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Unexpected challenges faced by people living long term with HIV: I thought I was a survivor but it turns out I am a pioneer.

Ron Rosenes, Vice Chair, Canadian Treatment Action Council

Thank you for the opportunity to paint a picture for you of how things are turning out – unexpectedly – for people like me who have been living long term with HIV.

It is now well over 30 years, since the earliest days of the epidemic, that I have been living with HIV. Yes, there are a number of long term survivors, I am not alone, not the world record holder though probably close to setting a record for living with a disease that was only identified 30 years ago.

I am a survivor, a witness and now, it turns out, a pioneer.

Survival can be attributed to a number of factors (good genes, a wimpy virus, devotion to a vigorous yoga practice, lots of sleep and a healthy diet).

I have been a survivor and I have been a witness. Over the years working in this community, I have made many wonderful friends. In the 1980s and 90s I lost many of these wonderful friends who, in retrospect, didn't live long enough to benefit from the incredible advances in treatment we now call HAART. I was at the Intl AIDS Conference in Vancouver in 1996 when many of us thought we had been saved, that HIV could in fact be eradicated using these powerful medications. I remember being interviewed by the CBC and being photographed walking off into the sunset along English Bay. (I thought at the time that if I had a wheel chair, I would fling it into English Bay). As we now know, Dr. David Ho's dream of eradication was not to be. It was built on a faulty mathematical model that had not taken into consideration that HIV continues to hide in reservoirs and sanctuaries such as the lymph nodes and that to this day we are still not able to flush HIV out of those reservoirs, although it is interesting to me that there is a renewed push to search for a cure today that seems to many to be within our grasp. A functional cure, not a sterilizing cure but that is another talk.

Why do I say I am now a pioneer?

It is 2011 and the meds we take in combination therapy to suppress the replication of HIV are more effective, have a lower pill burden and generally have fewer unwanted side effects. Treatment is less toxic and the number of patients who are able to reach and sustain today's holy grail of an undetectable viral load and regain a relatively normal number of CD4 cells is high, particularly for people like me for

whom the social determinants of health are not so much of an issue. Of course, adherence to therapy can look a lot different for a young person who is street and drug involved or an individual dealing with mental health or addiction issues. For many people with HIV today, the virus can be the least of their concerns. Food and income security, stable housing, the next fix – can all be viewed as more urgent issues.

But, while many of us are doing well on our meds, there is something ominous and troubling going on. We are starting to see signals that all is not well with those of us who were thinking we might in fact have had the good fortune to reach our golden years despite many years on treatment for HIV. So I feel like a pioneer, standing once again on the edge of a precipice although it is far from clear if and when I might fall and how far the drop.

So what exactly is going on?

This past year we lost the amazing James Kreppner, a well-known lawyer and advocate for the haemophiliac community, co-infected with HIV and hepatitis C. We might not have lost James so soon had he been able to receive a liver transplant. On the west coast, we learned of the sudden death of a colleague working in the HIV community, barely 40 years old, from a massive heart attack. The Secretary of our Board at CTAC, a man still in his 40s, who lives in St. John's where, for a time, they were without an ID specialist, is dealing with anal cancer. In Montreal, we recently lost another CTAC Board member in his early 50s, a giant of a man both physically and metaphorically, after a short sharp battle with lung and brain cancer.

Less serious, but of equal concern, is the complaint of another friend who tells me he increasingly goes in search of words he knows well and seems to have misplaced. He is in his 50s, is a chartered accountant and investment adviser and he recently decided to stop giving advice to private clients because of mild but increasing cognitive impairment.

I have been pretty fortunate so far though as I approach my mid 60s, I can feel the winds gathering. Diagnosed with Osteoporosis almost 10 years ago, I am fortunate that it was discovered and I remain on treatment that manages it. In addition to a bisphosphonate, my own holistic osteo program includes physiological amounts of testosterone (under my doctor's supervision) and a vigorous yoga practice. Sometimes the yoga and the testosterone make me feel like the "belligerent Buddhist" but that's another talk. Fortunate to be living in Toronto, I have also undergone baseline screening for cognitive function as well as a follow up 4 years later, which, knock on wood, seems to be holding its own. But how many of us are being screened for bone density or HAND (HIV Related Neurocognitive Disorder) especially those who are living with HIV and other co-morbidities outside of a major urban centre?

