

aids treatment update

herbal medicine: what are you on?

When the BBC polled 1,200 Britons about their use of complementary and alternative therapies in 1999, the findings made interesting reading. One in five had used complementary therapies in the previous year; twice as many compared to a similar exercise completed six years earlier. Average spending came to £160 per year, which extrapolates to some £1.6 billion on a national level. The most popular therapy was herbal medicine, which is the subject of our lead article this month.

In the UK and elsewhere, herbal medicines are frequently self-prescribed without professional medical advice, and the very fact that they are not classified as medicinal products means that, under UK law, they cannot be accompanied with written recommendations in the absence of a personal consultation. Herbal medicines are associated with side-effects – of both the mildly irritating and the much more serious variety – and harmful interactions with other medications, which in some cases we are only just beginning to understand. Sharing information about your use of complementary medicines with your HIV doctor or pharmacist is essential to you receiving the highest quality care from them.

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herbal medicine

2 after recent reports of harmful interactions and side-effects, are the benefits worth the risks? by anna poppa

systematic reviews

Systematic reviews are an effective way of reviewing results from several clinical trials, all of which had a common aim, such as assessing the effectiveness of St John's wort in treating depression. A researcher will gather the results of all studies on a given subject which have been published in medical journals, analyse their quality, and summarise their results.

buyer beware

According to UK law, products which claim to treat, prevent or cure disease are considered to be medicines and so require approval before being supplied to consumers. Approval will only be granted if the product's safety and efficacy has been adequately demonstrated. Vitamin and mineral products, and other supplements which do not make *explicit* claims about their effect on health, are considered to be foods, and are not subject to the same evaluation or legislation. However, under UK law, foods are expected to be safe, and must be accurately labelled.

Expenditure on herbal medicines in the UK and USA amongst both HIV-positive and HIV-negative people is substantial, and much of this concerns over-the-counter preparations. As many are sold as dietary supplements or 'herbal remedies', they are not subject to the same scrutiny, and controls, as pharmaceutical medicines. Users therefore face a number of risks – aside from often dubious claims of benefit, some herbal medicines undoubtedly have potent effects which can cause harm.

As we reported in last month's issue, researchers in the US are now advising against the use of garlic supplements alongside the anti-HIV drug saquinavir (if it is being taken as a sole protease inhibitor), following their discovery that an interaction between the two can result in a reduction in saquinavir levels, and consequent HIV treatment failure. St John's wort, an over-the-counter herbal antidepressant, is contraindicated with antiretrovirals, and many other medications, now that its potential for interactions is better understood. And in the UK in December, manufacturers of products containing kava kava, a herbal medicine which can reduce anxiety, removed their products from sale after reports of liver problems emerged from Germany and Switzerland.

In this article we consider the available evidence about the positive effects of herbal medicines, and about their risks.

Effectiveness of herbal meds

Of all the practices collectively referred to as complementary medicine, herbal medicines lend themselves comparatively well to placebo-

controlled trials – the most rigorous method of evaluating a medicine's efficacy and safety. Systematic reviews (see sidebar on this page) of published results from randomised, controlled trials demonstrate a positive effect in the following cases:

- St John's wort for mild to moderate depression¹.
- Ginkgo biloba to slow progression of dementia².
- Saw palmetto for benign prostate hyperplasia (where the prostate becomes increased in size, but is not cancerous)³.
- Horse chestnut seed extract for chronic venous insufficiency, a circulatory disorder⁴.
- Gamma-linolenic acid (GLA) for rheumatoid arthritis⁵.
- Kava extract for anxiety⁶.
- Phyllanthus for chronic hepatitis B infection⁷.
- Echinacea for prevention and treatment of the common cold⁸.
- Evening primrose oil for atopic eczema⁹.
- Ginger for nausea and vomiting¹⁰.

In relation to the use of herbal medicines for the treatment of HIV, there has been very little original research published, and much of it concerns Chinese herbal medicine (see below). One exception is a report on the use of herbal medicine to treat herpes zoster attacks (shingles) in people with HIV in Kampala, Uganda¹¹. In this non-randomised study involving 206 people who were compared to 107 historical controls receiving either herbal medicine or the antiviral drug acyclovir, there were similar rates of resolution of the attacks across the two groups.

