

aids treatment update



hiv and the kidneys

hiv and kidney disease

who is at risk, and how to avoid problems *page 4*

tenofovir and the kidneys

does this anti-HIV drug damage the kidneys? *page 8*

PEP update

the latest on preventing hiv infection *page 3*

treating syphilis

why new guidelines recommend fewer injections *page 14*

news in brief

how the disability discrimination act affects you *page 12*
regular timing important for anti-hiv drug success *page 13*

in this issue

Inside this month's *AIDS Treatment Update* is a copy of our reader's survey. This is your first opportunity to let us know exactly what you think of *ATU* since we redesigned the newsletter last October.

Your opinions really matter to us. After all, *ATU* is produced to help people like you living with HIV understand the latest information about treatments and other HIV-related health issues. Please take a few minutes to fill out the survey and help us make *ATU* even better in the future.

If you are reading a copy of *ATU* which isn't your own (in your HIV clinic, for example) and which doesn't have a survey inside, you can also fill in the survey online at: www.aidsmap.com/atu/survey. Why not sign up for your own personal subscription (free for anyone affected personally by HIV) at the same time?

I would also like to ask you to consider joining *ATU*'s new readers' panel. Members of the panel will help shape future editions of the newsletter through regular feedback via the web. Those selected, and who remain actively involved, will receive free copies of the latest editions of NAM's *AIDS Reference Manual* and *HIV/AIDS Treatment Directory*.

Please visit: www.aidsmap.com/atu/readerspanel for more details.

page 3 This month's *Upfront* provides an update on PEP (post-exposure prophylaxis) a month's supply of anti-HIV drugs that can be given as an emergency treatment to HIV-negative sexual partners soon after probable exposure to HIV in order to prevent infection.

page 4 *HIV and kidney disease* examines who is at risk of kidney problems and how to best prevent future complications. There's also a guide to what the kidneys actually do, and information about the different kidney function tests that might be done at your HIV clinic.

page 8 In *Tenofovir and the kidneys* Liz Highleyman examines what effects the anti-HIV drug tenofovir (*Viread*, also in *Truvada*) may have on the kidneys.

page 12 Amongst the items in *News in Brief* are the findings from a new study about adherence to anti-HIV drugs: it's not just the number of doses, but also the interval between doses that matters. You can also find out more about how the Disability Discrimination Act affects you.

page 14 New guidelines from the British Association for Sexual Health and HIV (BASHH) on treating syphilis in people with HIV now recommend two penicillin injections over two weeks. Find out why, and who might need more (or less).



aids treatment update

editor Edwin J Bernard
sub-editing & proofreading
 Anu Liisanantti
production Thomas Paterson
design Alexander Boxill
printing Cambrian Printers
ISSN 0969-4706
copyright ©NAM Publications
 2006 All rights reserved
charity number 1011220

AIDS Treatment Update
 was founded by Peter Scott

contact details

Lincoln House, 1 Brixton Road,
 London, SW9 6DE, UK
 tel: 020 7840 0050
 fax: 020 7735 5351
 email: info@nam.org.uk
 web: www.aidsmap.com

medical advisory panel

Dr Fiona Boag
 Dr Ray Brettle
 Professor Janet Darbyshire
 Heather Leake Date MRPharmS
 Dr Martin Fisher
 Professor Brian Gazzard
 Professor Frances Gotch
 Dr Margaret Johnson
 Dr Graeme Moyle
 Dr Adrian Palfreeman
 Kholoud Porter PhD
 Dr Steve Taylor
 Professor Jonathan Weber
 Dr Ian Williams
 Dr Mike Youle

For more information about *ATU*'s
 medical review panel, please visit
www.aidsmap.com/atu.

about NAM

NAM is a charity that exists to support the fight against HIV and AIDS with independent, accurate, up-to-date and accessible information for affected communities, and those working to support them.

For more information, and details of our other publications and services, please contact us, or visit our website, www.aidsmap.com.

disclaimer

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.

supported by



The Derek Butler Trust

PEP update

by Edwin J Bernard

Post-exposure prophylaxis (PEP) following sexual exposure to HIV is in the spotlight right now because an HIV-positive man is taking the government to court, accusing it of failing to implement an equitable policy regarding access to PEP. His 'equal access to PEP campaign' argues that whilst HIV PEP is available to all healthcare workers accidentally exposed to HIV, there is widespread inequality within the United Kingdom when it comes to PEP access after possible sexual exposure to HIV.

What is PEP?

HIV PEP requires a month of anti-HIV drugs be given as soon as possible to someone who is HIV-negative after probable exposure to HIV.

The concept of HIV PEP has been around almost as long as antiretrovirals themselves, but for many years was provided only to healthcare workers who were accidentally exposed to HIV.

Published data exist regarding the effectiveness of PEP for healthcare workers, although a recent European survey found that some cases of HIV transmission occurred in healthcare workers despite their receiving PEP within several hours after exposure.

The first data on PEP following sexual exposure were published at the end of the 1990s, and recent reports from Amsterdam and San Francisco have found that PEP following HIV exposure during sex between men is effective, although not 100%

protective, and that the availability of PEP neither led to a huge increase in demand, nor generally to more risky sex following PEP.

An emergency treatment

The British Association for Sexual Health and HIV (BASHH) published draft guidelines for the use of PEP following sexual exposure more than two years ago, and they were reviewed in the March 2004 issue of *ATU*.

The guidelines were published in their final form in February, and in April the government's Chief Medical Officer, Sir Liam Donaldson, issued a letter informing all hospitals (and the health authorities that control them) about the PEP guidelines: "PEP is an emergency treatment, and to be effective in preventing HIV, it must be prescribed as soon as possible after potential exposure to the virus...I would therefore ask you to ensure that PEP is part of the spectrum of sexual health services for your local populations."

When should PEP be taken?

The BASHH guidelines recommend the following: "The use of PEP following potential sexual exposure to HIV is only recommended where the individual presents within 72 hours of exposure."

However, several pages earlier in a discussion of factors that influence the effectiveness of PEP, they also suggest the following:

"PEP may be less [effective] or ineffective after 72 hours of the exposure, but may be considered after this time if the exposure is 'high risk'."

This means that PEP after 72 hours may be considered on a case-by-case basis depending on how likely it is that someone has been exposed to HIV.

Some experts argue that the 72-hour deadline is arbitrary, based on theories of biological plausibility obtained mainly via animal studies. One study suggests that the window of opportunity to abort HIV infection is between 48-72 hours, since it takes that long before HIV can be detected in lymph nodes. Other studies suggest it can take up to five days before HIV can be detected in blood. Nevertheless, most experts agree that PEP is an emergency treatment that has the best chance of working when it is accessed within hours, rather than days, of exposure.

