HIV AUSTRALIA

24th Annual Keith Harbour Address

By Dr Edwina Wright

This is a transcript of an address delivered by Associate Professor Edwina Wright on 20 November 2016, at the 2016 Victoria AIDS Council (VAC) Annual General Meeting. It was originally published on VAC's website.

On 5 June 1981, I was studying first year medicine at the University of Sydney. I had just moved to Sydney from the United States where I had spent three years living with my mother and her new husband. I had been studying at George Washington University in Washington DC and through sheer boredom I had finally turned my mind to studying. Despite failing to matriculate in Melbourne, my marks at George Washington University were enough to earn me a place at Sydney University.

During my busy first year as a medical student, I do not recall hearing about the now famous report that came out of the Centers for Disease Control and Prevention that day in June 1981. That report notified the world of five homosexual men from Los Angeles who had been diagnosed with Pneumocystis Pneumonia and other illnesses seen in advanced immunosuppression. At the time that the report was published, three of those men had died.

Westmead Hospital 1986

After that report came out, I was not to meet a person living with HIV for five years when in 1986 I was an intern at Westmead Hospital and went down to see a man in the emergency department who had just been diagnosed with PCP.

He had acquired his HIV from a blood transfusion years earlier and I remember his gentle nature which was distorted a little by his bewilderment at being in the hospital setting, surrounded by hospital staff, like myself, who were fully gowned, gloved, masked and goggled, moving about him slowly and purposefully as though there was little gravity in his room and as though at any minute the staff might accidentally fly up and around the room, losing control like novice astronauts.

It was a surreal and distorted way to care for a person and this was the way that HIV positive people were cared for in hospitals for some time until we realised that HIV was only infectious through sex, blood transfusions, sharing injecting equipment, mother-to-child transmission and breastfeeding.

Over the next four years at Westmead Hospital I was involved with the inpatient care of more people with HIV and AIDS and most of my memories of the late 1980s were of how young people were and how profoundly unwell they were by the time they were admitted to Westmead Hospital.

For many of them they had a dual diagnosis when they were admitted: you are HIV positive AND you have AIDS.

During that time in the late 1980s in Sydney I decided to become a medical specialist, and there was a lot of study to do for the exams. As a young doctor, I was working hard during the day in many different areas of medicine – geriatrics, rehabilitation, palliative care, cardiology, haematology – and during the nights and weekends I was studying. All of these different medical disciplines played a role in my future care of HIV positive people.

So, HIV infection was not the centre of my world during those years. But I broadly remember how HIV infection fascinated the media at that time and the general public. I remember how the Food and Drug Administration (FDA) licensing of azidothymidine in the late 1980s excited the medical and scientific world.

In 1989 I passed my specialist's exam and decided to become an infectious diseases physician. However, in June of 1989, in the middle of a cold Melbourne winter, my stepfather returned my mother and their young son, age 10, to our family home in Melbourne.

My mother had recently been diagnosed with early onset Alzheimer's disease. She was in her mid-fifties. That winter she arrived in Melbourne with a suitcase full of summer clothes because my stepfather had told her that they were going to Russia for the summer. The greater truth was that he was not a

strong enough person to cope with her illness and his solution and escape was to fall in love with another woman. And so, he brought my mother and my little brother back to Melbourne so that the rest of her family could begin to take care of them and thereby allow him to return to America. My mother never saw her lovely house in Washington DC again; nor did I.

Fairfield hospital 1990

So, in early 1990 I uprooted my life and moved back to Melbourne and began working at Fairfield Hospital as a first-year infectious diseases trainee and along with my other brother, began caring for our mother and young brother.

Fairfield Hospital had been the Fever Hospital of Victoria since the early 1900s. It was lodged safely north of the city and cared for people with all forms of infectious diseases: typhoid, diphtheria, tetanus, malaria, tuberculosis, leprosy, cholera, small pox and polio. It was the natural destination for those living with diseases that made them human outcasts. And so of course it was the medical destination for most Victorians who were diagnosed with HIV.

Ward Four was the HIV ward at Fairfield Hospital and I entered it on the first day of my new job in 1990 with some anxiety - but it was only performance anxiety. I wasn't anxious about opening each of those doors down Ward Four's long corridor to meet each young man, take their medical history, examine them and then try to fathom the right diagnosis and treatment. And behind each door there was, invariably a man - very occasionally a woman - with a rare infection or cancer, or dementia that signified that that person's immune system had become depleted and exhausted by HIV and had thereby succumbed.

Fortunately, many of the AIDS-associated opportunistic infections and some of the cancers could be treated so we were in a position to treat people and return them to a level of health that allowed them to be discharged. AZT was available through a special access scheme but not everyone was on it. But of course, single agent treatment -at that time - was doomed to fail and people returned again and again to Ward Four with new AIDS illnesses. We could not cure people from the effects of HIV on their immune systems. And so, they died.

