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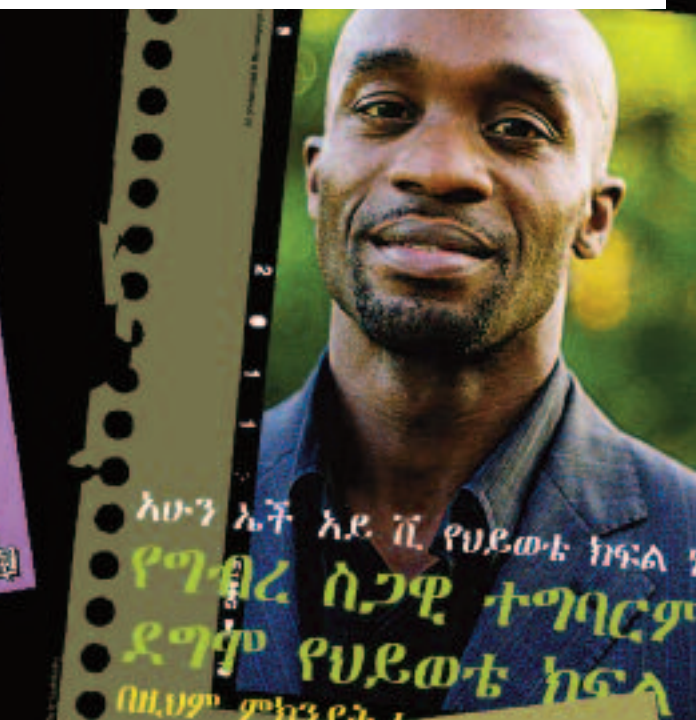
hiv treatment update



Gus Cairns

in this issue

As an interviewee in *The World Next Door* (page 4) says, UK Africans may accept the need for HIV prevention advice, they just don't want to be targeted for it.

The estimated proportion of people with HIV among the UK's African community is similar to that amongst gay men. And the proportion who become infected in the UK appears to be rising. Clearly, therefore, there's a need.

But, as the widely differing portrayals of Africans in the national campaigns conducted thus far shows, deciding exactly what they need to know and how to reach them is a very different thing. Portrayals in the posters and leaflets have swung from people who looked like office workers, through grittier images, which even included a bit of man-on-man action, to a sitcom Peckham dad.

'UK Africans' is an impossibly broad group of people to engage using one series of posters. Mass-media campaigns trying to grab their attention may be a waste of money.

This May, the British National Party (BNP) misused statistics to 'prove' that the UK's HIV problem largely results from African immigration. Individually, someone may be extremely likely, or not likely at all, to have HIV and because of stigma may be sensitive to messages that imply that they do.

Our numerous local African organisations, however, are having success in contacting their local community. It's on the street, in clubs, shops and churches, that people will be reached and educated.

We also celebrate some extremely good news. In *Combinations and Conundrums* (page 8), while stressing the complexity of hepatitis C therapies, we mark recent trials' successes: at least 50% more people cured in half the time, including many who had failed therapy before.

In our news section we celebrate a couple of historic decisions (or near-decisions: both could still be reversed).

One is the decriminalisation of gay sex in India (page 12). The importance of this can't be overstated: it overturns a 150-year-old law that has been used as the template for similar anti-sodomy statutes in several ex-British colonies. Furthermore, the Delhi High Court based its decision on a piece of judicial bedrock: its country's own constitution. Legislating against gay men, it said, violates their rights to liberty and privacy. This sets the stage for challenges in other countries.

The other is the proposed ending of the travel ban on HIV-positive people by the USA (page 14). This is significant because the US Health Department went further than expected and essentially declared that HIV-positive visitors and immigrants were not a significant threat to public health. This could shame the countries that still bar travellers with HIV, and serve as additional 'ammo' against the likes of the BNP.

The next issue of HTU will come out in September as we now have a pause for the NAM team to attend the IAS conference. Enjoy your summer and, if you missed sponsoring our team in the Crusaid Walk for Life, don't forget that our intrepid NAMmers will also be entering the London Triathlon on 1 August to raise money for HIV. Just go to **www.justgiving.com** and search for NAM.

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

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

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upfront

Thunder, lightning, torrential rain…and Walk for Life!

Laura Wigzell, NAM's Funding Development Assistant, reports on NAM's latest fundraising effort.

Last month, NAM staff and supporters dusted off their trainers and got involved in Europe's largest sponsored walk to support those affected by HIV and AIDS – the Crusaid Walk for Life.

This annual, 10-kilometre walk around London is now in its 20th year – but this was NAM's first time. Luckily for us we had an amazing team of supporters, HTU readers and suppliers walking with us and helping us every step of the way.

Undeterred by the early morning thunder, lightning and torrential rain we made our way to the starting point at Tower Bridge, complete with wellies and umbrellas and ready for the worst…

By 10am, the sun was shining, the sky was blue, and everyone was raring to go. What a sight! Over 2300 people all kitted out in bright yellow T-shirts (and some brilliant fancy-dress costumes!) walking through the heart of London on a busy Sunday afternoon, raising awareness and getting people talking wherever we went!

"I support NAM and Crusaid because of the valuable information and advice I received when I was diagnosed and want to make sure I do my bit to ensure others get equally good help during what can be a difficult time."
Ricki, London

Walkers crossed the finish line to rapturous applause, picked up their medals and enjoyed the afternoon entertainment in the sunshine. As for Team NAM, we put our feet up, raised our celebratory bananas and toasted a job well done. Until next year…

We'd like to say a huge thank you to everyone who generously gave up their time to walk with us on the day and who helped us to raise so much money. And thank you to everyone who sponsored us.

"I suffered a heart attack in January of this year and was determined that I would get this walk under my belt."
Tony, London

With your help we have so far raised over £4000 for NAM and Crusaid. But we can still keep fundraising until September 7th. To sponsor us, simply visit **www.walkforlife.com** and search for NAM.

The money we raise will help us continue to provide the latest HIV information and news.

Inspired by the success of this year's Walk for Life, we are determined to make next year even bigger and better. Would you be interested in putting together your own team and walking on NAM's behalf? If so, please contact us on 020 7840 0050 or email info@nam.org.uk

We also have brand new online justgiving.com pages so you can fundraise on NAM's behalf any time of year. Are you doing a challenge event this year, running a marathon or putting on an event? Or perhaps you have a big birthday coming up? Then why not turn it into a fundraiser and support the work of NAM? Just search for NAM at **www.justgiving.com** to get started!

And maybe we'll see you next year at the Crusaid Walk for Life!

