

## My toxic world

Created 13 Oct 2005 - 1:08am

The beautiful beaches of Rio de Janeiro are hardly the place in which you'd imagine your thoughts would start turning to mortality, but for a while there not even the incredible, hunky, tanned Adonises strutting before me could distract me from thoughts of impending doom.

You see, on my first day at the International AIDS Society Conference on HIV Pathogenesis and Treatment in Rio I made the mistake of attending a drug company stand in the display area, where they were doing free tests to analyse your cardiac risk.

(It may be hard at first to understand why they would do this in a room where a good percentage of HIV-positive people on [lipid](#) [1] A fat.-elevating treatment regimens are strutting around, but there is method to this madness, as you will see.)

Without really thinking about the likely result, I stumped up for the test and was later given a sheet of results that stated: "Your risk of cardiovascular disease (CVD) over the next ten years is 35.9 percent." Not only that, but according to accompanying graphs, nothing I could do (reducing my total [cholesterol](#) [2] An essential component of cell membranes and nerve fibre insulation, cholesterol is important for the metabolism and transport of fatty acids and the production of hormones and Vitamin D. Cholesterol is manufactured by the liver, and is also present in certain foods. High blood cholesterol levels have been linked to heart disease and may be a side effect of some anti-HIV medications., increasing my HDL cholesterol, controlling my blood pressure or improving my [diabetes](#) [3] [Diabetes mellitus] A disorder in which sugars in the diet cannot be metabolised into energy due to a lack of the enzyme insulin. Late-onset diabetes mellitus may be a long-term side effect of some anti-HIV drugs. management) would take me out of the danger zone.

I was, according to the smiling nurse, a 'very high risk'. But, she said, if I were to switch to that company's product, my lipids would be likely to reduce considerably (although it still wouldn't get me out of the 'high risk' category).

So that was what this marketing exercise was all about!

## Learning about your disease

There is nothing like a reality check on your future prognosis to get you to pay attention when a session on 'Metabolic Disorders and Cardiovascular Disease' presents itself on the conference program, delivered by Australia's own Professor David Cooper (on behalf of one of its co-authors Dr Andrew Carr, also from Australia).

David proceeded to outline all the [antiretrovirals](#) [4] A medication or other substance which is active against retroviruses such as HIV. which put people at most risk of cardiovascular disease and metabolic complications (see table). Of course, yours truly is on a number of them: ritonavir and d4T to increase my cholesterol, triglycerides and [insulin resistance](#) [5] A diabetes-like condition in which, while adequate amounts of insulin are produced by the pancreas, the body does not respond normally to the action of insulin. In the wider community, insulin is related to obesity, while in HIV it may be related to lipodystrophy., and fosamprenavir to increase my cholesterol and [trigs](#) [6].

On top of this I'm told that the D:A:D study of 23,500 people with HIV around the world showed an increased risk of [heart attack](#) [7] A life-threatening emergency in which the blood supply to the heart is suddenly cut off, causing the heart muscle (myocardium) to die from lack of oxygen. if you were older, male and had a family history of heart disease (for all of which I qualify). For every year of being on combination treatment your risk of CVD increased to 26 percent over the first 4-6 years of treatment. The study also showed that people with diabetes were more than twice as likely to have a heart attack as those without the condition.

Before I started to get cross with my doctor for putting me on these supposedly risky combinations, I realised that there are reasons why I am limited to these drugs and that my current combinations, for all their toxicities, have given me a healthy CD4 count and almost undetectable [viral load](#) [8] A measurement of the quantity of HIV RNA in

the blood. Viral load blood test results are expressed as the number of copies (of HIV) per milliliter of blood plasma.

I was already on treatment for years before combination therapies came along, and was introduced to [HAART](#) [9] Highly Active AntiRetroviral Therapy ??? aggressive treatment of HIV infection using several different drugs together. in ways which we now know were far from perfect. Doctors didn't yet know what they do today about how to avoid or minimise the risk of developing drug resistance, so after many years on single or double nucleosides, I was put onto proteases and non-nucleosides as soon as they became available, and soon developed resistance to several of them. Many other people have similar stories.

Because of this, my current combination cannot do without that pesky, lipid-elevating, insulin-resistance-producing ritonavir booster.

My doctor is faced with a dilemma – deciding whether it's more important to keep the [virus](#) [10]A small infective organism which is incapable of reproducing outside a host cell. under control by using the most effective antiretrovirals for my circumstances, or limiting drugs (like d4T and ritonavir) which could increase my cardiovascular risk.

At least I guess the lipids and insulin resistance can be treated (with limited success) but nothing can replace effective control of the virus.

