

aids treatment update

measles, mumps, rubella... and HIV?

The Silly Season it may have been, but the participation of an unfamiliar Oxford politician in a small, preliminary HIV vaccine study last month made headline news in the UK. In Britain, where we often like to think that we invented everything, local involvement in the first few steps towards the prospect of an end to AIDS would naturally prove seductive. Of course, the Oxford study fits into a far broader worldwide effort, which we invited Julian Meldrum to review for ATU readers this month. Julian is Special Advisor on Vaccines to the National AIDS Trust, as well as being a consistently expert commentator on the subject.

As it's October, we're including our annual readers' survey questionnaire with this issue. It's short, it's confidential, it comes with a reply-paid return envelope, and it would really mean a lot to us if you filled it in. Last year's survey was important in shaping ATU's new format, and in guiding editorial decisions about content. We really do listen – so please use this opportunity to tell us what you'd like from ATU, and from NAM, next.

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closer to a vaccine?

2 a clinical trial which has just begun in Oxford does represent something new, even though it has been a long time coming by julian meldrum

Has Dr Evan Harris, the Oxford Liberal Democrat MP, recently noticed any soreness in his arm? This question is an essential part of an HIV research project at Oxford University, where Dr Harris is a volunteer in the first safety trial for a new kind of HIV vaccine. The research is jointly funded by the Medical Research Council and the International AIDS Vaccine Initiative (IAVI) with the aim of testing a possible preventive vaccine against HIV, to be given to people who are HIV negative to protect them against AIDS.

Meanwhile, in North America and Thailand, two vaccines are now in Phase III trials, to find out whether they work. There have been other vaccine trials before – even a couple in Britain – and there will be many more. What is different about the Oxford trial is that it represents new kinds of vaccine, a new kind of partnership to develop them, and the use of a new technology to evaluate vaccines, as this article sets out to explain.

The vaccines

Dr Tomas Hanke, working with Professor Andrew McMichael at the Medical Research Council's Human Immunology Unit, has designed a DNA sequence which he calls 'HIV-A'. This is built into two different vaccines which will be used in combination, one after the other. The HIV-A DNA sequence is to be presented in two different ways, firstly as a DNA vaccine and secondly built into an MVA vaccine. Such 'prime-boost' designs are currently seen as the most effective way of using DNA vaccines, which have generally been disappointing when given on their own to human volunteers.

The goal is a cellular immune response to HIV (the kind which enables the body to destroy virus-infected cells without producing antibodies), which is stronger than any previously seen with an HIV vaccine. Experiments conducted in animals suggest this is likely.

Where the Oxford study is breaking new ground is that it is the first DNA vaccine to be based on African strains of HIV. It is also the first designed for human use as a primer with a matching recombinant virus as a booster.

The partnership

Natural cellular immunity seems to have been able to protect a small minority of heavily-exposed African women from HIV infection.

The big question is whether a vaccine can induce levels of cellular immunity that are even more effective than natural immunity in protecting people against HIV. And can it protect more than the small minority who would naturally be protected, perhaps because they were only exposed to very low levels of HIV, or perhaps because their immune systems were particularly good at dealing with it?

If the Oxford trial goes well, the plan is to carry out further small-scale trials in Nairobi, Kenya, also looking at safety, in preparation for a much larger trial to test the ability of the vaccine to protect people in Kenya against infection with HIV.

The Oxford/Nairobi partnership is the most advanced of a number of similar partnerships which are springing up around the world under

the influence of IAVI, which is co-funding the Oxford work as one of its four initial projects.

Building on the Oxford work, IAVI has announced that its fourth partnership, with Robert Gallo's Institute for Human Virology in Baltimore, Maryland, will build Dr Hanke's

infection with a laboratory-adapted strain of HIV. Fortunately for the monkeys, but unfortunately for the research, HIV-1 doesn't cause illness in those monkeys, which leads some people to regard this as weak evidence for the effectiveness of the vaccine. But it is still encouraging evidence.

