

aids treatment update

Herbs and HIV: *caveat emptor*

This month, *ATU* examines herbal medicines and HIV. It's a difficult and potentially emotive subject, not just because there are so few data on the interactions between prescription medicines and herbal remedies, but also because belief in all kinds of complementary medicine appears to be stronger now than at any time since the Great Plague of the 17th Century.

Herbs and other supplements are rightfully important to many people living with HIV. We use them to counteract side-effects of both HIV and the drugs used to treat it, and they help us to feel a little more in control of our health and our bodies. But it's worth remembering that many herbs have not been subjected to the rigorous scrutiny given to prescription drugs.

"The quantity and quality of data for most herbal products is much lower than the kind of data licensed pharmaceuticals have to submit to the regulatory authorities before they can be approved," says HIV pharmacist Heather Leake Date. "And we know that, even then, nasty surprises can be discovered after the drug has been on the market for a while!"

Most herbs have Latin names. Two more Latin words are very relevant here: *caveat emptor*. Buyer beware!

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Summary

- There's absolutely no evidence that any herbal product can substitute for your anti-HIV medication.
- As with vitamins and supplements, there is limited evidence that some herbal products may improve some symptoms and quality of life.
- Be aware that herbal remedies are just as capable of creating unpleasant side effects and allergies as prescription drugs.
- Always consult a reputable and qualified herbalist.
- Be suspicious of any claims of 'miracle cures' - especially if the 'miracle cure' is expensive.
- Always tell your HIV healthcare professional and/or HIV pharmacist if you are taking a particular herbal remedy or a herbal prescription from a traditional medicine practitioner, as they may interact with the prescription drugs you are taking.

Where HIV is concerned, the use of herbal medicine is a particularly complex area because, unlike vitamin supplements, herbal supplements are not 'pure' substances. Whether by taking a particular herb you are taking chemical substances in their most effective or least toxic form is a very difficult question to answer. However, in the hope that herbal remedies may contain something new and unknown to science, or be more effective or safer than prescription drugs, people living with HIV often take herbs without realising that they may, at best, be a waste of money, and at worst, be harmful. Although one in seven adults in the UK use herbal remedies, it doesn't necessarily follow that they all work or are beneficial for all people with HIV. As Professor Janet Darbyshire, Director of the Medical Research Council's Clinical Trials

Unit warns, "The key issue to remember is to think of herbs as complementary, not alternative, medicine, and to be sceptical about the claims for herbs as well as cautious about how they are used with prescribed drugs."

Be wary of so-called 'miracle cures'

There is a lot of misinformation out there, peddled by people with a commercial interest in herbs, often claiming a particular remedy as a cure-all. Many herbal fads over the years have capitalised on fear, denial and a mistrust of Western medicine among people with HIV, the most recent of which is noni juice. The people behind the multi-million-pound business that sells the juice - which comes from the fruit of the Tahitian mulberry, *Morinda citrifolia* - claim that it cures virtually anything, from yeast infections to cancer, poor memory to HIV. There is some research indicating that some chemicals in noni may be useful as a preventative for liver cancer¹ or heart problems². However, according to expert herbalist Ray Sahelian, "There are no scientific data to support the use of noni juice as a substitute for any standard medical treatment for HIV."

Herbs can be toxic too

Herbal products may not only distract people from taking vital medications, they may themselves be toxic. In April 2004, the US Food and Drug Administration banned supplements made from the plant Ephedra (which were already restricted in the UK), after the death of a well-known baseball player who had been using an Ephedra nose spray. A similar controversy was caused by the herb kava or kava-kava (*Piper methysticum*), a natural

Researching the unresearchable

George W Carter certainly believes herbs are responsible for his good health. "I'm hepatitis C positive, and a supplement called *Hepato-C* is the only thing that's ever normalized my liver enzymes," he says. *Hepato-C* is a blend of 15 different Chinese herbs including Astragalus, which several studies have shown helps to reduce drug-induced liver damage (in rats) and Scutellaria or Baikal skullcap, which has anti-HIV activity³². Carter, an ex-heroin user, was one of a core of activists who set up buyers' clubs for people with AIDS to buy supplements and herbal medicines at a time when they had few conventional options. He is now a director of the Foundation for Integrative AIDS Research (FIAR). FIAR was set up with the ambitious aim of becoming, as Carter says, "the alternative AMFAR" - a reputable scientific research organisation investigating the properties of what he defines as "non-patentable interventions".