## What to do about it?

So what does Professor Cooper say we can do if we have high lipids and insulin resistance from HAART combinations? Switching off proteases is the number one strategy, although we know that many nucleosides and non-nucleosides also contribute to these problems so it may not be that simple.

Using a combination including abacavir is worth considering if there is no resistance to the drug, as it has been shown to reduce total cholesterol as well as increase HDL ('good' cholesterol) and possibly help insulin resistance.

Tenofovir is also a good option with less effect on cholesterol than d4T. Cutting out d4T and AZT generally produces a slow but significant improvement in limb mass although it doesn't improve the adiposity (central fat accumulation – distended stomach) or insulin resistance problems significantly.

Of the proteases, atazanavir is a good option with improvements noted in lipids and insulin resistance. Saquinavir may have a minimal effect on those areas as well although further studies are needed to demonstrate a long-term benefit. Those who are prepared to endure the injecting process can take solace that the entry inhibitor T-20 has not been seen to increase cholesterol, triglycerides or insulin resistance.

The first thing that should be tried with people with these problems should be changes to diet and lifestyle, and these should be continued even if drug regimens are changed or other therapies added.

The greatest reduction in cardiovascular and diabetes risk you can make is to give up smoking. The most recent HIV Futures survey found that 48.3 percent of HIV-positive people smoke. According to NSW Health, five years after quitting the risk of stroke returns to that of the general population, and after 15 years the rate of heart disease is similarly reduced.

There is also only limited success likely in reducing insulin resistance from diet and exercise but of course it should be tried before introducing new agents with their potential side effects.

There are a range of lipid-lowering medicines that we now have experience with in people with HIV. Most of these fall into two categories: fibrates (e.g. gemfibrozil) and statins (e.g. simvastatin, fluvastatin and lovastatin).

Fibrates are reasonably good at lowering triglycerides and, to a lesser extent, increasing HDL ('good') cholesterol. They don't do much to reduce LDL ('bad') cholesterol, however. Gemfibrozil has been tested in people with HIV with modest positive effect.

Statins are less effective than fibrates at lowering triglyceride levels, but are better at reducing LDL cholesterol. In

one trial, fluvastatin showed an 18% decrease in cholesterol by Week 4 (although no effect on triglycerides and HDL). Certain statins have been shown to interact with HIV medications (particularly simvastatin and lovastatin) and these should be avoided. For some reason statins seem to be generally less effective on people with HIV than in the general population.

A third option is to use fish oils such as maxEPA. These can have a positive effect but because they are relatively weak a high dosage is needed.

Metformin is the drug of choice to treat people with insulin resistance for those without advanced lipoatrophy. It is thought to also help reduce central fat accumulation and may help with lipids – as well as possibly helping with blood pressure if that is a problem. If its use is combined with exercise though, loss of subcutaneous fat has been observed in some people, David Cooper said. This is to be avoided and use of Metformin should be closely monitored in people with severe lipoatrophy as it may make it worse. Rosiglitazone is useful for those with insulin resistance although an earlier trial on people with HIV showed no improvement in lipoatrophy.

For various reasons, most of the above options have either been tried or ruled out by my doctor so there was little joy for me in this presentation. If anything it increased my respect for my treating doctor as I realised the complexities involved in deciding on each therapy for a treatment-experienced patient like me. Even the drugs you use to treat the side effects can have problems themselves, sometimes interacting with antiretrovirals. There seemed to be so many pros and cons for every option to be considered.

### **[Salvage](#) [11][salvage therapy] A treatment strategy for managing HIV in people who have developed resistance to existing therapies. Therapy**

There was some hope though in the presentation on salvage options by Steve Deeks from the USA. He spoke of the POWER 1 Study (which [recruited](#) [12]The act of signing up participants into a study. Generally this process involves evaluating a participant with respect to the eligibility criteria of the study and going through the informed consent process. from Australia and the US) that showed that 67 percent of patients on T-20 and the new protease inhibitor TMC-114 were undetectable at 24 weeks. Tipranavir was also effective with T-20 in trials if the patient's viral load had not increased more than fourfold. TMC-114 provoked considerable interest during the conference as the “next big thing” and it seemed to have a low side effect profile.

Deeks also presented on resistance with NRTIs. He argued that even when there was considerable resistance to drugs in this class, they still have residual antiviral activity. He spoke of a study where 16 patients had been on AZT and 3TC for many years and suddenly stopped the drugs. Despite all having resistance to both drugs, each patient's viral load increased rapidly when the drugs were stopped. Likewise, a 3TC monotherapy study showed continuing [clinical](#) [13]Pertaining to or founded on observation and treatment of participants, as distinguished from theoretical or basic science. benefit to patients even though they all had the 184V mutation which signifies resistance to 3TC.