Another question is how to deploy such a vaccine, and in what populations. If people who would otherwise have been using condoms, which are close to 100 per cent effective when properly lubricated, switched to vaccines that were 50 per cent effective, the result would be a public health disaster.

HIV-A sequence into a third kind of vaccine. This would be a harmless vaccine strain of salmonella, which could be given orally, both to reduce the costs of vaccination and to stimulate immunity at mucosal surfaces (inside the anus and vagina) more efficiently than injected vaccines usually do.

A vaccine design similar to the one being tested in Oxford is now being developed in Australia, supported by the US National Institutes of Health (NIH), with a view to eventual tests in Thailand. The Australian team was able to show that a combination of a DNA vaccine followed by a poxvirus vaccine protected pigtail macaque monkeys from

Evaluating immune responses

The Oxford trials can't tell us whether the vaccines on trial will protect anyone against HIV. However, the trials are using new methods of measuring cellular immune responses. The new evaluation technology to be used in the Oxford trial includes a blood test called a 'tetramer assay' which can pin-point 'killer' T-cells that respond to specific elements of HIV contained in a vaccine. One test can't be used for everyone, and it can't be used to measure all the responses that may be going on in one person's body. Other tests have to be used alongside the tetramer assay to monitor the overall levels of cellular immune responses

DNA & MVA

DNA vaccines consist of DNA (deoxyribonucleic acid, the material in the nucleus of a cell where genetic information is stored) extracted from bacteria. This makes them relatively cheap and simple to manufacture. DNA vaccines work very well in mice, less well in other animals and in people. So a variety of special methods are being used to make them more effective.

MVA is a version of the smallpox vaccine, Vaccinia. The letters stand for Modified Vaccinia Ankara, a strain named after the Turkish capital. MVA was given to hundreds of thousands of people in the final stages of the global campaign to eradicate smallpox, so its safety record is well established. It is given by intramuscular injection, not into the skin. MVA is particularly good at inducing a cellular immune response, hence the interest in using it to carry HIV elements.



closer to a vaccine? continued

to HIV or any other microbe. This could advance research on the use of vaccines as treatments ('therapeutic vaccines'), by allowing the measurement of immune responses to at least some of the HIV-related elements of a vaccine, even in a person with HIV whose immune system is already responding to the virus.

The question would still remain as to whether the new responses due to the vaccine were of clinical value. That question would still take a long time to answer if a vaccine is used in addition to other treatments. But at least if we know the vaccine is producing a measurable immune response, we can have some confidence that such trials will not be a complete waste of time

The VaxGen trials

It was recently announced that both of the world's first two full-scale efficacy trials for an HIV preventive vaccine had recruited all the volunteers they needed. It is also reported that drop-out rates of volunteers have been lower than expected. Both of these trials are sponsored by a Californian biotech company called VaxGen.

VaxGen's 'AIDSVAX' products use the outer envelope protein of the HIV virus, gp120. The main problem with basing a vaccine on this protein is that it seems to be most diverse in those regions which the immune system most readily recognises and which give rise to neutralising antibodies.

The two VaxGen trials differ in design and are testing slightly different vaccines against different modes of transmission.

The first trial has recruited more than 5,000 HIV negative people at high risk of sexual transmission across numerous sites in the US,

Canada, Puerto Rico and Amsterdam. Most of the volunteers are gay men; people using injection drugs were excluded.

The second trial recruited 2,500 injecting drug users from treatment centres across Thailand. Feasibility studies reported some years ago that these men and women remain at risk of HIV despite access to treatment for their drug dependency.

Both vaccines are 'bivalent', mixing two different versions of the gp120 protein. In the first trial, these are both from subtype B viruses. In the second trial, one is subtype B and the other the so-called 'subtype E' (now reclassified as a 'circulating recombinant form' of HIV). Both subtype B and 'subtype E' viruses circulate in Thailand.

