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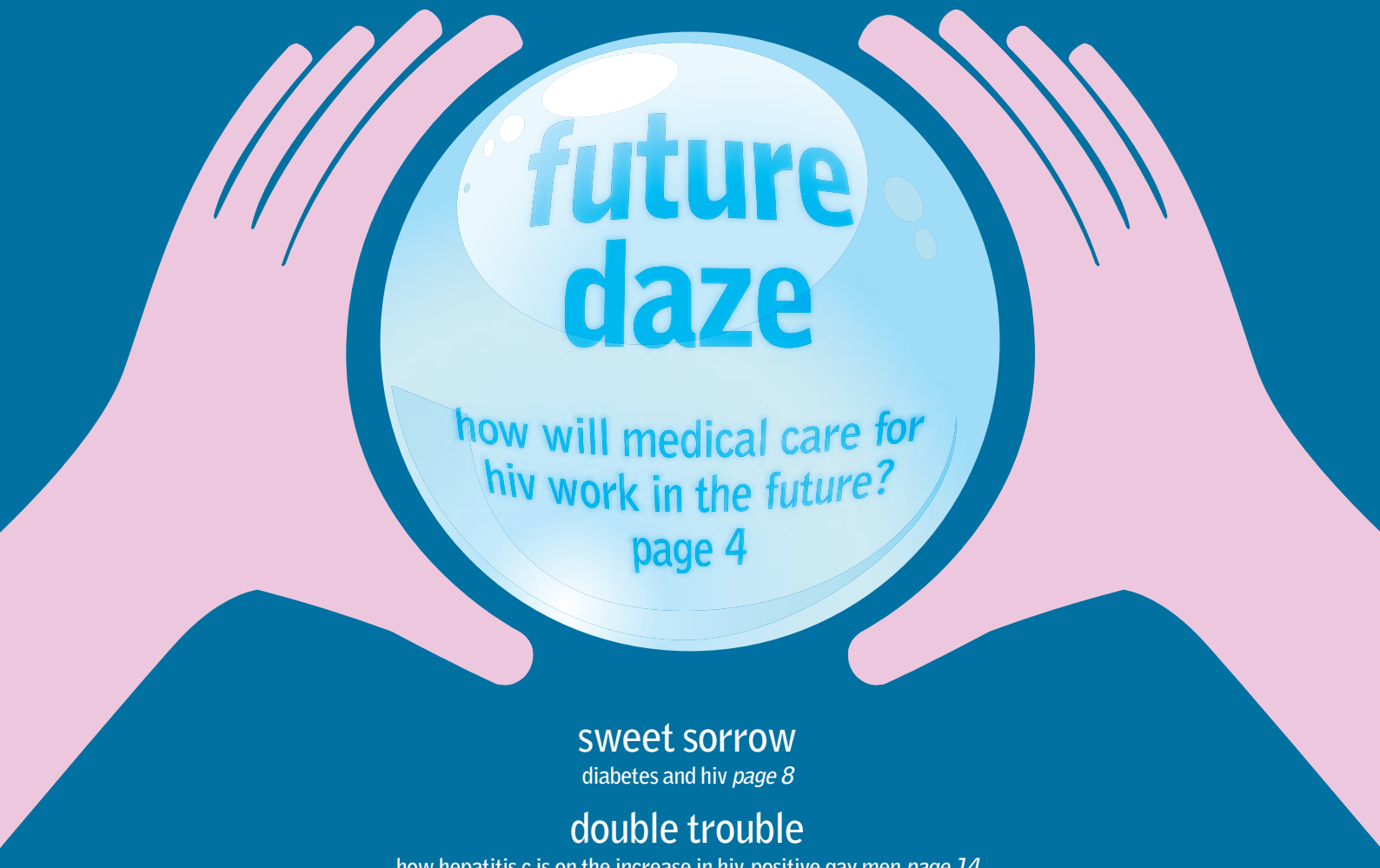
hiv treatment update



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in this issue

Gus Cairns

Firstly, well, hello everyone. This month I take over from Edwin J Bernard as editor of *HIV Treatment Update* and I'm immensely looking forward to being at the helm of a newsletter I've read virtually since its first issue in 1992.

It's almost a cliché to say how much things have changed since then. To give you some historical perspective, there was a piece in that first HTU on the then-novel idea of using more than one HIV drug at a time.

There was also a piece on a new class of drugs called TIBO derivatives. That research line eventually resulted in a drug, etravirine, which was licensed last year. This month saw the first hint of success in a trial of an idea that has been around for even longer – a microbicide against HIV (see *Microbicides and the trouble with good news* opposite).

Some of you may know of me already, and this isn't a personal blog, but as a way of introducing this issue, one curious fact is that in accepting the editorial baton from Edwin, an older guy is taking over from a younger one (I'm 52 and he's 45 – I've just checked if he minds me saying that).

People with HIV now have the questionable luxury of developing the diseases of old age. There were a lot of studies of the impact of things like heart disease and dementia on people with HIV at the recent Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal, which NAM attended and reported on; some of that is in the *News in brief* section in this issue (see page 12) and I intend to cover what to expect as we get older in forthcoming issues.

This issue we look at a common and often age-related condition we haven't looked at in detail before – diabetes (see *Sweet sorrow* on page 8).

Unlike the exotic zoo of opportunistic infections that comprise AIDS, these are conditions people with HIV share with the population in general. It's possible that your HIV specialist isn't the best person to monitor them and in some cases your GP might do a better job. Or might they? And do you want them to know you have HIV? We explore the likely expansion of the role of primary care in HIV treatment in *Future daze* on page 4. How people get their care is as important as what the care is and we'll be returning in future issues to the NHS as it changes.

One more thing before I sign off. The diabetes piece sprang from a patient who emailed NAM wanting to let us know about his treatment story, and I would like to feature many more patient voices in *HTU*. If you have an issue you think worth airing, email info@nam.org.uk.

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upfront

Microbicides and the trouble with good news

by Gus Cairns

As we report in this issue, the 16th Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal featured the first ever non-negative result in a trial of a microbicide.

We say 'non-negative' rather than 'positive' because the 30% reduction in HIV infections seen in women who used the microbicide PRO2000 wasn't 'statistically significant'. It could have been a chance finding.

Despite this, the first thing to do is to celebrate. The idea for a microbicide has been around since 1990 when the South African epidemiologist Zena Stein published a piece called "HIV Prevention: The Need for Methods Women Can Use", pointing out that whether to use a condom was essentially the man's choice and women were often in a position where it wasn't possible to "choose safer sex".

Nearly 20 years later we at last have a hint that microbicides could work. This is a testament to the scientific belief and persistence that has got us this far – often driven by feisty advocates, mostly women and gay men – and the success of some of the most difficult research studies ever attempted in the history of medicine.

But what about statistical significance? This is a complex area and misunderstanding it was the reason why the headlines about the trial ranged from the confident "Vaginal gel effective in preventing HIV infection" (*Hindu Times*) to the disappointed "Microbicide Gel Falls Short of Showing Significant Efficacy" (*Doctor's Guide*).