"When we opened our store (DV8 in Soho), it was our company ethos to do as much as we could to support HIV charities and help raise HIV awareness. Having worked with NAM before, it was a great opportunity to join them on the Walk for Life – a perfect way to help others who may be going through or facing some of the difficulties I have witnessed. And I have to say it's also one of the most relaxing and enjoyable days I've had all year. I totally recommend it!"
Jason, DV8 Soho, and Diesel the dog

Some of the NAM Walk for Life team with HTU editor Gus Cairns at left (with big grin and waistcoat). For more photos from the day visit www.aidsmap.com/walkforlife.

the world next door

africans and hiv prevention in the uk

HIV prevention in the UK, with its campaigns and images largely intended for gay men, has had to change in response to a new community with parallel – but different – needs. *Gus Cairns* investigates.

Henderson Mmangisa, outreach worker for the Centre for All Families Positive Health, Luton's African HIV support agency, is taking me into a world that has long been on my doorstep. I've just never stepped through its door. Henderson is its Condom Man.

High Town Road is one of those areas, which often fringe town centres, where the most recent wave or two of newly arrived cultures to the UK have set up shop. We wander down the narrow street dropping off bags of condoms and proffering information leaflets at barbers' shops, money exchanges, small food stores – but not the pub, which has refused his free goods. Reception varies from the familiar ("Yeah, we've run out. Just put them on the shelf by the door") to the nervous ("I'll have to ask the manager").

If you do HIV prevention work you become hyper-aware of the sexual undercurrents that permeate any city scene. Who will use our goods over the next week? The two boys glancing back at the busty girl? The young men admiring their razor-cuts in the barber's mirror?

Who is the 'UK African community', anyway? Are its members really at risk of HIV? And if so, are they getting the right kind of help to avoid it?

UK Africans and HIV

The last census in 2001 estimated that there were about half a million people in the UK who were born in Africa – not the same as people of African ethnicity – and the Home Office estimates that during the first half of this decade there was a net inflow of around 66,000 people from Africa every year.[1] This inflow may have slowed since then: the more recent BASS Line survey[2] found that 4.4% of its respondents had been in the UK less than a year, which would imply about 25,000 new arrivals.

The Health Protection Agency (HPA) estimates that 4.9% of UK Africans – one in 20 – has HIV, of which 25% are undiagnosed (22% of women and 30% of men).[3]

This is over 30 times higher than HIV prevalence in the general population, and about the same as prevalence in gay men outside hotspots like London, Brighton and Manchester.[4] So one might expect rough parity between the amount spent on prevention in the African and gay communities. In fact, CHAPS, the gay men's HIV prevention partnership, got £1.7 million from the Department of Health last year, but NAHIP, the National African HIV Prevention Programme, only got £750,000, plus another quarter of a million for managing the African AIDS Helpline.

But are Africans transmitting and acquiring HIV at the same rate as gay men? The HPA estimates that the number of Africans in the UK with HIV has been increasing by about 3400 a year, but that four out of five of these infections are brought in from Africa and only 700, one-in-five new infections, are caught within the UK. Although this is not an insignificant number, it still represents only about half of the number of infections caught in the UK by non-African heterosexuals.

This figure could be wrong. Community-generated surveys like Mayisha 2 in 2005[5] and BASS Line, which recruited over 4000 people of African ethnicity in 2007, find much higher HIV prevalence rates: 14.4% in Mayisha and 15.5% in BASS Line – as high as HIV prevalence anywhere globally, except southern Africa. However these surveys may have over-recruited from higher-prevalence communities, in the case of BASS Line via HIV agencies, so are more likely to have been answered by people already with HIV, and at risk of HIV.

The HPA's Brian Rice says: "The assignment of place of infection can be difficult, and is open to a number of biases. For instance, allocation of country of infection may be based on the assumption that if someone was born in Africa and hasn't been in the UK long, they must have been infected in Africa."

In certain places new HIV infections may be occurring at a much higher rate in the UK. Rice adds: "London data indicate that approximately 30% of African-born people diagnosed in London in 2007 possibly acquired their infection within the UK."

The HPA's unpublished data are backed up by a study by Fiona Burns from the Centre for Sexual Health and HIV Research at University College, London.[6] They estimated that between 25 and 35% of their subjects had acquired HIV in the UK, which would indicate about 1200 new infections a year in the UK.

Burns comments: "The absolute number of new HIV diagnoses in Africans may not increase further, but the proportion infected here probably will.

"HIV is invisible over here to a lot of the African community," she adds. "I continue to encounter patients who tell me 'I thought I was the only positive African here'. There is a very high awareness of HIV in general, but somehow it doesn't translate into an appreciation of personal risk."

Perception, knowledge and risk

It does appear that many UK Africans believe that they left HIV behind when they left Africa. The BASS Line survey found that a majority of its respondents – 53% – had never had an HIV test (compared with 38% of UK gay men[7]) and when asked why they hadn't, seven out of ten said it was "because I've no reason to think I have HIV". Worryingly, one in five who had tested positive had doubts about whether they actually had HIV.

Some UK Africans may be more likely to acquire HIV than they think. A third of respondents to BASS Line had been diagnosed with a sexually transmitted infection (STI), one in ten in the last year. One-in-eight men (but only one-in-18 women) had had more than five partners in the last year, and nearly half of men and a quarter of women had at least one sexual partner in addition to their main partner.

A third of men and a quarter of women reported 'always' using condoms over the last year, but a fifth of both sexes reported 'never' using them. Over a third of people who answered the survey (38%) felt they were not in control of whether they became infected with HIV, and the impact of stigma came through in the finding that 30% of people "would worry about what people thought of me" if they carried a condom.

The influence of faith

One finding of qualitative surveys of African women with HIV[8] and heterosexual men[9] is how important the church is as a source of strength and support. One woman said:

"*It is only in church that I feel really integrated, because you know there is one common ground for girls and boys that have problems. I feel good about myself for a change. It makes me feel better.*"

However, these surveys also found that some people had experienced rejection and ostracism from their local church, or feared it.

NAHIP conducted a survey and series of workshops with Christian faith leaders and congregation members in 2007-08. The report on these workshops, *Faith and HIV in Action*, makes interesting reading.[10] Only a small proportion of people in the survey expressed punitive attitudes towards people with HIV such as "HIV is nearly always contracted as the result of 'sinful' sexual relations" (80% disagreed) and "HIV/AIDS is punishment from God for sin" (84% disagreed).

But strong beliefs were expressed that HIV is curable with the help of God. Only just over half of respondents agreed that "There is no cure for HIV infection once someone has it," and three-quarters believed that "There are people who have been cured of HIV/AIDS by the power of prayer alone (i.e. without medication)". In the workshops, the report adds, one participant insisted he had been cured by God.

On the other hand, no one thought that people who took HIV medicines had "a lack of faith in God".