VaxGen claims that it has seen evidence of neutralising antibodies in the blood of volunteers in earlier-stage trials using these products. Their scientific critics question whether the quantity and quality of these antibodies will be enough to protect people against the virus.

If, against the odds, VaxGen proves to be right, we should know either when a first interim analysis of the results of the first trial becomes available towards the end of next year, or – if the trials continue to the end – in 2002 or 2003.

It is already clear that the vaccines will not be 100 per cent effective. Some volunteers in earlier trials became infected, despite vigorous immune responses to the vaccine. The question is whether a lower level of effectiveness will be seen, and if so, how low. The trials have been designed to pick up anything down to 30 per cent effectiveness, during the course of the trials and for six months afterwards.

If there is evidence of some effectiveness, say 50 per cent, what questions arise after that? One question is how long such effectiveness may last. Some researchers argue it is important to have longer follow-up, in case a neutralising antibody response not only fades but is transformed into something worse than useless, an antibody response that can actually enhance HIV infection.

Another question is how to deploy such a vaccine, and in what populations. If people who would otherwise have been using condoms, which are close to 100 per cent effective when properly lubricated, switched to vaccines that were 50 per cent effective, the result would be a public health disaster. On the other hand, if people who are unable to use condoms or other means of protection were given such a vaccine, it could have a profound and positive effect on the future course of the epidemic. Given to women, it could safeguard their role as mothers to a generation of children at risk of becoming orphans.

Through the trials, the fact that one third (in the first trial) or one half of volunteers (in the second trial) are receiving a placebo injection

may be enough to discourage anyone from relying on the vaccine to protect them in place of condoms or other risk-reduction strategies.

The proof of this must be in the full evaluation of risks taken by volunteers through the trials. It is hoped that risk-taking will decline over the three years of repeated clinic visits and questionnaire-filling that volunteers must undergo. Indeed, an early report at the Durban conference on the reported behaviour of Thai trial volunteers supported this expectation.

After these trials, when the effectiveness of the vaccine is known, what then? Trials of other vaccines should not wait on the VaxGen results, though it is unlikely that other efficacy trials will have recruited all their volunteers by the time VaxGen's results are out.

If AIDSVAX 'fails' there is clearly every reason to press on with other trials. But what if it is a partial 'success'? If so, the very existence of such a vaccine should galvanise both vaccine research and the other approaches to prevention with which it must be combined. Making sure this happens would be a challenge for us all.

HIV subtypes

Until recently, most vaccine research was based on subtype B viruses, which are only a small minority of HIV cases worldwide. This is because subtype B is dominant in the US and Europe, where most of the research is.

The classification of subtypes began with HIV's env (envelope) gene, which may be more varied than other parts of the virus. There may be more similarity among versions of the other genes of different subtypes: no-one knows if the differences are more important than the similarities, when it comes to a possible vaccine.

In Kenya, as in Uganda, most people with HIV have either subtype A or subtype D virus or, increasingly, recombinant viruses with elements of both subtypes. This contrasts with southern Africa and Ethiopia, where subtype

C is dominant. In West Africa, yet another pattern is emerging, with a very complex pattern of recombinants between subtypes A, G, and several other viruses.

In Thailand, a circulating recombinant form known as 'subtype E' (which contains elements of subtype A) is the commonest version of HIV, alongside a local version of subtype B.

