of new drugs with which to construct a regimen, some people might suggest that you stop treatment altogether in order to stop the accumulation of drug resistance in your virus population.

Whilst some researchers have suggested that protease inhibitor resistant virus is less harmful to CD4 cells, research presented in Chicago suggests that only saquinavir resistant virus had this effect in animal experiments. The long-term benefit of protease inhibitors in people with detectable or rising viral load may be associated with their ability to reduce rates of apoptosis (cell suicide of CD4 cells), independent of their effect on HIV replication.

A PERSONAL VIEW

Alison Gray, Treatments Officer at the Terrence Higgins Trust, recently came off treatment after two and a half years on a variety of regimens. "I first stopped treatment two days before Christmas in 1997. I was taking d4T/3TC/ ritonavir and had a constant metallic taste in my mouth. I decided that I wanted to taste my Christmas dinner, so I stopped taking ritonavir. I remember looking in the fridge at the capsules that night and just thinking "No". It wasn't a considered decision!"

Alison stayed on d4T/3TC and added nevirapine about a month later, but at this time she didn't have accurate information about her viral load because the test being used at her clinic couldn't measure her HIV strain accurately. By the middle of 1998 the new combination was showing signs of failing, and Alison decided to take a complete break.

"I made sure I got a resistance test before I stopped so I knew which drugs were failing, and if you can't get resistance testing at your clinic yet, I would advise getting a blood sample stored that can be tested later on."

"Given my general health, which is fairly good at the moment, and my travel plans over the next few months - several trips abroad - I decided to have a rest for a few months before starting on a six or seven drug regimen. After two and half years of taking pills the psychological breathing space is important to me".

Summary:

Alison Gray's experience highlights how a decision to stop treatment might be reached for many different reasons, including:

- Planned interruptions to therapy due to lifestyle factors such as holidays or recreational drug use.
- Stopping due to side-effects or illness.
- Stopping after loss of virological control and exhaustion of alternative treatment options.
- Stopping or interrupting therapy to stimulate an immune response.

Guidance:

- If you are planning to stop for any reason, talk to your doctor first!
- It may be best to stop all drugs at the same time, not just the drug which is inconvenient to take or which is causing side-effects, though this will depend on the drugs you are taking.
- If you are stopping ritonavir and switching to other drugs you may need a 'washout' period to allow your liver to go back to normal, otherwise it may flush some new drugs out too fast.
- Although a few cases have been reported in which brief interruptions to treatment might have long-term benefit, these people all began treatment soon after infection.
- Evidence suggests that drug holidays lead most often to viral load rebound and a risk of drug resistance, narrowing future treatment options.
- If you are having difficulty remembering to take medication, talk to your doctor, an HIV pharmacist or other HIV specialist services as soon as you detect a problem. Don't wait for your next clinic visit to discuss problems of this sort.
- Until you are advised otherwise, missing any doses is a problem that needs to be reviewed with your doctor or pharmacist in order to work out how to avoid it in the future.

WHATS NEW

Immune Therapies

Immune therapies are treatments which influence or modify certain components of the immune system. Apart from drugs designed to attack HIV directly, a number of immune therapies are also being investigated for use by people with HIV for the purpose of boosting immunity and to try to correct the abnormalities seen in HIV infection.

Interleukin-2 (IL-2)

Cytokines are chemical messengers secreted by immune cells which co-ordinate and control the intricate workings of the immune system. IL-2 is a type of cytokine which encourages the growth of CD4 T-cells. Genetically engineered, or recombinant, IL-2 is being tested as an immune therapy for people with HIV

IL-2 is a very efficient trigger of HIV replication, because when it activates CD4 cells it also activates HIV-infected CD4 cells. For this reason, IL-2 has tended to be tested in combination with anti-HIV therapy to suppress the HIV activation.

A current UK study is investigating its use alone. Other research is looking at whether IL-2 might have a role in attempts to purge HIV from the reservoirs of long-living immune cells which appear to be persistently infected despite long periods of potent anti-HIV therapy.

People treated with IL-2 plus anti-HIV therapy experience a significant, sustained improvement in their CD4 counts compared to people who receive anti-HIV therapy alone. It is not clear whether this signifies improvement in the function of these CD4 cells. It's also not clear at present whether IL-2 will affect the long-term risk of disease and death.

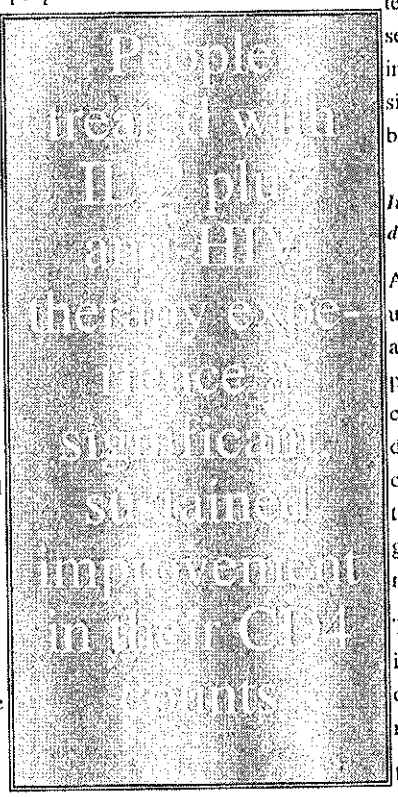
Today, IL-2 tends to be given in five day cycles which recur every couple of months. Treatment is given by subcutaneous (under the skin) injection to improve the rate of side-effects. However, side-effects can still be very unpleasant, often described as similar to a bout of flu.

Remune

A vaccine is a substance intended to stimulate the body's own immune defences against a micro-organism. While preventative vaccines are designed to protect the recipient against initial infection with a micro-organism, therapeutic vaccines are designed for people who are already infected with a micro-organism.

In HIV research, the lead candidate in this category is Remune, a therapeutic vaccine made from HIV particles which have been made harmless. The theory is that by injecting these particles into people who are already infected with HIV the immune system may be stimulated to mount a greater response not only to the killed HIV particles in Remune, but also to real virus particles and HIV-infected cells in the body.

Current trials suggest that, in the test tube, Remune increases CD4 cell response to HIV to a higher level even than that seen in long-term non progressors, at least over the relatively short period studied so far. It is unclear if this will translate into a benefit in terms of protection against illness and death over the longer term, and this is the subject of several ongoing trials. Other than infections around the injection site, side-effects from Remune have not been reported.