Statistical significance is an arbitrary limit that scientists impose on the data they get from experiments, in order to decide what means something and what doesn't. Odd things can happen that are purely due to chance: if you toss a coin for long enough, eventually you'll get 20 heads turning up in a row.

Researchers work out the probability that the findings from their study are due to chance. If there's a less than one-in-20 chance that the result is random, then that is 'statistically significant'; if there's a more than one-in-20 chance, it is 'not significant'. In the microbicide study, the probability that the 30% reduction in HIV infection seen was not real was one-in-ten, so it was not significant...

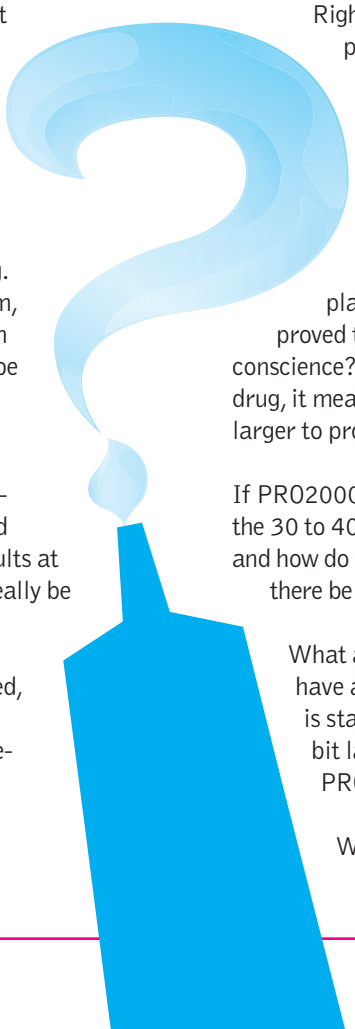
...which, to put it another way, means that there was a 90% chance that it was real.

Still, you may say, 30% isn't very impressive. Would you trust a condom that was 30% effective? PRO2000 is, nonetheless, promising rather than disappointing because:

- For some people, 30% may be better than nothing. As Professor Abdool Karim, the principal investigator in this study said, "This may be a niche product for women with no other choices."
- If the still ongoing three-times-bigger UK-supported study produces similar results at the end of this year, we'll really be on to something.
- The more gel women used, the more protected they were. In women with above-average adherence to PRO2000, HIV infections were reduced by 44%.

It may work even better than this. You can't ethically test a prevention product without offering women the best in existing methods, and condoms and safer sex advice were freely available. A woman who is a regular condom user has already protected herself against nearly nine in ten possible HIV infections. Adding a microbicide won't reduce her risk much further.

But for a woman who doesn't use condoms at all, a microbicide may add a considerable amount of protection. In the group of women who used condoms rarely but PRO2000 frequently, it stopped 68% of infections. This could be closer to its 'real' efficacy, but we don't as yet have the figures to support that conclusion with confidence.



Right now the result of the trial poses more questions than answers.

Do we start using PRO2000 as the comparator drug in forthcoming microbicide trials because it will be unethical to use an inert placebo? Or can we say "It wasn't proved to work" with a clear conscience? If we use it as the comparator drug, it means new studies will have to be larger to prove an effect.

If PRO2000's efficacy is confirmed to be in the 30 to 40% region, is it worth developing and how do we ethically market it? Will there be pressure to market it anyway?

What about gay men and others who have anal sex? A rectal safety study is starting this year, but isn't that a bit late if they decide to license PRO2000?

Would **you** use it?

It's five years from now. The number of people living with HIV in the UK is well over 100,000, and you're one of the new ones.

You were tested as part of a routine sexually transmitted infection (STI) check-up at your local polyclinic, a sort of 'health mall' with a late-evening sexual health shop. You had blood tests done to check whether you have any HIV drug resistance and hepatitis – oh, and your CD4s too, though these days nearly everyone starts treatment straight away. It turns out you don't need any special meds, so they prescribe one of the once-a-day combination pills for HIV. After three initial, monthly appointments to check the medication is working, you settle down into quarterly visits with the practice nurse after work. You don't even have to go to the chemist for your pills as they are home-delivered. You've been told a hospital consultant has reviewed your notes but you don't see any reason why you should ever have to see her personally. You have better things to do than worry about HIV.

Could having HIV really be that trouble-free? Well, maybe for some. Here's an alternative scenario…

You're diagnosed with HIV by your GP when an HIV test was, unbeknownst to you, included among a battery of tests they are paid to do (it was in the small print on the consent form). You develop depression, which he assumes is a reaction to your diagnosis. You're sure it's a side-effect of your pills, and you don't have adherence explained to you adequately so you only take them intermittently. Your last blood sample went astray and it takes six months before you find out your HIV is resistant to two classes of drugs. You go to the local hospital for your second anti-HIV regimen. This is prescribed after a delay that was caused, you later find out, by your GP and the hospital arguing about who pays for it. The new regimen sends your cholesterol sky-high. Your GP prescribes the wrong statin, which reacts with your HIV drugs, causing severe muscle and kidney problems. You come off HIV medication altogether, your CD4s plunge and you spend so much time shuttling between appointments you have to stop work.

Neither of these scenarios is likely to be the typical patient story. But they have one thing in common, namely the increasing proportion of care that will be undertaken by your local GP or their equivalent – primary care. How can we ensure that the first scenario is closer to reality?

A Sexual Revolution

"At some point in the next few years, the current model of HIV care is going to become unsustainable," says Paul Ward, Deputy Chief Executive of the Terrence Higgins Trust. "We just can't go on having more people with HIV cared for by the same number of specialists. There is no money to expand clinic capacity."

Ward is talking about a policy document called A Sexual Revolution,[1] which was issued last summer. In this, the Terrence Higgins Trust maps out a model of care for sexually transmitted infections (STIs) and HIV that aims to avoid specialist hospital-based services cracking under the strain while not transferring too much of HIV care to GP practices without HIV experience.

As well as a number of proposals for improving STI services and HIV testing, the document envisages "a major shift to deliver HIV clinical care for the 'well person with HIV' out of hospital" (but overseen by HIV specialists), thereby ensuring the existing HIV specialist capacity is used sparingly and is available for those who need it most.

Amongst other measures, it proposes:

- the average "well person with HIV" would see specialist nurses in polyclinics, larger general practices and other community health settings for their health care;
- the setting up of 'e-consultation clinics' via the internet for people to get specialist help when they need it;
- home delivery of HIV treatment, home-administered CD4 testing and "as the technology allows", home viral load testing;
- an integration of HIV health care with HIV social care. This would mean that, for instance, social workers and benefits advisers would work alongside nurses dealing with HIV, drink and drugs problems, mental health and sexual health in a local centre.

At some point in the next few years, the current model of HIV care is going to become unsustainable. We just can't go on having more people with HIV cared for by the same number of specialists.
Paul Ward, Terrence Higgins Trust

What patients think

Many patients feel that hospital-based HIV services are already moving this way. "My hospital-based clinic in London already looks something like the model service of the future that *A Sexual Revolution* describes," comments Matt Williams on the UK Community Advisory Board (UK-CAB) patients' web forum.[2]

Brian West comments that, in Scotland, a significant part of his health care is already GP-delivered, but emphasises that measures had to be put firmly in place to avoid the 'scenario two' possibility.