While the significance of HIV subtypes for vaccine design is unknown, it must be prudent to match the subtypes of currently circulating viruses when designing vaccines to be tested in Africa or Asia. Doing this is also symbolic of good intentions in international vaccine research, in giving the best chance of access to a working vaccine to communities that most need it.

glossary

recombinant
Genetically reconstructed.
strain

A variant characterised by a specific genetic make-up.

vaccine

A substance that contains antigenic components from an infectious organism. By stimulating an immune response (but not disease), it protects against subsequent infection by that organism.

women & viral load

6 is there a gender difference in the progression of HIV disease, and should women be treated differently as a result? by anna poppa

In 1998, a team of researchers from Baltimore published a report on a large group of HIV-positive injecting drug users called the ALIVE cohort¹. The group found that viral load levels amongst women in the cohort tended to be lower than in men, even when CD4 counts were matched. Women subsequently developed AIDS-defining illnesses at a similar speed to men, despite having lower viral load. The implication of these findings, the team concluded, was that treatment guidelines, formulated largely on disease progression studies completed in men, may be inappropriate for women and should therefore be re-examined. Over the past two years, this issue has continued to rumble, generating a series of reports from other cohorts of people with HIV which include both men and women.

Viral load early after infection

At a session devoted to gender issues in disease progression at the recent XIII International AIDS Conference in Durban, a further report from the ALIVE study was released². This involved 202 seroconverters (156 men and 46 women) – people who had contracted HIV between March 1989 and December 1998. Comparing men who did and did not progress to AIDS, the average viral load after seroconversion was 78,000 copies in progressors and 41,000 copies in non-progressors. Initial viral load levels following seroconversion were significantly lower in women. Women who progressed had a median viral load of 17,000 copies in comparison to 12,000 copies in non-progressors, a difference which was not statistically significant. Despite the lower viral load levels seen in women,

MACS: How well do these results apply to women?

In the 1980s, the US Multicenter AIDS Cohort Study (MACS) enrolled over 1600 HIV-positive gay men and tracked the progression of their HIV disease. The study confirmed that viral load predicts the future risk of disease progression. The table shows the varying risk of developing AIDS over a three year period according to one's viral load and CD4 count. For example, men with viral load over 55,000 and CD4 counts over 750 had a 32.6% risk of progression to AIDS within three years. The risk increased to 85.5% in men with the same viral load level but with CD4 counts below 200. The MACS men did not take anti-HIV therapy, and so these figures predict the likely course of HIV disease if left untreated, and not what may happen if people begin treatment. As this article describes, because MACS is a men-only cohort, it's possible that these results may not apply so well to women. Source: Mellors JW. *Annals of Internal Medicine* 126:946-954, 1997.

MACS & progression of HIV disease

Percentage of people who develop AIDS within 3 years, assuming no anti-HIV treatment

viral load	CD4 count				
	below 200	201 to 350	351 to 500	501 to 750	above 750
below 1500	**	**	**	3.7	0
1500 to 7000	**	**	2.0	2.0	2.0
7001 to 20000	**	8.1	8.1	8.1	3.2
20001 to 55000	40.1	40.1	16.1	16.1	9.5
above 55000	85.5	64.4	42.9	32.6	32.6

Viral load levels relate to results using RT-PCR method, such as that used in the Roche *Amplicor* test. ** indicates lack of data.

there was no gender difference in the time to development of AIDS. In other words, the viral load level after seroconversion in women was not a good predictor of their risk of developing AIDS, and appears not to carry the same meaning in terms of future health as in men.

Researchers working with the two largest natural history HIV cohorts in the US, the Women's Interagency HIV Study (WIHS) and the Multicenter AIDS Cohort Study (MACS), have recently published similar conclusions³. Their analysis included 1,256 untreated women from WIHS, who were compared with 1,603 men from MACS. Because different viral load tests had been used during the study periods (NASBA in WIHS, bDNA in MACS), data from both cohorts were standardised to values equivalent to the RT-PCR method of

measuring viral load. This conversion is important given that previous data on this subject have been seen as inconclusive because observed differences between different study populations could have been due to differences in the tests used.

The team found no differences in viral load between men and women at CD4 counts below 200 cells, but did find differences at other levels, particularly at higher CD4 counts. At CD4 counts between 200 and 350 cells, viral load was 32% lower in women. The difference at 350 to 500 cells was 50% lower, and at CD4 counts over 500 it was 46% lower.