Be prepared

Since you might already have HIV that is resistant to some anti-HIV drugs, it makes good sense to talk to your HIV doctor about the best PEP combination for anyone you might accidentally expose to HIV through sex in the future. You can then pass this information on to your partner, along with information about your current anti-HIV regimen (if you are on treatment), should the need ever arise. ■





Summary

- Kidney problems, although less common than liver problems, are a growing concern for some HIV-positive people
- People of African heritage or ethnicity are most at risk of HIV-associated kidney disease (HIVAN)
- However, HIVAN affects very few people and can often be treated by anti-HIV drugs alone.
- Kidney disease is also being seen in HIV-positive people with diabetes, high blood pressure, and hepatitis B and/or C coinfection.
- Kidney problems are usually asymptomatic in the earlier stages, but various tests can be used to identify kidney disease before symptoms occur.
- Kidney transplants are now available for HIV-positive people, and survival rates are similar to their HIV-negative counterparts.

hiv and the kidneys

who is at risk, and how to deal with it, by Edwin J Bernard

Until recently, chronic kidney disease in HIV-positive people was a subject very much 'under the radar', especially since the prevalence of liver-related problems is much higher.

Now, however, experts are recognising that the number of people with kidney-related problems may be increasing as people with HIV live longer, and last year, guidelines were produced in both the United States and the United Kingdom addressing the prevention and treatment of chronic kidney disease in people with HIV.

The Infectious Disease Society of America's (IDSA) chronic kidney disease management guidelines^[1] are the first of their kind, and recommend screening for kidney disease at the time of HIV diagnosis in order to identify people at risk of developing kidney problems. They also recommend that those at high risk of developing kidney disease should be screened every year.

Also last year, the British HIV Association (BHIVA) published their groundbreaking guidelines on kidney transplantation^[2] - the final option for people with end-stage kidney disease, after dialysis - which asserted that any HIV-positive person with end-stage kidney disease should be eligible for kidney transplantation if they were medically fit.

Hopefully, though, if all HIV-positive people are screened for kidney problems early on, and those at risk are monitored regularly, fewer people will develop end-stage kidney disease in the future reducing the need for dialysis and kidney transplants.

As Dr Samir Gupta, lead author of the IDSA guidelines says, by recommending that everyone with HIV be screened for kidney problems at diagnosis they are "trying to shift gears from how you

treat the HIV-infected patient with severe kidney disease to [looking] for the ones who are at risk of developing severe kidney disease and taking care of them early so they don't have to end up going on dialysis."

Who is at risk?

Although previous studies have suggested that about one-in-three people with HIV have some low-grade abnormal kidney function due to their HIV infection, most were conducted more than ten years ago prior to the advent of modern combination therapy.

As you will see below, more recent studies suggest that treating HIV with potent anti-HIV drugs often reverses even severe HIV-related kidney problems. This suggests that, as long as kidney-toxic drugs are not used without first checking that the kidneys are functioning well, most people with HIV won't have to worry about HIV damaging their kidneys.

However, as people with HIV live longer, it is anticipated that we may also be more susceptible to other illnesses that are associated with kidney problems, including diabetes, high blood pressure (hypertension) and hepatitis B and/or C coinfection. Other studies have also identified smoking for over ten years^[3], and older age^[4] as possible risk factors for kidney disease.

According to the IDSA guidelines, people at a higher risk of kidney disease include:

- HIV-positive people of African heritage or ethnicity.
- HIV-positive people with advanced HIV disease (CD4 counts below 200 cells/mm³ or with HIV viral loads above 4000 copies/ml).
- HIV-positive people with a family history of kidney disease.

Nevertheless, the US guidelines recommend that *everyone* who is diagnosed with HIV infection should be screened at diagnosis for the presence of protein in the urine (proteinuria) and undergo one of two sensitive kidney function tests (either creatinine clearance or glomerular filtration rate; see 'kidney function tests' for more on these).

These recommendations make sense in the US, because HIV is disproportionately affecting African Americans, and people of African heritage are particularly prone to kidney problems. However, current UK HIV treatment guidelines from BHIVA do not mention screening for kidney problems, despite the increasing numbers of people of African ethnicity living with HIV in the UK. This is likely to be addressed when the guidelines are updated later this year, but until then, if you are concerned about kidney problems, you could discuss this with your HIV doctor at your next visit.

Certain drugs used to treat either HIV or many of the infections associated with more advanced HIV disease, can also make previously undiagnosed chronic kidney disease worse. That's why screening for kidney problems makes sense, especially before starting anti-HIV therapy or the drugs used to treat HIV-related infections.

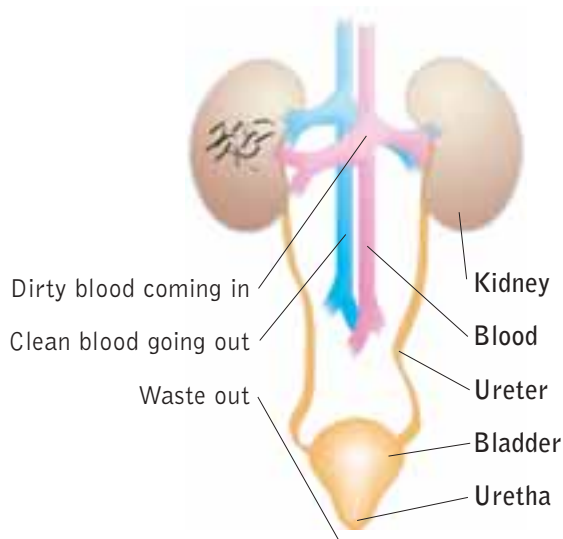
Although many of these drugs can still be used in people with kidney problems - with dose adjustments - it's particularly important to screen for any undiscovered kidney problems before starting on the anti-HIV drug tenofovir (*Viread*, also in *Truvada*) because it is prescribed to people with HIV so frequently. See 'Tenofovir and the kidneys' for more details on this.

kidney basics

1 The kidneys are a pair of fist-sized, bean-shaped organs (about 11cm long, 5cm thick, and weighing about 150 grams each) located around the middle of the back, just below the rib cage. Although most people have two kidneys, even one healthy kidney is enough for normal functioning.

2 The kidneys have several functions, including acting like sieves, filtering waste and excess fluid from the blood. Blood passes through the kidneys and is cleaned before returning to the heart. Each day, the kidneys process about 190 litres of blood through 145 miles of small tubes (tubules) and millions of mini filtering systems called "nephrons".