Traditional Chinese medicine

Traditional Chinese Medicine (TCM) has been advocated for treatment of several chronic viral conditions, including hepatitis B infection. A single randomised trial found the Chinese herb kuorinone as effective as treatment with interferon-alpha¹². However, a systematic review of nine randomised trials of Chinese herbs for chronic hepatitis B infection, which was published in *Liver* in 2001, found these trials to be of low quality and to provide no compelling evidence in favour of TCM¹³. A Chinese herbal preparation known as CH-100 was reported to be more effective than placebo in reducing liver enzyme levels in people with chronic hepatitis C virus infection¹⁴.

Two systematic reviews have found no evidence to support the use of TCM for eczema^{15,16}, and one of these concluded that TCM may do more harm than good. A randomised trial in the *Lancet* reported that Chinese herbs were effective in treating a skin condition called atopic dermatitis in adults¹⁷. A further systematic review could not find evidence to support the use of TCM for acute respiratory (breathing) infections, but concluded that *Shuang Huang Lian* appeared effective for treating lower respiratory infections¹⁸. Both standardised and individualised Chinese herbal preparations have been found effective in treating irritable bowel syndrome¹⁹.

TCM in HIV infection

In a Swiss study, 68 people with HIV were randomised to receive a six month course of treatment with 35 Chinese herbs, or placebo²⁰. At entry, all had CD4 counts below 500, and were matched according to prior antiretroviral use, and their viral load and CD4 count. After six months, there was no difference in viral load, CD4 count, symptoms, or psychometric markers (which assess psychological health) between arms. CD4 counts fell in all participants who were not taking concomitant antiretrovirals, regardless of which trial treatment they were allocated. Gastrointestinal disturbances were more common amongst TCM recipients (79% versus 38%). The study concludes that this particular standardised TCM formula was not effective, and caused significant side-effects.

In a US study, thirty symptomatic people with HIV, with CD4 counts between 200 and 499, were randomised to receive a twelve week course of a standardised preparation of 31 Chinese herbs, or placebo²¹. The study found no difference in effect between the two groups in relation to symptoms or life satisfaction measures. Another San Franciscan study reported that a Chinese herbal formulation called *Source Qi* had a modest effect on pathogen-negative diarrhoea (that is, no causative germ could be detected) in people with HIV²². Treatment in this small trial was open-label, meaning that participants and investigators were aware of the trial treatment they were receiving.

A review of research into the *in vitro* anti-HIV effects of Chinese herbal medicines appeared in the *American Journal of Chinese Medicine* in 2001²³. The authors emphasised *Scutellaria baicalensis Georgi* as being worthy of further investigation.

Side-effects and safety issues

Whilst a number of herbal medicines are clearly of some benefit, their use presents a range of possible risks. Herbs are not normally subject to stringent quality control, and different preparations may differ in the amount of active ingredient present. Misidentification, adulteration and contamination may all be responsible for causing side-effects, and in extreme cases, poisoning.

There has been considerable publicity attached to recent reports of poisoning by Chinese herbal medicines. In 2000, eighteen patients at a private weight-loss clinic in Belgium were found to have developed cancers of the urinary system when the Chinese herb *Aristolochia*, already known to cause serious kidney problems, was accidentally substituted for another herb²⁴.

In September 2001, the UK's Medicines Control Agency (MCA) reported having found potentially dangerous and illegal substances in herbal preparations sold as TCM remedies in the UK²⁵. These included *Aristolochia*, mercury and arsenic compounds, and prescription-only steroids (which, ironically, some individuals may use TCM in order to avoid). The MCA is

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.

placebo A pill or liquid which looks and tastes exactly like a real drug, but contains no active substance.

protease inhibitor Family of antiretrovirals which includes amprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir.

randomisation The process of selecting by chance the treatment that a clinical trial participant will receive.

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.

further reading

This article includes extracts from NAM's forthcoming *Directory of Complementary Therapies in HIV & AIDS* which we will be sending to all ATU readers who have a free subscription in the Spring. A review of the safety and efficacy of the six best-selling herbal medicines in the US was published recently: Ernst E. The risk-benefit profile of commonly used herbal therapies: ginkgo, St John's wort, ginseng, Echinacea, saw palmetto, and kava. *Ann Intern Med* 2002;136:42-53.



herbal medicine continued

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working with a number of professional bodies which represent Chinese medics in the UK, but has warned against the purchase of unlabelled products, or those which do not list ingredients in English (unless you are a Chinese speaker).