"The key here is to ensure access to new drugs and technologies for people who need them, when they need them. I have no problem at all with the transfer of care when everything is going OK. But how quickly will I get access to a specialist when things get difficult? And will my specialist's advice be the last word? We know that GPs can and have been used as both the gatekeepers to the hospital system, and as agents of medical rationing."

The doctors write...

Many HIV doctors share his concerns. The British HIV Association (BHIVA), the HIV clinicians' organisation, has concerns that while the THT paper makes some sensible recommendations, it was issued without consultation with HIV consultants. Although it recommends "fast track referral arrangements with specialist hospital HIV services", HIV clinicians were not asked about what these should look like and how they should work.

BHIVA issued its own *Standards for HIV Clinical Care* in 2007.[3] At that time, however, they assumed that the majority of HIV care would remain within, and be paid for by, hospitals. The *Standards* only devoted 70 words of a 12,000-word document to general practice and primary care. BHIVA is now writing an annexe to the *Standards* on extending the role of primary and community care in HIV, to be presented later this spring.

This paper emphasises that all providers of HIV care should have clear and fast referral arrangements with hospital-

based services to cover complex cases, people with treatment failure, people who are diagnosed late with AIDS, and people with co-infections like hepatitis.

BHIVA says that because HIV medications still have potential for interaction with many other drugs, only specialists should prescribe them, regardless of where patients are seen. This, plus the potential for wasteful duplication of tests and rows about who should provide particular treatments, requires top-quality communication between GP and hospital services. This raises questions of confidentiality, and also means that it won't necessarily cost less to get GPs to provide HIV care.

The paper acknowledges that primary and community care could have benefits for people with HIV such as ease of attendance and GPs' greater experience with certain issues such as heart disease and diabetes. They acknowledge that the subset of patients with complex psychosocial issues might well be better served by an effective local GP practice with good links to community mental health, addiction and social care services.

Models of care

Dr Ian Williams, an HIV consultant at London's Mortimer Market Centre (MMC) HIV clinic, comments that there are already models to choose from.

I have no problem at all with the transfer of care when everything is going OK. But how quickly will I get access to a specialist when things get difficult? And will my specialist's advice be the last word?
Brian West, UK Community Advisory Board

"If you're going to improve patient health care, you need to do it in a collaborative way," he says. "There are many different possible care models and shared care arrangements already for people with long-term health conditions. We don't want to reinvent the wheel here."

The BHIVA paper suggests three models:

- Specialist outreach clinics in large health centres and polyclinics;
- Training local GPs to provide non-HIV related care, with tight liaison with the local HIV clinic;
- Providing primary care trust-funded GP services within an HIV clinic.

Some preliminary research on HIV patients' preference for these options has already been done. Chris Sandford runs the patient group at the MMC clinic.

"In our survey 58% of patients preferred the idea of an in-clinic GP, even though 77% had 'come out' as HIV positive to their own GP," he says.

What commissioners think

Whatever solution is adopted locally, a higher proportion of care needs will be met, and paid for, by primary care trusts in the future, not least because this is the declared policy of the Department of Health (DH).

In January 2009 the DH issued a document called 'Supporting People with Long Term Conditions: Commissioning Personalised Care Planning'.[4] It says that every one of the one-in-four people in the UK who has a chronic health condition should have a personalised care plan, a collaborative agreement between the NHS and the patient on how to handle their case. The paper doesn't mention HIV specifically, but makes it clear that care planning for patients with 'less complex needs' should be undertaken at the GP level, and a lot of HIV patients will fall into that category.

Stuart Rowe is the interim director of the London HIV Consortium, the group of NHS commissioners who collectively purchase and allocate HIV services in London.

"There is a possibility that parts of HIV might be reclassified as long-term care rather than specialist care," he says. "If this does happen then the HIV Consortium would continue to commission the same range of services as it does now, though the possibility of providing non-complex long-term care in a primary care setting may become an option in future." The consortium is writing a draft service specification for the commissioning of such a combination of care, which will be out for consultation this summer.

Where does that leave the hospital specialist? Good practice apart, the most problematic issue in any move from hospital to primary care can be boiled down to four words: "Who'll be in charge?" This is not just about professional territory-marking. As the BHIVA document points out, doctors are legally responsible for the consequences of their prescriptions.

Ian Williams says that imposes a responsibility on doctors to draw up a good model for future HIV care. "If we don't," he says, "they'll commission a bad one."

The ageing population

Margaret Johnson is Ian Williams' predecessor as Chair at BHIVA.

She says that, whatever happens, it will still be important that each patient should have, somewhere at the top of the pyramid, an HIV specialist who should be the ultimate supervisor of their care.

"There's lots of evidence to show that being linked into expert care produces better outcomes. If, say, I was a diabetic I would want to know that even if I was stable I was linked to an expert in a regional centre who could make decisions if something went wrong."

She agrees that patients with poor adherence and lifestyle issues might be better served by local care. "I agree 100% with Paul Ward. He's throwing down a gauntlet and saying 'things need to be better for the kind of patient who isn't well served by the big clinics'."

But she's concerned about what will happen as people with HIV age, especially as ageing with HIV may look very different to ageing in the general population. "HIV patients are likely to get things like chronic obstructive pulmonary disease (such as emphysema) faster. When they get co-morbid conditions like that, the best place to link them to is the hospital where they get HIV services. What has worked well in HIV is the lack of compulsion about where you go."

Paul Ward says we shouldn't presume anything. "I don't think we've collectively yet got an obvious model for the care of people with HIV as they get older. For the majority of the older public the GP is the primary care giver, why not HIV? Over the next 10 to 15 years we will acquire knowledge about how to handle HIV, and of course the specialists will have a role to play. What we need to do is change the model of service delivery beneath the specialist so that community services and GPs take on a greater responsibility for day-to-day care, thereby ensuring there is enough HIV specialist capacity to go round all people with HIV."

The GP's role

HIV and GPs don't always fit well together. A pilot programme in one London borough offered local GPs an extra payment if they performed the common blood tests for patients with HIV such as CD4 counts.

"All that happened," says a local HIV consultant, "is that the patients still came to the hospital clinic for their blood tests, and we got pestered by GPs wanting the results so they could record them and get their extra money." It's important to weed out any perverse incentives like this from an integrated HIV care service.

One way of doing this is for GPs to get together and plan a joint service. One such programme is running in Brighton, where Jonathan Wastie is a local GP.

"A number of local GP practices in 2005 made a bid to the local commissioners to run what's called a Locally Enhanced Service (LES) to look after the general practice needs of HIV-positive people," he says.

"We don't do CD4s, viral loads or prescribe antiretrovirals (ARVs). What we do is offer a cardiovascular risk screen, treat high cholesterol and blood pressure, treat depression, provide safer sex advice, cervical smears and contraception, and annual flu jabs. We ask HIV-positive people round for an annual health MoT, and do annual mental health reviews with a psychology-trained general practice nurse, treating any depression. There's a pretty good pick-up rate. Patients can choose to have different levels of interaction with us; some just want a flu jab."