Immune restoration with anti-HIV drugs

At present, the most commonly used immune boosting therapy is anti-HIV treatment itself. Most people who respond well to combination therapy have a dramatic increase in their CD4 count in the first few months of treatment, followed by a more gradual rise during subsequent months.

This later phase is accompanied by improved function and restoration of a wider range of immune responses.

Until relatively recently, there was concern that immune recovery may not be possible for people whose immune damage had reached a 'point of no return'. However; there are now many studies showing that even people with extremely low CD4 counts can experience very substantial increases in their CD4 cells during combination therapy. This recovery of immune capacity is responsible for the declining disease and death rates seen amongst people with HIV in much of the developed world.

P.O.Box Private

I advertised for a relationship at the end of last year. It began with encouragement from my community haemophilia nurse that perhaps now was the time to start looking for a new relationship. Egged on by friends of mine I composed an advert with them and then after a few more bottles of wine one of them rang up the phoneline. My friend then presented the phone to me and a voice demanded my name and address and drunken message. Fortunately I received a letter in the post a few days later that explained when my message would appear in the paper and how I could re-record the message. I started writing a new one and then recorded a sober version of the message.

Early thirties, living in Brighton, likes food, drink and European cities; hates Barbara Cartland novels, horse racing on TV and Country and Western music; I speak English German and after a few pints, crap. I want to meet an intelligent woman who will tell me to shut up when I start talking rubbish.

The advert was to be printed three weeks later which sadly was the start of a week's holiday for me. So everyone who left a message had to wait a week before I replied. The ad was quite successful with 17 woman leaving messages - it took half an hour just to listen to them all. I also had writers cramp after taking the details of each one down. I managed to speak to twelve of them on the phone with the rest being unobtainable or sounding dull.

From the twelve I met six and one either did not show up or was lost in the crowd that suddenly appeared where we had arranged to meet. There was no reply each time I rang her afterwards. It took over a month to see all of them as I had another trip out of the country planned and everyone was getting flu. Some were nice but dull, one was really fun and one was really stunning. This latter one said her friend wanted a medical report on any possible lovers because she kept going with out disabled people and ending up looking after them.

From the six, I saw three a second time. One then did not ring me or answer messages after the second date and I was left with two; T..... and M..... With the number down to a manageable level I could also throw away the notes I had kept to ensure I did not call anyone by the wrong name or ask about the wrong job. By now I had friends across half of Europe wanting information about these women along with my original friends and the community nurse. And all of them asking the same questions - Have you snogged any of them ? When will you sleep with one of them?

I spoke to both of them quite a lot on the phone but decided I should talk about my status face to face. I told T.... that I had haemophilia and HCV the second time I met her which was not particularly easy. Especially as she was the one who'd said she did not want to end up looking after someone again. I planned to do it half way through the evening so that there was plenty of time for me to explain afterwards but it was not the first thing I said. It seemed to go fairly well or as well as these things can go. She rang me later and asked how could I say these things ten minutes before she had to go which I suppose shows how time flies when you're having fun. It felt like a very long hour to me but when I asked if I could see her again she agreed.

Christmas then intervened, as it does at the end of every year and I decided not to tell M.... my status until she returned from her parents. I then got a stomach bug, (why is it when ever I tell someone I have HIV I always get flu or a stomach bug within the next fortnight and scare the hell out of them), T.... looked in on me after work a few times which was very nice. One particular evening though, after she had been at my house for about an hour, she got up abruptly and left. I was not sure what I had said but felt I had probably fucked it up somehow. Then she rang me from her mobile and said that she felt she had to go because otherwise she would have wanted to make love to me.

Then we were cut off as mobiles always do at crucial moments. However after much flattery and begging she agreed to come back to my house. This ensured I did at least have a traditional Christmas, all morning cooking a turkey, all afternoon drinking and half the evening having drunken sex. It was a great day. She dumped me on Boxing Day.

We saw each other on Boxing Day and had a very adult type discussion about what had happened. She felt she could not handle a relationship with someone who was positive and the inevitable stress it would cause for her and her family. After a long talk she changed her mind and decided she could go out with me. I naturally instantly changed my mind and decided that I did not want to go out with her now. She then left messages for me on my answerphone and I rang her the next day. I stuck to my line of not going out with her, she was not impressed. In the meantime M...., having said she would call me after returning from Birmingham had not. I Left a message but still nothing. T..... and I decided to try and be friends and went out a couple of times to the cinema and for a drink which seemed to go very well. And on the third time I saw her we slept together again. The next day M.... rang.

She had been ill with flu quite badly and stayed an extra week at her parents. We chatted and I promised to ring her in a week when she would hopefully have recovered. T..... and I continued to get on better and we even decided to go for a weekend away. The problem with living in Brighton though is where the hell do you go for a dirty weekend. We decided on the short lighthouse on the coast between Cardiff and Newport.

I rang M.... of course and decided to tell her the next time I saw her that I was now with someone. She however beat me to it. I was not the only advert she had answered and was now seeing someone else through the paper called Matthew.

Could we have a part two,. or an update please? (Ed)

Letters Page

Heavens Above

Dear Macfarlane Trust

I wish to protest about the cover of your last newsletter. I am a live registrant of the Trust and feel the cover was extremely insensitive. To be reminded of my friends' deaths and my own impending on Christmas Eve when it arrived was highly dispiriting.

The Trust has consistently given a poor service to widows and for those without children leaves them with nothing after six months. It has always worked on the basis that the longer a registrant lives the better for their family financially rather than attempting to alleviate the suffering once a registrant is dead. With that as the backdrop, to place this tacky icon of a saint wearing a cow on his head with a T-shaped Jesus and virgin mother in hand, (very relevant to the lives and deaths of HIV infected heamophiliacs) is crass.

I would also like to point out that it has taken 15 years for a memorial to go up and happens quite by chance in the year the Chairman's son dies. Whilst your Trustees may highlight that it has not been around for that length of time and has not been involved in this icon's production they are almost exactly the same group of people who bickered about a memorial for those who died with Aids when they were Haemophilia Society Trustees.

Secondly it is in a protestant christian church and has suddenly transmogrified into one for deaths from contaminated blood products. Is Aids too dirty a word for St. Botolphs without Bishopsgate? Or are haemophiliacs with HCV supposed to flock there as well? Are Jewish, Catholic and those with other beliefs supposed to produce their own memorial or is there to be an independent one somewhere else as well ?

I suppose on a positive note it means at least it will not have to be amended for when we all start dying of mad cow disease.