Any product intended for human consumption which contains *Artisotlochia* is illegal in the UK. More information on these, and other compounds used in traditional Chinese and Ayurvedic medicine which fall foul of UK law, is available at <http://www.mca.gov.uk>.

These cases demonstrate the need to ensure that any practitioner of herbal medicine you approach is qualified, experienced and

reputable. Approaching professional accrediting bodies is recommended.

Care must be taken whenever conventional medicines are used with other therapies as there may be harmful or unhelpful interactions. Do ensure that your HIV doctor or pharmacist knows of any herbal therapies you're considering before taking them, and be proactive in inquiring about the risk of interactions.

Herb-drug interactions?

The pharmacological properties, and active agents, of many herbal medicines are not well described, and so the potential for harmful interactions is unclear. In 2001, *published reports* of interactions between herbal medicines and pharmaceutical drugs were reviewed for the *British Journal of Clinical Pharmacology*²⁶. It's likely that many cases go unrecognised and unreported, and of the 108 cases of suspected interactions identified in this review, the vast majority were not evaluable due to poor reporting. The following table summarises the findings:

Herb	Drug
Betel nut	Fluphenazine, Flupenthixol
Chili pepper	ACE inhibitor
Danshen	Warfarin
Devil's claw	Warfarin
Dong quai	Warfarin
Eleuthero (Siberian ginseng)	Digoxin
Evening primrose oil	Anaesthetics
Garlic	Warfarin
Gingko	Trazodone, Warfarin, Aspirin, Thiazide
Ginseng	Warfarin, Phenelzine
Kava	Levodopa, Alprazolam
Papaya extract	Warfarin
St John's wort	Theophylline, Cyclosporin, Phenpro-coumon, Warfarin, Combined oral contraceptives (ethinyloestradiol and desogestrel), Paroxetine, Sertraline, Nefazodone, Venlafaxine, Loperamide

The next table is taken from a review of *potential* herb-drug interactions published in *Archives of Internal Medicine* in 1998²⁷. In some instances, concern about interactions

relates to the overlapping, and therefore potentially additive effects of the medicines, such as taking both St John's wort and a pharmaceutical antidepressant.

Herb	Conventional drug	Potential problem
Echinacea for more than 8 weeks	Anabolic steroids, metho-trexate, amiodarone, ketoconazole	Liver toxicity
Feverfew	Non-steroidal anti-inflammatories	Inhibition of herbal effect
Feverfew, garlic, ginseng, ginkgo, ginger	Warfarin	Altered bleeding time
Ginseng	Phenelzine sulphate	Headache, tremulousness, manic episodes
Ginseng	Oestrogens, corticosteroids	Additive effects
St John's wort	Monoamine oxidase inhibitors, SSRI-type antidepressants	Safety of concomitant use not established
Valerian	Barbiturates	Additive effects, excessive sedation
Kyushin, licorice, plantain, uzara root, hawthorn, ginseng	Digoxin	Interference with pharmacodynamics and drug level monitoring
Evening primrose oil, borage	Anticonvulsants	Lowered seizure threshold
Shankapulshpi	Phenytoin	Reduced drug levels
Kava	Benzodiazepines	Additive sedative effects, coma
Echinacea, zinc	Immunosuppressants, e.g. corticosteroids, cyclosporin	Antagonistic effects
St John's wort, saw palmetto	Iron	Tannic acid content of herbs may limit iron absorption
Kelp	Thyroxine	Iodine content of herb may interfere with thyroid replacement
Licorice	Spironolactone	Antagonism of diuretic effect
Karela, ginseng	Insulin, sulphonylureas, biguanides	Altered glucose concentrations, so should not be prescribed to diabetics

key conclusions

- Herbal medicines have some benefits in treating a wide range of health conditions, though there is no evidence they are useful in treating HIV infection.
- Herbal medicines are associated with significant risks. They may cause both minor and serious side-effects, and cause harmful interactions when taken with other medications.
- Before you take herbal medicines, talk to your HIV doctor or pharmacist about possible interactions and side-effects.