Carter has had to scale FIAR back (he originally had hopes of a \$1-2 million research budget) in the face of sceptical attitudes from funders such as the National Council for Complementary and Alternative medicine (NCCAM), but it is now recruiting for its first studies. One is a 40-person placebo-controlled study of the herbal remedy milk thistle in New York, while the other, in collaboration with the Indian Council of Medical Research, is a study in Tamil Nadu state of a mix of herbs used in Ayurvedic (traditional Indian) medicine, called Siddha.

The UK Medicines and Healthcare products Regulatory Agency (MHRA) decided to consider the new evidence last August, though it has yet to decide whether to lift the ban.

Herbs can interact with medicines

Herbal products can also interfere with the levels of prescribed drugs in the body. The best-known example in the HIV field is St. John's wort (*Hypericum*). This herb has proven anti-depressant properties, and one recent study found it produced a 25% greater reduction in depression symptoms than the antidepressant drug paroxetine (*Seroxat*)³. However, two different studies have found that St John's wort reduces the concentration of the protease inhibitor (PI) indinavir⁴ and the non-nucleoside (NNRTI) nevirapine⁵ in the body, in the case of indinavir by 80%. Heather Leake Date, principal HIV pharmacist at Brighton and Sussex University Hospital says: "St. John's wort actually has more drug interactions than many of the licensed antidepressants, with potentially very serious consequences. It doesn't just interact with anti-HIV meds, it also reduces oral contraceptive pill levels, potentially resulting in unwanted pregnancy, and interacts with anticonvulsants, potentially resulting in someone having a seizure or epileptic fit."

Other herbs that affect liver enzymes in a way that could cause worrying drug interactions include ginseng, *Sutherlandia* and *Hypoxis* (African potato)⁶. African potato is the source plant for the supplement *Moducare*⁷, which is used by some people with HIV as an immune stimulant.

Other interactions that have been studied look less worrying than first feared. Garlic supplements are often taken to reduce cholesterol - though there's not much evidence they do - and because garlic's active ingredient allicin has anti-parasitic⁸ and antibiotic⁹ properties when used for gut problems. Milk-thistle (*Silybum marianum*) is taken by a lot of people who are coinfecting with hepatitis C or who have HIV drug-induced liver problems, and some studies¹⁰ point toward its possible usefulness in this area. But the same team that examined St John's wort found that garlic supplements reduced the concentration of the PI saquinavir (*Invirase/Fortovase*) by over

sedative similar to Valerian, which is derived from a Pacific vine. In August 2002, reports from Germany implicated kava in liver problems in more than 40 people, including three deaths and six cases of liver transplant. The UK banned kava in December 2002. However, kava producers based in the Pacific nations, who lost their livelihood from the ban, refused to take it lying down. They produced a safety assessment saying that the German products had been prepared incorrectly (as alcoholic tinctures instead of tea), resulting in massive overdoses.

further reading

The Foundation for Integrative AIDS Research have a website located at <http://www.aidsinfonc.org/fiar/>

further reading

NAM's *Directory of Complementary Therapies in HIV and AIDS* is available free to people living with HIV. For a copy please email info@nam.org.uk or call 020 7840 0050.

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A-Z of herbal remedies

Astragalus (milk vetch) A mainstay of traditional Chinese medicine, astragalus is a non-specific immune enhancer with activity on T-cells, antibodies and cytokines¹⁴. For this reason, as with Echinacea and ginseng, it should be used with caution in people with HIV, as it may enhance rather than suppress HIV replication.

Bacopa see Ginkgo

Berberine A chemical found in various members of the Berberis family including barberry, Oregon grape (*Mahonia*) and golden seal (*Hydrastis*). Used as a remedy for diarrhoea: some studies have found its effectiveness against bacteria such as *E.coli* to be comparable with antibiotics. Golden seal is now an endangered species due to medicinal use; buy the alternatives.

Butterbur (*Petasites hybridus*) May help allergies. One study¹⁵ found it suppressed hay fever symptoms as effectively as the antihistamine cetirizine (*Zirtek*).

Bitter Melon (*Momordica*) see main article.