3 First blood enters the kidneys via the renal artery. Then, inside the kidneys, the nephrons sieve the blood. Substances that the body needs are reabsorbed and waste products and excess fluid are removed in the form of urine. The clean blood returns to the body through the renal veins. The urine is carried from the kidneys to the bladder by tubes called ureters. The bladder stores the urine until it is full, when the urine passes out of the body via the urethra.



4 Kidneys also release hormones, including erythropoietin, which stimulates the production of red blood cells, and renin which regulates blood pressure; and convert vitamin D into its active form, which is essential for healthy bones.

5 The medical field that studies the kidneys and diseases affecting the kidney is called *nephrology*, from the Greek name for the kidney; the adjective meaning 'kidney-related' is *renal*, from the Latin.

Noticing symptoms

Although there may be no symptoms, early signs for some people that the kidneys are not working properly include the passing of a lot of urine (polyuria) and an excessive or abnormal thirst (polydipsia): these are also symptoms of diabetes.

If you have protein in your urine, it may look 'frothy'. Excessive protein loss may cause fluid accumulation, which may be particularly noticeable in the legs.

The symptoms of more severe kidney problems may include a general feeling of being unwell (malaise), tiredness, nausea, headaches, muscle cramps, reduced urine flow, drowsiness, itchiness and, later, darkening of the skin.

HIV and kidney disease

HIV-associated nephropathy (HIVAN) is the leading cause of serious kidney disease among HIV-positive individuals. Recent studies have found that between 25% and 50% of HIV-infected people not on anti-HIV therapy in Kenya^[5] and Uganda^[6] have HIVAN. In the UK as well, HIVAN is mainly affecting people of African heritage or ethnicity.

A study presented in March at the BHIVA conference in Brighton^[7] found that all 50 cases of HIVAN that were diagnosed at ten hospitals in London and one in Brighton between 1998 and 2004 were in people of African heritage or ethnicity, notably from Africa (74%) or the Caribbean (20%). The majority (82%) were diagnosed with HIVAN at the same time as their HIV diagnosis, and this was invariably a late HIV diagnosis: the median CD4 count was 66 cells/mm³ and the median viral was 114,000 copies/ml. All 50 had never taken anti-HIV drugs before, and no-one was co-infected with either hepatitis B or C.

Although HIVAN only seems to be affecting people of black ethnicity in the UK, it should be emphasised that HIVAN is relatively rare. In fact, HIVAN was diagnosed in only one-in-100 (1.1%) HIV-positive people of black

ethnicity in London and Brighton between 1998 and 2004. However, the study's authors point out that they may have underestimated HIVAN prevalence because HIVAN is not always considered in undiagnosed HIV-infected people with acute kidney failure.

In contrast to the days before potent anti-HIV therapy, when the prognosis for someone with HIVAN was poor, things have significantly improved now: the study found a four-year survival rate of 84%. The most significant predictor of survival was the complete and durable suppression of HIV replication with potent anti-HIV drugs.

Dialysis and transplantation

Although the incidence of HIVAN has decreased since the introduction of powerful combination therapy in the developed world, the number of HIV-positive people on dialysis is actually increasing^[8] due to the amount of people now surviving with chronic severe kidney disease.

Dialysis involves the filtration of the blood by a dialysis machine, which takes over the function of the kidneys. Although dialysis is an option for HIV-positive patients with end-stage kidney disease, BHIVA's kidney transplantation guidelines make it clear that transplantation is a preferable option to long-term dialysis. This is because remaining on dialysis complicates the use of anti-HIV and other drugs, and also greatly affects quality of life.

Until recently, HIV infection was considered an absolute contraindication to kidney transplantation in both the US and Europe. However, kidney transplantation is now a viable option for people with end-stage kidney disease because potent anti-HIV therapy has reduced the risks associated with immunosuppressive drugs (which are used to prevent rejection of the transplant) and the risk of death from HIV itself.

The IDSA guidelines say that "renal transplantation may be considered" as long as it is carried out by surgeons with "adequate experience", and BHIVA's kidney transplantation guidelines note that survival is now comparable to non-HIV infected kidney transplant recipients. The BHIVA guidelines provide a great amount of detail regarding the transplantation process, and can be downloaded in full from BHIVA's website (www.bhiva.org).

However, the BHIVA guidelines do point out that "there are still a number of issues that need addressing, including the long-term survival of grafts and recipients, the long-term impact of immunosuppression on HIV reservoirs and CD4 cells, and the [drug-drug] interactions between antiretroviral and immunosuppressant therapies. Many of these questions will be answered with increasing experience and well-designed studies."

kidney function tests

The most basic kidney function tests involve looking for the presence of protein in the urine and measuring the levels of a protein called creatinine in the blood. Kidney function is said to be impaired if protein is found in the urine. Measuring levels of creatinine in the blood alone is not always reliable: high levels of creatinine in the blood are usually only elevated if there is marked kidney damage, and levels can also be elevated after intensive muscle activity, for example weight-training.

Creatinine clearance is considered to be a more accurate measure of kidney function. Measuring the formal creatinine clearance involves the collection of all urine that is passed over a 24-hour period. Along with a blood sample, this is sent to a laboratory to see how well creatinine is being excreted from the kidneys. Serious kidney disease is usually suspected if creatinine clearance is below 60ml/min. However, creatinine clearance is usually estimated using a calculation that involves serum creatinine, weight, age and gender (known as the Cockcroft Gault estimation).

An alternative calculation (MDRD) that includes creatinine levels, age, gender, and ethnicity, is used to estimate the glomerular filtration rate (GFR). The GFR measures the volume of water filtered out of blood plasma through glomerular capillary walls into Bowman's capsules per unit of time.

If tubular or glomerular leakage is suspected, the degree of leakage and extent of tubular damage can be assessed by comparing the ratios of creatinine and phosphate in the serum and urine, or the ratios of creatinine and protein in the urine.

The only reliable test to establish (or rule out) the presence of HIVAN is a kidney biopsy. This involves taking a small sample of kidney tissue for examination under a microscope. Enlarged kidneys seen through ultrasound may also be diagnostic of HIVAN, rather than other kidney diseases. Another reason for a biopsy would be when the cause of kidney disease is unclear in people with more than one possible cause of kidney problems.

tenofovir and the kidneys

are tenofovir's effects on the
kidneys really harmful?
asks Liz Highleyman

Summary

- Tenofovir (*Viread*) is one of the most widely-used anti-HIV drugs in the developed world.
- Most experts agree that, on the whole, tenofovir is one of the safest anti-HIV drugs available.
- So far, serious tenofovir-related kidney toxicity is very uncommon.
- When problems do occur, it is usually in people with pre-existing kidney problems or those taking other potentially kidney-toxic drugs.
- Although most kidney toxicity occurs within the first 6-12 months, later emergence has been reported.
- Although kidney toxicity is rare, it is still important to continue kidney function monitoring for as long as you take tenofovir.