Robert James

HEPATITIS C WORKERS REPLY

Dear Gareth

I am writing in response to your personal piece in the last edition of the Birchgrove (issue 14) entitled "The things they don't say?". In this article you talked about some of the unpleasant side effects which you have suffered since staring on combination therapy for HIV.

You also made a comment about your discussions with the medical professionals involved in your care, stating that you are able to sit down and discuss "all problems and issues surrounding haemophilia, HIV & AIDS, and if I'm really bored, HCV".

You were giving a personal view of your own situation but I know from discussions with members who have hepatitis C- both with and without HIV co~Infection- that there are many people for whom HCV is not boring. I do not wish to minimise what you have been through, but I would like you to know that hepatitis C is having a very real effect on people's lives; health-wise, socially, financially, emotionally, and I know that your comment has been interpreted by others as a negation of what they have suffered.

Thankfully, there are also people on whose lives hepatitis C has had less impact, but for any of your readers who do have concerns or questions about hepatitis C, please encourage them to contact me or Steve Fouch for more information, or just for a chat.

With best wishes

Lucy McGrath Hepatitis Worker Haemo Soc

Dear Lucy

I thank you for taking the time to reply, but I would question on who's behalf your replying. I don't have a problem with what you are saying, but I think I have a right to deal with my viruses in my own way and if, during a period of my life when family and friends are preparing for my death from AIDS, I write that I find HCV boring, then I make no apologies for doing so.

Many people who take the time to get to know me, know that I work for the benefit of all haemophiliacs whether infected or not. I was instrumental in persuading Birchgrove Wales into providing support for Hepatitis C only infected people and have attended many meetings and spoken at many seminars on HCV only. I give my time and energy freely providing services and support, to Hepatitis C only haemophiliacs and we also provide support for people affected only by Haemophilia. But I respect all individuals' rights to deal with their haemophilia, HIV/AIDS or HCV in there own way and I will work in my voluntary capacity to support them. But all I asked is they respect me and the way in which I deal with my problems. People who take the time to get to know and understand me, will get back more than I will take from them. I have hundreds of letters of support from people in all walks of life thanking me for the support I have given them. But as I said they took the time to get to know me. " I'm not that bad really "

Gareth (personal capacity)

Keeping them safe

HIV can be transmitted from an HIV-positive woman to her child either during pregnancy, or during labour and delivery, or by breast-feeding. In Europe and the USA, about 15 to 20 per cent of babies born to HIV-positive women who are not taking anti-HIV drugs are infected. In most cases, HIV is thought to be transmitted during the last weeks of pregnancy or during delivery.

Factors that increase the risk A child is more likely to be infected with HIV from its mother if she has advanced HIV infection or AIDS; she has high viral load or a low CD4 count; her waters break at least four hours before delivery; she has a vaginal delivery (as opposed to a planned caesarean section); the labour is difficult, requiring episiotomy or forceps; she has a genital infection (e.g. a sexually transmitted disease, such as chlamydia); she uses illicit drugs during pregnancy; or she breast-feeds. Becoming infected with HIV during pregnancy is also likely to increase the risk.

Breast-feeding The risk of infection is roughly doubled to around 1 in 3 if the mother breast-feeds her child, and so women are advised not to if there is a safe alternative to breast milk. In the UK it is safe to bottle-feed your new-born baby.

Treatment with AZT The anti-HIV drug AZT (zidovudine) has been shown to reduce the risk of transmission. In one study, pregnant women received AZT tablets during the last six months of pregnancy and intravenous AZT during labour and delivery, plus AZT syrup for their babies for the first six weeks after birth. They were also advised not to breastfeed. These women were much less likely to transmit HIV to their babies than women who did not take AZT. The use of AZT during pregnancy has reduced transmission rates to about 1 in 20 in parts of Europe and the US.

Studies in the developing world have shown that even when AZT is started later in pregnancy, or around the time of delivery, this can still reduce the risk of transmission by about half.

AZT alone is inadequate treatment for the woman herself, and could limit her future treatment options if she becomes resistant to the drug. Studies so far suggest this does not happen often when AZT is used in pregnancy only. AZT may not be quite as effective at reducing mother-to-baby transmission in a woman who has already taken AZT before pregnancy.

Caesarean delivery The risk of transmission is reduced if the baby is delivered by planned caesarean section, rather than by vaginal delivery. This is called an 'elective caesarean', and is scheduled for the 38th week of pregnancy, or performed sooner if labour begins early. Research suggests that anti HIV therapy during pregnancy plus planned caesarean delivery may reduce the risk of transmission to as low as 2% (1 in 50). Caesarean delivery itself can carry some risk for the mother.

Drug combinations in pregnancy Women who become pregnant when their CD4 count is high and viral load is low are less likely to pass on HIV to their child. These women may not require treatment themselves, and so they are advised to begin AZT some time after week 14 of their pregnancy.

Pregnant women are encouraged to take the treatment which they require regardless of their pregnancy. (An exception is the new anti-HIV drug efavirenz, which is not recommended in pregnancy.) This means that combinations of anti-HIV drugs, considered standard treatment for adults with HIV, are now more widely used by women who become pregnant. There is no information about whether these are more effective than AZT alone in preventing HIV transmission, but it is assumed that they could be because they are much more able to reduce the mother's viral load.

Women who conceive whilst on treatment During the first 14 weeks of pregnancy, the fetus is most vulnerable to any toxic effects of drugs. Taking anti-HIV drugs during this time may increase the risk of birth defects. However, stopping treatment may increase the risk of transmission, as viral load would be expected to rise, and it is recommended that women continue their treatment throughout their pregnancy.

Side-effects in the baby To date, children born to mothers exposed to AZT in pregnancy show no increased risk of birth defects or growth problems, though their continued monitoring remains important. Much less is known at the moment about the safety of other anti-HIV drugs. One small study of pregnant women taking AZT and 3TC, with or without protease inhibitors, found a high rate of premature births, and a small number of abnormalities at birth. However, other studies have reported no increase in premature delivery or congenital abnormalities.

NAM also publishes a monthly newsletter, AIDS Treatment Update, free to individuals affected by HIV. For details of this and our other HIV treatment publications, call 0171 627 3200 or write to NAM Publications,

FREEPOST LON277, London SW4 7YY

Interpreting viral load result

Viral load

A viral load result is usually described in terms of the number of HIV RNA copies per millilitre of blood (copies/ml). In HIV-positive people who have not developed symptoms, a viral load higher than 100,000 is considered to be high, and below 10,000 is considered low.

