



AIDS TREATMENT UPDATE

FEBRUARY 1999

ISSUE 74

Measuring drug levels

How problems with drug absorption can contribute to treatment failure

BY ANNA POPPA

In last month's *AIDS Treatment Update*, we previewed a number of developments which are expected to have some impact on the medical care of people with HIV in the coming year. One of these, tests that investigate drug absorption by measuring the amount of a drug which reaches the blood stream, may well become an important tool for monitoring the effects of combination therapy.

HOW ARE DRUGS ABSORBED?

Once swallowed, anti-HIV drugs pass through the digestive system where they are absorbed into the blood stream and distributed throughout the body. The rate at which they are absorbed varies between individuals. This means that if two people take identical treatment at the same doses and with the same foods, the amount of drug which will reach their blood streams can be very different.

To a certain degree, this variability is unimportant. In order to be effective against HIV, antiretrovirals must reach a level in the blood which falls within a range that is established when new drugs are first developed. A blood level which is higher than this "therapeutic range" can lead to more side-effects. A lower level will allow ongoing HIV replication, which provides the circumstances for drug resistance to develop, causing the treatment to fail.

Drug levels reach their peak soon after they are taken, and then taper off over the subsequent hours to a lower "trough level" before the next dose. It is this trough level which is likely to be pivotal in determining a drug's efficacy. For example, early study of the NNRTI delavirdine found that the drug's activity followed a typical dose-response curve – that is, at

very low blood levels there is no anti-HIV activity at all, but above a certain trough level there is a rapid increase in activity as the dose is raised.

VARIABILITY IN PROTEASE INHIBITOR LEVELS

Amongst the antiretrovirals, the greatest degree of variability in blood levels is seen with protease inhibitors (PIs). They are processed (metabolised) into inactive products relatively quickly, hence the need for frequent dosing. Their metabolism is dependent on the liver, involving a "pathway" called the cytochrome P450 system, which is responsible for processing many other drugs and nutrients. Interactions between these different substances can affect the speed at which they are metabolised, causing blood levels to rise or fall.

The activity of P450 is itself variable – some people are rapid P450 metabolisers and others are slow, and this produces variation between individuals in PI levels in the blood. Tests designed to distinguish between rapid and slow metabolisers, one example being an erythromycin breath test, have so far been unable to predict response effectively.

Contents

Measuring drug levels	1
News on HIV in children	5
Hepatitis C and HIV	6
Glossary and Notices	8

Much of the data on variable drug absorption and its relationship with viral load response to anti-HIV treatment relates to PIs (see page 4). At the 1998 Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in San Diego, Italian researchers reported on 16 people taking indinavir at the standard dose, 800mg three times daily. Most were also receiving other antiretrovirals and five were using methadone, which is known to interact with PIs. Indinavir blood concentrations were measured by the most commonly used method (called HPLC) about every hour following dosing. The study found that there was a wide variation in indinavir levels between participants.

At the same conference, data on problems with drug absorption in children (discussed elsewhere in this issue), were also presented. 57 children taking part in a study investigating the use of the PI nelfinavir in combination with the NNRTI efavirenz, underwent drug level monitoring two weeks after starting treatment. Dose adjustments were then made on the basis of these tests. However, repeat testing after six weeks found that efavirenz levels were outside the normal range in 30% of participants, and for nelfinavir the figure was 18%.

A NEW FACTOR

Another factor is growing in importance in our understanding of variations in drug absorption, particularly of PIs. Poly-glycoprotein, or P-gp, is a protein found on the surface of cells in the gut, the blood brain barrier, kidneys, liver and around one in ten CD4 cells, the immune cells which HIV targets. It flushes drugs out of cells and back into the gut, and so it limits the absorption of PIs in the blood and prevents their activity in the brain.