In June 2009, the African HIV Policy Network (AHPN), as part of the NAHIP programme, launched two faith toolkits – **Breaking the Loud Silence** for Christian faith leaders and **Life and Knowledge** for Muslim faith leaders – as part of the *Changing Perspectives* anti-stigma campaign.[11]

Men who have sex with men

One of the most intriguing findings in the BASS Line survey was that a high proportion of African men reported having sex with other men, but still considered themselves heterosexual. Fifteen per cent of men who answered the survey reported sex with men in the last year, two-thirds of them with both men and women and one-third with men only. Fiona Burns estimates that half of the men who have sex with men (MSM) who had HIV acquired it in the UK.

Yet despite having sex with men, 58% of men who also had sex with women, and even 12% of men who only had sex with other men, reported that they were *exclusively* attracted to women. How can that be?

Titise Kode, Chief Executive Officer of the AHPN, says: "It's all about stigma and self-loathing. In African culture you have to be a MAN and you have to have a woman and have kids."

Jabu Chwaula, NAHIP's Programme Development Officer, adds: "People's social support may consist of places where it's simply impossible to be a 'gay man'. It's a mistake to think people become less African just because they come over here."

During my rounds with Henderson in Luton, we passed a couple of gay pubs and I asked him if any openly gay men had approached CAFPH for help and support. He could only recall one, and seemed very impressed by the man's courage, or foolhardiness, in coming out as gay: "He had just been diagnosed, and really didn't know where to go for help at all," he said. He personally didn't know who ran gay HIV support services in the town.[12] This reinforces a finding by a qualitative survey from 2006[13] that African MSM currently fall through the gap between gay and African HIV prevention programmes.

Evaluations

Ibi Fakoya has been working at the Centre for Sexual Health and HIV Research and wrote the evaluation reports on NAHIP's campaigns (see panel below).

The report on *Better to Know* found that the campaign was too rushed, that workers were only trained on implementation halfway through the campaign, and that minor partners in the campaign didn't feel consulted. As a result of this *Beyond Condoms* was mandated by the Department of Health to develop its message by means of a painstaking series of consultations with all partner agencies. Because of this there were "significant delays in the formative and development stage", which was supposed to take six months but in the end took 18.

The report comments that the central message of the campaign was subject to "Campaigning by committee ... issues that appeared finalised in one meeting would be subject to scrutiny in the next, with seemingly no single organisation having a definitive final word".

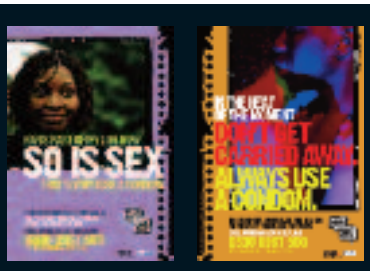
The message was at the start of the campaign intended to be bold and innovative, questioning penetrative sex as the only kind of worthwhile sex; abstinence was to be mentioned as a valid choice as

Prevention programmes

What HIV prevention help has been provided to the UK African community? Historically, voluntary-sector HIV services for this audience have been split between a high number of small local agencies, and NAHIP has 19 current partners in contrast to the gay men's programme, CHAPS, which has nine.

NAHIP has overseen three major programmes.

It's Better to Know: This was an HIV testing campaign originally developed by the Terrence Higgins Trust and rolled out in 2004 as NAHIP's first multi-partner campaign. Twenty-seven sites were involved, with 4600 posters and 62,000 booklets and cards distributed. They featured smartly-dressed, professional-looking models saying "Now I've had an HIV test I can get on with my life," and directed people to the THT Direct helpline.



Beyond Condoms: This campaign, run between 2006 and 2007, was developed collaboratively by the NAHIP partners. The first national African campaign to actually talk about sex and sexual behaviour, it sought "to encourage debates within communities not only of condom use but also on other safer sex practices that reduce

were oral sex and masturbation. In the end, however, users felt that "the messages being used were not new and were not challenging", and that it was ironic that "While the finalised materials did contain a consistent message, this message was quite simply 'Use a condom'."

Nonetheless, *Beyond Condoms* produced a permanent doubling in the number of calls to the African AIDS Helpline.

The report on *Do it Right* is soon to be published, and despite the campaigns' different feels and messages, Fakoya comments that certain themes stand out. She questions the assumption that members of the African community have the same needs and that therefore only one message needs to be addressed to them. "Specific messages need to be tailored to specific needs," she says.

She urges more sophisticated research be undertaken to see if campaigns are actually making an impact: "Documenting an increase in calls to the African AIDS Helpline is very distant from making a difference to HIV infections. There should at least be an element of ongoing behavioural research built into every campaign."

Values

Chwaula agrees that within the community people will have very different needs according to their age, sexuality, religious beliefs, HIV and socioeconomic status.

"We need to stop saying 'Here's a group of Africans – let's throw an HIV intervention at them'."

He adds that in the next few years AHPN's priorities will be to strengthen their work with faith communities and on gender issues.

They would also like to run a multi-year testing campaign, looking at the models that are employed in various parts of Africa and which may resonate and be relevant to Africans in the UK. However, Kode warns advocates who are currently urging the adoption of early HIV treatment as a prevention method not to ignore the concern that having pills lying around will force a person to disclose their HIV status. "People have needs other than protection against HIV," she warns, "including enjoying the support of their local community."

"If you're an undocumented migrant," she adds, "this becomes even more crucial because you can't go to social services and demand that they meet their obligations – you HAVE to rely on informal networks."

Burns comments that "Doing prevention work in a non-stigmatising way is really important. Africans often want HIV prevention messages to be universal and not to focus on them as such. They don't want to be seen to be targeted, and aiming HIV prevention messages at Africans in general may simply fuel stigma.

"Interventions with limited budgets will need to use more innovative means of addressing groups at higher risk."

I asked Fakoya what she would do for the African community if money were no object.

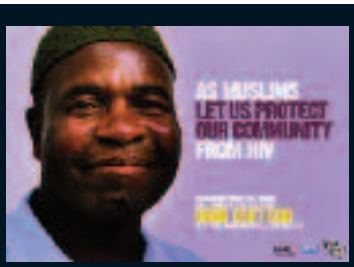
"I'd invest in trying to adapt group workshops that had had proven efficacy in the USA", she says. One is called Project SAFE,[14] a three-session workshop for African-American and Mexican women that achieved a 30% reduction in STIs (high for a behavioural intervention).

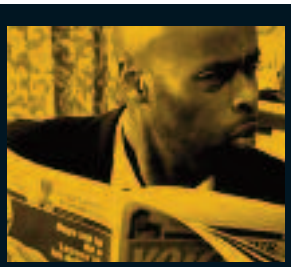
"It would cost money," adds Fakoya. "Messages would have to be tailored for UK Africans, and you'd need to train facilitators to a high level of skill."