These numbers are often written in a form known as the logarithmic scale, such as 10^5 (which is spoken as 'ten to the power five'). This means that the actual number is 10 x 10 x 10 x 10 x 10. Another way of thinking of 10^5 is as 1 with the decimal point moved five places to the right, which is the same as 1 plus 5 zeros - 100,000. Changes in viral load are also described using this log scale; for example:

***A one log change is a ten-fold change. An example of a one log fall might be 40,000 copies to 4,000 copies. Put another way, this is a 90% fall.**

***A two log fall might be 40,000 copies to 400 copies. This is a 99% or hundred-fold fall.**

***A three log fall might be 40,000 copies to 40 copies. This is a 99.9% or thousand-fold fall.**

So for each log fall, cross off one zero from the number you start with to get some idea of the magnitude of the change. Fractions of logs are harder to remember, because they don't correspond to round-number percentages. For example, a 0.5 log fall in viral load is a 66.6% or two-thirds fall in viral load. A 1.5 log fall is approximately a 96% reduction.

In the past, trials have tended to measure changes in viral load using the log scale; for example, a treatment may be said to have reduced viral load by 1 log. It is important to remember that this is a relative measurement - a one log decrease is a reduction to a tenth of the starting value, such as from 1,000 to 100, or from 10 to 1.

This means that it is easier to show a 1 log reduction in viral load among people who have a high initial viral load than in those with lower viral load, simply because they have more virus to start with.

Factors that affect viral load

Changes in viral load tend to precede and mirror changes in the CD4 count – as the viral load increases over time, the CD4 count decreases – although anti-HIV drugs can reverse these changes, at least in the short- to medium-term. Researchers no longer believe that HIV maintains a stable set point for years. Instead, there is evidence that if HIV is untreated, then viral load steadily increases from the set point over the years. One study analysed blood samples taken over a 17 year period. It found viral load increases by an average of 0.12 log per year, although a higher rate of increase was predictive of more rapid disease progression. Another study looked at eight men in the MACS study and found that viral load increased gradually over several years and that disease progression was associated with a viral load of about 100,000.

As with CD4 counts and other laboratory tests, what matters most is the trend in viral load over time, rather than any one single test result. The same viral load test used on the same sample of blood can produce a different result because of the degree of variability in the test.

The degree of variation may be anything up to 0.3 log, so two separate tests on the same blood sample might come up with two different results. For example, the difference between 50,000 and 100,000 copies is just 0.3 log, yet this is also the difference between a medium and a high disease progression risk. Similarly, the difference between 25,000 copies and 50,000 copies is also 0.3 log, and this is the difference between low and medium viral load in some guidelines for treatment.

Various factors can cause a temporary blip in the viral load, especially things that stimulate the immune system such as vaccinations. People who develop an opportunistic infection tend to experience a temporary increase in viral load of around 1 log, which usually returns to its previous level within a couple of months of the successful treatment of the infection (although there is some evidence that TB may lead to a permanent increase in viral load).

It is also possible that viral load, like the CD4 count, follows a diurnal rhythm, so that it will always be lower at certain times of the day.

Some clinics recommend that patients have blood drawn at a similar time on each visit to avoid this sort of confounding factor. It may also be influenced by the menstrual cycle, like the CD4 count, and there is not yet any information about the degree of day to day variation that might be expected in viral load measurements due to fluctuations in the CD4 count.

Finally, viral load is also influenced by the conditions in which the blood is stored and the length of time it is kept at room temperature, and last but not least, the potential for human error in carrying out laboratory tests.

For all these reasons, it is important not to make changes on the basis of a single viral load count.

References

Donovan RM et al. "Changes in viral load markers during AIDS-associated opportunistic diseases in human immunodeficiency virus-infected persons".

Journal of Infectious Diseases 174:401-403, 1996.Mullins J. "Consistent features of HIV-1 evolution in vivo". 38thInterscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, abstract S-100, 1998.Sabin CA et al. "The natural history of viral load over 17 years of HIV infection". Fourth Annual Meeting of the British HIV Association. Oxford, abstract 11, 1998.

Gene Therapy

THANKS TO "PEN" NEWSLETTER USA

Hope and Hype - Gene Therapy - Is this the Answer ??

A number of developments have made it even more likely that this new technology will hold the key to a cure. Yet a practical cure may still he years away.

Over the past few months, haemophilia gene therapy has made news on a number of fronts. During its annual meeting in October, The National Haemophilia Foundation unveiled its new "Campaign for a Cure," a $5 million fund-raising program focusing exclusively on research into curing haemophilia. In November, the NHF sponsored a Gene Therapy Workshop at the Salk Institute in La Jolla, California, where leading gene therapy researchers presented their latest research findings and discussed future direction for the field. In December, Transkaryotic Therapies, Inc. (TKT) announced that it had started the first human clinical trials using gene therapy to treat haemophilia A. And most recently, in January, several scientific papers demonstrated the potential for using gene therapy to treat haemophilia B.

Real hope for our children ? It's soothing to hear something positive and concrete at last. It's also natural to jump to the conclusion that gene therapy will work, and that a cure is on its way. Jumping to these conclusions, some parents have approached PEN, asking how to "sign up" their children for clinical trials. Believing that a cure is imminent, these parents want to be first in line, without investigating potential risks. Other parents show more caution. "My child is doing fine on his factor concentrate," said one mother to PEN. "I would rather wait fifteen years after its approval to see how well gene therapy will work."

Her comment is valid. While one company, TKT has finally begun human clinical trials, most researchers cautiously avoid any prediction of a practical cure in the near future. Even as they spread the word about gene therapy's hope, many researchers and educators also warn against the "hype." A closer look will illuminate some of the reasons the haemophilia community is watching gene therapy with both excitement and caution.

Part of the problem when examining the success of gene therapy is defining exactly what we mean by a cure. If we stick to a narrow definition of cure - merely correcting a clotting disability - then it appears that we do have a cure, at least for some animals like dogs and mice. Two separate research teams presented data at the NHF'S La Jolla workshop in November, and later published papers showing they had partially corrected the clotting deficiency in animals with haemophilia B. Dr. Mark Kay of Stanford University, working with researchers at Cell Cenesys in Foster City, California, announced that his group had been able to treat haemophilia B-affected mice and dogs with a type of gene therapy that uses an adeno-associated virus to deliver the Factor IX gene into the animal's liver cells. Some of the treated mice showed improved clotting function for the rest of their lives. Another team, led by Dr. Katherine High of Children's Hospital in Philadelphia, used a similar method to deliver the factor IX gene to the muscle cells of dogs with haemophilia B. Again, the treated animals showed improved clotting function for more than 18 months. Both research groups hope to begin human trials soon. They are optimistic that their methods eventually will be able to make at least a partial improvement in clotting function among haemophilia B patients. But the definition of 'cure' goes well beyond the ability of the blood to clot. A liver transplant will "cure" haemophilia, but is it practical or safe? Such drastic and risky treatment has ruled out liver transplantation as a realistic cure for haemophilia. A cure must help blood to clot normally, but must also be safe, practical and widely available.