In many ways the doctors and nurses in Fairfield Hospital were like reverse midwives, really, birthing the patients as gently as we could, *out* of this world.

Because we could not offer a cure or even a chance at long term remission from HIV infection at that time, we did break rules in terms of how we could engage with our patients. In this regard Dr Ron Lucas and Dr Anne Mijch were my role models. Anne Mijch, as many of you would know, would give the shirt off her back for her patients; she was a fearless physician and fearsome if she found that you had in any way not provided the optimum patient care. She gave patients money; she drove patients to places they needed to go; she paid their rent; she filled me with awe.

Ron Lucas was a very important mentor to me also. He was strict and circumspect and highly scientific in his approach to the practice of medicine. But even he was moved by the sorrows that day-to-day medical care engendered on Ward Four, so much so that even he shifted the boundaries in the traditional patient- doctor relationship. One day on a ward round, being led by Ron Lucas, we entered a patient's room. The patient was dying from a lymphoma in the brain. He had not eaten for days as he could find no appetite. Ron implored him to think of something that might spark his appetite just a little. The patient thought for a while and then said he could eat a meat pie with sauce on it. At that, the whole ward round left the patient's room, we went down to the hospital shop, Ron bought a pie with sauce, cut it up on the plate and returned it to the somewhat surprised patient. So that day I was given permission to shift my boundaries as well.

And an example of that was when I let a patient do something for me. One of our patients who was frequently admitted with intractable Mycobacterium avium complex (MAC) infection was a gorgeous fellow. He never complained when, night after night his temperature would rise to 39C, 40C with sweats and chills. He became so tanned because of the treatment we were giving him and with his platinum blonde hair and moustache and slim physique he was very beautiful. I think he felt sorry for me labouring away trying to help make him feel better. I think I was probably a complete pain in the arse in my medical fussings and ministrations. It is hard when you are young and you have not yet figured out that you cannot fix everything. But being a hairdresser, he offered to dye the unruly roots that had emerged in my own dyed blond hair! I was a little hesitant, but I let him do so in his hospital room in Ward Four, using the tiny basin and some hospital towels after work one night. He didn't have a hairdryer and I don't recall that there was much conditioner used in the process, but I was, if you like, baptised by him to become a doctor who could withstand being vulnerable and could accept the help of someone I was technically supposed to be tending. HIV has expanded many doctor-patient and I think nurse-patient relationships thus so.

What I remember of the people I cared for on Ward Four and later Ward Two was their bravery and their humour despite suffering from really awful diseases, the types you see in medical textbooks. It is worth noting that nothing competes with Kaposis's Sarcoma (KS) in terms of its ability to distort and disfigure a person's face and body. In this sense, leprosy is just a country cousin to KS. But young men walked the streets of Melbourne with KS all over their faces and bodies, perhaps emboldened by some makeup that rarely hid their condition.

Importantly I remember that despite their advanced, often terminal illnesses how sexual and beautiful so many of the gay, male inpatients at Fairfield Hospital remained. And I can confidently say, "sorry HIV, and sorry religions, and sorry families, and sorry stigma, but you were unable to rob these men of their essential sexiness."

Occasionally people were angry, but it takes energy to be angry and people either didn't have that energy or chose

to use it to make sense of their situation and to make peace with what was left of their lives and the people in them.

I remember Keith Harbour as an inpatient only. I did not know him outside of the medical setting. I remember the irony of him being unwell, but at the same time he was ebullient and so physically robust. He was bemused by doctors with our questions and pokings. He seemed to not have the time to indulge his illness because he had better things to do. Coming in and out of hospital seemed like a dry process to him.

I did not know that the reason he was so keen to get out of hospital was that he was an activist and was working to help establish People Living with AIDS Victoria and he was caring for HIV positive people in their worlds, outside of Fairfield Hospital. Looking back, I see now that he knew what was coming and I remember him as being completely unafraid of dying; death for him was a distraction from much more important things.

We all had a way of coping with how HIV affected our lives. For me I focussed on undertaking research into HIV dementia. This illness affects up to 20% of people with advanced, untreated HIV infection and is one of the only treatable dementias in the world and it's treated with antiretroviral therapy.

Young men would be admitted to Ward Four with HIV dementia. They were slow in their speech and manner and demeanour. They were detached from the world. They became progressively dependent on those around them. They became bed-bound. Their lover became their carer. It was naturally challenging for me to go home from work at night and live with my mother progressively dementing, mourning her marriage and her life, but bravely and without ever complaining just like my patients at work.