What's the role of injecting drug use?

The findings of studies involving injecting drug users (IDU) may or may not be applicable to

glossary

antiretroviral

A substance that acts against retroviruses such as HIV.

CD4

A molecule on the surface of some cells onto which HIV can bind. The CD4 cell count roughly reflects the state of the immune system.

cohort

A group of people who share at least one common factor (e.g. being HIV-positive) and are studied over a long period of time.

HAART

Highly Active Antiretroviral Therapy, a term used to describe anti-HIV combination therapy with three or more drugs.

seroconversion

The time at which a person's antibody status changes from positive to negative.

viral load

Measurement of the amount of virus in a sample. HIV viral load indicates the extent to which HIV is reproducing in the body.

women & viral load continued

people who do not have a history of drug injection, and this was one of the key criticisms levied at the ALIVE study group. However, the WIHS/MACS study, which involved people with and without a history of IDU, found that gender differences in viral load were greater amongst non-IDU women. Whilst race, gender and IDU were all found to be associated with variations in viral load level, the biggest difference observed overall was between white men and non-white women – 60%, or 0.4 log, lower in the latter at CD4 counts above 200 cells.

An analysis of 1,299 men and 712 women enrolled in the Italian ICONA cohort also found viral load to be 0.13 log lower in women than in men (similar to the difference seen in the ALIVE study), and 0.25 log lower in women whose route of infection was presumed to be heterosexual, rather than through injecting drug use⁴.

Not all cohorts agree

Data from the Swiss HIV Cohort produced somewhat different findings⁵. The analysis included 456 men and 286 women who were injecting drug users, and 234 men and 361 women who were heterosexually infected. Whilst viral load levels were slightly lower in women IDUs than male IDUs (0.13 log), no difference was detected between heterosexually infected groups. The Swiss team also found no evidence of a gender difference in disease progression, or in the predictive value of viral load results.

Earlier this year, researchers from the US government Centers for Disease Control (CDC) analysed combined data from three large CDC-sponsored cohorts: the Adult and Adolescent Spectrum of HIV Disease Project,

the HIV Epidemiology Research Study, and the HIV Outpatient Study⁶. Of 3,776 people studied, 2,467 (65%) were men and 1,309 (35%) were women. Viral load results from participants were adjusted to control for variations in the viral load test used. In common with studies reported above, women's viral load levels were generally lower than those seen in men. At CD4 bands of 0 to 199, 200 to 499, and over 500 cells, it was estimated that women had viral load levels that were 40%, 48% and 57% lower than in men, respectively.

However, in this study, gender was not associated with time to first AIDS-defining illness, or with length of survival time – that is, there was no difference in disease progression between the sexes at given viral load levels.

Differences in CD4 counts?

It's well known that in HIV-negative people, CD4 counts in women tend to be higher than in men. In the WIHS/MACS study, the rate of CD4 cell decline was not predicted by baseline viral load in women, and was faster in women than in men. Last year, a study involving 221 female and 443 male injecting drugs users found that women developed AIDS at higher CD4 counts than men⁷. This difference implies that the initiation of antiretroviral therapy may occur later in women than is appropriate for them. Clearly, the suggestion that women have lower viral load levels than men provides further potential for this to happen.

Response to anti-HIV treatment

However, there is little evidence from the body of research into the effects of anti-HIV therapy that women do less well on treatment than men – though it's sometimes argued that

women may be less likely to take part in trials than men. Researchers from Harlem, New York, reviewed this issue for the Durban conference⁸. Data from patients who had been randomised to begin an anti-HIV treatment regimen within studies completed as part of the Community Programme for Clinical Research into AIDS (CPCRA), within the last decade, were analysed. This included 730 recipients of dual therapy (Group 1; 62 women, 668 men), and 885 recipients of three drug HAART (Group 2; 136 women, 749 men). Median follow-up was 26 months in Group 1 and 21 months in Group 2. Whilst a history of injecting drug use was associated with a higher risk of disease progression, no significant difference was noted between men and women in progression of HIV disease, or in the rate of survival in the study overall. These findings were consistent across each of the drug trials analysed.