And given current funding levels? "Essentially, fewer mass-media interventions." She thinks that NAHIP and its partners have done an excellent job accessing members of the African community: "Their figures on contacting recently arrived people are impressive." As a result she feels that big mass-media campaigns in papers like the *African Times* are unnecessary. "Africans love to talk together, and what you do is build on a sense of local community and solidarity."

AHPN mentions this as a specific value in its campaigning. "Ubuntu," says Jabu Chwaula, "is a word in southern African languages that means 'I am who I am because of other people' – or to use the English quotation, 'no man is an island'. It's about nurturing the African sense that you are dependent on the dignity and respect others accord you – and that you in turn extend dignity and respect to them." Whether Ubuntu can be harnessed as a way of helping Africans stay safe from HIV remains to be seen. ■

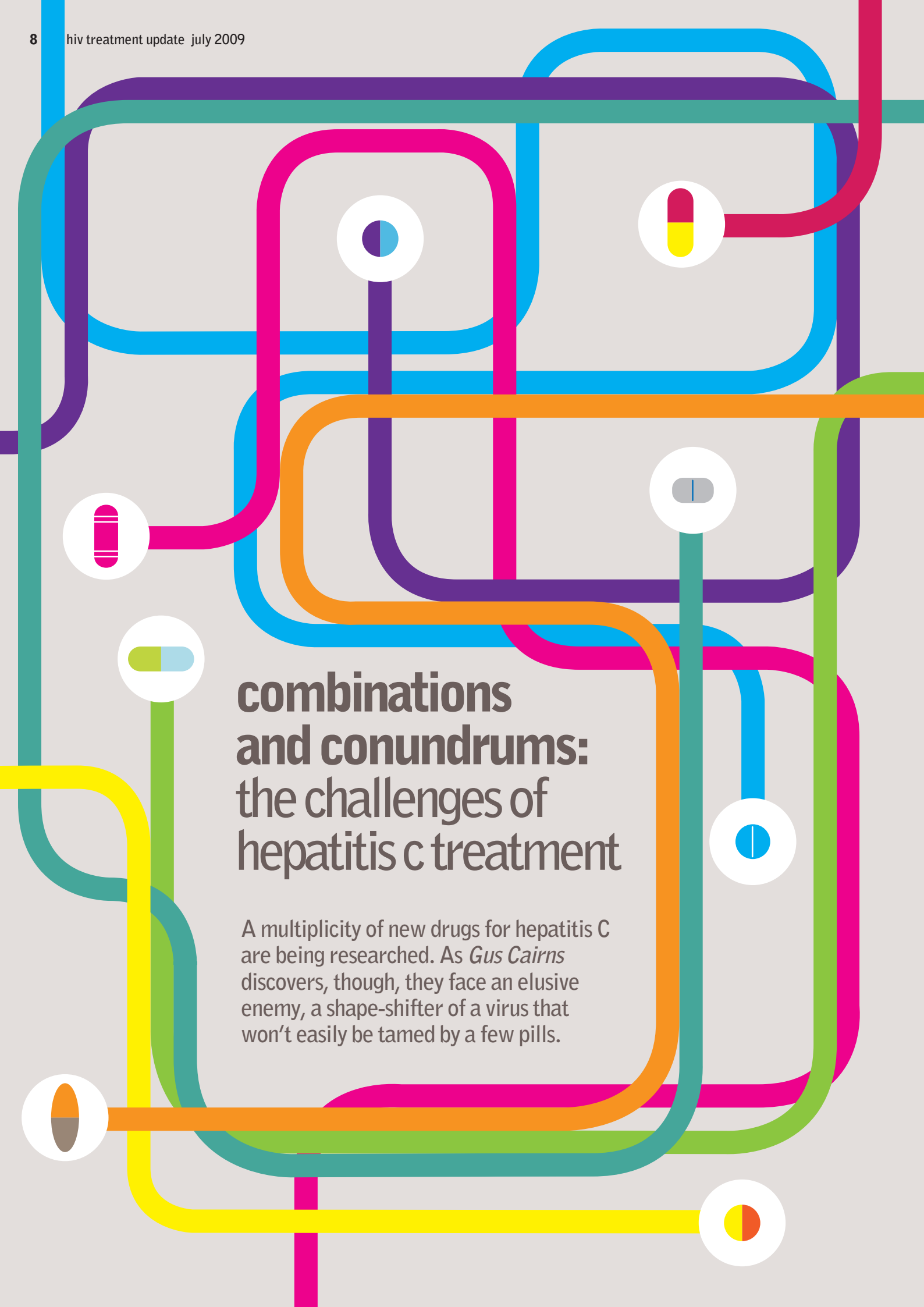
Images courtesy of AHPN/NAHIP ©





the spread of HIV." It was considerably larger, with 20,000 posters and 200,000 leaflets and booklets distributed at over 750 venues. The posters had a grittier tone, with ones directed at MSM and at young people, and said things like "HIV is part of my life now, so is sex". People were directed to the African AIDS Helpline.

Do it Right: subtitled *Africans Making Healthy Choices*, this is the current campaign, with an altogether slicker feel and its own website at www.doitright.uk.com. Its printed materials simply inform people of some basic facts about HIV and direct them to sexual health services, but in its website, developed as a teaching and workshop aid, there is a strong emphasis on gender and the roles of women and men. An amusing set of videos called *Kobana's Stories* features a fallible and old-fashioned African dad struggling with a wife who's had an HIV test because she (rightly) doesn't trust him, a mistress wanting him to use condoms, a son who may or may not be gay, and a newly dating daughter. Deeper on the website there are also discussions about men and sexual violence with a couple of powerful films shot in South Africa for MTV's *Staying Alive* campaign.



combinations and conundrums: the challenges of hepatitis c treatment

A multiplicity of new drugs for hepatitis C are being researched. As *Gus Cairns* discovers, though, they face an elusive enemy, a shape-shifter of a virus that won't easily be tamed by a few pills.

In the April issue, *HTU* 185, we looked at how hepatitis C infections are rapidly increasing in gay men with HIV in Europe and parts of the USA. Since then, new studies have continued to document its spread and possible consequences for health.

More on the new epidemic in gay men

A recent study[1] has found genetic evidence that the different outbreaks seen in European cities since 2000 are in fact one connected outbreak of hepatitis C – an outbreak that seems to be growing at a rate of about 20% a year in HIV-positive gay men.[2] This study found that 86% of gay men co-infected with HIV and hepatitis C in Europe shared their virus in a 'cluster' with other men in the study.

The study also found an apparently separate outbreak of hepatitis C among HIV-positive gay men in Australia. Only one case was found of infection by a European strain of hepatitis C and it also seems to feature different risk behaviours. Whereas few men affected by the European and US outbreaks of hepatitis C injected drugs, a large proportion of the Australian gay men did.