Echinacea (purple coneflower) Like Astragalus, a non-specific immune enhancer. Although it appears to be safe when used in the short-term (i.e. less than a week), people with HIV should definitely avoid long-term use.

Ephedra now banned. See main article.

Evening primrose The oil from *Oenothera* plants is a rich source of the essential nutrient gamma-linolenic acid (GLA). As well as being a popular way to reduce hot flushing and other menopausal symptoms, GLA has shown promising results in the treatment of neuropathy¹⁶ and high cholesterol¹⁷.

Garlic (*Allium sativum*) see main article.

Ginkgo biloba and **Bacopa monniera**. Both these herbs have been used to combat stroke, dementia¹⁸ and memory impairment¹⁹. They work, in part, by reducing the tendency of the blood to clot, so should not be taken if you have a low platelet count or take other blood-thinning medications such as aspirin or warfarin.

Ginseng, Korean (*Panax ginseng*) A well-known pick-me-up, although since it is expensive many 'supplements' contain little or none of the active herb. Has been used in Korea to delay the start of HAART and in one intriguing study²⁰ there was a far lower rate of AZT resistance mutations in patients given ginseng alongside AZT monotherapy. **Siberian ginseng** (*Eleutherococcus senticosus*) has similar effects. Like Astragalus and Echinacea, however, ginseng may stimulate the 'wrong' parts of the immune system in people with HIV²¹, so they should not take it on a long-term basis.

Hypoxis (African potato) see main article.

50%¹¹ and milk thistle reduced saquinavir levels by 25%¹². However, this was *unboosted* saquinavir, given to HIV negative volunteers, and although there have been no studies of ritonavir-boosted saquinavir, it seems likely that the significant boost given by ritonavir will mask any drug level problems caused by these herbal interactions.

Some herbs could be very useful allies

There are some natural substances that may be very useful for people with HIV. According to a review published last year¹³, certain natural chemicals do have some degree of anti-HIV effect, although, as yet, there is no evidence of their clinical benefit.

- **Lectins** These slimy, long-chain molecules stick to HIV's outer surface and can act as entry inhibitors. Derived from plants such as snowdrops and nettles, they are being used as the bases for experimental microbicides.
- **Triterpenoids** These are soluble resins found in tree bark. One, betulinic acid, derived from birch bark, is the chemical template for PA-457, a promising new HIV drug which acts against the HIV protease enzyme in a completely novel way (see 'News from CROI' for more information).
- **Flavonoids** A huge class of chemicals derived from leaves and bark, often pigmented and bitter-tasting. One of the most interesting, *epigallocatechin gallate*, is

Kava (*Piper methysticum*) Currently banned in UK. See main article.

Liquorice (*Glycyrriza glabra*) is the most widely used herb in Chinese medicine. In the pre-HAART era, several studies suggested that its active ingredient, glycyrrhizin, had anti-HIV effects. Its use was revived in a trial in Zambia²² in 1999, where it appeared to delay progression to AIDS.

Lutein and lycopene These anti-oxidants, found in green vegetables and tomatoes respectively, have become the most popular herbal products of all in the last two years, thanks to their becoming incorporated in many multivitamin supplements. As yet there's not much hard clinical evidence for their efficacy, but lutein reduced the occurrence of an age-related eye condition in one trial²³.

Milk thistle (*Silybum*) see main article.

Mistletoe (*Viscum album*) Used for hepatitis C. In one open-label study²⁴, mistletoe used alongside lycopene reduced liver fibrosis in patients with chronic hepatitis C, and in another²⁵, 25% of patients given the therapy were cured of chronic infection. The authors admit this is half the cure rate of standard hepatitis C therapy, but mistletoe might be an option for the many people who can't tolerate interferon.

Pau d'Arco or lapacho (*Tabebuia impetiginosa*). A South American remedy, tea made from this

rain forest tree was a popular anti-HIV therapy in the pre-HAART era and remains a cancer treatment alternative, though there's not much evidence of its efficacy. Intriguingly, more recently, pau d'arco has shown activity²⁶ against the so-called 'superbug', MRSA.

Polycosanols are waxy substances derived from rice bran and sugar cane that appear able to reduce cholesterol. In one study²⁷, rice bran oil reduced 'bad' LDL-cholesterol by seven per cent.