Why might there be a sex difference?

The reason for the sex difference in viral load observed in some of these studies is unknown. A number of possible explanations have been put forward, often involving potential hormonal effects. Sex hormones have been

shown to affect the functioning of immune cells and the production of cytokines, which act as chemical messengers between body cells. A cytokine called TNF-alpha which is associated with activation of the immune response and subsequent replication of HIV, may be inhibited by the female hormone oestrogen, perhaps lowering viral load.

Social factors such as poor access to welfare and care services, which may disproportionately affect women, might also be expected to influence disease progression. The negative effects of social deprivation may also explain – at least in part – the variations observed in injecting drug users and in non-white people.

Treatment guidelines

The current recommendation in both the UK and US is for anti-HIV treatment to be started at the same viral load levels in women as in men. The 2000 US DHHS guidelines, however, assert that “theoretical concerns exist” in relation to whether modifications may be needed on gender lines, and encourage continued efforts to enrol more women into clinical trials in order that these concerns may be scrutinised more fully.

key conclusions

- There is some evidence that viral load levels may be lower in women than in men, particularly at earlier stages of HIV disease.
- Whether this difference results in an altered pattern of disease progression is less clear, as some studies have found evidence of this and others have not.
- Some people believe that existing treatment guidelines should be changed to reflect these variations between men and women.
- There is little evidence to suggest that women respond less well to anti-HIV therapy than men.

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Treating depression

A randomised, controlled trial comparing a herbal therapy with a pharmaceutical drug called imipramine, has found that both drugs were equally effective for treating mild or moderate depression, but that the herb caused fewer side-effects. However, St John's Wort, the herbal treatment studied, may not be an appropriate remedy for some people with HIV due to the potential for dangerous interactions with anti-HIV drugs, and other treatments.

324 people with mild to moderate depression were randomised to receive a six week course of either 250mg hypericum (St John's Wort) extract twice daily, or 75mg imipramine twice daily, (plus a placebo so that participants would not know which treatment they had been allocated). Both St John's Wort and imipramine are used for treating depression. Imipramine is an antidepressant from the tricyclic group. In the UK, St John's Wort is an over-the-counter herbal treatment which is not approved for any medical purpose. However, in Germany, where this trial took place, it is licensed for treating depression and prescribed under the brand name *Romativ*.

Though the six week treatment period might be considered quite short, at the end of this time, both treatment groups reported improvements in their mood, with no significant difference between them. Recipients of St John's Wort, however, found their allocated treatment more tolerable and

reported fewer side-effects (39% St John's Wort versus 63% imipramine). 3% of St John's Wort users withdrew because of side-effects, and 16% of imipramine recipients.

However, St John's Wort recently hit the headlines in less positive circumstances. The drug is processed through the liver using a route which several anti-HIV drugs also pass through, and this can cause interactions between different drugs as they compete for the same limited set of liver enzymes. St John's Wort has been proven to reduce the blood levels of some anti-HIV drugs, leading to drug resistance and treatment failure. For this reason, it's recommended that people taking anti-HIV therapy do not take St John's Wort at the same time, and that anyone taking St John's Wort discuss the potential for drug interactions with their doctor or pharmacist.

Because St John's Wort is unlicensed in the UK, it does not appear on the formulary of drugs which UK doctors may prescribe on the NHS. It's quite expensive to buy over-the-counter, costing about £15.00 for one month's supply. Discounted vitamin schemes available through some HIV organisations may offer a cheaper means of getting hold of the drug.