The upshot of this is that, even when resistance is present, nucleoside drugs continue to show benefit and should remain the backbone of HAART combinations for people whose drugs are failing them – at least until new options become available.

While there are many delights to be had in travelling overseas (and believe me, Rio has many of them!) those of us with diabetes can find it challenging to control your diet when you are away from your normal routines. Brazil had many temptations – lots of fatty meats supplemented by pastries or sweets and not a lot of vegetables to be had anywhere. I couldn't bear to prick my finger every day for glucose tests, knowing full well I was misbehaving.

When I arrived home my diabetes doctor read me the riot act on seeing my glucose averages and I fear that it won't be long before my diabetes will only be controlled by regular insulin injections. Toxicity has become a daily issue for me, whether from my regular HAART-related gastric problems or insulin resistance.

You can only grin and bear it and hope something better comes along soon. Hopefully few readers will be dealing with the same headaches as me, some of which are hardly surprising given my 17 years of taking HIV [antivirals](#) [14]A medication or substance which is active against one or more viruses. May include anti-HIV drugs, but these are more accurately termed antiretrovirals. – although some of you will be. I cheered up a little when I read a recent NAPWA/ATPA publication on cardiovascular disease that points out that the DAD Study revealed an overall

mortality rate of two percent in the [cohort](#) [15] In epidemiology, a group of individuals with some characteristics in common. A cohort study is a special kind of clinical trial which looks at a treatment or treatment strategy in a cohort of people..

My risks obviously increase the older I get and the longer I stay on HAART, but it is worth reflecting on what my mortality would be if I didn't have those drugs in the first place! Maybe I will make it to that old aged people's home one day, fighting off senility, but hopefully not too soon.

### Antiretroviral drugs associated with lipid and glucose abnormalities

Protease inhibitors	Effect on lipid levels	Effect on glucose metabolism
Atazanavir (Reyataz)	No change	No change
Fosamprenavir (Telzir)	? Cholesterol & TG	No change
Indinavir (Crixivan)	? Cholesterol & TG	? insulin resistance
Lopinavir (Kaletra)	? Cholesterol & TG	? insulin resistance
Nelfinavir (Viracept)	? Cholesterol & TG ? HDL	No change
Ritonavir (Norvir)	? Cholesterol & TG	? insulin resistance
Saquinavir (Invirase)	No change	No change
Tipranavir (Aptivus)*	? Cholesterol & TG	Unknown
<a href="#">Nucleoside analogues</a> [16] A type of anti-HIV drug that works by inhibiting a stage of the HIV life cycle called reverse transcription.	Effect on lipid levels	Effect on glucose metabolism
Non-nucleosides work in a similar way, but are chemically different.		
ddl (didanosine, Videx)	Generally unknown; probable lipoatrophy effect when administered with d4T	? insulin resistance
d4T (stavudine, Zerit)	? total cholesterol & TG levels, especially in those with lipoatrophy	? insulin resistance
AZT (zidovudine, Retrovir)	Generally unknown; probable lipoatrophy effect	? insulin resistance in those with lipoatrophy
Non-nucleosides	Effect on lipid levels	Effect on glucose metabolism
Efavirenz (Stocrin)	? Cholesterol, HDL & TG	No change
Nevirapine (Viramune)	? HDL No change in TG	? No change

**Key:** ?, increases; ?, decreases; TG, triglycerides; HDL, high-density lipoprotein ('good' cholesterol)

Source: [clinicaloptions.com](http://clinicaloptions.com)

- [diabetes](#)
- [heart disease](#)
- [Lipodystrophy and lipoatrophy](#)
- [rosiglitazone](#)
- [treatment side effects](#)

#### Links:

- [1] <http://www.napwa.org.au/glossary/term/100>
- [2] <http://www.napwa.org.au/glossary/term/88>
- [3] <http://www.napwa.org.au/glossary/term/95>
- [4] <http://www.napwa.org.au/glossary/term/122>
- [5] <http://www.napwa.org.au/glossary/term/99>
- [6] <http://www.napwa.org.au/glossary/term/114>
- [7] <http://www.napwa.org.au/glossary/term/103>

[8] <http://www.napwa.org.au/glossary/term/416>

[9] <http://www.napwa.org.au/glossary/term/96>

[10] <http://www.napwa.org.au/glossary/term/125>

[11] <http://www.napwa.org.au/glossary/term/111>

[12] <http://www.napwa.org.au/glossary/term/489>

[13] <http://www.napwa.org.au/glossary/term/475>

[14] <http://www.napwa.org.au/glossary/term/123>

[15] <http://www.napwa.org.au/glossary/term/477>

[16] <http://www.napwa.org.au/glossary/term/104>