MEASURING PROTEASE INHIBITOR LEVELS

The main rationale for PI drug level monitoring, is to identify those people who begin a protease inhibitor but do not achieve an adequate trough level. This involves a one-off blood sample taken in the morning, just before the first dose of the day is due when the concentration of the drug in the blood will be at its lowest. The earliest this test should be done is around two weeks after starting the drug when blood levels should have stabilised.

People whose trough level is too low then have the option to modify their treatment, for example by continuing with their current combination and adding a small amount of

ritonavir. Ritonavir inhibits the effects of both P450 and P-gp, and this is why its use in combination with other PIs raises the blood levels of the other drug.

An alternative application for drug level monitoring is to identify users of ritonavir who are absorbing the drug quickly and getting very high peak levels just after a dose, which may cause unpleasant side-effects. In these circumstances there is the option to split the ritonavir dose (change from 600mg or 7.5ml twice daily to 300mg or 3.75ml four times daily) to iron out the peaks.

WIDENING AVAILABILITY

Therapeutic drug monitoring is infrequently performed outside research settings at present. Given that this is a new and investigational area of HIV management, it seems unlikely to become widely available very quickly.

“I’m uncertain whether it’s a doctor’s role to act as a policeman on compliance”
- Dr Graeme Moyle

The doctors we spoke to all raised the need to set priorities, often mentioning the economic pressures relating to the parallel introduction of monitoring tests for drug resistance. It was their view that people taking PIs, or a regimen containing either two PIs or one PI plus an NNRTI, are the group with most to gain from the use of drug level testing.

Dr Ray Brettle of Western General Hospital, Edinburgh, said “Ideally everyone on a protease inhibitor should have the level checked to prevent or reduce side-effects and ensure efficacy. An alternative approach would be to use drug monitoring particularly for [people beginning] salvage therapy in conjunction with resistance testing. After selecting, if possible, sensitive drugs one would want to check that they achieved good levels in the blood”.

People with liver disease or people who use methadone may also be prime candidates for monitoring, as both of these factors can affect metabolism of PIs.

WHAT ABOUT OTHER DRUGS?

Testing for blood levels of other drugs is less relevant because of the way they are processed in the body. Nucleoside analogues, e.g. AZT or ddI, require an additional step in their metabolism inside target cells (called phosphorylation) in order to reach their active form. Measuring their concentration in plasma may not provide an accurate reflection of intracellular levels of this active form.

UK CLINICS

At present the only UK laboratory which performs therapeutic drug monitoring is the Department of Pharmacology and Therapeutics at the University of Liverpool, led by Professor David Back. The cost is relatively low, but the turnaround time is two to three weeks, which hampers rapid decision-making. Whilst making use of the services on offer at the Liverpool research base in limited circumstances, a number of clinics, including London's Chelsea and Westminster Hospital and the Royal Sussex County Hospital in Brighton, are currently trying to set up local testing facilities in the south east.

Some health authorities are reluctant to make an investment without more data to support the clinical use of drug monitoring. Indeed one of the clinics we spoke to has received funding to set up a new testing service from one of the protease inhibitor manufacturers rather than through NHS sources. Dr Mike Youle of London's Royal Free Hospital, whose Trust will not pay for drug monitoring at the moment said: "A nice, small population study would be useful".

Such a trial is currently underway in the Netherlands. The ATHENA Project is a 600 person, prospective, randomised study of HAART (using a PI or an NNRTI), with or without access to therapeutic drug monitoring. It is expected to report preliminary results in late 1999.

ADHERENCE IS VITAL

Aside from the biological factors which influence drug absorption discussed above, a central factor in ensuring that blood levels remain within the therapeutic range is treatment adherence – always remembering to take your pills on time and within any recommended food guidelines.

Data from the French Trilege study, reported at a recent conference in the US Virgin

Islands, has been important in raising debate about the relationship between adherence, inadequate drug levels and a poor response to treatment. Participants in Trilege started treatment with indinavir/AZT/3TC and after three months some de-intensified to either AZT/indinavir or AZT/3TC. This "induction-maintenance" strategy was unsuccessful – those people who continued on the triple drug combination were more likely to maintain undetectable viral load than those who switched to two drugs.