St John's wort (*Hypericum perforatum*) see main article.

Sutherlandia (Cancer bush) see main article.

Turmeric (*Curcuma longa*) Turmeric's yellow pigment curcumin is an inhibitor of the gene transcription protein nuclear factor kappa B (see main article). Although one curcumin study in the mid-90s found no impact on HIV viral load²⁸, more recent trials have found that it exerts subtle effects on HIV gene expression²⁹ and the way HIV disturbs the immune system³⁰.

Valerian (*Valeriana officianalis*) Probably the best herbal tranquilliser and sleep remedy in the absence of the banned kava. Tea brewed from the smelly root of this plant has been shown³¹ to reduce insomnia in a number of studies.

found in green tea. Flavonoids have not only been shown to act against HIV, but are also antioxidants, mopping up reactive chemicals that result from body processes and that could otherwise damage cells.

■ **Calanolides** Among a class of chemicals that give new-mown hay its smell, calanolides A and B are extracts of a tropical tree called *Calophyllum lanigerum*. Calanolide A is in phase II studies as a non-nucleoside reverse transcriptase inhibitor.

■ **Caffeic and chicoric acids** Derived, as their names suggest, from coffee beans and chicory, these chemicals were originally thought to be active against the third HIV

enzyme, integrase. However it now looks as if they act as entry inhibitors.

■ **Ribosome-inactivating proteins** These 'jam up' the chemical messaging system HIV uses in the cell. Two, alpha and beta momorcharin, are found in the bitter melon plant *Momordica charantia*, which has been used as a complementary therapy for HIV for years.

■ **Nuclear factor inhibitors** NF-kappa-B is a protein found in human cells. HIV prods it into action, and it makes the cells divide and produce more HIV. Both curcumin (the yellow pigment in turmeric) and cepharathine (from a Chinese medicinal herb called *Stephania cepharantha*) dampen down this protein's action.

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About CROI

The Twelfth Conference on Retroviruses and Opportunistic Infections (also known as CROI, or the Retrovirus conference), held in Boston at the end of February, was the first of three important international HIV treatment conferences this year. Scientists and drug companies tend to wait for CROI to release important new treatment information, and this year was no exception.

However, the most significant finding to emerge from the conference was a report from Uganda suggesting that deaths, rather than the controversial US-led prevention policy of behaviour change (known as 'ABC'), have been the main cause of the decline in HIV prevalence seen in Uganda during the last decade. This is particularly important because of current political debates about funding life-saving treatments and the relative contribution of 'ABC' - abstinence, behaviour change (or be faithful) and condoms - to the containment of the HIV epidemic in resource-limited countries.

Prevention: fear, disappointment and monkeys

Just before CROI, frightening news reports of a New York man apparently infected with an "aggressive" strain of HIV that is "impossible to treat" were widely circulated. Fuelled by the fact that the man was a user of methamphetamine ('crystal meth', 'ice' or 'tina') and had had unprotected anal intercourse with many partners, most reports were quick to warn of the dangers of drug abuse and gay promiscuity — despite the fact that the original information came from a press release that contained little medical or scientific information.

At a special session, David Ho of the Aaron Diamond AIDS Research Center detailed the science so far (which can be read in full on aidsmap.com) and emphasised that this isolated case report does not indicate that the HIV strain found in this man is especially aggressive, and may be due to an exceptional HIV strain or an exceptional patient¹.

It has long been thought that pre-exposure prophylaxis, or PREP - where people at high risk of HIV infection take anti-HIV drugs before exposure to HIV - could bridge the gap in the absence of a preventative vaccine. This is an especially interesting idea at present, because a symposium at CROI on HIV vaccine development served as a reminder that we are probably decades away from an effective vaccine. However, the conference heard that a trial using tenofovir (*Viread*) as PREP against rectal exposure to monkey (simian) HIV in rhesus monkeys produced disappointing results.

The monkeys were given weekly rectal inoculations of HIV virus in a concentration equivalent to about 3-5 times the maximum viral load found in human semen during newly acquired HIV infection - the most infectious period. The scientists found that tenofovir delayed but did not prevent infection; all the monkeys eventually became infected, after an average of about seven weeks. Although animal studies cannot reliably predict what will happen in humans, this adds another worrying dimension to the controversial tenofovir PREP studies that are currently underway amongst high-risk gay men in the US and high-risk heterosexual women in Africa and Asia - studies that have already been stopped by governments in Cameroon and Cambodia, and which are now being demonstrated against by activists in Thailand².