With its once-daily dosing schedule and overall good side-effects profile, tenofovir disoproxil fumarate (*Viread*) has become one of the most widely prescribed anti-HIV medications in developed countries. Tenofovir is a nucleotide analogue anti-HIV drug, manufactured by Gilead Sciences. It was granted accelerated approval by the US Food and Drug Administration (FDA) in 2002, European Union approval followed in 2003, and full, traditional FDA approval was granted in February 2006.

Truvada, a combination pill containing tenofovir plus FTC (emtricitabine, *Emtriva*), was approved in Europe and the US in 2004. A new combination pill containing tenofovir, FTC, and the non-nucleoside efavirenz (*Sustiva*) – submitted for FDA approval in April – may soon offer what many thought impossible a decade ago: a one-pill, once-daily HIV regimen. Tenofovir is also being tested as part of a pre-exposure prophylaxis (PREP) combination to see if it can prevent HIV-negative people from becoming infected.

Does tenofovir harm the kidneys?

But whilst tenofovir may look like a wonder drug, no drug is perfect, and tenofovir has the potential for kidney toxicity. Preclinical studies showed that high doses of tenofovir could cause kidney failure in animals, and researchers were concerned about the drug's side-effects because two related compounds, adefovir and cidofovir (*Vistide*), are known to cause severe



kidney toxicity. In fact, adefovir was not approved as an anti-HIV therapy for this reason, though a lower-dose formulation (*Hepsera*) was later approved as a treatment of hepatitis B.

Tenofovir, like adefovir and cidofovir, is a chemical known as *acyclic nucleosidephosphonate*, which can damage the renal tubules (tiny tubes inside the kidney) where blood is filtered and nutrients and water are reabsorbed into the body. Tenofovir is processed and eliminated by the kidneys, and can build up to dangerously high levels. When this happens, the drug can cause the death of kidney cells (necrosis), leading to symptoms ranging from mildly elevated serum creatinine levels and low phosphate levels, to Fanconi syndrome (where nutrients are excreted in urine rather than absorbed into the bloodstream) and acute kidney failure. The mechanism by which tenofovir and its relatives cause kidney toxicity is not fully understood, but it may be related to damage to mitochondria (a cell's energy source).

What does the research show?

In the large randomised clinical trials that led to the drug's approval, it appeared that tenofovir did not share the toxicity of adefovir and cidofovir. Most studies showed that serious kidney problems were rare, occurring in 1% or less of patients taking tenofovir – about the same rate seen in people taking other anti-HIV drugs or placebo (an inactive pill). However, individuals with pre-existing kidney problems or taking kidney-toxic drugs were excluded from these trials.

At the International AIDS Conference in Barcelona in 2002, researchers reported safety data from several different phase II-III trials that included nearly 700 people taking tenofovir. Mildly elevated creatinine levels occurred in similar proportions of people taking either tenofovir or a placebo; after six months of treatment, none experienced severe kidney toxicity or discontinued treatment for this reason^[1]. Kidney toxicity was also rare (less than 1%) among the nearly 7000 treatment-experienced participants in the tenofovir expanded access programmes (EAPs) in Europe, Australia, and North America^[2].

Once tenofovir was on the market, however, case reports about kidney toxicity began to trickle in. The first report came from Paris in December 2002, concerning a 45 year-old woman who developed Fanconi syndrome, diabetes, and acute kidney failure five months after starting tenofovir; although within a month after stopping the drug, her kidney function returned to normal^[3]. Several other cases were reported at the annual Retrovirus conference in February 2003, including three cases by French doctors, although two of the patients had low creatinine clearance before starting tenofovir^[4].

Although such isolated cases continued to be reported – today numbering more than 50^[5] – longer-term data from most clinical trials still showed that tenofovir was not associated with an increased risk of serious kidney problems. In Gilead's 903 study, which

included 600 treatment-naive participants without pre-existing kidney impairment, tenofovir was no more likely to cause kidney-related laboratory abnormalities or serious clinical kidney toxicity than d4T (stavudine, *Zerit*) through 144 weeks; no-one taking tenofovir experienced serious kidney problems nor discontinued due to kidney toxicity^[6,7]. In Gilead's 934 study, which included about 500 treatment-naive participants, those taking tenofovir plus 3TC (lamivudine, *Epivir*), were less likely to stop treatment for any reason than those taking AZT (zidovudine, *Retrovir*) plus 3TC and, again, no-one discontinued due to kidney problems^[8,9].

“Real world” data

As noted above, people with pre-existing kidney problems and those taking other potentially kidney-toxic drugs were excluded from the tenofovir clinical trials and EAPs. Some experts suggested that this might account for the low rates of kidney problems seen in these groups, since most case reports of tenofovir-related kidney toxicity have involved people with pre-existing kidney impairment or kidney disease.

However, more recent data have shown that serious tenofovir-related kidney toxicity is still uncommon even under “real world” conditions. In 2004, after looking at the records of more than 4000 patients, doctors from London's Chelsea and Westminster Hospital reported that tenofovir was no more

likely to cause kidney problems than other anti-HIV drugs. Although about eight percent of their patients did experience moderate kidney impairment, most had causes other than tenofovir^[10]. And in a Spanish study with more than 1350 participants, kidney toxicity was again rare^[11].

At this year's Retrovirus conference, Gilead presented four-year data on the more than 10,000 people who had received tenofovir through EAPs worldwide, as well as post-marketing safety reports received until April 2005 (representing more than 455,000 person-years of tenofovir use)^[12]. In the EAPs, half of one percent of people experienced serious kidney problems; in the post-marketing database, which included people with pre-existing kidney impairment, the rate of serious kidney-related toxicity was a very low 43 per 100,000 person-years. However, this may be an underestimation as it relies on doctors' reports, and not all doctors report all cases.

The bad news

Other studies, however, have found higher rates of at least mild kidney toxicity in people taking tenofovir, especially when more sensitive kidney function tests are used. An analysis from the US Centers for Disease Control and Prevention (CDC), which included medical records from 11,362 HIV-positive individuals in ten cities, found that people taking tenofovir were 60% more likely to have some degree of kidney impairment; however, further

analysis found that this was mild-to-moderate, not severe, impairment^[13].