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vaccine development

6 London immunology lab wins major role in global HIV vaccine effort interview by michael carter

In December last year it was announced that an immunology laboratory within Imperial College and Chelsea and Westminster Healthcare NHS Trust in London had won a contract with the International AIDS Vaccine Initiative (IAVI), which would place the lab at the heart of the global search for an HIV vaccine. Here we interview Professor Frances Gotch, Professor of Immunology at Imperial College based at Chelsea and Westminster Hospital, about what the partnership will involve.

The laboratory is housed within the St Stephen's Centre, Chelsea and Westminster Hospital, which is the largest HIV unit in Europe, and which cares for almost 4,000 people with HIV. Professor Gotch is also a member of NAM's Medical Advisory Panel.

Michael Carter (MC): What is involved in your lab's partnership with IAVI?

Frances Gotch (FG): The lab will be providing an essential part of the IAVI infrastructure. Let me explain. Since it was founded in 1997, IAVI has made considerable progress in getting the search for an HIV vaccine firmly on the scientific and political agenda. This has been achieved by their financial support, with the object of getting as many potential vaccine candidates into Phase I clinical trials – to assess the safety and potential of provoking an immune response in healthy, HIV-negative volunteers – as possible.

Furthermore, IAVI has funded research groups around the world, and funded the manufacture of stocks of pilot vaccines for trials in humans.

Of crucial importance is IAVI's funding for the establishment of an *infrastructure* for vaccine trials, and they've provided the cash for the establishment of centres around the world to

undertake Phase I trials. There are sites in Oxford, Kenya, and a trial centre in Uganda will be completed shortly. In the pipeline are facilities in India, China and South America.

However, although many vaccines can be tried in Phase I trials only one or two of the most promising vaccine candidates can be taken forward into Phase II and Phase III trials. To be able to do this you need to be able to do head-to-head comparisons. This requires all the trial centres to be using the same methodology. All the labs have to work to standard operating procedures; they have to be quality controlled; everything they do has to be validated; they all have to be using the same agents, maybe even the same plastic tubes. So what was needed was a central core laboratory, which would validate tests, analyse and archive data, and crucially, train staff for IAVI trial facilities worldwide.

IAVI recognised the need for these services and we, at Imperial College made a successful bid in cooperation with the Chelsea and Westminster Hospital NHS Trust. A key factor in being chosen by IAVI was, I think, our very strong and well-established links with the developing world. We have a laboratory with state-of-the-art equipment and eight personnel in Uganda which undertakes basic research into HIV.

Coincidentally, the refurbishment of the St Stephen's Centre, where HIV services at the Chelsea and Westminster Hospital are based, included the provision of new laboratories modernised to an extremely high standard, part of which IAVI was able to lease on our behalf for almost immediate use.

The contract with IAVI was signed late in 2001. The labs are functional and an excellent research team is in place.

MC: So which studies will be taking place?

FG: There is a trial just starting, called ICOX, run from St Mary's Hospital in London and Oxford University. It's a continuation, in a slightly modified form, of the recent IAVI-supported study organised by the universities and Nairobi and Oxford. We'll be running this trial and validating it at the same time. [Editor:

This is a trial for HIV-negative volunteers; see aidsmap.com for more information].

There's also the European Union-supported EUROVAC, which might hold promise for southern Africa. They're one of a number of organisations which have recognised the value of the quality control which we can provide. We are more than happy, under IAVI's auspices to do this, but EUROVAC will be providing the funding.

MC: And what timescale are you working to?

FG: Work has already started. We have highly trained staff and state-of-the-art equipment. The first trials we are supporting are the ICOX trial and the ongoing Nairobi/Oxford study. In addition, the first field trial in Uganda will start in mid-2002. The facility in Uganda has been constructed and IAVI is currently recruiting scientists. As I mentioned earlier, a key part of our role will be their training and I'm looking forward to providing training to personnel from Uganda very shortly.

Within two or three years, with all the field labs in place this is going to be a very busy facility.

IAVI has leased the lab for five years, with an option for a further five years.

MC: So what all this adds up to is a very central role for your lab in the broader search for an HIV vaccine.

FG: Absolutely. We'll be providing the central infrastructure and training necessary for vaccine trials to be progressed. The establishment of the lab is also a real indication of how seriously the quest for a vaccine is now being taken. There is a feeling in the HIV community that a vaccine has to be the number one research priority. I can understand that people with HIV, particularly those in the developing world who do not have access to drugs might think that the funds might be better spent on drugs.