In an analysis of all participants whose viral load rebounded, low blood levels of indinavir were seen frequently. The researchers assessed treatment adherence by looking at clinical records and performing pill counts. Poor adherence was documented for all those with viral load rebound on triple therapy and half of those on indinavir/AZT. This poor adherence correlated with poor indinavir blood levels, leading the study group to conclude that treatment failed because it wasn't being taken.

Without open acknowledgement of adherence difficulties between people with HIV and their doctors, drug level monitoring is likely to yield misleading results about the true cause of poor absorption. The idea, proposed by some researchers, that these tests could be used by doctors to identify poor compliers is controversial. Dr Graeme Moyle of London's Chelsea and Westminster Hospital commented: "I'm uncertain whether it's a doctor's role to act as a policeman on compliance".

Key conclusions:

- ◆ There is wide variation in drug absorption amongst people with HIV, and this is particularly the case for protease inhibitors.
- ◆ Poor treatment adherence is a significant cause of drug levels in the blood being inadequately low.
- ◆ Several biological factors, and interactions between drugs can also influence drug levels.
- ◆ Low drug levels in the blood may cause treatment to fail.
- ◆ A small number of treatment centres are planning to begin testing drug levels, primarily in people taking protease inhibitors.

ACCESS
Therapeutic drug monitoring is offered by the University of Liverpool at a cost of £25 per sample per drug (exclusive of transportation and handling costs). Those requiring further information should contact Professor David Back or Sara Gibbons at the Department of Pharmacology & Therapeutics, University of Liverpool.
Telephone: 0151 794 5553. Their excellent website is at <http://www.liv.ac.uk/hivgroup>

PI drug levels and effect on treatment

In this section, research on the extent and possible causes of protease inhibitor absorption, and the effect this has on the success of treatment is reviewed.

NELFINAVIR AND SAQUINAVIR

Dutch researchers investigated the relationship between blood levels of nelfinavir and hard-gel saquinavir (*Invirase*) and HIV clearance rates in a sub-group of 29 people from the ADAM induction-maintenance study. Higher exposure to nelfinavir resulted in a faster viral load drop in the first eight weeks of treatment. A more rapid decline in viral load after starting treatment may be important in delaying the emergence of resistance.

At the 1998 World AIDS Conference the same research group presented data on 130 people receiving *Invirase* plus two nucleoside analogues. Saquinavir plasma concentrations correlated with viral load responses. Those participants with trough levels above a cut-off of 50ng/mL were significantly more likely to have sustained a 2 log reduction in viral load after 48 weeks.

Data from Agouron's 511 study of nelfinavir was presented at the 1998 ICAAC conference. Participants were treatment naïve and received AZT/3TC with nelfinavir in either 500mg or 750mg doses three times a day. Baseline viral load, 4 week viral load and nelfinavir plasma levels at weeks 2 and 8 were found retrospectively to be independent predictors of the 48 week viral load response. (Though plasma level was less predictive than the other two). Plasma level was a significant predictor regardless of the dose taken.

Data from the MIKADO trial of the use of soft-gel saquinavir (*Fortovase*) with d4T/ddC in people new to treatment was presented at a conference in the Virgin Islands in December.

10 of 29 people followed for 24 weeks had viral load above 200 copies. They were matched with a control group of 10 people from the same trial who had viral load below 200 copies. *Fortovase* blood levels were measured at week 24, and genotypic and phenotypic resistance testing were performed at baseline and after 24 weeks. The genotypic mutation commonly associated with saquinavir resistance (L90M) was found in only 2 of the 10 people with detectable viral load. There was no evidence that phenotypic resistance affected viral load response, as phenotype did not change over the study period, even in those with the L90M mutation. Drug absorption tests showed 7 of 10 in the control group had saquinavir levels in the range of therapeutic values compared with 1 of 10 of those with detectable viral load.