Another large analysis of nearly 1300 participants in the international CHORUS cohort found that about six times as many people were classified as having at least mild kidney impairment when using a combination of glomerular filtration rate (GFR - see 'kidney function tests' on page seven) and clinical symptoms, rather than simple serum creatinine levels^[14].

So, who is at risk?

The number of serious tenofovir-related kidney problems is so small that it is difficult to make generalisations about the level of risk in different groups of people. Nevertheless, some trends are apparent. In the CDC study, being older than 50 was associated with a 3.5% increase in the risk of severe kidney impairment; in another study from Seattle^[15], older age doubled the risk.

The Seattle study also found that low body weight increased the chances of kidney problems (a five percent greater risk per kilogram below average body weight). Body weight may be a factor in kidney toxicity because lower-weight individuals receive a relatively higher amount of tenofovir, which is not dosed-adjusted based on weight.

There is some expert disagreement about whether race/ethnicity plays a role in tenofovir-related kidney toxicity. Although people of African descent are more likely to have HIV-associated

nephropathy (HIVAN; see 'HIV and kidney disease' for more on this), a study of 96 African Americans treated at a Texas clinic concluded that tenofovir was no more likely to cause kidney toxicity than AZT, and that the degree of impaired creatinine clearance (which was mild) was similar to that seen in studies with a majority Caucasian population^[16]. Clearly more "real world" studies are needed in people of African ethnicity, however.

Several studies have suggested that tenofovir-related kidney toxicity is more likely in people with advanced HIV disease. In both the Gilead EAP/postmarketing study and the CDC study, low CD4 cell count was an independent risk factor for kidney toxicity. This finding may be due to the fact that people with advanced HIV disease are more likely to take kidney-toxic drugs to treat opportunistic infections.

However, the highest risk for tenofovir-related kidney toxicity is pre-existing kidney impairment. In the early case reports and in large "real world" studies, most people with kidney toxicity had at least pre-existing elevated creatinine levels, if not more serious kidney disease, before starting tenofovir. This strongly suggests that all people thinking of taking tenofovir should undergo kidney function tests before starting the drug.

Additive drug toxicity

The data linking tenofovir toxicity with the use of other kidney-toxic drugs are



ample and growing. For example, in an analysis of 27 people who experienced serious kidney damage while taking tenofovir, 75% were also taking ritonavir (*Norvir*) or *Kaletra* (lopinavir/ritonavir), and many were taking ddI (didanosine, *Videx*) or atazanavir (*Reyataz*)^[17].

Low-dose ritonavir used to boost many protease inhibitors and *Kaletra* (which includes a small dose ritonavir alongside lopinavir) can boost tenofovir levels by as much as 30%, increasing the risk of kidney toxicity. Atazanavir, even when used without ritonavir, (although this is not licensed in Europe) has also been shown to increase tenofovir levels. On the other hand, tenofovir can raise ddI levels by as much as 50%, which may increase the risk of kidney damage related to mitochondrial toxicity.

Finally, there is a risk of additive kidney toxicity when tenofovir is used with certain medications used to treat opportunistic infections, including foscarnet (*Foscavir*), ganciclovir (*Cymevene*), and cidofovir, all used to treat CMV retinitis; amphotericin B (*Fungilin/ Fungizone*) for fungal infections; pentamidine (*Pentacarinat*) for *Pneumocystis* pneumonia; and antibiotics such as tetracycline and the aminoglycoside drugs, such as gentamicin. Although aciclovir (*Zovirax*) for herpes simplex and other herpes-type viruses may also increase the risk of kidney toxicity when taken with tenofovir, this is rarely seen in

clinical practice. People co-infected with HIV and hepatitis B should avoid using tenofovir with adefovir.

How to minimise the risk

The best way to reduce the risk of kidney toxicity whilst taking tenofovir is careful kidney function screening before starting the drug. This includes, at minimum, assessment of serum creatinine and phosphate levels, and protein in the urine; some experts believe creatinine clearance and glomerular filtration rate are better measures than simple creatinine level but these can be calculated based on simple measurements (see 'kidney function tests' on page seven).

The current European Medicines Agency (EMA) guidelines advise monitoring every month for the first year, then every three months, although in the UK this rarely happens, and most people without pre-existing kidney problems are monitored every three months. More frequent monitoring (as often as every 1-2 weeks) is recommended for people who have pre-existing kidney problems, are taking other potentially kidney-toxic drugs, or are otherwise at increased risk for kidney problems.

Gilead advises that people with severe pre-existing kidney dysfunction (creatinine clearance below 50mL/min) should not use tenofovir. Those with mild-to-moderate kidney impairment should have their tenofovir dosing interval lengthened based on creatinine clearance rates,

since it takes longer for the drug to be eliminated from their kidneys. Gilead also advises that the *Truvada* combination pill should not be used by people with creatinine clearance rates below 30 mL/min, since the tenofovir dosing interval cannot be adjusted without also changing the dose of FTC.

Although this is clearly spelt out in the tenofovir package insert, Gilead – at the urging of the EMA – sent a letter to healthcare providers in the UK in March reminding them of the importance of dosing-interval adjustment, since several reported cases of tenofovir kidney toxicity have occurred in people with known kidney impairment who should have been taking less frequent doses.

Vigilance is key

Fortunately, serious kidney damage can usually be avoided by stopping or adjusting the dosing of tenofovir at the first signs of trouble. In most cases, kidney function returns to normal within a few weeks after the drug is appropriately adjusted or discontinued (although some cases of long-term dysfunction have been reported).

Tell your doctor immediately if you experience any symptoms suggestive of kidney impairment such as excessive thirst, very frequent or very sparse urination, painful urination, pain on the side of the body between the ribs and hips, or muscle pain or weakness. Vigilance is the surest way to prevent lasting problems. ■

news in brief

mental health

Good mental health news

Two recently published studies provide good news for those of us concerned about our mental health. Previous studies have found that HIV-positive individuals are more likely than their HIV-negative counterparts to experience a range of mental health issues such as depression, and there is also concern that HIV may affect the brain, leading to reduced mental functioning.

Some experts believe that HIV-positive people with mental health problems won't do as well with HIV disease, due to problems like poorer adherence to anti-HIV treatment. However, an Australian study which included more than 500 individuals over 16 years, has found that this isn't the case, and that HIV-positive people with mental health problems live just as long as those without.

The study did find, however, that people with mental health problems took more anti-HIV drugs and spent more time in hospital.