But the drugs we currently have are far from perfect. For a start they're extremely expensive, and well beyond the reach of most of those

glossary

antibody Protein substance produced by the immune system in response to a foreign organism.

antiretroviral A substance that acts against retroviruses such as HIV.

chronic A long-term condition.

clinical trial A research study with people, usually to work out how well a new drug or treatment works and how safe it is.

immunotherapy A therapy which changes an aspect of the way the immune system works.

opportunistic infection Specific infections which cause disease in someone with a damaged immune system.

recombinant Genetically reconstructed.

seronegative Negative result in a blood test.

seropositive Positive result in a blood test.

T-cell A type of immune cell which is damaged in the course of HIV infection.

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.

vaccine development continued

infected with HIV. As your readers will be all too aware, although HIV antiretrovirals have been remarkably effective in cutting the incidence of opportunistic infections and deaths from AIDS, they can cause side-effects and resistance can emerge. Therefore a vaccine is of paramount importance in the fight against HIV.

MC: Could you give me an overview of HIV vaccines currently in clinical trials?

FG: There is a vaccine in Phase III trials [from] VaxGen, which is being investigated in people vulnerable to HIV infection in Thailand and the USA. The problem with vaccine trials is that they always lag behind the most cutting-edge science. For instance, the VaxGen product is based on an envelope protein of HIV. The idea is that it will induce an antibody response which will be protective against the virus. Interim results are expected at the World AIDS Conference in Barcelona this summer.

However, there's widespread agreement that this vaccine is not going to offer anything like protection for 100 per cent of the population against HIV – maybe no vaccine will offer *everybody* immunity to HIV. Therefore we could well be faced with a decision of what to do with VaxGen's product, or another candidate vaccine which offers protection against HIV to only part of the population – say 25 per cent. Do we start mass vaccination? Protection against HIV for a quarter of the population might have some impact on the HIV pandemic, but it's not really anywhere near good enough. I doubt very much if, say a polio vaccine which provided immunity to only a fraction of the population would be acceptable.

But having said this, getting a potential vaccine to Phase III is a huge achievement and very encouraging for the future.

However, the most up-to-date thinking on HIV vaccines is that immune responses on mucosal surfaces would be a promising area for further research – particularly if you are hoping to offer sterilising immunity – that's to say a vaccine which stops the virus penetrating the body's defences at all. For this to be achieved it's essential to have protection on the mucosal surfaces in the sexual organs, anus and throat, where HIV normally enters the body.

Another area being intensively investigated is the cellular immune response. Key to this research are the very few exposed seronegative people – those who have been exposed to HIV and not become infected. There are several small cohorts comprising such individuals around the world under investigation, the most highly studied being one of female commercial sex workers in Nairobi, Kenya. These people's immune systems have made responses to the HIV and apparently cleared it from the body. It is important to emphasise that they are *HIV-negative*, not *HIV-positive*. [One type of] antibody [IgG] which is seen in seropositive people hasn't developed and therefore didn't play a part in clearing the virus from their bodies. However, in females, it appears that [another type], IgA, on mucosal surfaces may have been important in providing protection.

We can also see HIV-specific T-cell responses in seronegative individuals, which also seems to be offering protection against infection with HIV.

However, within the Nairobi cohort, some of the women who gave up commercial sex work and subsequently returned seroconverted to become HIV-positive. It looks as if these IgA antibody and cellular responses need constant exposure to the virus in order to maintain protective levels against the virus. This has potentially worrying implications for vaccine development,

suggesting as it does that continual booster vaccination may be necessary.

Live recombinant vaccine candidates are also in Phase I trial. These use other pathogens, such as canary-pox, which have been engineered to express small, harmless parts of HIV, with the hope of provoking an immune response which would neutralise HIV.

An interesting, but highly problematic area of research is the use of live attenuated HIV, that's to say a version of HIV which is altered so it is harmless to humans but offers protection against fitter, harmful strains of the virus. In animal models this looks very promising, offering 100 per cent protection. However, such a vaccine could not be used in humans as there are worries about its long-term safety – in particular, reversion – the virus used in the vaccine evolving to become harmful again, and the potential for the attenuated version of HIV to recombine with fit HIV. The 100 per cent protection offered by live attenuated HIV has nevertheless become a goal of many researchers who are looking at how they can provide similar protection using an engineered parts of HIV which could neither revert, nor recombine.