This rule applies to gene therapy as well.

The good news is that at present it appears increasingly likely that a gene therapy method can be developed that will enable the treated cells to make factor, perhaps even enough to achieve normal clotting ability. It is also likely that a method will be developed that will last for extended periods, perhaps even the patient's lifetime. Still in question is whether these methods will be safe and can be used routinely for all patients. Even if the question of effectiveness is resolved, issues of safety, cost and practicality remain. The Hippocratic Oath sworn by physicians requires doctors to ensure the safety of a patient even before considering the benefits of any treatment. Similarly, the Food and Drug Administration's (FDA) first requirement for any new drug or treatment is safety; all clinical trial programs for new drugs must begin with "Phase I trials"- a series of experiments designed solely to test and demonstrate a product's safety. Only when a product's safety has been demonstrated does the FDA allow Phase II and Phase III trials to study the product's effectiveness.

Tragedies, like the "thalidomide babies" born in the 1950s, warn of the danger, of rushing treatments into use without adequate safety tests. They also show why safety studies must be

Cont Pg 10

Who offers what ?

Dear Birchgrove,

I recently attended a focus group run by the MFT's strategic review survey. I look forward to its final report as it raised many issues. From a personal point of view this year has been quite traumatic as my CD4 dropped sharply to 50, my viral load approached 1 million and my health declined rapidly. This put me in a position where I needed help, advice and support which subsequently made me more aware of the organisations available to me.

The THT and ATP helplines have been excellent with their advice and knowledge about HIV drugs and all their implications, until haemophilia is mentioned. No one could tell me anything about PI's and increased bleeding, increased arthritic pain or the use of anti-retroviral drugs and other haemophilia related problems.

I needed specialist help and that's when I became scared about who I had for support. The Haemophilia Society, The Birchgrove Group and The Macfarlane Trust are all set up for us, but what support or help do I receive from these organisations?

I feel the Haemophilia Society have little interest in HIV+ haemophiliacs and give us minimal support. The fact that they do not include us in their Hep C compensation campaigns is clear evidence. Maybe its taken a while for the penny to drop, but it certainly did when the Haemophilia Society sent me xmas raffle tickets with a first prize of a holiday in the USA. I personally found this insulting and illustrates to me that the society have little insight into the deep feelings and emotions I still have. If any of us wins first prize it would mean smuggling our drugs through customs like criminals, risking humiliation and being sent back on the next plane or having to disclose our medical history and status to try and apply for a special visa.

I returned my tickets unwanted and still have received no reply or explanation. Credit where it's due though, as Steve Fauch at the society did provide me with some useful information, but the society as a whole does not work for me.

The MFT was set up to provide a financial support for HIV infected haemophiliacs so I have never expected any other kind of support from them. Over the years however I have been refused financial aid from them because my request was not within their guidelines. At a time when I was feeling very depressed and stressed about my health, money was refused for a holiday when I really needed one. Money was also refused for a fridge when my old one stopped working on the same grounds. This made me reluctant to approach the MFT overall in the past and made me feel almost guilty that I was sending begging requests.

My suspicions about the MFT were increased this summer when their post franking machine proudly boasted MFT in large letters on the envelope of my mail. This has now been removed after many complaints. It wasn't that it happened that concerned me the most but the fact that someone thought it would be a good idea to boost the image of the trust. Are they thinking of recruiting more members? It made me wonder about who was making decisions within the MFT.

There are no consultations with any of us when they make their decisions and no HIV+ haemophiliacs on their board of trustees. I hope they are not consulting with the Haemophilia Society as that would give me no hope at all. I hope the focus group will address these issues as people making decisions about my health, well being and any kind of security I may have should know how I feel and what my fears are. One of which is that my postlady may now know that I am a HIV+ haemophiliac, and that is the least of my fears.

Now to the Birchgrove Group. The newsletter seems to have almost dried up and the phone rarely gets answered. I realise that it is staffed by individuals in the same position as myself and I fully appreciate that ill health and low energy levels are not conducive to running an effective service. I only recently discovered that there are other Birchgrove groups running in other parts of the country, such as the group in Manchester which are succesful.

I hope the MFT's strategic review will highlight some of the inadequacies in the services we rely on and improve them. Attending the focus group gave me an opportunity to meet other haemophiliacs and it was quite evident that although we all had similar fears and problems our individual needs were quite diverse. Clinics we attend, advice given, support services, opportunities and help shouldn't be a geographical problem. There are only around four hundred of us still alive and we all know we are not going to live for ever (that's what the doctors keep telling me) so lets get it together and improve the services, support and communications for the time we do have left.

Am I alone in my feelings?

Yours sincerely

P B

" Dear P B.

Yours is not an isolated case we deal with many similar phone calls every month. We have been talking about the problems with Visas for the last three years.

Some people listen, but don't hear.

Hope or Hype

carried out carefully and for extended periods, especially when the long-term risks are unknown. The haemophilia community has only to look at the contaminated factor products of the 1970s and 1980s to see that having a product that is effective that "works"- is not nearly as important as having a product that is safe. While one of the major advantages of haemophilia gene therapy is that it could free patients from relying on frequent infusions of factor, thus reducing the risk of infusion related infection, it is still critical to remember that gene therapy is not just one more drug; rather, it is an entirely new method of treatment whose long-term safety is not clear.

Gene therapy has some inherent risks, which must be carefully examined before any forms of treatment gains widespread acceptance. An end to uncontrolled bleeding - this is the hope of parents when they consider gene therapy. Even though the first gene therapy methods may work for only a limited time, the long-term goal is to develop a permanent, lasting cure.

Permanence, which is the key to gene therapy, carries some risk; along with positive changes may come lasting negative changes. Many drugs can have side effects, such as headache, nausea or rashes. Often these effects are short-term, and can be reversed simply by discontinuing treatment. Gene therapy is complex; it involves adding DNA to a patient's cells, perhaps even altering some of the patient's own DNA. Once made, these changes could be extremely difficult or impossible to reverse. Gene therapists hope that they can avoid any undesirable effects of modifying the patient's DNA. They want to add one function making factor without altering any other genetic processes. But no practical method currently exists to simply put genes into a specific location in a patient's cells. Genes can probably be put into a patient's cells in a way that allows them to function and make factor, but current gene therapy methods cannot control exactly where in the cell the new genes will end up ! There is a theoretical possibility that the new DNA could join the patient's DNA in regions where oncogene genes that can cause cancer are located, and that the intrusion of the new gene could activate an oncogene and eventually lead to tumor formation or other types of cancers.