I have continued to do research in the area of HIV dementia and have contributed *very modestly* to this area of medicine. I have led research that described the prevalence of HIV neurological disorders across the Asia and Pacific regions, other research in the SMART Neurology Substudy that found that hypertension and high cholesterol have an impact on the cognitive health of virally suppressed HIV positive people, and I led the START Neurology Substudy, where we found that for people who are well with CD4+ cells over 500, early versus deferred antiretroviral therapy does not make a difference to their neurocognitive performance. At the Alfred we are continuing to study the effects of treating hypertension on neurocognitive function in HIV positive people and we have been running the HIV Brain Bank Project since 2004.

Time passed and in the early 1990s clinical trials showed that using two versus one antiretroviral proved better in terms of controlling HIV infection.

Vancouver 1996

1996 was the turning point in terms of taming HIV infection's power over the human immune system. It was announced at the 11th International AIDS Conference in Vancouver in July 1996 that by combining three antiretroviral agents, especially if the combination included a protease inhibitor, that AIDS, death and hospitalisation rates would fall dramatically. Thus, the highly active antiretroviral therapy (HAART) era began. At the same time Fairfield Hospital closed and we moved to The Alfred Hospital where we were able to successfully continue our culture of care.

For several years, until we had better tolerated drugs like Efavirenz and Tenofovir, the toxicity of the HAART era was very tough for patients, but people tolerated it because they had their lives back, in a sense.

Peripheral neuropathy, lipoatrophy of the face and limbs, lipohypertrophy of the abdomen and neck, nausea, high lipids, osteoporosis and increased risk of cardiovascular disease and other non-AIDS comorbidities were to follow.

For many years I remember how we struggled to decipher patients' HIV genotypes. People who had been started on monotherapy and then double therapy back in the late 1980s and early 1990s had unwittingly fostered viruses that could overcome many different antiretroviral agents, so even if you used three drugs at once they may not have worked. Also, because so many of the new agents were so toxic, patients were unable to adhere well to the HAART regimens, which allowed HIV to develop further resistance.

Interpreting HIV genotypes was like breaking codes for the allies in World War 2, trying to put together three antiretroviral agents that could silence a person's HIV infection. Fortunately, it was not to last. I admit to being sceptical when an infectious diseases doctor visiting the Alfred Hospital from Israel and its Occupied Territories told us in the mid-2000s that future HIV treatments would be so potent and well tolerated that we would no longer need to do genotype tests because, so few patients would fail treatment.

Now, in 2016

He was absolutely right: it is now only once or twice a year that I would ever have to study a person's genotype because antiretroviral treatment has become highly tolerable and potent.

Last year the START study demonstrated that immediate versus deferred treatment in people with greater than 500 CD4+ cells significantly reduced the likelihood of combination of AIDS events, non-AIDS events and death. This means that we now offer people treatment as soon as they are diagnosed with HIV. Within a few days or even hours of their diagnosis, people in Australia can commence a single tablet with few side effects that will make their plasma HIV viral load undetectable, sometimes within a matter of weeks. This remarkable news is now the subject of VAC's current 'Treat HIV Now' campaign.

I was on the Australian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) Board for a number of years until 2014. During the three years while I was president of ASHM, I think that one thing I achieved of value for Australian residents living with HIV was to lead a community submission from ASHM, (NAPWHA and AFAO to the PBAC to overturn the criteria that only people with CD4 cells less than 500, or those

with symptoms of HIV infection, could have access to antiretroviral therapy. The submission was successful and since April 2014 all Australian residents can access antiretrovirals (ARVs) irrespective of their CD4 cell counts and overall health. In parenthesis, of course, I am saying that non-residents cannot access subsidised antiretroviral therapy which remains unjust and an indictment on us. At the same time, I was involved in work with colleagues in the United States looking at the benefits of commencing people on treatment within four months of becoming infected with HIV and we found that if people commence ART within four months, they have a significantly greater chance of restoring their immune health to levels that approximate their pre-HIV infection immune health. And we published that work in the *New England Journal of Medicine*.

What we did not know when HIV positive people commenced on HAART in 1996 - with all of its associated toxicities - is that they were practising Treatment as Prevention (TasP). We now know that if people are on suppressive ARV treatment that their risk of transmission of HIV to others is incredibly low. The PARTNER study enrolled heterosexual and gay serodiscordant couples practising condomless sex, where the positive partner had an undetectable HIV viral load. After 58,000 episodes of condomless sex there were no linked HIV transmissions in this study. The absolute risk of transmission was not zero however, using statistical boundaries of confidence and further follow up of gay male couples is happening in the PARTNER-2 study to try and find a more precise estimate of risk for condomless anal sex. But the overall risk will be remarkably low, I expect.

The HIV Prevention Trials Network (HPTN) 052 study enrolled heterosexual, serodiscordant couples who were using condoms and found that after 10 years there was a 93% reduction in HIV transmission if the HIV positive partner was virologically suppressed. None of the transmissions that occurred in this study over those ten years did so when the partner was fully virologically suppressed.