A study presented at the Drug Therapy in HIV Infection conference in Glasgow last November found evidence that absorption of saquinavir decreased over time in a group of 20 people who received the drug with nelfinavir and nucleoside analogues. Over the eight months of follow-up, however, this did not appear to affect viral load response, which remained below 500 copies for all participants.

INDINAVIR

A number of studies presented at the Geneva World AIDS Conference investigated the relationship between indinavir drug levels and viral load response. The Dutch researchers whose work on nelfinavir and saquinavir is reported above, presented data from a prospective 24 week study of 65 people taking indinavir (800mg three times daily) plus two nucleoside analogues. 78% had prior experience of combination therapy, 35% with PIs. Indinavir blood levels were measured by HPLC at regular intervals. A low indinavir level was highly predictive of viral load above 200 copies at week 24. Those whose blood level averaged less than 75% of the normal therapeutic level were three and a half times more likely to have detectable viral load at 24 weeks than those whose average level was above this point.

However, a number of studies found no relationship between low indinavir levels and viral load response. One was presented by the drug's manufacturers, Merck using data from 95 people who received indinavir monotherapy at various doses in early Merck indinavir studies. 75 of these received more than 2400mg, the standard daily dose. No relationship was found between total indinavir exposure, or the trough level, and viral load response at weeks 4 or 24.

In a French trial, indinavir plasma levels were found to be highly variable in 95 people receiving indinavir (800mg three times daily) plus two nucleoside analogues. Participants were then interviewed and low concentrations were found to confirm poor adherence. However, no relationship was found between indinavir levels and viral load response.

Researchers from Spain performed a prospective analysis of 31 indinavir users (taken 800mg three times daily in combination with 2 nucleoside analogues) who they described as "fully compliant". After six months, 10 of 11 with undetectable viral load (below 80 copies) and 17 of 20 with detectable viral load were reported as having maintained indinavir levels above the normal therapeutic range throughout. Poor absorption could not, therefore, explain the differences in outcome.

REFERENCES

- 12th World AIDS Conference, Geneva, 1998: Hoetelmans RMW et al (abs 42261); Chodakewitz J et al (abs 42266); Perello L et al (abs 42272); Burger DM et al (abs 42275); Dalmau D et al (abs 42276). 38th ICAAC, San Diego, 1998: Chan S et al (abs A-11); Gatti G et al (abs A-66); Starr SE et al (abs LB-6). 4th International Conference on Drug Therapy in HIV Infection, Glasgow, 1998: Khaliq Y et al (abs P43). International Conference on the Discovery and Clinical Development of Antiretroviral Therapies, US Virgin Islands, 1998: Brun-Verzinet F et al (abs 15); Calvez V et al (abs 19). Hoetelmans RMW et al. The effect of plasma drug concentrations on HIV-1 clearance rate during quadruple drug therapy. *AIDS* 1998, 12:F111-F115.

News on HIV in children

Forthcoming developments in paediatric treatment and care

BY MEGAN NICHOLSON

The effectiveness of early treatment for HIV infected infants will be an area the Paediatric European Network for Treatment in AIDS (PENTA) will be focusing on in 1999. Similar to seroconverter studies in adults, the PENTA 7 study will investigate the effect of early treatment with three or possibly four drugs on infected babies born to positive mothers.

There is some evidence from US research that early, aggressive treatment of HIV infected babies may cause dramatic reductions in viral load, despite the very high levels seen in babies. PENTA 7 hopes to recruit 20-30 infected infants who will be given three anti-HIV drugs early in life, including the protease inhibitor nelfinavir. A review of the first few cases will be conducted early on, and the potency of the combination may be increased if results are disappointing.

In addition to the ongoing PENTA 5 trial for children who have not received previous antiretroviral therapy which will be completed in 1999, a new trial in children who have prior experience of treatment is also in the planning stage through PENTA. Although study details have not been finalised, researchers are interested in examining the effects of hydroxyurea and/or drug resistance testing in children. Dr Di Gibb from the MRC Clinical Trials Unit and Great Ormond Street Hospital, London, told *AIDS Treatment Update*, "Many unresolved questions remain about resistance testing generally. There is a possibility that resistance may be different in children and the uses of resistance testing have not been widely studied in children".