Daniel Fierer, the HIV physician who first documented a rash of new hepatitis C cases among gay men in New York, told a hepatitis C and HIV workshop in Lisbon in June that the development of liver fibrosis (the scarring caused by hepatitis, which eventually leads to cirrhosis) appeared to be proceeding five times faster in his patients than in co-infected patients in previous studies, and the longer the interval was between hepatitis C diagnosis and liver biopsy, the more severe the fibrosis was.[3] The liver is such a resilient organ it can do its job with this degree of scarring and people may have no symptoms; the concern is more about what may happen to these patients in the future.

So, to summarise, we are talking about an outbreak of a chronic and progressive liver disease among gay men. But they are not the people who need new treatments for hepatitis C most badly.

The global consequences of hepatitis C infection

While one in eleven HIV-infected people in the UK have hepatitis C,[4] in the countries of southern and eastern Europe and elsewhere in the world where a significant proportion of HIV-positive people have acquired HIV through sharing injecting equipment, hepatitis C infection is extremely common.

In the USA about one-in-five people with HIV is co-infected with hepatitis C,[5] in Italy and Spain one in two,[6] and in Russia up to 80%.[7] Some of these people may have had hepatitis C for decades and are starting to develop severe liver disease.

Hepatitis C is also one of the most significant causes of mortality and of poor health in people with HIV. A study from Denmark in 2006[8] estimated that a person diagnosed with HIV at the age of 25 and on HIV treatment could expect to enjoy 39 more years of life. In a person diagnosed with both HIV and hepatitis C that life expectancy was halved to 20 years. People with hepatitis C are more likely to be injecting drug users and have other health risks, but some of the higher death rate may be due to far higher rates of hepatitis-related liver disease.

Given that only about half of HIV and hepatitis C co-infected people respond positively to the current standard regimen of pegylated interferon and ribavirin, and fewer than a third of those infected with the harder-to-treat genotype 1 and 4 subtypes, there are a lot of people out there in urgent need of new approaches to hepatitis C treatment.

Luis Mendão, a Director of the European AIDS Treatment Group, is 51 and from Portugal. He suffers from the fluid accumulation, tiredness, diabetes and clotting disorders characteristic of cirrhosis – a condition in which the liver barely manages to keep performing its vital functions. He was diagnosed with HIV in 1996, with a low CD4 count, and with hepatitis C in 1998, though he had probably had both viruses for a long time.

"There was no record of my ever having had a hepatitis C test, but I kept having toxic hepatitis, so I insisted on one," he says.

His experience of hepatitis C treatment was pretty disastrous. He had had an undetectable HIV viral load for seven years and a CD4 count of 950 when he decided to try pegylated interferon and ribavirin in 2003.

"I lasted three months. The hepatitis C treatment barely made an impression on the virus but my HIV viral load jumped to half a million and my CD4s crashed to 60 in two months." He developed new AIDS-related illnesses and was only able to go back to full-time work this year.

New drugs

The good news is that there is a huge research programme underway looking at new treatments for hepatitis C and more than 50 candidate drugs are under study in human trials.

Firstly, companies are looking at new versions of interferon, like *Albuferon*, a slow-release formulation that may only need to be injected once a month. But though this may be more convenient for the patient, it does not appear to achieve higher rates of sustained viral response (SVR). An SVR is the goal of hepatitis C treatment: it means there has been no reappearance of hepatitis C by the sixth month after the end of treatment, and is essentially a cure.

The challenge, therefore, is to develop hepatitis C drugs of new classes. Initially, and for the foreseeable future, these new drugs would not replace interferon. The reason for this is that most of the hepatitis C drugs in development work like HIV drugs: they prevent the virus replicating but do not clear it. This means that if they are stopped the virus will reappear, and if too few are taken they will cause resistance. In contrast, interferon creates a stronger immune response to hepatitis C. So far there have been a couple of animal experiments in which an SVR was achieved without interferon, using only oral drugs, but clinical application is probably ten to 15 years away.[9]

Like HIV therapy, the new hepatitis C drugs come in a number of classes. The two classes under the most scrutiny are the protease inhibitors and the polymerase inhibitors. The latter are the equivalent of reverse transcriptase inhibitors in HIV treatment. Many other classes are under investigation. Most of them stop viral replication as described but some have different modes of action.[10]

The ones furthest along in development are the **protease inhibitors**. Positive results have come from clinical studies of two drugs, Schering-Plough's boceprevir and Vertex Pharmaceuticals' telaprevir. In several different trials, these drugs were added to pegylated interferon and

ribavirin and given to HIV-negative patients with genotype 1 of hepatitis C. In both cases an increased proportion of patients (about 65% instead of 45%) achieved an SVR.[11,12]

Perhaps just as importantly, these rates of SVR were achieved in half the length of time of normal therapy – 24 weeks instead of 48, which is a significant improvement for anyone trying to put up with often taxing side-effects of interferon and ribavirin. Even more promisingly, one of the three telaprevir trials targeted patients who had failed previous pegylated interferon and ribavirin therapy and achieved SVR rates of 50%, compared with 14% in those taking a placebo – an unprecedented result in a population that has already experienced interferon therapy failure.[13]

Next in line are the **nucleoside polymerase inhibitors (NPIs).** These appear to be very potent drugs, achieving large reductions in viral load, and active across a number of different varieties of hepatitis C. The first large phase 2 clinical trial of an NPI, Roche's R7128, was announced in April.

Alongside these are the **non-nucleoside polymerase inhibitors.** These have a less potent effect on hepatitis C and are only active against specific subtypes, but they seem to cause fewer side-effects. The vanguard drug in this class is Gilead's GS9190, currently in a phase 2 trial. (Phase 2 trials typically involve several hundred subjects and try to find out the optimum dose, establish the frequency of side-effects, and so on. They lead on to phase 3 trials, which may involve thousands of patients and establish the actual efficacy of a drug in a clinical population.)

A number of other antiviral classes are in early-stage development, including the **NS5a inhibitors**, which work against a component of the hepatitis C virus whose function is uncertain.

There are a number of **non-antiviral** drugs too. Some of these are improved formulations of interferon like *Albuferon*[14] and *Locteron*[15] that require less frequent dosing. Others are versions of ribavirin which aim to be less toxic, like taribavirin, though a trial of this drug last year found it had relatively few advantages.[16]

Hepatitis C...produces a viral load about 100 times higher than HIV, has a much greater genetic variability, and an even higher propensity to develop drug resistance. This variability is a major stumbling block for hepatitis C drug development.

Many more classes of drugs are in development. Some, as interferon does, work on the machinery of the human cell which hepatitis C subverts in order to replicate itself, rather than the virus. These are potentially exciting drugs because they are less likely to cause resistance than antivirals and may be the best candidates eventually to replace interferon.