Another study from Sweden intensely examined HIV's effects on the brain in a small group of HIV-positive individuals between 1989 and 1996. Although HIV was found in the central nervous system of all the participants - and none were on powerful combination anti-HIV therapy because it wasn't available at the time of the study - the investigators found that there was a low risk of HIV causing disorders of the brain and nervous system, like reduced mental (cognitive) function, or dementia.

Treatments for mental health problems can work well in people with HIV, and today's powerful anti-HIV drug combinations can also help improve mental functioning - although efavirenz (*Sustiva*) may cause depression in a small minority of people. Many HIV treatment centres have mental health specialists, and help is always available, so talk to your doctor if you are concerned about your mental health.

hiv and the law

HIV and protection under the law

Since last December, the Disability Discrimination Act 2005 has protected people living with HIV from the moment of diagnosis. This law gives HIV-positive people rights in the areas of employment, access to goods and services, education and housing.

The government agency that monitors this law is the Disability Rights Commission. Together with the National AIDS Trust (NAT) they have produced a leaflet called *Positively Employed* that specifically outlines the new rights given to HIV-positive employees as well as the duties of employers. It can be obtained free of charge from the Disability Rights Commission by calling 08457 622 633 (textphone 08457 622 644) and quoting reference EXT1. NAT also has information about HIV and the law on their anti-HIV prejudice website, www.areyouhivprejudiced.org.

One of the main questions people have about this new law is whether your employer has to know that you are HIV-positive in order for you to be protected. After all, disclosing your HIV status to your employer might not be something you want to do.

To help you make the right decision about this - as well as to help to you decide about how or whether to disclose your status to partners, friends, relatives, dentists, doctors, insurers and immigration and government officials - the Terrence Higgins Trust (THT) have produced an updated version of their booklet *Should I Tell?* It can be ordered or downloaded directly from www.tht.org.uk or by calling THT Direct on 0845 12 21 200.

Updated information on HIV and the law and issues around disclosure can also be found in the new edition of NAM's comprehensive *Living with HIV* book, which will be available this summer. You can also find the newly updated information online now at www.aidsmap.com under the main heading of 'Living with HIV'.



new drugs

New *Kaletra* tablet due in July

Abbott's new tablet formulation of *Kaletra* (lopinavir/ritonavir) received a positive opinion from the scientific committee of the European Medicines Agency (EMA) in April, and should receive marketing approval by July.

The new tablet, which is already approved in the United States, will reduce the daily pill burden from three capsules twice daily to two tablets twice daily. The tablet version does not need to be taken with food, and does not need to be refrigerated. In addition, studies in HIV-negative volunteers suggest that the new tablet may mean fewer problems with diarrhoea.

Within a few months of the new tablet being approved, however, the current orange gel capsule formulation is likely to be withdrawn. If you are currently on a non-standard dose of *Kaletra* – for example, two or four capsules twice-daily – you will not be able to obtain exactly the same dose from the new formulation, because there is more ritonavir and lopinavir in the tablet (hence the lower pill burden).

Abbott tells *ATU* that they are committed to helping people who are on non-standard dosing, and are developing a half-dose tablet to replace the foul-tasting liquid *Kaletra* aimed at children – although this will not be available until at least the end of next year. In the meantime, the capsules may become available on a named-patient basis once they are withdrawn. Talk to your HIV doctor now about how the changes in *Kaletra* formulation might affect your treatment.

latest research



Regular timing important for anti-HIV drug success

A new study has further underlined the importance of proper adherence to HIV treatment, this time finding that it's not just the number of doses that matters, but also the interval between doses.

For anti-HIV treatment to work effectively, it is essential to take it properly. This means aiming to take all your doses every day, at the right time and in the right way, making sure you observe any food requirements.

Previous studies have found that at least 95% of all doses need to be taken to provide you with the best chance that your anti-HIV combination will work well over a long period of time. In practice, this means missing no more than a dose a month if you are taking once-daily treatment, or a couple of doses a month if you are taking twice-daily treatment.

This new study, involving 129 people with HIV and lasting for a year, found that people who took their treatment close to the same time every day – and definitely no more than three hours late – had lower viral loads than people who did not stick as well to daily doses at regular times. The results of the study strongly suggest that taking your anti-HIV combination very close to the same time every day provides you with the best chance of long-lasting treatment success.

references

hiv and the kidneys [page four]

- 1 Gupta SK et al. *Guidelines for the management of chronic kidney disease in HIV-infection patients: recommendations of the HIV Medicine Association of the Infectious Disease Society of America*. CID 40, 1559-1585, 2005.
- 2 Bhagani S et al. *Guidelines for kidney transplantation in patients with HIV disease*. <http://www.bhiva.org/guidelines/2005/renal/rfs.html>
- 3 Miguez-Burbano MJ et al. *Renal disease in HIV infected subjects: the deleterious effect of smoking*. 15th Intl. AIDS Conf. Bangkok, abs MoPeB3274, 2004.
- 4 Gupta SK et al. *Prevalence of proteinuria and the development of chronic kidney disease in HIV-infected patients*. Clin Nephrol 61: 1-6, 2004.
- 5 Muloma E et al. *Renal disease in an antiretroviral naïve HIV-infected population in western Kenya*. 3rd IAS Conf, Rio de Janeiro, abs MoPe11.6C23, 2005.
- 6 Pepper L et al. *Prevalence of renal disease in patients attending the HIV/AIDS clinic at Mbarara University Teaching Hospital*. 3rd IAS Conf., Rio de Janeiro, abs TuPe15.3C02, 2005.
- 7 Post F et al. *The epidemiology of HIV-associated nephropathy (HIVAN): the London HIV- nephropathy study*. HIV Med 7 (suppl. 1), abstract 013, 2006.
- 8 Rao TK et al. *Human immunodeficiency virus infection in end-stage renal disease patients*. Semin Dial 16: 233-244, 2003.

tenofovir and the kidneys [page eight]