Such a scenario might be extremely unlikely, but at present there is no way to determine the real risk. And since such a situation might not be apparent for many years, it might never be clear whether the gene therapy was responsible for any cancer that developed years down the road. A key issue for gene therapy researchers will be deciding how long to monitor patients in clinical trials (and animals in pre-clinical studies) to ensure that the short-term and long-term risks are well understood.

Virtually all medical treatments, from infusions to organ transplants to vaccinations, involve interaction with our immune systems. The immune system is the body's natural defense mechanism against disease. It is a complex system, easily disturbed. To be effective, any medical treatment must work cooperatively with the immune system, and avoid undesirable immune reactions. Because the immune system can be so finicky, immune reactions may represent the biggest obstacle to successful gene therapy for haemophilia. The immune system's basic function is to recognise and react to "foreign" substances-like viruses, bacteria and toxins-that invade the bloodstream. But the immune system doesn't evaluate whether a substance is "good" or "bad." It cares only whether a substance is "natural" or "foreign." Natural substances, those seen as belonging to the body, will be left alone. Foreign substances will be attacked.

Most drugs seek to escape the notice of the immune system, to avoid being seen as foreign. When a drug is identified as foreign by the immune system, the patient may experience an allergic reaction. In some cases, as in haemophilia patients with inhibitors, the system may actually manufacture antibodies against the "foreign" substance. One type of drug that does not seek to escape the notice of the immune system is the vaccine. Vaccines are specifically designed to overstimulate the immune system. Vaccine manufacturers intentionally formulate their products to be easily recognized by the immune system, and to provoke an aggressive attack of any "foreign" substance that looks like the vaccine. To accomplish this, frequently vaccines are made from killed or mutated viruses that stimulate the immune system to produce cells and antibodies that can attack the virus if it infects the patient at a later time.

Unfortunately, some gene therapy treatments currently under consideration use components that act more like vaccines than drugs. That is, instead of silently slipping into the body and doing their job, they set off alarms that trigger the immune system to react strongly against the invader. A major reason for this is that many of the leading gene therapy methods use viruses as vectors, or agents, that carry a new gene into the cells. These virus vectors can work like

Cont Pg 11

Gene therapy

cont from Pg 10

vaccines to stimulate an aggressive immune response by the body. Gene therapists fear that if an immune response does occur, it could limit the effectiveness of the treatment; perhaps even more troubling, an immune response could prevent the treatment from ever being used again in the same patient. Since many experts believe that the first gene therapy methods may be effective for only a limited time, it could be disastrous if the first treatment leads to side effects that make it impossible to treat the same patient again in the future.

Many early gene therapy experiments using viral vectors did fail because of immune responses. Today, some researchers, like those at TKT, are developing methods that do not use viruses. Others are trying to modify the viruses to lose their immune-stimulating properties. Still others, like Drs. Kay and High, are optimistic that they can avoid significant immune problems by using viruses that do not ordinarily arouse a significant response by the human immune system. Unless one or more of these methods proves effective, the immune response issue will continue as a major obstacle to successful gene therapy.

If the immune system could be overstimulated by gene therapy, would gene therapy be more likely than factor infusions to lead to inhibitor formation. The answer is not yet clear. Some scientists believe that constant production of relatively low levels of factor, which would occur with gene therapy, may arouse a weaker immune response than does the relatively large amount of factor shot into the system in typical infusion treatment. So far, no strong data exists from which to draw conclusions.

However, at the NHF's La Jolla workshop, one researcher reported that a dog that had never exhibited inhibitors when treated with infused factor did develop antibodies against factor when it underwent gene therapy treatment.

While only a single case, this result alarmed a number of researchers. Could the way inhibitors develop in gene therapy patients be different from the way inhibitors develop in infused patients? When recombinant products were introduced, clinical results indicated that the risk of inhibitor formation was similar among patients regardless of whether they used recombinant or blood-derived products; patients who had a history of receiving blood-derived factor without developing inhibitors would be unlikely to develop inhibitors to a recombinant product. The possibility that patients undergoing gene therapy might be at risk for a new form of inhibitors is disturbing. The haemophilia community must continue its vigilance, and closely follow this issue in upcoming safety trials.

It's easy to get excited because the first human clinical trials are underway in Boston. But don't expect too much too soon. We do know that a practical, safe gene therapy won't be commercially available for a long while - parents are shocked to hear that it may be even a decade or longer. TKT's Phase 1 trials in Boston are expected to last several years, or as long as it takes to ensure safety. If during this period improvements are made to the process, additional safety testing may be required for the improved process before Phase II and Phase III trials can begin.

And once a procedure enters Phase II or Phase III trials, it may prove to be only partially effective; it may work in some, but not all, patients. Or the treatment may increase factor levels by only a small percentage. Realistically, we should expect that early gene therapy procedures may be suitable for only a limited number of patients, with gradual improvements in treatment over many years. We shouldn't expect to wake up one day and find a "cure" available for one and all.

Let's assume that a gene therapy procedure is developed that works well and is safe. It's ready to hit the market. Who will be eligible for treatment? How much will it cost, and who will pay for it? Will it require just one treatment, or frequent repeated treatments? Will it be available to everyone? Because gene therapy is still out of reach, so far not much attention has been paid to the practical side. And it's certainly too soon to answer any of these questions with confidence. Yet it may be helpful to begin thinking about some of the practical issues, while we still might have time to influence outcomes. One of the biggest questions may be cost, and who will pay. Insurance coverage will most likely be affected by the price of gene therapy, and several factors will influence price: production costs; recovery of research costs; the number of times the therapy must be performed; only once, or requiring a "booster" every few years. Special considerations will arise from the specifics of the gene therapy method; will the treatment consist of a simple injection, or will it require more complex surgical procedures? Can it he done at a local hospital or treatment center, or will it be available only at selected locations with specialised staff? Will it be a mass produced product that can be packaged in vials like factor, or will it be tailor made on an individual, patient-by-patient basis?

Cont Pg 14

AIDS or Mad Cow Disease

Brain Teazer !!