How do they handle the confidentiality issue? "We never mention HIV in letters. We'll say things like "As a patient at the Claude Nicole Clinic, you're entitled to an annual general health check". In my experience most patients are pleased we're taking an interest. We are bound by the same confidentiality rules as an HIV clinic; you can't disclose anything without the patient's permission."

One of the accusations levelled at GPs and primary care in general is that GPs have regarded HIV as a forbiddingly complex area.

"I think it's about confidence in both directions. Patients need to feel confident in using their GPs, and GPs *were* unconfident in the days when HIV patients went to hospital clinics for all their needs. To join the LES, GPs have to do a two-day course which covers HIV testing, confidentiality and disclosure, recognising HIV-related symptoms, and the different parts of the body affected."

Stuart Rowe maintains that NHS chiefs will never force HIV patients to go to GPs and wouldn't want to.

"You can't replicate the critical mass required to deliver tertiary specialist services in a general practice. But if patients *want* to visit their local GP for routine visits rather than travel into the major centres, then we need to put in a system that will allow that to happen." ■

sweet sorrow:
diabetes and hiv

HTU spoke to a patient, George, about the complexities of managing diabetes and HIV.

George's introduction to diabetes was rougher than most.

"In 2000 I started taking a combination therapy regime containing ddI. I was fine for four weeks then started suffering agonising abdominal pain. I stopped my HIV drugs and two days later the pain went away. But by that time the damage had been done."

Blood tests made it clear he'd had pancreatitis (inflammation of the pancreas). As he subsequently found, the ddI in his regimen had turned someone with a family history of diabetes into someone with the condition, and a quite severe form at that. It's resulted in a long struggle to find an HIV therapy that doesn't make things worse.

What is diabetes?

The pancreas, a long organ sitting in the middle of your body, performs two vital tasks. Most of its cells secrete enzymes such as amylase that help to digest food, especially fats.

Scattered amongst these cells are different cells that secrete several important hormones into the bloodstream. One of these is insulin, a hormone that performs a vital role in regulating the amount of sugar in the blood.

Lack of insulin or a lack of ability to respond to it cause, respectively, type 1 and type 2 diabetes.

Diabetes is common, and getting more so. About 17 million people worldwide suffer from it or 2.8% of the global population.[1] This figure is expected to double by 2030, largely due to the adoption of western diets by people in Asia and Africa. Tony Wierzbicki (see over) estimates that 5 to 10% of the population of the UK is at risk of developing diabetes.

Type 1 diabetes is caused by a partial or complete loss of the insulin-producing cells. Its most common cause is when the body's own immune system stops recognising the insulin-producing cells and starts killing them off. As there is no or little insulin circulating in the body its treatment usually requires insulin injections.

Type 2 diabetes is caused when the body stops being able to respond to its own insulin. In its mild stages this is called insulin resistance. Exactly how this happens is still unclear,[2] but type 2 diabetes is strongly associated with obesity and especially with accumulation of fat inside the abdomen ('lipohypertrophy' or visceral adipose tissue – VAT).[3]

A third type of diabetes exists caused by toxic damage to the pancreas. Although the most common cause is heavy alcohol use, it can also be caused by some drugs, including HIV drugs, which is what happened to George.

The definition of diabetes is the same in all cases: more than 7 mmols/l (millimols per litre) of glucose in the blood eight to twelve hours after food. The symptoms are the same too. People may first notice fatigue, weakness and muscle aches, then – as glucose levels rise – the production of large amounts of dilute urine and a corresponding thirst. A life-threatening condition called ketoacidosis which involves an acute worsening of these symptoms can occur, but often the symptoms of type 2 diabetes are initially mild or absent – so easy to ignore.

They should not be ignored, however, as high glucose levels produce chronic symptoms that affect many parts of the body. Glucose damages the cells in many organs. This causes poor wound healing, and damage to blood vessels in the eye can cause blindness. Nerves can be damaged too, leading to the pain and numbness of neuropathy. Overworked kidneys can fail and muscles deprived of energy at the right time can waste, including the heart muscles.

Diabetes is the most common cause of amputations, blindness and kidney failure in the developed world.[4] Tony Wierzbicki says: "Eighty per cent of people with type 2 diabetes will get a heart attack or stroke compared with 35% of the general population".

George received differing reactions to his pancreatitis from his HIV doctor and a diabetologist he subsequently saw. "My HIV doctor said 'Your amylase levels were up 25% and we normally only start worrying if they're up 50%'. The diabetologist said 'It's a good job you stopped the ddI when you did or you'd have ended up dead'."

He feels HIV physicians are overly focused on HIV and have not given his diabetes and its treatment sufficient attention. Repeated requests to be referred to a diabetes specialist have been met with delay and reluctance. "I found out about the diabetic team at my former hospital via my GP," he says.

The pancreatitis had scared George off from taking HIV drugs and he went on a treatment break for 18 months. His diabetes at that time was manageable with diet and exercise. When he restarted, at a CD4 count of 150, he went on AZT/3TC (*Combivir*) and nevirapine – chosen with diabetes in mind[5] – and did well for another 18 months. Then unfortunately in 2003 he became resistant to the nevirapine.

After some chopping and changing he was eventually kept on the Combivir and switched to a boosted protease inhibitor – indinavir plus ritonavir. His glucose levels suddenly doubled to 12 mmols/l. Indinavir, as it turns out, may have been exactly the wrong thing to put him on.

It feels like the early days of awareness of increased heart attack risk in people with HIV. Diabetes takes longer to develop, so we're only just beginning to recognise that it may be a big problem in the coming years.
Tony Wierzbicki, St Thomas's Hospital

HIV drugs and diabetes

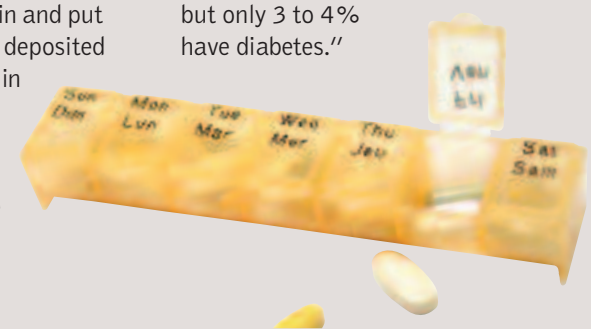
"Insulin resistance appears to be triggered by some antiretrovirals," says Dr Graeme Moyle of London's Chelsea and Westminster Hospital. "Initially we suspected protease inhibitors (PIs),[6] but found an association last year with d4T and AZT and, rather unexpectedly, not with PIs.[7] I suspect that of the PIs only indinavir and full-dose ritonavir are implicated in insulin resistance and they damaged the reputation of the class.[8]

"HIV may itself cause diabetes. We haven't much direct data, though one US study[9] did find more diabetes in patients with HIV in California than age- and sex-matched people in the general population. So when people start HIV therapy any diabetic effects of therapy may be masked by an improvement of the effects of HIV."[10]

Another phenomenon, Moyle comments, is so-called 're-feeding'. This was first noticed in World War II prisoners and later in anorexics.[11] "If thin people start eating again and put fat on quickly, it doesn't get deposited evenly. They accumulate fat in the abdomen (visceral adipose tissue or VAT) instead of under the skin. And VAT is exactly what we see in some people on HIV treatment."