NELFINAVIR DOSAGE

Recent product information released by Agouron (who produce nelfinavir), in the US recommends an increase in the recommended dosage of nelfinavir for children. All the key nelfinavir trials have adjusted the dosage accordingly. The previously recommended dosage for children was 20-30mg for every kg of body weight three times daily. However doses of around 20mg/kg are now considered to be sub-optimal. The newly recommended nelfinavir dose for children is at least 30mg/kg three times a day. Dosing for infants under three months has not yet been determined. The recommended twice daily paediatric dose is 50-55mg/kg per dose.

"Children metabolise protease inhibitor drugs more quickly than adults, hence they

need to take higher doses for their size", Dr Gibb explained. "Nevertheless, I think the increase in the paediatric dose of nelfinavir raises questions about the standard adult dose." Based on the new paediatric dosing, older children and adolescents would be on higher doses of nelfinavir than adults, and according to Dr Gibb, there is not a great deal of evidence that drug metabolism differs in older children compared with adults.

NNRTIS IN CHILDREN

The NNRTI nevirapine has also been more widely prescribed as part of triple combination regimens for children, and a study investigating its use in the UK and Ireland is in progress. Provided the child does not experience rash, this drug is considered by some to have advantages for longer term adherence compared to nelfinavir.

Other paediatricians, however, suggest that the liquid form of efavirenz, which should become available soon, may be worth waiting for instead. Cross resistance amongst all the drugs in the NNRTI group means that people who become resistant to nevirapine are not expected to benefit from using efavirenz, and vice versa.

HIV TESTING OF PREGNANT WOMEN

The push to encourage all pregnant women, particularly those in high prevalence areas such as London, to be tested for HIV has intensified over the last year given the clear evidence that antiretroviral treatment during pregnancy can dramatically reduce a woman's chance of passing on HIV to her baby. A combination of avoidance of breast feeding, anti-HIV therapy and elective caesarian (planned for 38 weeks' gestation, or sooner if labour begins early) can reduce the rate of transmission to as low as 2%.

There is some evidence of a shift towards routine testing with higher levels of uptake of testing in London, according to Dr Gibb. Although figures are not yet available for 1998, Dr Gibb said that anecdotally, the percentage of pregnant women being tested in some of the major London hospitals has increased over 1998. It appears that greater awareness of the benefits of treatment during pregnancy, as well as professional guidelines and better training of midwives, is slowly having an effect.

PENTA 5

The PENTA 5 trial is an ongoing partially blinded trial where children are randomised to receive a double nucleoside analogue combination (two of either AZT, 3TC or abacavir), with or without nelfinavir according to their disease stage. More details, and contacts for participating treatment centres can be found in NAM's *HIV & AIDS Treatment Directory* and on our website at <http://www.aidsmap.com>

TREATMENT IN PREGNANCY

New data about the safety of anti-HIV treatments during pregnancy are due to be presented at the Chicago Retroviruses Conference in early February 1999. Research presented at the Geneva World AIDS Conference in 1998, and recently published in the journal *AIDS*, raised concerns that combination therapy may increase premature labour and birth abnormalities among babies born to women on such treatment. A review of American data found no evidence of increased prematurity, though the issue of birth defects remains unresolved and will require long-term follow-up. (See Lorenzi P et al. "Antiretroviral therapies in pregnancy: maternal, fetal and neonatal effects". *AIDS* 12:F241-F247, 1998.)

Hepatitis C and HIV

What are the treatment options for people who are co-infected?

BY KEITH ALCORN

Many people in the UK infected with HIV through injecting drug use or blood products have also been infected with the hepatitis C virus. Whilst hepatitis C co-infection does not appear to have any effect on the course of HIV infection, co-infection with HIV and hepatitis C does seem to increase the risk of hepatitis C-related liver disease and liver cancer.