- 1 Cheng A et al. *Safety profile of tenofovir DF in treatment-experienced patients from randomized, placebo-controlled clinical trials*. 14th Intl. AIDS Conf., Barcelona, abs TuPeB4460, 2002.
- 2 Nelson M et al. *The Viread expanded access program (EAP): safety and efficacy of tenofovir disoproxil fumarate in antiretroviral treatment experienced patients*. 14th Intl. AIDS Conf, abs TuPeB4468, 2002.
- 3 Verhelst D et al. *Fanconi syndrome and renal failure induced by tenofovir: a first case report*. Am J Kid Dis 40(6): 1331-1333, 2002.
- 4 Reynes J et al. *Renal tubular injury and severe hypophosphoremia (Fanconi Syndrome) associated with tenofovir therapy*. 10th CROI, Boston, abs 717, 2003.
- 5 Roling J et al. *HIV-associated renal diseases and highly active antiretroviral therapy-induced nephropathy*. CID 42: 1488-1495, 2006.
- 6 Staszewski S et al. *Three-year analysis of the renal safety of tenofovir DF (TDF) versus stavudine (d4T) when used in combination with lamivudine (3TC) and efavirenz (EFV) in antiretroviral-naïve patients*. 15th Intl. AIDS Conf., Bangkok, abs WePeB5917, 2004.
- 7 Izzedine H et al. *Long-term renal safety of tenofovir disoproxil fumarate in antiretroviral-naïve HIV-1-infected patients: data from a double-blind randomized active-controlled multicentre study*. Nephrol Dial Transplant 20:743-746, 2005.
- 8 Pozniak AL et al. *Superior outcome for tenofovir DF (TDF), emtricitabine (FTC) and efavirenz (EFV) compared to fixed dose zidovudine/lamivudine (CBV) and EFV in antiretroviral naïve patients*. 3rd IAS, Rio de Janeiro, abs WeOa0202, 2005.

- 9 Gallant JE et al. *Tenofovir DF, emtricitabine, and efavirenz vs. zidovudine, lamivudine, and efavirenz for HIV*. NEJM 354(3): 251-260, 2006.
- 10 Jones R et al. *Renal dysfunction with tenofovir disoproxil fumarate-containing highly active antiretroviral therapy regimens is not observed more frequently: a cohort and case-control study*. JAIDS 37: 1489-1495, 2004.
- 11 Estrada V et al. *Renal safety of tenofovir DF in HIV treatment-experienced patients with adverse events related to NRTI use (RECOVER Study)*. 44th ICAAC, Washington, abs H-169, 2004.
- 12 Nelson M et al. *The safety of tenofovir DF for the treatment of HIV infection: the first 4 years*. 13th CROI, Denver, abs 781, 2006.
- 13 Heffelfinger J et al. *Renal impairment associated with the use of tenofovir*. 13th CROI, Denver, abs 779, 2006.
- 14 Becker S et al. *Beyond serum creatinine: identification of renal insufficiency using glomerular filtration: implications for clinical research and care*. 12th CROI, Boston, abs 819, 2005.
- 15 Crane H et al. *Didanosine and lower baseline body weight are associated with declining renal function among patients receiving tenofovir*. 13th CROI, Denver, abs 780, 2006.
- 16 Lewis S et al. *Comparative evaluation of renal function in HIV-infected, treatment naïve patients of African American descent receiving HAART regimens containing either tenofovir DF or zidovudine*. 15th Intl AIDS Conf., Bangkok, abs TuPeB4599, 2004.
- 17 Zimmermann AE et al. *Tenofovir-associated acute and chronic kidney disease: a case of multiple drug interactions*. CID 42: 283-290, 2006.
- 18 Izzedine H et al. *Antiviral drug-induced nephrotoxicity*. Am J Kid Dis 45: 804-817, 2005.

hiv and syphilis [page fourteen]

- 1 Nandwani R et al. *2006 United Kingdom national guideline on the sexual health of people with HIV: Sexually Transmitted Infections*. Available from the BASHH website, www.bashh.org/guidelines.asp
- 2 Rolfs RT et al. *A randomized trial of enhanced therapy for early syphilis in patients with and without human immunodeficiency virus infection*. NEJM 337(5): 307-314, 1997.
- 3 Babu C et al. *Syphilis reinfection in HIV-positive men: a new challenge*. HIV Med 7 (Suppl 1) P107, 2006.

news in brief [page twelve]

Good mental health news

- 1 Mijch A et al. *Increased health care utilization and increased antiretroviral use in HIV-infected individuals with mental health disorders*. HIV Med 7: 205 - 215, 2006.
- 2 Samuelsson K et al. *The nervous system in early HIV infection: a prospective study through 7 years*. Eur J Neurol 13: 283 - 291, 2006.

Regular timing important for anti-HIV drug success

- 1 Liu H et al. *Repeated measures longitudinal analyses of HIV virologic response as a function of percent adherence, dose timing, genotypic sensitivity and other factors*. JAIDS 41: 315 - 322, 2006.

treating syphilis

why new guidelines recommend fewer penicillin injections, by Edwin J Bernard

Syphilis has returned with a vengeance in the United Kingdom over the past few years. Between 2000 and 2004 new diagnoses of this sexually transmitted infection (STI) rose by 717% in gay men; 583% in heterosexual men, and 255% in women, although HIV-positive gay men are much more likely to be affected than HIV-positive heterosexuals. Since syphilis can be harder to cure in people with HIV, it is particularly important that the infection is diagnosed early and treated appropriately.

Last month, the British Association for Sexual Health and HIV (BASHH) published the first ever comprehensive set of guidelines for the management of STIs in HIV-positive individuals^[1]. The STI guidelines include an important update to BASHH's 2002 syphilis and HIV guidelines.

The recommended treatment of early syphilis in HIV-positive individuals has now changed from up to three weeks of consecutive daily intramuscular injections of procaine penicillin to a more manageable and less painful treatment using two doses of intramuscular benzathine penicillin given one week apart.

What exactly is early syphilis?

Syphilis is a complex infection caused by bacteria. Early syphilis refers to both primary and secondary syphilis, when

most cases of syphilis are diagnosed in HIV-positive people in the UK.

Primary syphilis occurs soon after infection when a painless chancre (sore) appears at the site of infection (mouth, penis, vagina, or anus). Since some chancres can be hidden away, or mistaken for herpes, syphilis can easily be missed at this stage.

Syphilis is much more likely to be diagnosed when it has progressed to the secondary stage - within six months of exposure - when it shows up in blood tests. Secondary syphilis can also cause symptoms. These include a rash, swollen glands, fever, muscle pain, headache, ringing in the ears, and in rare cases, meningitis. Dark brown sores, about the size of a penny piece may also appear on the hands and feet. The rash and sores are highly infectious.

Why the change?

The guidelines' authors explain that the change of recommendation came about because there is currently a UK shortage of procaine penicillin (although supplies are available and being imported from Spain and Australia for people who really do need this treatment); because taking (and giving) 10-21 consecutive days' worth of large volumes of penicillin into the buttocks is difficult for everyone involved, especially the patient; and because there has been "a shift in expert opinion in the UK on the adequacy of benzathine penicillin" to treat syphilis.

What the old guidelines said?

There were good scientific data supporting the 2002 recommendations. A pivotal 1997 study^[2] found that after six months almost one-in-five HIV-positive people treated with a single injection of benzathine penicillin still had detectable levels of syphilis bacteria in their blood. That's why up to three weeks of daily procaine penicillin injections was recommended.