Results from early studies of two drugs from a class called **cyclophilin inhibitors**, which stop cells making new hepatitis C viruses, were presented this April. Importantly, one of the drugs, Debio 025, produced significant viral load drops when given to people with HIV and hepatitis C co-infection for whom the standard pegylated interferon and ribavirin regimen had previously failed,[17] though it was still only effective when combined with these other two drugs.

Then there are a few wild cards like **nitazoxanide.** This is an antibiotic that was in trials for the AIDS-defining gut illness cryptosporidiosis. It was serendipitously found to have activity against hepatitis C infection – no one yet knows why. In one trial the efficacy of pegylated interferon and ribavirin therapy was increased from 50 to 80% in HIV-negative patients when they were given one to three months of nitazoxanide before starting therapy.[18]

This is by no means a complete list. Further off, in pre-clinical development, are drugs of many other classes: TLR agonists, micro-RNA agents, A3AR agonists, anti-phospholipids, more thiazolide antibiotics like nitazoxanide, pancaspase inhibitors, glicosidase inhibitors ... whatever the challenges, it cannot be said that hepatitis C is not receiving enough attention from the scientific community.

When looking at the exciting new developments in hepatitis C treatment, however, we should be guided by caution. Two particular considerations come to mind.

The resistance problem

The first is that hepatitis C replicates furiously and makes numerous mistakes while doing so. This means it produces a viral load about 100 times higher than HIV, has a much greater genetic variability than HIV and accordingly an even higher propensity to develop drug resistance.

This variability is a major stumbling block for hepatitis C drug development. It means that some of the new drugs only work against one genotype or even one sub-genotype of hepatitis C. It also means the new drugs absolutely cannot be taken alone[19] – and they must be tested and developed together.

At the hepatitis C co-infection meeting in Lisbon, Alan Perelson of Los Alamos Laboratory in the USA said that in the billion viruses one would find in any untreated person with hepatitis C, one would expect to find not just every possible mutation (change) the virus is capable of producing in its genetic make-up, but every possible combination of two changes.[20]

That means, if you were relying on antiviral drugs alone, you would need at least four drugs, if each of them stopped working after just one viral mutation. In the recent telaprevir study, 95% of the patients whose hepatitis C viral load

became detectable again, either during or after therapy, developed drug resistance, and Perelson said that the time it takes for resistant virus to predominate in patients taking telaprevir as the only therapy – or any similar drug – would be two to three days.

If you need to study the effect of combining two experimental drugs, this poses problems. Firstly, pharmaceutical companies need to co-operate and share commercial secrets, which takes time and negotiation. And the regulatory authorities that license drugs do not like the idea of two experimental drugs being combined in one trial, both because it muddies the data (it's difficult to establish the relative contribution of each drug), and because of the increased risk of side-effects.

Nonetheless, a number of double studies are underway or proposed. Furthest along is Roche, a company with several hepatitis C drugs in its portfolio, which is studying a combination of its nucleoside polymerase inhibitor R7128 with a protease inhibitor called R7227. Giving both these drugs for two weeks to 57 HIV-negative patients has produced large drops in viral load and no acute side-effects.

Another solution to make the drug burden better for HIV and hepatitis C co-infected people would be a drug that works against both viruses. This has greatly simplified therapy for chronic hepatitis B co-infection, because the HIV drugs tenofovir, 3TC and FTC also work against hepatitis B. This year Roche and its biotech collaborators Rigel Pharmaceuticals and Medivir announced the discovery of two drugs called RO-0622 and RO-9187 that worked against both hepatitis C and HIV.[21] These are very early test-tube studies but we now know that a single regimen for both infections is not inconceivable.

Drug interactions and side-effects

The second consideration especially concerns patients with HIV – drug interactions.

"HIV and hepatitis C protease drugs don't work in the same way, so you'll need to take two protease inhibitors," says Dr Janice Main of St Mary's Hospital in west London. "But they do affect the liver the same way. So drug developers are very nervous about co-infected people taking handfuls of drugs that may interact."

The result is that studies in co-infected people have hardly begun. Anger and concern among activists led to the Sitges Declaration, an agreement signed in 2007 by companies, regulators and community representatives that urged that co-infected people be included in hepatitis C drug trials.

Spanish activist Joan Tallada was one of the architects of this resolution. "The first clinical trial in co-infected people is about to start," he says. This will test if boceprevir strengthens the response to pegylated interferon and ribavirin.

There is some disagreement about who should enter trials, with some activists wanting patients who have run out of options entered into trials to save lives, while others urge that the less complex patients who are likely to do better should enter trials first because the results will be clearer.

Side-effects will certainly be a concern, as the new hepatitis C drugs are by no means free of them. Boceprevir, like ribavirin, may cause anaemia and in its phase 2 trial 50% of patients on both drugs developed anaemia despite discretionary use of the anti-anaemia drug erythropoietin.[22] Telaprevir also causes mild anaemia but its main side-effect is a rash, which was sufficiently unpleasant to nearly double the proportion of patients who discontinued the trial compared with those taking a placebo.[23]

The dilemma of resistance was also exemplified in the boceprevir and telaprevir trials. Patients who fail to respond to treatment in such trials may develop resistance, and may therefore fail to benefit from better drugs of the same class in future. We have seen this before in HIV and need to avoid it again.

How can we avoid the problem of resistance? In the boceprevir trial, patients were started on a 'lead-in' dose of pegylated interferon and ribavirin for four weeks before starting boceprevir. The idea is to suppress hepatitis C replication far enough to make the development of resistance less likely.

In the telaprevir trials, on the other hand, all three drugs were given from the start to maximise the suppression of hepatitis C, but in the second half of the study telaprevir was withdrawn. Various yardsticks – such as the proportion of patients with undetectable viral load at weeks four and twelve – are being used in trials to predict who will eventually achieve an SVR so that those unlikely to benefit from the new regimen under trial can be taken off before they develop resistance.

Conclusion

A few years ago it may have looked to both researchers and patients as if a new era of convenient, tolerable hepatitis C antiviral therapy was just round the corner. We know, however, from previous experiences such as the struggle to develop an HIV vaccine that such assumptions are often disappointed. Hepatitis C is a complex, slippery virus that may take a lot of pinning down. And unlike HIV, where the introduction of new drugs has led to far better health outcomes for patients who fail first-line regimens, no treatments will be available in the near future for people who have failed the current drugs, and who desperately need other options.

Nonetheless, it's important to emphasise that hepatitis C, unlike HIV, is in some cases already curable. We just have to make the cure work for more people, with the more difficult-to-treat genotypes. Significant progress is already being made and we may only be a year or two away from drugs that can strengthen, shorten and sweeten the course of hepatitis C therapy. Watch this space. ■

news in brief

India

Delhi decriminalises gay sex

In a historic ruling, the Delhi High Court has decriminalised 'sodomy' and freed one in six of the world's gay men and men who have sex with men from the threat of prosecution.