First Prize crate of Lager

A collection of statements from publications of the haemophilia society. See if you can guess which refers to nv CJD and which to HIV. Answer on a postcard to The Birchgrove Group, 110 Caerphilly Road, Cardiff CF4 3QG and first prize is a Crate of lager. (to keep your liver ticking over)

1) It is no good worrying about [it) without knowing whether it is actually a risk or not. At the moment the risk must be seen as minute; and the changes made by the Department of Health must have made the risks even smaller. However, it is possible that some people with haemophilia will have had injections of clotting factor made from the plasma of blood donors who were incubating this disease.

2) Assuming blood to be a transmission agent, the chances are that the risk involved in imported concentrates has been reduced considerably. It is also important to remember that we have not seen the massive increases in reported cases which were predicted earlier in the year.

3) If the cells involved with immunity like those in the tonsils are affected, then blood could also be a source of infection, because these cells are also found in the blood.

4) Thus the incidence is less than 1 in 1,000 patients at risk

5) This means that less than 1 in 20,000 blood donations would be from someone incubating the disease. When making clotting factors it would mean that infectivity in any one of these blood donors would be hugely diluted by the plasma made from non-infective donors. When this is done it indicates that the risk from (it) to people with haemophilia must be minute.

6) Our message remains unchanged: THE ADVANTAGES OF TREATMENT FAR OUTWEIGH ANY POSSIBLE RISK. We state again that the risk is tiny compared to the risks from untreated bleeding episodes. By refusing treatment or not following your Centre Director's advice you are probably exposing yourself to even greater risk. RISK has always been a feature of haemophilia and in time this risk too will diminish, especially given the volume of research being conducted.

Bearing in mind what little affect HIV had on us it's not very reassuring is it?

Referrences : Dealler S: (1998): The Bulletin. Issue 2 Page 4. Haemophilia Society: (1984): Haemofact Release Nr 3.

Visualisation

Visualisation is a technique which uses mental imagery to fight illness. In HIV-positive people for instance, visualisation therapy may take the form of conjuring mental images of HIV-infected cells being eliminated from the body, or imagining the whole body as healthy and active once more.

Visualisation has been used by many people with cancer, and a considerable amount of research now exists to show that whilst people are doing visualisation exercises, their bodies show a physical response.

Although some of these physical responses may simply be a consequence of relaxation and concentration, others are less easily explained.

A number of experiments, some more well-controlled than others, have shown changes in immune system function following visualisation exercises involving the visualisation of specific immune system cells.

These experiments included the use of guided imagery as part of a programme of relaxation and hypnosis in a group of HIV-positive men with symptoms. When compared to a control group, the treatment group demonstrated a significant decrease in HIV-related symptoms such as fever, fatigue, headache, nausea and insomnia, and felt more energetic and able to cope (Aeurbach).

Visualisation exercises are often sold as expensive packages of tapes and training courses, but if you want to test the usefulness of such exercises for yourself, you may find that making up your own exercises or working with a group of like-minded people will prove just as effective.

References

Aeurbach JE et al. 'A behavioural medicine intervention as an adjunctive treatment for HIV-related illness'. *Psychology and Health*, 1992.

For many years I practiced visualisation after attending a course run by a positive man,. I found it very relaxing and was able to attain a state of complete control over part of my immune system.

I'm not sure if it worked or not but with low CD4 counts and a high Viral Load I stayed off drugs until July 1998.

I've also continued to use Aromatherapy and various other complementary therapies. I'm not sure if they work but I certainly feel better after treatment.

So something must have been doing me good (Ed)

If anyone has an opinion to offer on the benefits of complementary therapies drop us a line and we will put them into the newsletter.

What is considered to be a good response to treatment?

It depends on how many drugs you are taking and whether you have taken anti-retroviral drugs before, and your viral load before starting treatment. It also depends on when the response is measured. It is generally agreed that the absolute minimum you should expect to see is 0.5 log (about 66%) after eight weeks. Anything less may be a natural variation in virus levels, not a treatment effect.

Treatment guidelines now recommend that in general, failure to suppress viral load to undetectable levels should be regarded as a sign of a suboptimal response to therapy, and should prompt a discussion about whether to change therapy to try to achieve greater suppression.

Isn't undetectable load the most desirable response to treatment?

Most experts would agree that this is the ideal response to treatment,because it indicates that viral replication has been reduced to very low levels indeed.

People with undetectable viral load after starting drug therapy have the lowest risk of disease progression, and a greater chance that their viral load will stay at very low levels, compared to people with low viral load which is nevertheless detectable.

Studies of highly active anti-HIV regimens, such as a triple combination that includes a protease inhibitor, have shown that a substantial proportion of treated people may achieve undetectable viral load.

While it appears to be particularly possible to suppress viral load to this extent among relatively recently infected people, it is also possible for a substantial proportion of people with advanced HIV disease who have taken many anti-HIV drugs before.

However, this alone does not mean that undetectable viral load is the only good outcome of treatment. Some people accept lesser suppression, especially if they are taking drugs to which resistance is unlikely to develop rapidly.

And in any case, for some people it is likely to be impossible to achieve undetectable viral load with the drugs available today.

My viral load is starting to rise again after nine months below the level of detection. It has gone up to just above 1,000 copies.

Should I change treatment now, or wait?

Most experts agree that if viral load increases by more than 0.5 log, this indicates that your current treatment is beginning to fail. If the limit of detection is 400 copies on the test used at your clinic (Amplicor), your viral load increase represents a change of at least 0.4 log.

This may be a sign that your treatment is failing, or it may be a temporary blip caused by an infection. It may even be a laboratory error. It is probably best in these circumstances to have another test as soon as possible (i.e. have the test within a week and get the result within a week) rather than to rush into changing treatment. If your viral load is still above the level of detection, that is a signal to consider changing.

Having said that, the main reason for changing drugs at this point is to reduce the risk of developing resistance to those drugs, and to others you haven't yet taken.

Several studies have shown that the overwhelming majority of people whose viral load begins to rise again after a period below the limit of detection do not develop any illness over at least a year of follow-up, and continue to enjoy a stable or rising CD4 count.

Viral load is not the only factor to take into consideration when choosing to change treatment; you run the risk of using up all your options very quickly if you change treatment at the first sign of viral rebound.

I've just started therapy on an AZT/ddc/ritonavir combination and my first viral load test, taken after I'd been on therapy 3 months, just came back. I'm not undetectable, although it has fallen 2 log to below 3,000 copies.

My consultant says not to worry, but shouldn't I be adding more drugs, or changing some of them?