So, treatment as prevention is a remarkable phenomenon and coupled with HIV Pre-exposure Prophylaxis (PrEP) we now have the biomedical tools to allow Victorians and Australians to meet our pledge from the 2014 International AIDS Conference that was held in Melbourne to end new HIV transmissions by 2020.

Currently there are two PrEP studies in Victoria – VicPrEP and PrEPX and I am principal investigator of both studies. Together these studies have enrolled over 2,500 people to receive Tenofovir/Emtricitabine. This has been a huge collective effort of activists like PrEPaccessNOW who have helped thousands of people in Australia to import generic PrEP, PrEP'DforChange who have raised awareness and educated people about PrEP, Time4PrEP, the peak organisations including Victorian AIDS Council (VAC) and Living Positive Victoria and Positive Women and others, the general practitioners in Melbourne who are supporting people to import PrEP and to enrol in to PrEP studies, Alfred Health which has embraced HIV prevention as part of its mandate, and the Department of Health and Human Services and the Victorian Ministry of Health who provided tremendous leadership in funding these PrEP studies. We are all watching new HIV notification rates very closely and hope that these two PrEP studies coupled with the personal importation of PrEP, will allow us to see in two to three years' time a significant decline in new HIV infection rates. Currently new HIV infection rates are ten per cent lower than they were at the same time last year and around 20 per cent lower than they were at the same time in 2014. I know that PrEP is bringing in other STIs: that is a problem for us to solve - but we can't throw the baby out with the bathwater.

One of the most remarkable things that we may see, and I think there is some early evidence of it now coming out anecdotally and also out of work from the VicPrEP study, is that through the widespread knowledge and use of PrEP that we are seeing a decline in stigma from HIV negative MSM towards MSM living with HIV. In turn I think that TasP perhaps to a lesser extent, has also achieved the same thing

So, we might be in a position to say that there is a pill for stigma!!

The future

Pills can do lot of things.

It is possible to be cured by a pill but not be healed by it.

This is a contentious thing to say in the current climate of hope around a HIV cure, but it is said in the spirit that a cure – although it is very likely to come – may not come for some time, perhaps not in some of our lifetimes in which case some people may feel that they lost out, that they missed out on a cure.

But until a cure comes, I think it is worthwhile pondering from time to time, what difference would a cure make to me as an HIV positive person, or as a person who is affected by HIV?

The reason I mention this is because a cure may not lead a person to be healed- they may still suffer physically because of how hard their journey with HIV has been, they may continue to suffer purely because of the psychological toll of their journey, they may continue to suffer because they are still grieving the life they never got to live, or they are grieving the lives of people whom they have loved who died from HIV infection.

What these thoughts mean to me is that we must not rely on a cure - in whatever form it takes - to fully heal us. We can begin that healing work now before the cure arrives. That is the truth for anyone with a chronic, medical incurable condition: diabetes, heart failure, severe arthritis and dementia. If we don't yet have a cure for our illness, let's at least make sure we are working on being healed from its effects.

Finally, to look to the broader and more distant future – say in 100 to 200 years - say 2216 - when people look back on this epidemic, would we be content to show them that we had identified the virus, found a treatment for it, found ways to prevent it and found ways to either put HIV into long-term remission, or to cure people of HIV? Here I should mention that the HIV field of medicine and research has greatly benefited other

fields of medicine including hepatitis C treatment and cure.

What would we regret not having done, alongside these magnificent scientific advances?

Given that HIV infects people when they are at their most human - during sex and sexual intimacy, during childbirth, during injecting drug use, during breastfeeding- and given that we didn't know much about the virus for a long time so we couldn't initially vilify the virus, it was destined that the focus of the HIV epidemic at least initially, would be upon what humans DO to acquire HIV rather than what the VIRUS DOES to humans. This is still the case in many settings - the focus is on nature of *people* and not on the nature of the *virus*.

So, I think that along with all the remarkable medical advances that we have already achieved and are likely to still achieve, that in 200 years' time we would want people to see that we had brought about a great change of fortune and a great carriage of justice for those who were most vulnerable to HIV back in the 1980s and 1990s and through the first hundred or so, years of the 2000s.

People who through poverty, sexual coercion, through the ugly chauvinism of big business, religion and corporate Christian power were denied their rights to live unashamedly as humans free to have sex, free to give birth, free to take drugs to relieve them of the existential pain of living on this fucking planet in this fucking Universe without fear of acquiring a virus which, unchecked would kill them in a terrible way in a period of some five to ten years. I am quite sure that Keith Harbour would want that as our legacy. Even if we found a cure for HIV today he would want us to keep fighting against the factors that made humans so vulnerable to HIV in the first place and continue to do so.

Thank you for your time and patience in listening to me today.

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