Hepatitis coinfection: more drugs for B, more liver damage seen in C

There was good news for the use of tenofovir as a potent anti-hepatitis B drug for patients coinfecting with HIV. Tenofovir was found to be at least as potent as adefovir - a similar drug approved only for hepatitis B - in controlling hepatitis B virus in coinfecting individuals. Since both adefovir and tenofovir show test-tube activity against 3TC-resistant hepatitis B virus, this suggests that tenofovir could be a very useful component of a second-line anti-HIV combination. However, the scientists have not yet analysed data looking at how successfully tenofovir treats 3TC-resistant hepatitis B virus in people³. Another drug, entecavir - an antiviral proven superior to 3TC in people infected with hepatitis B alone - was also shown to lower hepatitis B viral loads in people coinfecting with both hepatitis B and HIV. Unlike the other drugs used in coinfection (3TC, adefovir, and tenofovir), entecavir has no activity against HIV. This can be a benefit, since entecavir use cannot lead to HIV cross-resistance. In addition, entecavir does not interact with any protease inhibitors (PIs) or non nucleoside reverse transcriptase inhibitors (NNRTIs)⁴.

There was less good news for people coinfecting with HIV and hepatitis C virus, however. Results of a 61-person study found that liver damage (fibrosis) progressed faster than expected in more than one quarter of the participants, despite their first liver biopsy showing little or no fibrosis. Based on these results, principal investigator Mark Sulkowski of Johns Hopkins University suggested that HIV and hepatitis C coinfecting individuals who appear to have mild disease after their first biopsy may need a liver biopsy at least every three years, rather than the three-to five-year interval recommended for people infected only with hepatitis C⁵.

'Superbug' risks higher with HIV

Infection with the so-called 'superbug', MRSA or methicillin-resistant *Staphylococcus aureus*, is being seen more often among HIV-positive patients. Researchers from San Diego were surprised to discover that 60% of MRSA cases appeared to be community acquired, rather than picked up in hospital - which is the common assumption amongst UK politicians, who have put hospital cleanliness on the agenda in the run-up to the current election. They also found that people who had acquired HIV through heterosexual intercourse were 90% less likely to be diagnosed with MRSA than gay men or injecting drug users. HIV disease severity was also implicated: people with viral loads above 100,000 copies/ml were almost twice as likely to be diagnosed with MRSA as people who had viral loads below 10,000 copies/ml. And having a CD4 cell count below 50 cells/mm³ increased the risk of diagnosis with MRSA by 250%. However, being on antiretroviral therapy reduced the risk of MRSA by 40%. Although this is only one report from one clinic, and it is also possible that increased awareness of MRSA may have contributed to the increase in diagnoses seen in the study, it does suggest that community-acquired MRSA may be a concern for HIV-positive people, and that HIV disease severity has a direct effect on the risk of being diagnosed with the infection¹⁶.

further reading

All of these reports can be read in full in Conference News on aidsmap.com

international conferences

The next major international HIV treatment conference is the International AIDS Society's Third Conference, to be held in Rio de Janeiro, Brazil at the end of July. NAM will provide full daily conference news coverage on our website, aidsmap.com, and there will be selective in-depth coverage in the September/October issue of this newsletter.



New drugs: some soon, some later and some much later

Tipranavir is a new protease inhibitor currently available on a named-patient basis for individuals with experience of three classes of antiretrovirals and at least two prior PIs and who need the drug in order to assemble a viable regimen. Results of the combined RESIST trials - providing data from over 1000 participants - reported on at CROI by Stanford University's Jonathan Schapiro found that ritonavir-boosted tipranavir was superior to lopinavir (*Kaletra*), indinavir (*Crixivan*), saquinavir (*Invirase/Fortovase*), or amprenavir (*Agenerase*), all of which were also ritonavir-boosted. In fact, 41% of individuals with multiclass-resistant HIV who received boosted tipranavir had a tenfold decrease in viral load after 24 weeks, compared with only 19% of people taking the other boosted PIs. All of the regimens could be taken alongside an optimised background regimen that could include T20 (enfuvirtide, *Fuzeon*), regardless of the number of PI mutations. This is great news for people whose current options are limited due to PI resistance. Manufacturer Boehringer Ingelheim submitted a marketing authorisation application for tipranavir to the European Medicines Agency (EMA) last October; approval is expected in late summer⁶.