EFFECTS OF HEPATITIS C INFECTION

Hepatitis C virus (HCV) causes damage to the liver by mechanisms which are still poorly understood. After twenty to thirty years of infection with HCV alone, it is estimated that at least 20% of people will have developed serious liver disease – either cancer or scarring of the liver which leads to permanent changes in the way that the liver works, death of liver tissue and eventual liver failure.

However, up to 80% of people infected with HCV may report symptoms such as chronic fatigue, intolerance of alcohol, nausea, “brain fog”, joint pain and many other symptoms which may not, at first sight, be linked to HCV, but which nevertheless have a serious effect on quality of life and the ability to work.

It is considered that the progression of HCV disease is speeded up by HIV co-infection. Liver damage seems to happen much more quickly and more frequently. In haemophiliacs co-infected with HIV and HCV, liver cancer is now replacing AIDS-related illnesses as the major cause of ill health and death in Europe and America.

There are differences of opinion on this issue, however. Some doctors point out that many people with HCV do not know when they became infected, and argue that this hampers our ability to understand fully the relationship between HCV and HIV infection given the potential for differences in the length of infection. Dr Ray Brettell of Western General Hospital, Edinburgh, said “Most haemophiliacs were infected with hepatitis C well before HIV, and with a 20-30 year incubation period the appearance of liver disease in [people co-infected with] HIV is related to length of [hepatitis C] infection.”

HIV infection can make the diagnosis of HCV and its symptoms more difficult. HCV infection may not show up on antibody tests in HIV infected people, and levels of liver enzymes may not reveal the full extent of liver disease in HIV-infected people, leading to a false sense of security.

Goals of HCV treatment:

- ◆ Sustained normalisation of ALT (liver enzyme) levels
- ◆ Achieving undetectable hepatitis C viral load within three months of starting treatment. This is strongly predictive of achieving long-term suppression of HCV infection
- ◆ Sustained undetectable hepatitis C viral load (below 100 copies), thought to indicate clearance of the infection
- ◆ Improvement and disappearance of liver inflammation
- ◆ Prevent progression of liver disease to cirrhosis and liver cancer

WHO SHOULD RECEIVE TREATMENT?

As with HIV treatment, there is considerable debate about when to start HCV treatment:

- ◆ Symptomatic people with fibrosis of the liver are less likely to respond well to treatment
- ◆ People with high HCV viral load are likely to have a poorer response to treatment with interferon or ribavirin
- ◆ People with CD4 counts below 500 are less likely to respond to treatment, but this may be because this group are also more likely to have symptomatic liver disease
- ◆ There are at least six hepatitis C genotypes. These are named type 1, type 2, type 3 etc. Type 1b is less likely to respond to therapy than types 2 or 3 but is the most aggressive genotype for liver disease
- ◆ Genotyping (testing for the type of HCV) should be conducted before deciding on treatment, suggest some experts, because it may save money. However, like HIV resistance testing, it is still not widely available
- ◆ People with fewer symptoms tend to be better responders, but they may have a lower risk of disease progression in any case (for example, people with type 1 HCV probably have a lower risk of liver

cancer than people infected with other sub-types)

- ◆ People who do not achieve a sustained response to interferon-alpha may still have a positive response to dual therapy with interferon and ribavirin, but the characteristics of interferon non-responders likely to benefit still need to be defined
- ◆ Some experts argue that it is possible that even amongst people who are not long-term responders, interferon-alpha treatment may still reduce the level of damage to the liver, but this is currently unproven

For a detailed discussion of the pros and cons of interferon-alpha treatment, see *The Hepatitis C Handbook*.

TREATMENT OPTIONS FOR HCV

Treatment for HCV is not lifelong. It consists of 24 week or 48 week courses of treatment. Side-effects may be very severe, though they tend to reduce as treatment goes on. They include high fevers, joint pain and depression.