The court ruled that section 377 of the Indian Penal Code, which has been used to criminalise gay sex, was unconstitutional when applied to sex between consenting adults. The law was also used to prosecute offences such as child sex abuse and bestiality, and the ruling clarifies that the law only applies to sex where one party cannot legally give consent.

The ruling applies to the whole of India unless it is struck down by the Indian Supreme Court. Vikram Doctor, the founder of India's biggest gay website www.gaybombay.org said: "We are confident that judges, lawyers and police officers across the country will understand and follow the Delhi High Court's lead."

In its judgement, the Delhi High Court ruled: "The criminalisation of homosexuality condemns in perpetuity a sizable section of society and forces them to live their lives in the shadow of harassment, exploitation, humiliation, cruel and degrading treatment... Section 377... grossly violates their right to privacy and liberty embodied in Article 21" [of the Indian constitution].

An important aspect of the ruling is that similarly worded clauses exist in the laws of many other ex-British colonies, and this ruling will help to strengthen other legal challenges.

Vikram Doctor commented: "Because the law no longer treats homosexuals as criminals it will make it easier for us to reach them for HIV/AIDS work."

HIV testing

Nearly half of new GP patients accept routine HIV test

In a pilot study,[1] 45% of patients registering with a large inner-London GP practice agreed to have a routine rapid HIV test as part of their initial health check. One patient tested positive and was later confirmed to have HIV at their local sexual health clinic.

It is estimated that about 30% of the estimated 77,000 people with HIV in the UK are undiagnosed. This is of concern because it has been estimated that anything from between a quarter[2] to half[3] of all new HIV infections originate with undiagnosed people and that people who only come to medical attention when they present with AIDS are at very high risk of death in the first few months.[4]

In a recent editorial, *The Lancet* described the failure to diagnose more people with HIV as "appalling".[5]

In the pilot study, a rapid HIV test performed by the practice nurse was offered to all 85 patients aged between 18 and 55 registering at the GP practice between December 2007 and March 2008. Of these, 38 (45%) agreed to have a test and, in interviews, the majority of those who agreed said that it was the routine nature of the test that persuaded them to do it. The 85 patients came from 34 different countries, and black African and Caribbean patients were significantly more likely to take a test.

Most participants were positive about the programme. One Nigerian man commented that: "If you go to a GUM clinic you will be stigmatised, but with a GP no-one will know you've had a test." However a minority of patients were worried that: "It's so quick – it could be a real shock," or felt that the test was "intrusive".

The investigators conclude that "Our study shows that the offer of rapid HIV tests is potentially acceptable to patients and staff in primary care."

HIV treatment

Drug could 'wake up' and destroy HIV infected cells

In test-tube experiments, Italian researchers have managed to selectively stimulate and then destroy previously dormant HIV-infected immune cells using a combination of two drugs.[1]

The experiment, by Dr Andrea Savarino and colleagues from Italy's Istituto Superiore di Sanità, is the latest to use an idea that has been dubbed "shock and kill". In this technique, quiescent HIV-infected cells are first genetically 'woken up' by one chemical so that they start to produce HIV and then selectively destroyed by another one. If every HIV-infected cell in the body could be enticed out of hiding and destroyed, this would amount to a cure of HIV infection.

HIV infection is lifelong because it can exist inside a reservoir of long-lived immune cells that are not actively dividing or producing virus and are therefore invisible to the immune system. During periods when such cells are active, they can be seen by the immune system, but they also recharge this reservoir.

Savarino and colleagues first used a drug called a class 1 histone deacetylase (HDAC) inhibitor to waken up cells. They then added a drug called buthionine sulphoximine which depleted cells of the vital antioxidant glutathione, making them more likely to self-destruct. The HIV-infected cells in the test tube died out while the non-infected cells stayed intact.

Dr Savarino commented that such molecular weapons "in combination with antiretroviral therapies, could hopefully allow people living with HIV/AIDS to get rid of the virus". However, he warned that cells may use many different ways of lying dormant and this specific technique might only work against certain ones.

Previous experiments using valproic acid, another HDAC inhibitor, found that activity in the test tube did not translate into reservoir depletion in humans.[2,3]

TB treatment

Drug shows promise against resistant TB

A new drug for multidrug-resistant TB (MDR-TB) is safe and effective, a study in the *New England Journal of Medicine* (NEJM) reports.[1]

In a small South African study of 47 people, TMC207, when added to a standard five-drug regimen for MDR-TB, made it twelve times more likely that people achieved a negative TB culture eight weeks after the start of treatment. The trial is ongoing and final results are expected next year.

The proportion of people with a negative culture at eight weeks was 48% for patients taking TMC207 and 9% for patients only taking the standard regimen.

MDR-TB is defined as TB resistant to at least isoniazid and rifampicin, the two most potent of the four drugs usually used to treat non-resistant TB. Globally, about 2% of people with TB, and 5% of people with TB and HIV, have MDR-TB.

TMC207 is the first TB drug with a new mode of action to be developed in over 40 years. The new drug produced nausea in a quarter of patients compared with fewer than one-in-20 patients on placebo. In an accompanying editorial the NEJM said that available safety data "urgently need to be expanded".[2] It predicted that initially TMC207 would only be used for MDR-TB, as it will probably interact negatively with rifampicin.

TMC207's developers, Tibotec, later announced that they had signed a royalty-free deal with the Global Alliance for TB Drug Development to take the drug forward into large trials.

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usa travel ban to depart at last

It has been a long time in coming and there have been many false dawns, but it really does look as if the ban on people with HIV entering the United States is coming to an end, says *Gus Cairns.*

Barring an unexpected challenge from the US Congress, the removal of HIV from the list of "communicable diseases of public health significance" should happen by the end of this year, and this should mean that people with HIV will be free not only to travel to, but apply to work and settle in, the USA.

The Office of Management and Budget (OMB) for the US Department of Health and Human Services (DHHS) issued a "Notice of Proposed Rulemaking" on 30 June containing a set of proposals to remove HIV from the list of diseases and delete references to it in public health and immigration regulations.

The initial regulations banning people with HIV were enacted by the DHHS in 1987. They were in the form of guidance to the US Immigration and Naturalisation Service (INS) that HIV should be among the list of diseases of public health significance, but the INS's application of the law was inconsistent as there was no consensus that HIV fell into this category.

In 1993, however, a measure called the Nichols Amendment, sponsored by the notoriously anti-gay Senator Jesse Helms, specifically required HIV to be classed as a disease of public health significance.