There are two views about this question. One argument is that you should do everything possible to get your viral load down as quickly as possible in order to minimise the risk of developing resistance during this period. So if your viral load is still detectable after 12 weeks on treatment, you need to intensify the drug combination, or perhaps even change some of the components.

continued on Page 14

cont from Pg 13

The other view is that there is no clear evidence that this will make any difference to the risk of resistance, and that a 2 log fall in viral load is a very good response at this stage.

If your viral load hasn't fallen further after a few more weeks or months, that is the point to think about what you want to do next. At that stage you might decide to try new options – or you may be content with the fact that the drugs have reduced your viral load to low (albeit not undetectable) levels that are likely to be associated with a much reduced risk of disease progression.

I've been on triple therapy for nearly six months and my viral load is now undetectable, having been 100,000 before I started treatment. But there's been very little change in my CD4 count. It's gone up from 90 to 120 so far. Why is this?

This represents a 33% increase in your count since you started therapy. Obviously it would be preferable to have a higher CD4 count at this stage, but we don't yet know whether those extra cells would actually confer greater protection from opportunistic infections, because in the first few months after starting treatment, it's probable that your immune system's memory is still full of holes - in other words, you could have the immune system of someone with 90 T-cells disguised as 250, and so you might still be at risk of PCP even though you want to come off prophylaxis.

Gradually however your immune system should generate new 'memory' to provide enhanced protection against OIs, but this doesn't happen overnight.

The time to be concerned will be in about a year's time if your immune system has not begun to generate new CD4 cells, and if your count has not risen further.

What's probably more significant at this stage is that your viral load is substantially reduced – in your case, to undetectable levels. Studies have shown that viral load reductions are strongly associated with a reduced risk of disease progression in the future.

I would like to thank Alison and wish her all the best for the future (Gareth)

GENE therapy

cont from Pg 11

Closely connected to the question of price is the question of availability; Will gene therapy be accessible to all? Will treatment be so specialized that it will be performed only at certain hospitals, with waiting lists lasting years? Will it be restricted to those with the best health insurance? Will it be available in the UK on the NHS. And finally, if the U.S. wins the gene therapy race, how will those in other countries gain access to care? It may seem premature to worry about cost and availability, but as patients and consumers, we should do all we can to ensure that the treatment, when available, is also accessible.

Gene therapy promises so much. In our desire to do what is best for our children, and our wish to see them lead "normal" lives we may too eagerly conclude that gene therapy is safe, effective, and near at hand. Our own hastiness and lack of complete information can fuel the hype that surrounds gene therapy, leading some families to volunteer to receive experimental treatment, or be crushed emotionally when they learn that actual commercial treatment may be a decade away.

We all hope for an immediate, safe cure. But our hopes can raise unrealistic expectations: hope can lead to hype We can always make the ideal our target, but we must also realistically accept that the first gene therapy treatments may fall short of this idea.

Will gene therapy eventually work? Yes, according to most expert opinion. Will it happen soon? Probably not, at least not in a widely available, commercial form. Yet we deserve to be excited that there is, for the first time, a defined plan for curing haemophilia, a plan that has realistic hope for success. It is thrilling to imagine that this new technology, gene therapy, will revolutionise medical care in the coming century and that we, the haemophilia community, may well be one of its first success stories.

But we must remain patient, even cautious, to ensure that the experimentation and research needed to develop gene therapy into a safe and effective cure is not rushed.

It is rare that a community has the opportunity to observe so closely, and participate so actively, in research that may cure a chronic condition. It is an opportunity we should accept with hope, enthusiasm and the determination to make sure that, this time, everything is done right.

Thanks to PEN Newsletter USA. KELLY COMMUNICATIONS

BIRCHGROVE IS A FORUM FOR:

- **The treatments of haemophilia and HIV**
- **Taking care of ourselves, through informed debate and argument**
- **Staying healthy with Haemophilia HIV & AIDS and HEP C**
- **Ways in which HIV affects love and sexuality**
- **The social and psychological aspects of haemophilia and HIV**

PEOPLE WITH HAEMOPHILIA AND HIV

- **Can be empowered and enabled to deal with HIV/AIDS through relevant information and mutual support**
- **Can improve their health and extend their lives by expressing feelings and confronting the issues directly**
- **Should be heard and have their needs recognised and not suffer in fear and isolation**
- **Have a role in the work of the HIV/AIDS community to inform and challenge the ignorance that exists about HIV**

The following information leaflets and back issues of the Birchgrove Newsletter are available from the Birchgrove Group, free of charge to those directly affected by Haemophilia/HIV or registrants.

Birchgrove Newsletter Back Issues

- ☐ BIRCHGROVE newsletter *Issue 6*
- ☐ BIRCHGROVE newsletter *Issue 7*
- ☐ BIRCHGROVE newsletter *Issue 8*
- ☐ BIRCHGROVE newsletter *Issue 9*
- ☐ BIRCHGROVE newsletter *Issue 10*
- ☐ BIRCHGROVE newsletter *Issue 11*
- ☐ BIRCHGROVE newsletter *Issue 12*
- ☐ BIRCHGROVE newsletter *Issue 13*
- ☐ BIRCHGROVE newsletter *Issue 14*

Birchgrove Information Leaflets

- ☐ Hepatitis C – Special Edition

We can also supply the following items.

☐ Red Ribbons (Cloth)	£0.50
☐ Red Ribbon Badges (Enamel)	£2.50
☐ Birchgrove Red Ribbons (Enamel)	£2.50

Name:

.....

Address:

.....

.....

.....

Send to:

The Birchgrove Group,
PO Box 9, Abertillery, NP3 1YD.
or Phone 01222 520029 Helpline
01222 520045 Fax

HIV Young People's Weekend

11th to 13th June,Langford Hotel, Hove Near Brighton

Report next Issue

If someone sends it in

??????

Newsletter
These are Frequent Comments
Why do I keep getting asked the same questions ?

When is the next Issue ?
Why is it taking so long?
Haven't seen an issue for a while.
These are not
Can I do anything?
Here's an article for the next issue !
How's it coming along?
Do you need a hand?
You've been ill, how can I help?
It must be hard with everything else on your plate
XXXXXXX
Remember it's yours so be proud, own this F..... Thing

One person cannot change the world, but many can make it a little easier.

(Volunteer & general dogsbody)

DISCLAIMER

The views expressed in each of the articles are those of the individual authors, and not necessarily those of the Birchgrove Group.

"BIRCHGROVE" is published by:

The Birchgrove Group,
P.O. Box 9, Abertillery
Gwent NP3 1YD.
Tel: (0345) 697231 (Helpline)
(01222) 520029 (Admin.)
Editor: Gareth Lewis