Other options for treating depression are available, however. The tricyclic class to which imipramine belongs may be less likely to be prescribed nowadays than the more modern type of antidepressants known as SSRIs (selective serotonin re-uptake inhibitors). This

group includes *Prozac*, *Cipramil*, *Seroxat* and *Lustral*, which are generally considered to have fewer side-effects than the tricyclics, though as the German study group acknowledge, even these can be challenging for people whose depression is mild. In addition, non-pharmaceutical interventions are important for many people with depression, e.g. counselling, exercise, complementary therapies – see *NAM Factsheet 34: Mental health* for more information.

Source: The German study was published in the *British Medical Journal* on 2nd September, 2000 and is freely available on their website <http://www.bmj.com> – Woelk H et al. *British Medical Journal* 321:536-9, 2000.

PEP talk

The UK's Department of Health Expert Advisory Group on AIDS has recently updated guidance on the management of post-exposure prophylaxis (PEP) – the prescription of anti-HIV therapy to people who have very recently been at possible risk of HIV infection. Whilst PEP has most often been regarded as an issue for healthcare workers who face infection risks through their work, the availability of HAART has introduced PEP to a wider group of people, for example people whose risk of infection was through sexual exposure.

Proving that PEP is effective is difficult – many of those exposed to HIV may never have become infected anyway. To have the greatest chance of success, it's recommended that PEP begins within 24 to 36 hours of exposure, and preferably within an hour. The new UK guidelines recommend PEP be administered to healthcare workers if they have had a significant occupational exposure to blood, or another high risk body fluid, from a patient or other source either known to be HIV-positive, or considered to be at high risk of being infected with HIV, but where the result of an HIV test is not available.

The use of PEP in people whose risk of infection was through sex has been less well studied, partly because most people with sexual risks will not reach medical services within the short period considered ideal for beginning treatment. Because of this lack of information on the effectiveness of PEP after sexual exposure, the Expert Group does not recommend in favour of, or against its use in these circumstances at present.

It is advised that every NHS Trust or healthcare setting should develop a post exposure policy and protocol. In addition, starter packs of anti-HIV treatment should be available on site to allow rapid intervention.

Previous guidelines advised that PEP involve a three drug combination of AZT, 3TC and indinavir, though this recommendation is not based on firm evidence of effectiveness. The new guidelines suggest indinavir may be replaced by nelfinavir, another protease inhibitor.

Source: HIV Post Exposure Prophylaxis: Guidance from the UK Chief Medical Officers' Expert Advisory Group on AIDS. Department of Health. July 2000.

And finally...

Researchers from Antwerp report the case of a 48 year-old truck driver whose anti-HIV therapy has been blamed for turning his hair from straight to curly. The man also developed peripheral fat loss, considered part of the lipodystrophy syndrome, and a side-effect of anti-HIV treatment. While his doctor suggests the hair change could be one more symptom of lipodystrophy, it's possible that an anal tumour, successfully treated during the same period, may have been the cause. Use of the protease inhibitor indinavir has been associated with a thinning and loss of hair.

Source: Colebunders R et al. *Archives of Dermatology* 136:1064-1065, 2000.

nam forum

This month's forum features a debate on *When to start anti-HIV therapy*, with arguments for and against early and late treatment put by members of the British HIV Association. It all takes place at the University of London Union, Malet Street, London WC1 on Halloween, Tuesday October 31st, 7-9pm. Entrance is free.

ABT US approval

Abbott's new protease inhibitor *Kaletra* (also known as lopinavir/ritonavir, or ABT-378/r) has been licensed in the US. See NAM's website aidsmap.com for a review of the drug.

HIV's origins

A meeting on the Origins of HIV at London's Royal Society of Medicine last month heard new evidence which disputes the theory that the AIDS epidemic was sparked by the use of a contaminated polio vaccine in Africa in the 1950s. See Keith Alcorn's meeting reports in the aidsmap.com News archive.

coming soon

Next month we report back from two recent AIDS conferences held in Toronto. Headline news stories from the 2nd Lipodystrophy Workshop and the 40th ICAAC are available on aidsmap.com.



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any questions

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