The exact wording of the law was that "*Any alien . . . who is determined... to have a communicable disease of public health significance,* ***which shall include infection with the etiologic agent for acquired immune deficiency syndrome***" was ineligible to receive a visa and ineligible to be admitted to the United States.

President Bill Clinton opposed the measure but – as it was packaged alongside a number of other public health measures he supported – felt he had to sign it into law or the whole bill would have fallen.

The law did not mean that there was no chance of people with HIV entering the USA. But it did mean that they had to plead to be a special case. Entry to the USA requires a visa in most cases. However, citizens of 35 countries, including the UK, are entitled to short-term entry of up to 90 days under the so-called Visa Waiver Program. Until recently this has involved filling in a green form, prior to travel or on the aircraft, which requires the applicant to declare, among other things, that they do not have a communicable disease.

HIV-positive people were officially denied this route. Instead they had to apply for a proper entry visa, be denied it and then, in a tortuous legal process, be issued with a different kind of visa waiver. This would involve a frequently lengthy and in-person interview at the US embassy, and a stamp in their passport which stated "Denied entry to the USA", accompanied by a waiver saying that as a special concession they would be let in after all.

The impact of this stamp was often worse when travellers subsequently sought entry to other countries as it flagged up that they had had a problem with the US authorities, but not what the problem was.

This meant that HIV-positive people faced a dilemma when deciding whether to travel to the USA. They could simply refuse to go. They could lie on their visa waiver form and risk denial of entry or deportation if their HIV medication was found in their possession. Or they could risk a stamp that labelled them a travel pariah.

In 2003, a study from the Lawson Unit HIV Outpatients' Clinic in Brighton[1] looked at whether HIV-positive patients travelling to the USA were able to obtain a visa waiver and/or medical insurance, and to establish how they managed their HIV medications when travelling.

The most striking finding was that fear about US entry restrictions affected the way people took their HIV drugs. Of the 83 respondents on antiretrovirals who travelled to the USA, 10 (12.5%) stopped their drugs for the duration of their stay. Five chose to take treatment interruptions prior to leaving for the States, and five tried to mail their drugs to the USA in advance but had problems doing so, either finding that they never arrived or were stopped at customs.

Of the three people who had short- or long-term problems due to their

treatment interruption, one subsequently developed NNRTI drug resistance (Y188L). "This was a highly drug-experienced patient who has subsequently run out of options now that he has also developed resistance to T-20," noted Dr Duncan Churchill, co-author of the study, at the time. The other two developed intermittent fevers, joint pain, headaches and diarrhoea, symptomatic of a viral load rebound, while in the USA.

The first crack in the US position came in February 2006, when the US government issued a blanket waiver allowing HIV-positive people to enter the USA to attend the Gay Games in Chicago. Importantly, the visa was issued on a special form instead of being placed permanently in passports.

In July 2008, George Bush signed into law a provision that removed the Nichols Amendment. However it did not remove the ban, but simply returned the power to refuse entry from Congress to the DHHS which was then asked to "initiate a rulemaking that would propose a categorical waiver for HIV-positive people seeking to enter the United States on short-term visas".

The new notice sets in motion a far more profound change than this. If enacted in full, it will not simply remove the categorical ban on people with HIV entering the USA, it will also enable people with HIV to apply for long-term residency and work visas. In its proposed rulemaking, the DHHS states that:

"*While HIV infection is a serious health condition, it does not represent a communicable disease that is a significant threat for introduction, transmission, and spread to the U.S. population through casual contact.*"

If this declaration remains unaltered, it means that not only will the USA be removed from the ten countries – out of the world's 200 – that automatically ban people with HIV on entry, and another ten or so who deport people instantly if they are discovered to have HIV, but also from the larger list of 50 or so countries that prevent people with HIV from seeking residency or work status. It would join the 99 countries that see HIV as irrelevant to a person's right to enter.

Barring unlikely opposition from Congress, the lifting of the ban, it is hoped, will take place by the end of 2009. There is a period for public comment till mid-August, after which DHHS may make adjustments to its proposal and send it back to the OMB for budgetary approval. After this there will be another review period which could either be 30 or 90 days. This means that the earliest it is likely to come into law would be mid-autumn.

Removing the ban would enable the International AIDS Society to start planning for the 19th International AIDS Conference in 2012 to take place in Washington, DC, as it said it would if the ban were to be lifted. The last International AIDS Conference to be held in the USA took place in San Francisco in 1990.

Lifting the ban will focus attention on the other countries that deny entry to people with HIV or deport them. Some, like Saudi Arabia and Sudan, are not known for their enlightened policies. But the list also includes some important world destinations such as Singapore and South Korea.

Two former banners, China and Russia, are in the process of changing their own regulations. China is currently conducting a consultation on lifting the ban. Russia, meanwhile, no longer denies entry but still requires an HIV test and an almost certain ban for people wishing to stay more than 90 days. Fifty countries including Canada, Australia, Israel, Poland and Malaysia still ban long-stayers.

It will also have important personal consequences for a lot of people wishing to travel or live in the USA. One is German national Heidemarie Kremer who moved to the USA to be with her HIV-negative husband.

She says: "I am currently in deportation procedures due to HIV. Fortunately, I was able to postpone the deportation hearing I had today. I guess this will now save my children and me from deportation." ■

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☐ We would like to be able to let you know about other resources and updates of this directory. Please tick this box if you would **not** like to be added to the mailing list.

☐ We occasionally undertake funding campaigns to help support our work. Please tick this box if you would **not** like to receive information about them.

For more information telephone NAM on 020 7840 0050.

thanks to our funders

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

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NAM would also like to acknowledge the generous support of its individual donors.

donate to nam

Every year NAM provides information resources, like *hiv treatment update*, to thousands of people living with HIV, completely free of charge. To do this we really do rely on the generosity of people like you to help us continue our vital work. You can make a difference today. Please make a donation by visiting **www.aidsmap.com/donate** or by ringing us on **020 7840 0050**.

where to find out more about hiv

- **Find out more about HIV treatment:**
  NAM's factsheets, booklets, directories and website keep you up to date about key topics, and are designed to help you make your healthcare and HIV treatment decisions. Contact NAM to find out more and order your copies.
- **www.aidsmap.com**
  Visit our website for the latest news about HIV & AIDS, a fully searchable treatments database and a complete list of sexual health clinics in the UK.
- **THT Direct**
  Offers information and advice to anyone infected, affected or concerned about issues relating to HIV and sexual health.
  0845 1221 200
  Mon-Fri, 10am-10pm Sat-Sun, 12pm-6pm
- **i-Base Treatment Phoneline**
  An HIV treatment phoneline, where you can discuss your issues with a treatment advocate.
  0808 8006 013
  Mon-Wed, 12pm-4pm