More good news for people with HIV resistant to all current PIs came from the Belgian biotech company Tibotec. The highest dose of their investigational protease inhibitor TMC114 managed to drop viral loads to below 50 copies/ml in five of 13 participants with resistance to all current PIs, suggesting that it may be a potent option for people with multiclass-resistant HIV. Among all people taking 600mg of TMC114 boosted with 100mg ritonavir twice a day, 47% had a viral load under

Treatment interruptions make a big difference to long-term immune recovery

Investigators from the Swiss HIV cohort, who followed people on highly active antiretroviral therapy (HAART) for seven years, have found that the greatest CD4 count increases occurred in people who had never interrupted therapy. People on continuous HAART had an average increase of 349 cells/mm³ over seven years, while those who had interrupted therapy had an average increase of 153 cells/mm³, despite the fact that the average length of therapy interruption was only 32 days. The study also found that the largest CD4 increases over the seven years were in the people who started HAART with the lowest CD4 counts (under 100), whereas people starting HAART with the highest CD4 counts (over 700) actually had a slight CD4 decline. Forty-two per cent of people in the Swiss cohort maintained an undetectable viral load for the study's seven years¹⁵.

50 copies/ml after 24 weeks of this 96-week study, and 72% had at least a tenfold drop in viral load. Just under 1% of all study participants dropped out due to side effects, which have been noted previously as gastrointestinal and liver problems. Expect more news from the full 96 weeks of this study by the end of the year⁷. Tibotec also have a promising investigational NNRTI called TMC278 in development, which may work against HIV resistant to other NNRTIs. An international study began last month to find the best dose⁸.

The conference also heard the results of the first dosing trial of an exciting new class of anti-HIV drug: maturation inhibitors. PA-457, a maturation inhibitor developed by Panacos

pharmaceuticals, is a derivative of the natural product betulinic acid, whose anti-HIV activity was only discovered two years ago. PA-457 works like no other anti-HIV drug: it creates a chemical bridge between two protein components so that HIV protease cannot separate them. In this very early dosing study, a viral load reduction appeared to last for over a week in people taking higher doses of the drug, which is very promising. Larger studies are planned before the end of the year⁹.

Lipodystrophy: new data on body shape changes, heart attack risk and the benefits of fish oils

Doctors have thought for some time that the nucleoside analogues (NRTIs) d4T (stavudine, *Zerit*) and, to a lesser extent, AZT (zidovudine, *Retrovir*) have been linked with fat loss. The conference heard more data that may help us make decisions about which NRTI 'backbone' drugs are more fat-friendly.

Graeme Moyle, of London's Chelsea and Westminster Hospital, and colleagues throughout Britain compared people who switched from d4T or AZT to either tenofovir or abacavir (*Ziagen*), and found that either switch led to a return of 12-15% of lost fat after 48 weeks. However, more people had to discontinue abacavir than tenofovir, and cholesterol and triglyceride levels after 48 weeks favoured tenofovir¹⁰. Another study, ACTG 5110¹¹ presented data that compared switching from d4T or AZT to abacavir *or* changing completely to an experimental NRTI-sparing combination of *Kaletra* and nevirapine. After 24 weeks, the 37 participants receiving the NRTI-sparing regimen had experienced an average increase of eight per cent in thigh fat, compared to no change in the abacavir group. This is the first study to detect an improvement in fat loss after only 24 weeks, although an eight per cent increase is unlikely to be noticeable. The switch to the NRTI-sparing regimen was found to be safe,

leading to a significant increase in CD4s and keeping viral load undetectable in most. However, another NRTI-sparing trial¹² found that people only gained an average 13% of lost fat after two years. Given that there appears to be little difference in lost fat regained between an NRTI-sparing regimen and a simple switch from d4T or AZT to tenofovir or abacavir, the long-term benefits of NRTI-sparing regimens on fat redistribution must be balanced against the likelihood that, without an NRTI 'backbone', HAART will not be as effective against HIV over the long-term.

