Looking into the eye of the tiger

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My concern started when an email with the monthly 'HIV Newsclips' arrived on my desktop. "People with diabetes [1][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. at greater risk of HIV-associated dementia," it said, and proceeded to outline research at the University of Hawaii where a higher percentage of positive people who had developed diabetes after taking HAART [2]Highly Active AntiRetroviral Therapy ??? aggressive treatment of HIV infection using several different drugs together. were showing signs of cognitive impairment.

My further investigation into risk factors for HIV-associated dementia (also known as AIDS Dementia Complex, or ADC) suggested that people who were older, had high cholesterol [3]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. levels and had a low nadir of T-cells in the past (below 200 for a reasonable period of time) were probably at greater risk of developing dementia later in life. Of course I fit into all categories — and with the exception of a low testosterone count, a prior injecting drug use experience or hepatitis C infection (other risk factors which I don't have) — I looked like a bit of a sitting duck.

Until I talked to Dr Edwina Wright, an infectious disease specialist at the Alfred Hospital in Melbourne who assured me that the rates of HIV-associated dementia had dropped significantly since the implementation of HAART in the mid-nineties and for many of those with it, dementia is treatable.

"HIV-related dementia is one of the few dementias which we have been able to treat relatively successfully in recent times," Wright said. "Of those people who had already developed HIV-related cognitive impairment when HAART arrived, about 50 percent responded to treatment with an ongoing improvement in cognition for up to a year or more."

Higher prevalence of cognitive impairment

Dr Wright said that before HAART came along, 15-20 percent of people with CD4 counts below 200 developed dementia — about 7 percent of that group per year. This has dropped to about 3 percent per year of those with T-cells less than 200.

Unfortunately, however, with more people living longer with HIV, there are more people living with a form of HIV-related cognitive impairment, sometimes even with relatively high T-cells, Wright told me. "Preliminary work suggests that these are people who experienced some form of 'cognitive insult' in the brain from HIV when they had low T-cells pre-HAART, although we are also realising from recent research that the current antivirals [4]A medication or substance which is active against one or more viruses. May include anti-HIV drugs, but these are more accurately termed antiretrovirals. are not completely controlling the virus [5]A small infective organism which is incapable of reproducing outside a host cell. in the brain in some people. The longer people live with HIV, the greater the chance that we will see some longer term cognitive deficits or damage becoming active."

The ' blood-brain barrier [6]A selective barrier (obstacle) between circulating blood and brain tissues that prevents damaging substances from reaching the brain. Certain compounds readily cross the blood-brain barrier; others are completely blocked.' prevents many antiretrovirals [7]A medication or other substance which is active against retroviruses such as HIV. from passing into the brain — but some drugs — including AZT, d4T, 3TC, nevirapine, efavirenz, abacavir and indinavir (boosted with ritonavir) — are able to get through this barrier.

For people who have kept their T-cells above 200 and who haven't developed any of the other associated risks (hepatitis C, injecting drug use, higher coronary [8]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. risk etc), HAART would seem to be very protective and to preserve cognition well. Even those who have previous AIDS-defining

illnesses and low T-cells still have a good chance of avoiding cognitive problems in the future particularly if they keep their viral load [9]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. low, but even for people who are unable to keep their T-cells high and viral load low, HIV-associated dementia is far from a foregone conclusion.

We will have to see whether the effects of ageing (itself involving a decrease in natural immunity) and the combined side effects of long-term use of HAART (diabetes, increased coronary disease risk and a greater chance of developing strokes) will increase the incidence of cognitive problems amongst the HIV+ population.

Research is currently being undertaken into HIV+ people with cognitive impairment (such as the Hawaii cohort [10]

For those who have been diagnosed with a form of cognitive impairment, Edwina Wright said that HAART can improve or preserve their brain function by choosing HAART combinations based on the drugs that do penetrate into the brain. In the future it is hoped more research will be done into the treatment and prevention of HIV-associated dementia, identifying the specific risk factors and enabling doctors to target those who need more intensive monitoring and treatment.

Other treatments which can be used include memantine (a drug licensed in the US for Alzheimer's disease), the antibiotic minocycline, and the antiinflammatories aspirin and ibuprofen to settle down some of the immune system's reactions to infection.
"For some people the cognitive impairment is reversed, for some it is stabilised and unfortunately for some, the virus is resistant [11]HIV which has mutated and is less susceptible to the effects of one or more anti-HIV drugs is said to be resistant. to treatment and their condition becomes worse and progresses to dementia," Wright explained.

Many causes of forgetfulness

" Many people with HIV fear they are developing dementia-like symptoms when they are just going through memory deficits which might come from tiredness, depression, use of sleeping tablets or opiates for pain control (such as for peripheral neuropathy), excessive alcohol or recreational drug use or the side effects of some antivirals such as efavirenz," said Wright.

"When I see a patient who is presenting with possible cognitive problems, I go through a battery of tests to exclude a range of other possibilities such as cryptococcal meningitis, syphilis, strokes, problems with thyroid function and other forms of dementia (such as Alzheimer's). The neuropsychologist will do tests to pick up on parts of the brain that HIV affects and look at whether people can still multi-task for instance, one of the early signs of brain damage."