The current standard treatment is interferon-alpha, but a recent study of 900 treatment-naïve people showed that only 13% had undetectable HCV viral load after 48 weeks, compared with 38% who received a dual combination of interferon-alpha and ribavirin, an anti-viral drug.

This combination is due to be licensed under the brand name *Rebetron* in Europe shortly. Other drugs, including HCV protease inhibitors are being tested in trials at the moment. The flu drug amantadine in combination with interferon is also being tested against HCV in treatment centres throughout the UK.

People with type 1 HCV are less likely to sustain undetectable viral load after stopping therapy, especially if they have a high viral load before starting treatment. Around 60% of people with type 2 and 3 HCV were still HCV-negative 6 months after stopping anti-HCV combination treatment, compared with 8-24% of people with type 1 HCV.

Many people with HCV have chosen to use alternative and complementary therapies to reduce symptoms. Chinese herbal medicine in particular is used quite widely in the UK, and there is a detailed discussion of the use of Chinese herbs in *The Hepatitis C Handbook*.

DIETARY CHANGES

Dietary adjustments and other changes in lifestyle are important. Reducing alcohol consumption or eliminating it entirely is likely to be beneficial, as alcohol consumption

increases the risk of liver damage in HCV infected people. Avoidance of trans-fatty acids (look for the words "hydrogenated vegetable oil" on labels to spot these) and animal fats may also be helpful, though some doctors advise that this may be less important in people who do not have symptoms.

HCV TREATMENT & CO-INFECTION

A large study is being conducted in the US to see whether stabilising HIV disease with HAART before starting dual therapy with interferon-alpha and ribavirin improves the rate of response to HCV dual therapy. Results are not expected for at least eighteen months.

HIV TREATMENT & CO-INFECTION

The immune system improvements seen with HAART can lead to flare-ups of HCV infection. However, it is believed that control of HIV replication will improve the outlook of people with HCV, reducing the risk of liver disease and reducing the risk of resistance to ribavirin.

Increases in liver enzyme levels associated with protease inhibitor treatment, especially ritonavir, develop more rapidly in people co-infected with hepatitis B compared to hepatitis C, but are least likely to go away when treatment is discontinued in people co-infected with hepatitis C. Treatment discontinuation due to liver toxicity is also more likely in people co-infected with HCV.

TRANSMISSION OF HCV

HCV is transmitted in blood, chiefly through injecting drug use. It is far more easy to transmit than HIV. According to research with health care workers who suffered needlestick injuries, hepatitis C virus is ten times more likely to be transmitted than HIV.

Injecting drug use equipment like spoons, filters, tourniquets and anything else which may become contaminated with tiny traces of blood could be routes of infection.

Epidemiologists have also traced infection to tattooing, ear piercing, barbers, biting and even snorting cocaine through rolled-up bank notes (tiny specks of blood from damaged nostrils are presumed to be responsible).

HCV can be passed from mother to child during pregnancy or childbirth. Treatment of HCV infection which lowers the mother's HCV viral load will reduce the risk of transmission.

Hepatitis C can also be transmitted sexually, through both vaginal and anal sex. There is some evidence that people infected with both HIV and HCV may be more likely to transmit HCV through sex, perhaps because they may have higher levels of HCV in their genital fluids than HIV-negative people.

REFERENCES

- den Brinker M et al. Fourth International Congress on Drug Therapy in HIV Infection, Glasgow, abs OP4.1, 1998.
- Melvin DC et al. International Conference on the Discovery and Development of Antiretroviral Therapies, US Virgin Islands, abstr 60, 1998.
- The Hepatitis C Handbook* by Matthew Dolan is published by Catalyst Press.