However, some experts argued that this was overtreating syphilis in most

HIV-positive people, and that two intramuscular injections of benzathine penicillin over two weeks would work just as well for HIV-positive people with early syphilis as long they didn't have very advanced HIV disease.

The new guidelines also point out that some doctors were also making it appear to their patients that the three-week course of procaine penicillin was a kind of punishment.

Is this enough?

The updated guidelines now recommend that anyone who is "not at significant clinical risk of developing opportunistic infection" and in whom there is "adequate follow-up" can be treated with two doses of benzathine penicillin one week apart.

Some experts still think that the three-week course of procaine penicillin still provides the best chance of a cure, and may well be preferable to incomplete symptom resolution and the possibility of more aggressive treatment later. However a recent report from Manchester^[3] found that three weekly injections of benzathine penicillin worked as well as nearly three weeks of daily procaine penicillin in men who were reinfected with syphilis: 89% had a good response when a single dose of intramuscular benzathine penicillin was used compared with 96% when three weekly injections of benzathine penicillin were given or when procaine penicillin was given for 17 consecutive days.

Alternatives to injections?

Some doctors say that many of their patients won't even have one penicillin injection, opting instead for oral antibiotics - including doxycycline, tetracycline, erythromycin, and ceftriaxone - although only azithromycin (*Zithromax*) has been shown to be as effective as penicillin, and then only as effective as a single benzathine penicillin injection (which means a one-in-five chance of treatment failure).

However, there have been recent outbreaks of azithromycin-resistant

syphilis amongst HIV-positive gay men in the United States and Ireland, and azithromycin-resistant syphilis may already be widespread in the UK (although there are no data on this yet).

Not enough for some?

Some people with HIV might still need to undergo a three-week course of daily procaine penicillin injections, however. The treatment is still recommended for people with very advanced HIV disease - those who might become sick with an opportunistic infection. However, since syphilis can temporarily lower CD4 counts, the guidelines recommend that an HIV specialist make a realistic judgement about whether someone is likely to need this stronger treatment.

The stronger treatment is also recommended if someone is diagnosed with late (tertiary) syphilis. In both cases, the guidelines note that it's important that "a full and informed discussion" about the reasons for this more difficult treatment takes place.

Choose wisely

Two benzathine penicillin injections a week apart may well balance the thorny issues of pain and potency. However, in some cases a single pill or a longer series of injections might still be the most appropriate treatment for you.

Treating syphilis - like HIV - is not a one-size-fits-all approach. If you are about to have treatment for syphilis, it makes sense to be aware of the pros and cons of all the treatment choices, and to discuss this with your doctor.

It's also worth remembering that earlier detection is better than later detection and the guidelines reiterate their 2002 recommendation that syphilis screening should be part of regular three-monthly HIV clinic blood tests.

It is also important to return for more tests after having syphilis treatment to make sure the syphilis bacteria is completely cleared from the blood and central nervous system. ■

thanks to our funders

NAM's treatments information for people living with HIV is provided free thanks to the generosity of:

Abbott Laboratories International & UK; Access 4; Ajahma Charitable Trust; Alan & Nesta Ferguson Charitable Settlement; Avexa; Birmingham PCT; The Body Shop Foundation; Boehringer Ingelheim International & UK; Bolton PCT; Bristol-Myers Squibb UK HIV & Hepatitis; British HIV Association (BHIVA); Cleopatra Trust; Corkery Group; Crusaid; Derek Butler Trust; Diana, Princess of Wales Memorial Fund; Government of the United Kingdom, Department of Health; East Sussex, Brighton & Hove area PCTs; The Elton John AIDS Foundation; Gilead International & UK; GlaxoSmithKline UK; Healthsure Charitable Trust; Hugh Fraser Foundation; International HIV/AIDS Alliance; Janssen-Cilag; Lloyds TSB Foundation for England and Wales; Lloyds TSB Foundation for Northern Ireland; London HIV & GUM Commissioning Consortium; MAC AIDS Fund; Merck Sharp & Dohme UK & International; Newcastle PCT; Norfolk PCT; Manchester city area PCTs; Miss Agnes H Hunter's Trust; Merton Social Services; Peter Moores Foundation; Pfizer UK & International; Positive Action (GSK); Roche Products UK Hep C; Roche Products International & UK; The Russell Trust; Salford PCT; Shire Pharmaceuticals; South East Essex PCTs; South West Essex PCTs; St. Stephen's AIDS Trust; Stockport Social Services; Thomas Sivewright Catto Charitable Settlement; Tibotec; Virco; West Sussex PCTs; Worcestershire PCT

NAM would also like to acknowledge the generous support of individual donors, and in particular Gavin Hay and Tim Cohen

Where to find out more about HIV

■ Find out more about HIV treatment:

NAM's factsheets, booklets, directories and website, keep you up to date about key topics, and are designed to help you make your healthcare and HIV treatment decisions. Contact NAM to find out more and order your copies.

■ Information events in London

On the last Monday of every month, an expert speaker discusses an HIV treatment related topic. Entry is free. The next topic is 'treatment interruptions', and will be held on 26th June 2006. For more details, go to www.aidsmap.com/forums.

■ www.aidsmap.com

Visit our website for the latest news about HIV & AIDS and a fully searchable treatments database and a complete list of HIV treatment centres in the UK.

■ THT Direct Phonenumber

Offers information and advice to anyone infected, affected or concerned about issues relating to HIV and sexual health.

0845 1221 200

Mon-Fri, 10am-10pm Sat-Sun, 12pm-6pm

■ i-Base Treatment Phonenumber

A HIV Treatment phonenumber; where you can discuss your issues with a treatment expert.

0808 8006 013

Mon-Wed, 12pm-4pm

nam

get aids treatment update for free every month

If this isn't already your own copy of *AIDS Treatment Update*, make it yours today by subscribing for free.

Simply call us on

020 7840 0050

or complete the form below



AIDS Treatment Update is written to help support you in the decisions you make about your health and HIV treatment.

Take control, subscribe today

name

address

postcode

country

email

subscription format paper email audio tape

- We publish a range of information resources on HIV & AIDS. Please tick this box if you would **not** like to be added to our mailing list.
- We occasionally undertake fundraising campaigns to help support our work. Please tick this box if you would **not** like to receive information about them.

please return this form to

NAM, Freepost LON17995, London, SW9 6BR

tel 020 7840 0050

fax 020 7735 5351

email info@nam.org.uk

web www.aidsmap.com

ATU