Unlike Alzheimer's disease, which largely affects the outer cortex, HIV-associated dementia strikes deep inside the brain, Wright told PL. This leads to a loss of 'motor coordination', which can show up as slowed speech and difficulties with gait, and slowing of thinking which might mean difficulty following the plot of a movie or needing to use lists to remember daily tasks. There may be a marked change in personality, with affected people becoming withdrawn and apathetic, and there are sometimes psychiatric complications as well. Memory loss, usually the first sign of Alzheimer's onset, is usually not an early factor.

Dr Wright is concerned that services are not really adequate for people with severe HIV-associated dementia, as placing these people in nursing homes with the aged is not a good mix, particularly as the people with HIV are likely to be considerably younger.

Geoff Cole from the AIDS Dementia and HIV Psychiatry Service (ADAHPS), which oversees much of the care of people with HIV-associated dementia in NSW, agrees that this is a problem. "With most nursing homes, we have to go back to previous decades in terms of their understanding about risks of HIV infection," he said. "Staff are often uncomfortable with taking our patients and they find the complexity of medication hard to deal with."

NSW has comprehensive service

ADAHPS is the only comprehensive service in the country dedicated to looking after people with HIV-related

neurological problems. It acts as a consultancy for service providers in NSW for patients with serious cognitive problems. Their services include a state-wide outreach team specialising in joint case management, neuropsychological and other assessment, carer support and coordination of The Bridge, a 12-bed facility in inner Sydney.

They also jointly manage The Villa, a pilot 'intensive supported accommodation' project which provides a shared community home and four places in a block of apartments for people who cannot live independently but do not require The Bridge's 24 hour care.

But ADAHPS's main work is supporting various community agencies via case management to care for people with complex needs (including HIV-associated dementia) in their own homes. This may involve the provision of nursing care but increasingly, according to Geoff Cole, this is being carried out by private agencies providing attendant care (help with personal care including showering, house cleaning, shopping etc). There are also a range of other services in NSW such as Bobby Goldsmith House, which provides medium to long-term accommodation for clients with medium support needs and North AIDS, which has a short stay facility.

"We thought that ADC was going to be a major problem in the early to mid nineties, then with HAART, we thought we might happily go out of business. This hasn't happened either," said Cole. "The incidence of lower order cognitive difficulties and complex mental health problems for people with HIV has meant that we're fairly busy still."

In fact, ADAHPS has estimated that they expect an increase in clients by 2007 as high as 20 percent. Five to 10 percent of people living with AIDS will have severe ADC (approximately 90 cases in NSW) and are expected to require heavy community support. Ten to 15 percent (another 90 cases) will have significant ADC requiring support, and 30 to 60 percent (540 cases in total) will have neurological complications of HIV disease.

Other states way behind

If these figures do eventuate (and Cole admits it is hard to be sure about these predictions) then the implications are possibly greater for states around the country which, while currently only having a relatively small number of cases of ADC, may have to improve their service delivery capacity considerably.

In Victoria, a Victorian AIDS Council in-home support program runs case management and attendant care support for a limited number of people with medium level support needs. The Alfred Hospital has set up five beds for people with HIV and complex needs (including ADC and cognitive impairment) at a supported accommodation service in East Melbourne and people with the condition can also use the Fairfield House facility at the hospital for respite for their carers, while they undergo medical treatment and investigations.

"Increasingly though, carers are harder to find for people with ADC," said Brian Price, HIV Coordinator at the Alfred Hospital. "As people live longer with HIV and cognitive impairment, it can be more difficult for relationships with family and friends to be maintained. Often, subtle changes in cognition over time impact on the maintenance of these relationships, often not helped with drug and alcohol issues." In this situation, paid community services are often expected to take up the slack in provision of support and long-term care.

"As the HIV-positive population gets older we are going to have to plan for longer-term care for those people who develop ADC and its complications," Price told PL. "Should we build up particular relationships with nursing homes that will take these clients? Should we push for our own facility with community involvement? Whatever happens, government agencies (state and federal) are going to have to start acknowledging that HIV ADC requires the same level of funding as the other dementias — and this will involve nursing home care and attendant care funding."

After researching this article, I feel a little more comforted that the chances of developing ADC are not so high — but that if I were to develop the condition, the clinical [12]Pertaining to or founded on observation and treatment of participants, as distinguished from theoretical or basic science. and research work being done by doctors like Edwina Wright and Professor Bruce Brew in Sydney (one of the world's leading researchers in this field) will help nip its development in the bud. If that didn't work, I hope that there is a considerable improvement in the quality and depth of care provided in the future — with hopefully more states following the example set by NSW Health in its funding of a range of community care interventions.

For the moment though, a suggestion from Dr Wright about monitoring for cognitive changes to prevent future difficulties makes the most sense. “If your T-cells go below 200, you need to have neuropsychological tests done as a matter of course. We make a fuss about monitoring lipids and blood glucose, why not also include cognitive functioning tests? We all have to become a bit realistic about the potential for ADC in the future. It’s important that people don’t ignore it altogether. People will benefit if they can deal with their fears about the condition, to be able to look into the eye of the tiger.”

- dementia

Links:
[1] http://www.napwa.org.au/glossary/term/95
[2] http://www.napwa.org.au/glossary/term/96
[3] http://www.napwa.org.au/glossary/term/88
[4] http://www.napwa.org.au/glossary/term/123
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