GLOSSARY

antiretroviral Something that attacks retroviruses such as HIV

CD4 Molecule on the surface of some cells onto which HIV binds. CD4 cell count roughly reflects the state of the immune system

cross resistance When resistance to one drug reduces the virological response to subsequent treatment with another drug which has not been taken before

log Short for logarithm, a measurement scale often used when describing viral load

NNRTI Non-nucleoside reverse transcriptase inhibitors: anti-HIV drugs that include nevirapine, delavirdine, and efavirenz

NRTI Nucleoside analogue reverse transcriptase inhibitors: anti-HIV drugs that include AZT, ddI, ddC, 3TC and d4T

protease inhibitor Anti-HIV drugs which target the protease enzyme, e.g. saquinavir, ritonavir, indinavir, nelfinavir

resistance A drug-resistant HIV strain is less susceptible to the effects of one or more anti-HIV drugs because of its genetic make-up

undetectable viral load A level of viral load that is too low to be picked up by the particular viral load test used

viral load The amount of virus in a sample. HIV viral load indicates the rate at which HIV is reproducing in the body

NOTICES

INFORMATION FORUMS

The next NAM Information Forum offers feedback from the Chicago Retroviruses Conference. Speakers are Dr Anton Pozniak of the Chelsea and Westminster Hospital, London and Edward King, HIV Program Director of Medscape. The forum happens on Monday 22nd February, 7-9pm, at the University of London Union, Palms Room, 4th Floor, Malet Street, London WC1. All welcome. A sign language interpreter will be available.

THANKS TO MEGAN NICHOLSON

Megan Nicholson, whose article on HIV in children appears on page 5 of this issue, has left NAM to return to her native Australia. Happily, Megan will continue to work with NAM as a freelance contributor to our website, AIDSmap. The Editor thanks Megan for her work on *AIDS Treatment Update* and wishes her well in her changed role.

NOTE

Our Factsheet 30 *Information: where to go* referenced a number of organisations which provide information services to people with HIV. We omitted to include *Continuum*, a bi-monthly magazine which covers alternative HIV and AIDS issues. For details call 0171 713 7071.

Subscriptions

Free to individuals in the UK affected by HIV or AIDS. Professional/organisational rate: £69/year. Voluntary organisation rate: £50/year. Overseas rate: within EU add £10/year; outside EU add £15/year. Tel: Helen or Letitia on 0171-627 3200

Medical Advisory Panel

Dr Fiona Boag, Dr Ray Brettle, Professor Janet Darbyshire, Dr Martin Fisher, Professor Brian Gazzard, Dr Diana Gibb, Professor Paul Griffiths, Dr Margaret Johnson, Dr Jacqueline Mok, Dr Graeme Moyle, Professor Tony Pinching, Professor Jonathan Weber, Dr Ian Williams, Dr Mike Youle

Thanks to our funders

NAM's treatments education for people living with HIV is provided free thanks to the generosity of: The Department of Health, the Inner London HIV Health Commissioners Group, Levi Strauss & Co, Glaxo Wellcome UK, Crusaid, Bristol-Myers Squibb, Boehringer Ingelheim, Roche Products, Pharmacia & Upjohn, Du Pont Pharma, Merck Sharpe & Dohme, Enfield & Haringey Health Authority, Abbott Laboratories, Barnet Health Authority, Redbridge & Waltham Forest Health Authority, Bexley & Greenwich Health Authority.

ANY QUESTIONS?

The following national agencies 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 Advisory Service
Face-to-face sessions in central London
Tuesday, Wednesday & Friday 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

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.

Donations towards production costs are welcomed.

AIDS TREATMENT UPDATE

Published monthly by



NAM Publications
16a Clapham Common
Southside
London SW4 7AB.
Tel: 0171-627 3200
Fax: 0171-627 3101
E-mail: atu@nam.org.uk

<http://www.aidsmap.com>

Editor:
Anna Poppa

AIDS Treatment Update
founded by Peter Scott
Copyright: © NAM
Publications 1999
All rights reserved

Design:
Positive Design Works,
London W10

Imagesetting & Printing:
Lithosphere Ltd,
London N7

ISSN: 0969-4706