MC: What does this mean for people who already have HIV?

FG: I'm going to answer that in two parts, looking first at people in the UK and other countries who have ready access to antiretrovirals and then at people in the developing world with little or no access to these drugs.

There's no doubt that when taken properly, antiretroviral therapy can dramatically reduce viral load, increase CD4 count and drastically cut the risk of developing an opportunistic infection. However, unless antiretroviral

treatment is offered very shortly after exposure to HIV, then HIV-specific cellular responses, which provide natural immune protection against the virus, do not come back. In chronically HIV-infected individuals therefore, immunotherapy in conjunction with antiretrovirals, may help to boost HIV-specific immune responses. This might enable people to stop taking medication. Who knows, we could dare to hope that immunotherapy might even hold the potential to eradicate HIV.

Autovaccination – vaccination with your own HIV – also seems to be promising and is something I'm very interested in. It involves people taking a short course of antiretrovirals until an undetectable viral load (below 50 copies) has been achieved, followed by structured treatment interruptions to induce immune responses. It's too much to hope for that we'll eradicate HIV from chronically infected individuals, but I'm hopeful that we might be able to use this strategy to prime people's immune systems and enable them to achieve a sort of 'long term non-progressor' status. That's to say, chronically infected individuals who are able to remain well, with low viral load and high CD4 count for at least ten years without the use of antiretrovirals.

We're also looking at the role which cytokines and human growth hormone can play in the restoration or reinstatement of HIV-specific immune responses.

Now, turning to the developing world. Although drug prices have come down they are still out of reach for most people. I'd hope that it might be possible to offer a relatively short course of antiretrovirals, say six months and then some immunotherapy which boosted the immune system to enable patients to control HIV without the need for drugs.

vaccines on the web

A thorough review of the state-of-play in HIV vaccine development is available at NAM's website aidsmap.com. From the homepage, use the drop-down menu *Take me to...* and scroll down to *Prevention technology: Vaccines*. For more information on the International AIDS Vaccine Initiative visit <http://www.iavi.org>

vaccines in print

If you don't have access to online information, you can read more about HIV vaccines in NAM's *AIDS Reference Manual*, a comprehensive guide to the social aspects of HIV and AIDS. Reduced price subscriptions, at £12.95, are now available to people personally affected by HIV. For details, contact NAM on 020 7627 3200.

Major HIV treatment trial begins overseas: UK sites likely

A major international study comparing two different methods of treating HIV has begun recruiting patients in the United States and Australia. The SMART study (Strategies for Management of Antiretroviral Therapy) will compare the strategies of beginning treatment after the CD4 cell count falls below 350 cells (and staying on treatment), with the strategy of waiting until the CD4 cell count has fallen below 250 cells to begin treatment (and stopping treatment once the CD4 cell count has moved above 350 cells).

The study is designed to investigate a number of important strategic issues, including the effects of earlier versus later treatment initiation, the relationship between drug exposure and side-effects, and whether starting and then stopping treatment results in more or less problems with adherence, quality of life and development of drug resistance.

SMART aims to enroll 6,000 patients, and people will be eligible to join the study even if they are already on HIV treatment, providing that they are willing to accept the possibility that they may be randomised to stop treatment. The study aims to detect differences in the rate

at which participants develop opportunistic infections, and so based on current data, SMART is planned to run for at least six years. Follow-up of this length has not been seen in HIV therapy trials for some time (though the Esprit study of IL-2 is an exception), as trials have moved towards focusing on 'surrogate markers' – viral load and CD4 changes – in place of the harder endpoints, such as serious illness and death. In the HAART era, clinical events occur much less frequently, and so trials must be bigger, and run for much longer, if they are to detect differences in the rate at which they develop.

In 2002, the aim is to recruit 1,000 patients in a pilot phase to prove that it is feasible to recruit patients to such a study and safe to manage HIV infection according to the protocol for stopping and starting therapy. If the pilot phase is successful, recruitment will be extended, with the possibility that the study will be extended to the UK and other countries.