Some surprising news came from the multinational DAD (Data Collection on Adverse Events of Anti-HIV Drugs) study, set up to examine the risks of heart attacks and other metabolic issues in people with HIV. Two years ago, after four years of follow-up, they reported a 26% increased risk in the frequency of heart attacks per year of antiretroviral drug exposure. Now, after six years, they have downgraded the risk to 17%. Other factors - especially smoking, aging, being male, having previous cardiovascular disease and/or a family history of heart disease - increased the risk of heart attacks even more than antiretroviral therapy. Frustratingly, the DAD statisticians have still not analysed heart attack risk according to antiretroviral drug class¹³.

The DAD study also suggested that raised blood fats (lipids, such as cholesterol and triglycerides) caused by anti-HIV therapy partially account for the inflated odds of a heart attack, and another study found that taking fish oil capsules can reduce some of those raised lipids. *Maxepa*, from Merck's Seven Seas brand, available over the counter and on prescription, is a formulation of fish oils rich in omega-3 fatty acids that has been shown to reduce triglyceride levels in adults without HIV infection. In this French study of 122 HIV-positive individuals on HAART, there was an average 26% reduction in triglyceride levels after eight weeks, but no changes in total or high density lipoprotein (HDL) cholesterol. Since there are no apparent side-effects, fish oil supplements appear to be a useful, non-toxic lipid-lowering option in people who can cope with the size of the pills, the high pill burden and the three-times-daily dosing¹⁴.

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16. Mathews C et al. abs 142.

HIV services in London face massive cuts

Cuts proposed by the Kensington and Chelsea Primary Care Trust will drastically reduce some important HIV services by 2007. Mental health support at the Chelsea and Westminster Hospital's Kobler Centre - the largest HIV treatment centre in the UK - will be drastically reduced after funding cuts of almost 60% (£500,000) over two years. Established by Dr Jose Catalan in 1989, the HIV mental health services team has an international reputation and has been at the forefront of HIV psychiatry and psychotherapy since its foundation. The proposed cuts would also affect other HIV services: funding for the Lighthouse, an HIV support centre, would be cut by £133,000 by 2007 and SW5, a health promotion agency working with young male sex workers, is facing cuts of £13,000 by 2007.

the investigators note that 62% of cases involved a sexual partner infected with HIV outside Europe. However, they concede that there has been a steady increase in the small numbers of heterosexuals infected with HIV in the UK and "as the number of heterosexuals living with HIV (diagnosed and undiagnosed) in the United Kingdom grows, the likelihood of heterosexual transmission within the country will increase, particularly among ethnic minorities."

Dougan S et al. HIV infections acquired through heterosexual intercourse in the United Kingdom: findings from national surveillance. BMJ: on-line edition, March 12th, 2005.

Two easier dosing formulations receive European go-ahead

European marketing approval has been granted by the European Commission for Gilead's once-daily NRTI 'backbone' pill, *Truvada*, which contains 300mg of tenofovir and 200mg of FTC (emtricitabine, *Emtriva*). This means that when combined with the 600mg pill of efavirenz (*Sustiva*), only two pills will need to be taken, once a day. In addition, a positive marketing opinion has been granted to a new formulation of Roche's hard gel saquinavir (*Invirase*). Full EU approval should follow soon of this new 500mg formulation, which is taken as two tablets twice daily and boosted by 100mg of ritonavir. The previous dose of boosted *Invirase* was five 200mg capsules twice daily, each dose taken with 100mg of ritonavir.

Kivexa correction

Last month, we reported on EU approval of the once-daily NRTI 'backbone' pill *Kivexa*, which contains 600mg abacavir and 300mg 3TC (lamivudine). When *Kivexa* is taken with the 600mg pill of efavirenz (*Sustiva*), the daily pill burden is only two pills once a day, not twice a day as we stated.