In addition, he adds, as patients with managed HIV both age, and come more to resemble the typical population, he's seeing more obesity in patients with HIV and therefore more insulin resistance and type 2 diabetes. "It's partly caused by demographic shift. Africans and South Asians have a greater genetic susceptibility to diabetes."[12]

Moyle refers all his patients with raised blood glucose to the diabetologist. "I may put them on diabetic treatment straight away if they have very high glucose levels, but a diabetologist can manage them better. They can decide to put them on medications like blood-pressure drugs to help their kidneys, do proper retinal exams for blindness, and can draw up tailor-made diets. After that I'd recommend they get managed by their GP, because GPs see a lot of diabetics. About 30% of my patients have raised blood lipids [fats] and so I'm experienced at managing them, but only 3 to 4% have diabetes."



"I felt really unwell," continues George. "With high glucose, you feel kind of speedy. I got very bad tempered and emotional, alternated between feeling hyper and exhausted."

When George's glucose levels shot up, he went back to his HIV doctor. "She said, 'It can't be the meds, it must be your diet,' and didn't propose any diabetes medications. I don't understand this; they give you statins for cholesterol as soon as your levels go over the limit."

In desperation he stopped his HIV meds again. "I had 250 CD4 cells and felt I had some time." He stayed off for four years, till June 2008.

"By this time my CD4s were down to 29. I went to a different hospital and basically blackmailed them. I said: 'I'm not going back on my meds till I speak to someone from the diabetic team'. I did see the diabetologist there; that's the very first time someone actually told me my diabetes was due to drug-induced pancreatitis."

George was put on the anti-diabetes drug metformin and, for his HIV, was put on a novel regimen of *Truvada* (which combines FTC and tenofovir), the protease inhibitor atazanavir and the integrase inhibitor raltegravir.

"Unfortunately my sugar levels went up the wall again, this time to 18 mmols/l." Oddly enough, it seems to have been not the atazanavir but the new integrase inhibitor that was to blame. "We stopped the raltegravir and so far things seem to be OK. I'm virally undetectable and my CD4s have gone up 50, though they're a bit worried that's on the low side."

George says: "If someone had listened to me in the first place, some of this could have been avoided. But I've had to fight for the right treatment because there's this attitude among HIV doctors these days that 'one size fits all' when it comes to HIV drugs. At the hospital, the HIV doctors don't know enough about diabetes and the diabeticians don't know enough about HIV – even though they're one floor away from each other."

● **For more information on diabetes, see www.aidsmap.com/cms1032578.aspx**

Diabetes treatments

Tony Wierzbicki is a lipid and cardiovascular risk specialist at St Thomas's Hospital in London. He expects to see a lot more type 2 diabetes in people with HIV in the future.

"When people had AIDS-defining illnesses they lost a lot of weight, which protected them. But we're now seeing increasing levels of diabetes. We see ddI-induced pancreatitis like George's and d4T-caused insulin resistance, but anyone with VAT is pushed up the diabetes risk scale."

The best form of diabetes treatment is prevention. "You can reduce your risk of type 2 diabetes by two-thirds if you work on being fit and not being overweight, and 50% of people with early diabetes can reverse it back to a pre-diabetic stage.[13, 14] Smoking contributes to insulin resistance,[15] so give that up. Dietary trials have usually been about reducing saturated fat, but the modern diet problem is now too much sugar rather than too much fat.

"Unfortunately, however, there is a point of no return after which type 2 diabetes will continue to progress. After this point we can use drugs to control glucose levels. These can help control the condition for decades before we have to start using insulin.

"The drugs either reduce the amount of glucose released into the blood (e.g. metformin), boost insulin production (e.g. gliclazide) or make body cells more sensitive to insulin (e.g. rosiglitazone).[16]

"Metformin is the number one strategy for management. Unfortunately it causes both diarrhoea and constipation.[17] It also induces fat loss, so if you have lipoatrophy it could make that look worse."

The second-line therapies are the sulphonylurea drugs like gliclazide. These boost insulin production but can cause weight gain and hypoglycaemia ('hypos', a condition familiar to insulin users, in which blood sugar falls drastically, causing fatigue, anxiety and eventually coma).

Dr Wierzbicki says, "Both metformin and sulphonylureas have long-term evidence of benefit."[18]

The third-line drugs are the thiazolidinedione (TZD) or 'glitazone' drugs, which induce the sluggish cells to be more sensitive to insulin. However, they may be associated with weight gain, fluid retention, possibly heart disease, and fractures.[19]

"There are a few new classes. One class is the DPP-4 antagonists which also increase insulin production.[20] The first one, sitagliptin, was licensed in 2007.[21] They reduce blood glucose in diabetics but only a handful of people with HIV have tried them. And there's a new injectable agent called exenatide,[22] which amplifies the action of any remaining insulin you have. Unfortunately it can also cause pancreatitis. I've only seen ten cases of it being tried in people with HIV."

Generally, Wierzbicki comments, "It feels like the early days of awareness of increased heart attack risk in people with HIV. Diabetes takes longer to develop, so we're only just beginning to recognise that diabetes may be a big problem in the coming years.

"That is slowly changing, but the average diabetologist knows nothing about HIV and I think HIV doctors need better training to try and manage patients with pre-diabetes in their units. We have a cardiovascular risk clinic in the HIV clinic here now, as do some of the other large London clinics. With complex cases, however, HIV clinicians will still have to know when to bail out and seek expert help."

news in brief

From the 16th Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal

side-effects

Abacavir and heart failure: stronger evidence

Two studies presented at Montreal strengthened the evidence that the nucleoside drug abacavir almost doubles the risk of heart attack. But they found that the risk does not increase much more with time spent on the drug and decreases after patients stop taking it. The studies also found risks which did increase over time associated with the protease inhibitors (PIs) lopinavir/ritonavir (*Kaletra*), indinavir (in one study) and fosamprenavir (in the other). It did not find any risk associated with tenofovir. The large D:A:D study[1] found tentative evidence that risk might increase with the length of time on abacavir, but this was not found in the other study[2] from the French National Health Research Institute.

A small, Irish, test-tube study[3] found tentative evidence to explain the link between abacavir and heart attack. It found that abacavir increases the tendency of blood to clot, but this evidence will need to be corroborated by a larger study.

hiv treatment

Start earlier, but how early?

Two studies presented at CROI agreed that starting treatment even earlier than the new guideline limit of 350 CD4 cells/mm^3 reduces the risk of death, but disagreed on how early it should be started. The large SMART study found three years ago that patients did better starting HIV treatment at CD4 counts up to 350 instead of waiting till they fell below 200, as guidelines at the time recommended. But scientists suspected that treatment at even higher CD4 counts would still be of benefit.