Participants will be able to take any drugs they choose, and will be able to change therapy whenever necessary. As new drugs come along, participants will be able to use them, because the study is investigating strategic approaches to therapy that are considered unlikely to become out of date within the next ten years.

The best time to begin anti-HIV therapy is not known, and whilst SMART cannot answer that

question directly, it aims to shed more light on the different outcomes attached to earlier versus later treatment. For more on this subject see the lead article in the November 2001 issue of *ATU*. More information on SMART is available at <http://www.clinicaltrials.gov>.

For the present, readers interested in ongoing UK trials which are evaluating the role of treatment interruptions in people taking anti-HIV therapy, should ask their treatment centre about the TILT study. More information is available on aidsmap.com.

Risk of birth defects in children born to HIV-positive mothers

Paediatricians from London have reported an apparent association between the use of anti-HIV drugs alongside certain other medications early in pregnancy, and birth defects in children born to women with HIV.

A review of 195 mother-infant pairs found birth defects in nine children (4.6%). All the children were born in London since 1994, during which time the use of antiretrovirals by mothers increased substantially, including use in the first three months (trimester) of pregnancy; this latter rate was 0% in 1994 and 27.5% in 1999. Thirteen children were exposed to both antiretrovirals and drugs from a class known as folate antagonists in the first trimester. Though birth defects overall were uncommon, the rate was much higher (23.1%) in this group of children than in those 148 children who were not exposed to either type of drug in the first trimester (4.0%). As there were no abnormalities in those children exposed to either one class of drugs or the other at this time, the increased risk *seems* to be associated with their combined use, (though the number of babies exposed to combined treatments was relatively small).

Drugs from the folate antagonist group include a number which are used to treat or prevent the

AIDS-defining pneumonia PCP, such as co-trimoxazole (*Septtrin*). These drugs lower levels of folate in the body. All women considering pregnancy are advised to take folic acid supplements prior to conception and in early pregnancy, as this reduces the risk of birth abnormalities. The study authors have reiterated the importance of this in women with HIV infection.

Reference: Jungmann EM et al. Sex Transm Infect 2001 Dec;77(6):441-443.

Boston man files suit over alleged HIV meds pharmacy error

A nurse from Boston, USA is suing his pharmacy after alleging that a prescription error left him taking the anti-HIV drug indinavir at the wrong dose for several weeks.

Newspaper reports say the man took indinavir at a half dose for three weeks before noticing the dosage was wrong. By this time his viral load was close to 200,000 copies – the highest result he'd ever had – and a drug resistance test indicated his virus was resistant to indinavir, amongst other drugs.

He is now suing CVS Pharmacy Inc for \$257,000 to cover projected lost wages. The pharmacy are reported to be challenging the suit on the grounds that the man's clinical circumstances cannot be proven to be directly associated with under-dosing of indinavir; but may have arisen anyway.

This case provides a timely reminder of the importance of checking that your medication prescription has been filled correctly before leaving the pharmacy.

Source: Boston Globe, 26th December 2001.

NAM forum

This month's NAM Information Forum takes place on Monday, 18th February and focuses on interventions to lower raised cholesterol, a side-effect of anti-HIV therapy. Guest speakers on the night will include a doctor, an HIV dietician, and a sports scientist. NAM forums are free and take place at the University of London Union, Malet Street, London WC1. They run from 7-9pm and a sign language interpreter, and refreshments, are available.





credits

editor
Anna Poppa

AIDS Treatment Update
founded by Peter Scott

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design
Alexander Boxill

printing
Cambrian Printers

ISSN
0969-4706

charity number
1011220

medical advisory panel

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

Department of Health, London HIV Commissioners
Consortium, International HIV/AIDS Alliance, Crusaid,
British HIV Association, Elton John AIDS Foundation,
GlaxoSmithKline, Bristol-Myers Squibb, Roche
Products, Bristol-Myers Squibb Pharma, Abbott
Laboratories, Boehringer Ingelheim, Merck Sharp &
Dohme, Agouron, Gilead, Roche Products Hep C
Division, Roche Molecular Systems, Serono, Visible
Genetics, Virco, and these health authorities: Barking &
Havering, Birmingham, East Surrey, East Sussex,
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any questions

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Professional/organisational rate: £75/year.
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