Vast majority of UK HIV transmission involves gay men

HIV infections acquired through heterosexual intercourse within the UK represent less than 10% of all HIV infections amongst heterosexuals diagnosed in the UK between 1985 - 2003, according to the UK's Health Protection Agency (HPA). Contrary to current public opinion, HIV transmission amongst gay men accounted for over 80% of HIV infections acquired in the UK during the same period. When heterosexual transmission did occur in the UK,

Viral load 'blips' are likely due to lab error and not cause for concern

An unexpected viral load measurement after consistently being 'undetectable' - known as a 'blip' - is the result of statistical fluctuations in the test used to measure viral load levels, and is not clinically significant, according to a new study. The researchers also found that there was no association between 'blips' and flu vaccination. The authors suggest that 'blips' are caused due to the "normal biological and statistical variation" that exists when viral load hovers around 15-20 copies/ml and say one-off 'blips' between 51 and 199 copies/ml "may not be cause for clinical concern". However, they add that "blips with a magnitude of greater than 200 copies/ml or blips that are detected in at least two independent or consecutive measurements may be more of a cause for concern."

Nettles RE et al. Intermittent HIV-1 viremia (blips) and drug resistance in patients receiving HAART. JAMA 293 (7): 817-829, 2005

UK HIV patients cost NHS £12,500 a year

According to two leading British HIV doctors, the annual cost of treating a person with HIV in the UK is "about £12,500". Angela Robinson from University College London Hospital and Brian Gazzard from London's Chelsea and Westminster Hospital calculate that "the lifetime costs of care for the current 50,000 infected individuals in the United Kingdom...[are] at least £12.5bn."

Robinson AJ et al. Rising rates of HIV infection. Br Med J 330: 320-321, 2005.

HAART could be safely interrupted for some

Individuals who started anti-HIV therapy with a lowest-ever CD4 cell count above 250 cells/mm³ and achieved a sustained increase in CD4 cell count above 500 cells/mm³ may be able to safely interrupt HIV therapy for over a year, according to a small study from Italy and Sweden. During the study, one person fell ill with PCP pneumonia

and herpes when his CD4 cell count was 205 cells/mm³, but there were no deaths. The findings need to be confirmed in larger trials, including the current SMART study, before treatment interruptions can be recommended.

International Study Group on CD4-monitored Treatment Interruptions. CD4 cell-monitored treatment interruption in patients with a CD4 cell count above 500 cells/mm³. AIDS 19: 287 - 294, 2005.

Some UK patients at risk of exhausting treatment options

A small but growing proportion of HIV-positive people in the UK may be in danger of exhausting current treatment options. But despite increased exposure between 1996 and 2002 to all three major classes of antiretrovirals, the HIV population as a whole has much improved CD4 counts and viral loads. However, "the immunological and virological status of patients who have experienced three-class failure remains relatively poor, showing that for a small number, treatment options are in danger of becoming exhausted," say the study's authors, who pooled data from six large HIV treatment centres in London and Brighton. "New drugs with low toxicity, which are not associated with cross resistance to existing drugs," are urgently needed for such patients, the authors conclude.

Sabin CA et al. Treatment exhaustion of highly active antiretroviral therapy (HAART) among individuals infected with HIV in the United Kingdom: multicentre cohort study. BMJ online first article, electronically published 4th March 2005, available at bmj.com

Methamphetamine use can worsen HIV brain damage

Long-term heavy use of methamphetamine ('crystal meth', 'ice' or 'tina') can worsen the damage to brain cells caused by HIV. Although both methamphetamine use and HIV infection contributed to brain damage, the study showed that their effects were additive, and not due to a more complex interaction between HIV and drug use.

Chang L et al. Additive effects of HIV and chronic methamphetamine use of brain metabolite abnormalities. Am J Psychiatry 162: 361-369, 2005.

news from



Future development of ATU

NAM is currently reviewing the design of *AIDS Treatment Update*, to improve its readability and ensure it responds to the needs of its readers. We are looking for people to give us their feedback on the new designs, and if you would like to be involved please email claire@nam.org.uk or call 020 7840 0050.

Lipodystrophy Forum

On the last Monday of every month, NAM facilitates a meeting between HIV experts and people living with HIV, to provide the latest information on a variety of treatment issues in a friendly, open atmosphere. NAM's April forum will be on the subject of lipodystrophy: causes, concerns, treatment and remedies. The forum will take place on Monday 25th April, from 7pm at the University of London Union, Palms Room, 4th Floor, Malet Street, London, WC1. Everyone is welcome, and refreshments are provided. Visit www.aidsmap.com/en/events/forums.asp for more details.

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