A US study[1] found that the risk of death was 60% greater in patients who started therapy at CD4 counts below 500 compared with ones who started at higher counts. But a UK study[2] found that the risk of death or AIDS was not reduced in patients who started much above the current guideline level of 350. These trials aren't directly comparable and don't give a final answer.

A large randomised controlled trial of 4000 patients called START is planned to begin soon, which will compare patients who start HIV therapy as soon as they are diagnosed with ones who wait until their CD4 count reaches 350.

new drugs

New boosters found

We may quite soon have other 'booster' drugs used to increase and sustain the levels of protease inhibitors (PIs) in the blood. In the late 1990s ritonavir (*Norvir* – also in *Kaletra*) was found to suppress the activity of a liver enzyme that clears drugs from the body. It meant that PIs could now be given in smaller doses once or twice daily and they became far more effective as a result.
But ritonavir has side-effects of its own including diarrhoea and raised cholesterol.

Two new booster drugs, Gilead's GS 9350[1] and Sequoia Pharmaceuticals' SPI-452[2], have now been found to boost the levels of other drugs at least as well as ritonavir, with fewer side-effects. Because they are not active against HIV themselves there is no chance of their causing resistance.

The companies seem to be moving ahead fast with development plans to co-formulate the new boosters with other drugs. Gilead has tested GS 9350 in a quadruple combination pill with elvitegravir and its licensed drugs tenofovir and FTC, while Sequoia intends to use SPI-452 to boost a new protease inhibitor called SPI-256.

new drugs

Immune therapy disappointment

Not all big, expensive drug studies produce positive results. One disappointment announced at CROI was the results from two studies of the immune-boosting chemical interleukin-2 (IL-2). This is a natural chemical made by the body that can also be synthesised artificially, which lengthens the life of CD4 cells and thus increases the CD4 count. It was hoped that the boost IL-2 gives to CD4 cells would result in fewer illnesses and deaths.

However the ESPRIT[1] and SILCAAT[2] trials, which started in 2002 and between them involved nearly 6000 patients, found that although IL-2 produced a rapid increase in CD4 cells, it did not result in fewer illnesses or deaths. The ESPRIT trial patients taking IL-2 had on average CD4 counts 150 cells/mm^3 higher and the SILCAAT patients 67 cells/mm^3 higher than those not taking it. But at the end of seven years, the risk of dying or developing AIDS was exactly the same in both trials regardless of whether patients took IL-2. IL-2 patients also had higher rates of deep vein thrombosis, a dangerous condition which also affects long-haul air passengers.

SILCAAT researcher Yves Levy said: "I don't see any possible benefit in continuing with IL-2 studies." However the immune-booster saga is not over, as he is researching a hopefully less toxic one called IL-7.

news in brief

From the 16th Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal

hiv prevention

Undetectable in blood is *not* undetectable in semen

Two studies presented at CROI have found that, in a minority of patients who achieve undetectable viral loads in their blood, HIV is still sporadically detectable in semen – sometimes at levels likely to be infectious. These studies provide evidence against the statement by the Swiss Federal AIDS Commission which in January 2008 said that people with undetectable viral loads do not transmit HIV.

In one study[1] 14% of men who had started HIV treatment had detectable viral loads in semen. In most the virus appeared sporadically but in one it was there all the time. The patients with the highest viral load – 16,000 – had semen that was shown in a laboratory experiment to be infectious. Even patients who had had an undetectable viral load on HIV therapy for years sometimes shed HIV in their semen. A French study,[2] which used a different viral load test, found that nearly 5% of patients with undetectable blood results had HIV in their semen, though the highest viral load here was 1250.

hiv prevention

Promising microbicide results, at last

A large two-year trial[1] of a microbicide in over 3000 women has found that the substance, PRO2000, reduced the chances of women becoming infected with HIV by 30%. Microbicides are compounds that can be incorporated into gels, creams or devices to be used during or before sex to prevent HIV transmission.

The 30% reduction may not seem much. But the trial was the first one to give a positive result in the field, after years in which candidate microbicides were found to be ineffective or even harmful.

The 30% reduction might have been a chance result, and will need to be corroborated – another trial is due to report results at the end of this year. But it did show that the more consistently women used the gel the higher their level of protection.

Principal investigator Professor Salim Abdool Karim said: "We cannot reach the definitive conclusion that PRO2000 is a microbicide, but it is a promising candidate."

● Also see *Upfront*, page 3.

references to all articles [continues on page fifteen]

Microbicides and the trouble with good news [page three]

1 Abdool Karim S et al. *Safety and effectiveness of vaginal microbicides BufferGel and 0.5% PRO 2000/5 Gel for the prevention of HIV infection in women: results of the HPTN 035 trial* 16th Conference on Retroviruses and Opportunistic Infections, Montreal, abstract 48LB, 2009.

Future Daze: How will medical care for HIV work in the future? [page four]

1 See *www.tht.org.uk/informationresources/publications/?pubid=27351*
2 See *www.ukcab.net*
3 See *http://www.bhiva.org/files/file1001299.pdf*
4 See *www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_093354*

Sweet sorrow: diabetes and HIV [page eight]

1 See *www.who.int/diabetes/en/*
2 Grinspoon S et al. *Mechanisms and strategies for insulin resistance in acquired immune deficiency syndrome* Clin Infect Dis. 37, Suppl 2:S85-90, 2003.
3 See for instance Gabriely I et al. *Removal of visceral fat prevents insulin resistance and glucose intolerance of aging: an adipokine-mediated process?* Diabetes 51:2951-2958, 2002; Grunfeld C et al. *Association of upper trunk and visceral adipose tissue volume with insulin resistance in control and HIV-infected subjects in the FRAM study* JAIDS 46:283-290, 2007.
4 See for instance *www.nfb.org/Images/nfb/Publications/vod/vod215/vodwin0701.htm*
5 Domingo P et al. *Switching to nevirapine decreases insulin levels but does not improve subcutaneous adipocyte apotosis in patients with highly active antiretroviral therapy-associated lipodystrophy* Journal of Infectious Diseases 184:1197-1201, 2001.
6 Justman JE et al. *Protease inhibitor use and the incidence of diabetes mellitus in a large cohort of HIV-infected women* JAIDS 32: 298-302, 2003.
7 De Wit S et al. *Relationship between use of stavudine and diabetes mellitus* 8th International Congress on Drug Therapy in HIV Infection, Glasgow, abstract PL9.5, 2006
8 Schwartz J-M et al. *Indinavir increases glucose production in healthy HIV-negative men* AIDS, 18:1852-854, September 3, 2004.
9 Currier JS et al. *Diabetes mellitus in HIV-infected individuals* 9th Conference on Retroviruses and Opportunistic Infections Seattle, abstract 677, 2002.
10 Koeppe J and Kosmiski L *Apparent resolution of type 2 diabetes mellitus after initiation of potent antiretroviral therapy in a man from African with HIV infection* Clin infect Dis 42: e79-e81, 2006.
11 Zamboni M et al. *Body fat distribution before and after weight gain in anorexia nervosa* International Journal of Obesity 21: 33-36, 1997.
12 Chandalia M et al. *Ethnic differences in the frequency of ENPP1/PC1 121Q genetic variant in the Dallas Heart Study cohort* J Diabetes Complications. 21:143-8, 2007; Chowdhury TA. *Type 2 diabetes in people of South Asian origin: potential strategies for prevention* Br J Diabetes Vasc Dis 7:279-82, 2007.
13 Lindstrom J et al. *The Finnish Diabetes Prevention Study (DPS): Lifestyle intervention and 3-year results on diet and physical activity* Diabetes Care 26:3230-6, 2003.
14 Knowler WC et al. *Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin* N Engl J Med 346:393-403, 2002.
15 Eliasson B et al. *The insulin resistance syndrome in smokers is related to smoking habits* Arteriosclerosis and Thrombosis 14:1946-50, 1994.
16 Bolen S et al. *Systematic review: comparative effectiveness and safety of oral medications for type 2 diabetes mellitus* Ann Intern Med 147:386-99, 2007.
17 Mulligan K et al. *Effects of metformin and rosiglitazone in HIV-infected patients with hyperinsulinemia and elevated waist/hip ratio* AIDS 21(1):47-57, January 2, 2007.
18 Holman RR et al. *10-year follow-up of intensive glucose control in type 2 diabetes* and *Long-term follow-up after tight control of blood pressure in type 2 diabetes* N Engl J Med 359:1565-76 and 1577-89, 2008.
19 Singh S et al. *Long-term risk of cardiovascular events with rosiglitazone: a meta-analysis* JAMA 2298:1189-95, 2007.
20 Bailey CJ *Drugs on the horizon for diabesity* Current Diabetes Reports 5:353-9, 2005.
21 Aschner P Diabetes 55 (Suppl. 1): A462, 2006.
22 Buse JB et al. *Effects of exenatide (exendin-4) on glycemic control over 30 weeks in sulfonylurea-treated patients with type 2 diabetes* Diabetes Care 27:2628-35, 2004.

Double trouble – how hepatitis C is on the increase in HIV-positive gay men

Studies at CROI showed how hepatitis C is gaining ground says **Gus Cairns**

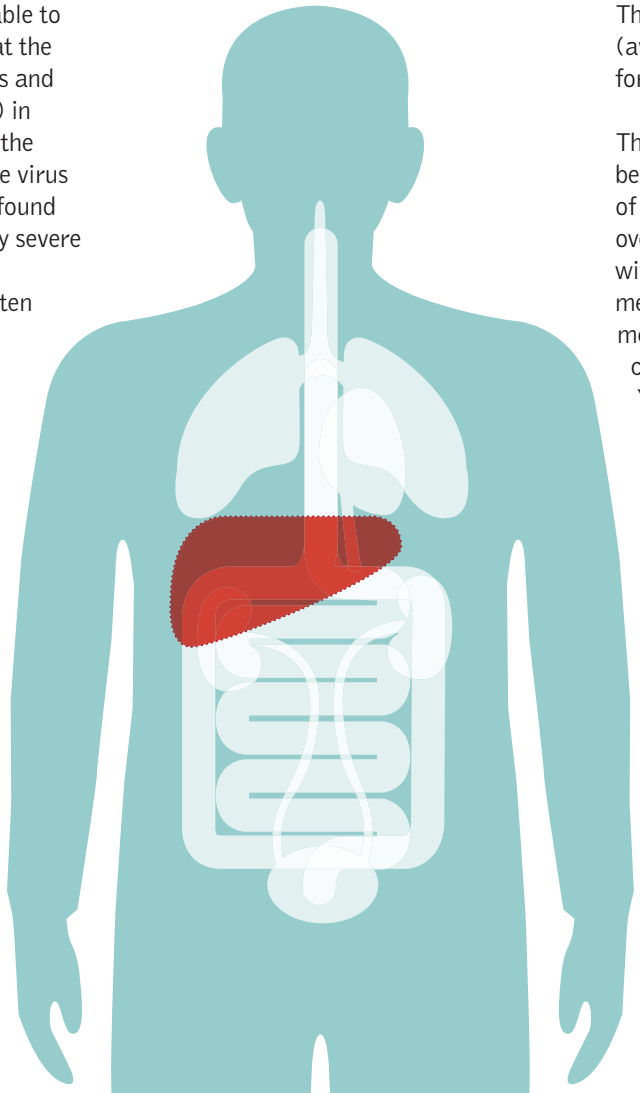
Last summer, an alarming study[1] presented at the International AIDS Conference in Mexico found that 20 out of a group of 157 HIV-positive gay men (18%) at a single clinic in Amsterdam had hepatitis C, a third of them with recent infection, and that hepatitis C prevalence was growing rapidly. In contrast, only two of 532 HIV-negative men (0.4%) had the virus – a similar proportion to heterosexual women.

At the time Kevin Fenton of the US Centers for Disease Control questioned the limited public health response to the outbreaks of hepatitis C in Europe and called for a greater sense of urgency.

We still don't fully understand why some HIV-positive men are so vulnerable to hepatitis C, but several posters at the 16th Conference on Retroviruses and Opportunistic Infections (CROI) in Montreal last month confirmed the existence of new epidemics of the virus among gay men with HIV. They found that it sometimes had potentially severe health consequences, although treatment, if taken, was more often than not successful if started early.

The UK may have a particular public health problem here. A study from New York compared behaviours in local and UK gay men who had been infected and found that on a whole range of indicators the UK men were taking more health risks.

Another study from Amsterdam[2] confirmed that hepatitis C infection among HIV-positive men is a recent and rapidly growing problem there. Although cases of recent infection were not as common as in the other Amsterdam patient group, they were increasing exponentially. There were two in 2003, one in 2004, nine in 2005, 12 in 2006, six in 2007 and 14 in the first eight months of 2008. That means that, by the end of 2008, one in every 66 HIV-positive gay men at the clinic might have become infected that year; 59% of patients, based on the timing of previous negative hepatitis C tests, had had it for less than a year. The doctors presume it must be being transmitted sexually because none of the patients had classic risk factors such as injecting drug use or medical exposure to infected blood.



One study[3] compared hepatitis C outbreaks in the UK and New York and looked at differences in the risk behaviours between 21 co-infected gay men in New York and 60 in the UK. The New York patients answered the same transmission risk survey that the UK patients had answered for a study in 2007.[4]

Soberingly, from a UK perspective, the majority of risk factors were a great deal higher on the European side of the Atlantic.

The New York patients were more likely to have ever injected drugs (24% versus 3%), and were more likely to have shared injection equipment (15% versus 1.7%): both 'classic' non-sexual risk factors.

The UK patients were somewhat younger (average 36 versus 40) and had had HIV for less time (3.7 versus eight years).

They also had the lion's share of risky behaviours. For instance, three-quarters of UK patients had been fisting 'tops' and over half of them 'bottoms' compared with a third and a quarter of New York men, respectively. Two-thirds of the UK men reported fisting in a group situation compared with one in eight New Yorkers, and the vast majority (94%) had had unprotected receptive anal sex in a group situation compared with three-quarters of New York men.

They were also much heavier users of non-injectable drugs. Eighty per cent of UK patients versus 24% of New Yorkers had used ketamine, 77% versus 38% had used cocaine, and 80% versus 38% had taken ecstasy. A third had used LSD compared with none of the Americans. The greater use of drugs in the UK was called a "notable finding" by the researchers. Having said this, one possible bias in the study is that, based as it was on a British questionnaire, they did not ask

about the use of methamphetamine (crystal meth), which is much more common in the USA.

The UK men also had higher rates of sexually transmitted infections (STIs) with 85% having had a lifetime history of STIs compared with 38% of the Americans.

Another study[5] was led by Daniel Fierer, who has previously documented alarmingly rapid liver fibrosis (scarring) in HIV-positive men who become infected with hepatitis C.[6] In a different group of 45 HIV-positive gay men with recent hepatitis C infection, 24 agreed to having a liver biopsy. One had stage 3 fibrosis; this is significant liver scarring and is one step short of cirrhosis. Most of the others had stage 2 fibrosis, indicating more-than-mild liver damage.

Four patients (13%) spontaneously cleared hepatitis C infection. The other 41 were offered pegylated interferon and ribavirin treatment. Of these 41, half chose to delay or refused treatment. Of the other 21, six are still awaiting treatment, and of the 15 treated eight achieved a sustained viral response, equivalent to a cure, while only two actually failed treatment. So at the very least, more than half of the patients who have undergone a course of treatment have found it successful.

Fierer also looked at risk factors by matching 21 men with similar hepatitis C-negative men. The only factors that reached significance were unprotected receptive anal sex, with or without ejaculation, unprotected oral sex with ejaculation, use of sex toys, and 'sex while high'. Fisting, often the biggest suspect when it comes to sexual hepatitis C transmission, was not a significant risk factor (as long as the men were telling the truth) but there was an interesting and unexpected difference between being a 'bottom', which was not a risk factor at all, and being a 'top', which was of borderline significance (one chance in 14 the association was not real). All we can say about this is that how hepatitis C is being transmitted remains unclear, and may differ between groups.

A French study[7] illustrated some of these similarities and differences. On one hand, the demographic and medical profile of the 45 New York and the 94 French patients was very similar. In both cases the men had an average age of 40, and 63 to 64% had an undetectable HIV viral load. French patients had had HIV for seven years and New York patients for ten.

But whereas in the other outbreaks documented at CROI, most of the patients had the genotype 1 variety of hepatitis C (the most common) half of the Paris patients whose full hepatitis C gene sequence was tested had the comparatively rare genotype 4. Furthermore, all of these 15 patients had almost identical viral strains, suggesting rapid transmission within a closely connected sexual network of gay men. Interestingly these viruses were very similar to genotype 4 viruses found in Paris in 2001-03, suggesting ongoing sexual transmission in the area.

The study also highlighted the suspected link between being infected with another sexually transmitted infection and acquiring hepatitis C. Twenty out of the 32 patients with full laboratory data had an STI diagnosed at the same time as hepatitis C, of whom 14 had syphilis. Only five patients cited fisting as a behaviour.

Next month, *HIV Treatment Update* will look at reasons for the spread of hepatitis C among HIV-positive gay men and will also look at treatment prospects. ■

references to all articles continues

News in brief [page sixteen]

All references below are to the sixteenth Conference on Retroviruses and Opportunistic Infections (CROI), Montreal. See www.retroconference.org.

Abacavir and heart failure: stronger evidence

1 Lundgren J et al. *Risk of myocardial infarction with exposure to specific ARV from the PI, NNRTI, and NRTI drug classes: the D:A:D study.* CROI, abstract 44LB, 2009.

2 Lang S et al. *Impact of specific NRTI and PI exposure on the risk of myocardial infarction: a case-control study nested within FHDH ANRS CO4.* CROI, abstract 43LB, 2009.

3 Satchell C et al. *A Case-control assessment of platelet function in HIV-1+ and HIV-1- individuals.* CROI, abstract 737, 2009.

Start earlier, but how early

1 Kitahata M et al. *Initiating rather than deferring HAART at a CD4+ count > 500 cells/mm³ is associated with improved survival.* CROI, abstract 71, 2009.

2 Sterne J for the When To Start Consortium. *When should HIV-infected patients initiate ART? Collaborative analysis of HIV cohort studies.* CROI, abstract 72, 2009.

New boosters found

1 Mathias A et al. *GS-9350: A pharmaco-enhancer without anti-HIV activity.* CROI, abstract 40, 2009.

2 Gulnik S et al. *Preclinical and early clinical evaluation of SPI-452, a new pharmacokinetic enhancer.* CROI, abstract 41, 2009.

Promising microbicide results, at last

1 Abdool Karim S et al. *Safety and effectiveness of vaginal microbicides BufferGel and 0.5% PRO 2000/5 Gel for the prevention of HIV infection in women: results of the HPTN 035 trial.* CROI, abstract 48LB, 2009.

Undetectable in blood is not undetectable in semen

1 Sheth P et al. *Persistent HIV RNA shedding in semen despite effective ART.* CROI, abstract 50, 2009.

2 Marcelin A-G et al. *Detection of HIV-1 RNA in seminal plasma samples from treated patients with undetectable HIV-1 RNA in blood plasma.* CROI, abstract 51, 2009.

Immune therapy disappointment

1 Losso M et al. *Effect of Interleukin-2 on clinical outcomes in patients with a CD4+ cell count of 300/mm³: primary results of the ESPRIT study.* CROI, abstract 90aLB, 2009.

2 Levy Y et al. *Effect of Interleukin-2 on clinical outcomes in patients with CD4+ cell count 50 to 299/mm³: primary results of the SILCAAT study.* CROI, abstract 90bLB, 2009.

Double trouble – how hepatitis C is on the increase in HIV-positive gay men [page 18]

1 Urbanus A *HCV is emerging as an STI among HIV-infected MSM: a threat to the MSM community?* XVII International AIDS Conference, Mexico City, abstract THPDC203, August 7 2008.

2 Van den Berk G et al. *Rapid rise of acute HCV cases among HIV-1-infected men who have sex with men, Amsterdam.* CROI, abstract 804, 2009.

3 Fishman S et al. *Age and risky behaviors of HIV-infected men who have sex with men with acute HCV infection in New York City are similar, but not identical, to those in a European outbreak.* CROI, abstract 801, 2009.

4 Danta M et al. *Recent epidemic of acute hepatitis C virus in HIV-positive men who have sex with men linked to high-risk sexual behaviours.* AIDS 21:983–991, 2007.

5 Fierer D et al. *Characterisation of an outbreak of acute HCV infection in HIV-infected men in New York City.* CROI, abstract 802, 2009.

6 Fierer D S et al. *Liver fibrosis during an outbreak of acute hepatitis C virus infection in HIV-infected men: a prospective cohort study.* J Infect Dis 198: 683 – 686, 2008.

7 Ghosn J et al. *Evidence for ongoing sexual transmission of hepatitis C (2006 to 2007) among HIV-1-infected men who have sex with men: France.* CROI, abstract 800, 2009.

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