I keep putting off the day long CV stress test I know I need despite having been able to maintain decent lipid numbers. You never can tell what's really going on inside those arteries.

Those of us living long term with HIV and on HAART have recognized this for some time and have begun to talk about it, to write about it, and more importantly to start asking questions of our health care providers, our epidemiologists, the research community, and ourselves. In the USA, **Error! Reference source not found.** of NATAP (North American Treatment Advocacy Project) has been pushing the issue daily on his listserv. The NATAP listserv coughs up at least 20 research reports each day and those reports can sound somewhat grim. They are confirming what we have suspected for some time now: that the population with HIV is aging at an accelerated rate with more frailty, non-AIDS related cancers, bone, heart, metabolic disease (including high rates of Type II diabetes) and cognitive impairment (as well as depression) when compared to the general population. The retrospective data being gathered from large cohorts around the world are compelling in terms of the picture that is now emerging BUT it is a picture of ASSOCIATIONS, one which leaves us in pretty much in the dark when it comes to understanding etiology or the CAUSAL relationships.

We recently formed CHARPA, the Coalition for HIV-related Aging Research, Policy and Advocacy. This is mainly a US based coalition but it provides an opportunity for people living with HIV to promote and advocate for increased funding for all of our research funding bodies to study the issue. (In the US, it's largely the OAR within NIH, in Canada, the CIHR, OHTN, CANFAR and CTN). No question, the problem has now been recognized and much work has been begun to better characterize it and to seek interventions.

Meanwhile, the statistics are compelling.

From 2000 to 2004, the Centers for Disease Control reported that the proportion of AIDS patients who are ≥50 years of age rose from 19% to 27% and that the number of adults ≥50 years of age living with HIV infection and/or AIDS more than doubled. Importantly, for that surveillance period, persons 40 to 49 years of age had the highest prevalence of HIV/AIDS and the steepest rise in prevalence. The number of older people with HIV/AIDS is expected to increase even further during the next decade. It is projected that by 2015, more than half of all HIV-infected individuals in the United States will be over the age of 50 [1].

An important point to remember here: age isn't everything. The increasing incidence rates among people over 50 confirms that people unfortunately continue to seroconvert in their later years. We must also bear in mind the number of babies, children and youth who are on treatment from an early age. Therefore, length of time on treatment will be a very important factor for researchers to consider along

with HIV disease process and not just an individual's chronological age. Modifiable behaviours such as smoking, poor diet, and sedentary lifestyle, along with depression – all of which are disproportionately high in my community – play a role.

Time was we were succumbing to Opportunistic Infections (OIs) that we don't hear a lot about today in the age of HAART (since 1996). We are no longer dying of toxoplasmosis, disseminated cytomegalovirus, PCP pneumonia, MAC (Mycobacterium Avium Complex) or KS (Kaposi Sarcoma). Today, we are more likely to die from a cancer that is unrelated to HIV, (anal, colorectal, melanoma, liver, lung, Hodgkins lymphoma) from cardiovascular disease, bone disease or organ failure – end stage kidney or liver disease. There is a growing epidemic of Type II diabetes and co-infection with hepatitis C that only complicates matters further. These are the new OIs, or co-morbidities as we prefer to call them today, and many of us wonder if cause of death is being correctly or comprehensively reported on death certificates. One wonders if HIV is getting lost in the process. Clearly this is a challenge that must be taken up by epi surveillance and all who track the mutating course of the epidemic in our various cohorts across North America and internationally.

We know what happens when HIV is left untreated. We know that treatment can do much to restore immune function but its ability to restore immune function is imperfect. Virus bounces back when treatment is stopped and the gains of many years can be lost within weeks. Even with perfect adherence, we are now beginning to understand there is underlying disease progression that is only now beginning to be understood as the result of low-level viraemia, virus that may for example be escaping from latent reservoirs, causing inflammation and immune activation. There is the early senescence of immune system cells which lead to activation of the immune system (think of a machine that is constantly left on and running, never turned off and generating heat in the process) and a state of ongoing inflammation (aye there's the heat and the rub!) which appears to lie at the heart of the acceleration of the aging process when compared to the general population.

The three big questions with regard to the accelerated aging we are seeing in HIV are:

1. How much is due to the HI Virus itself and other ongoing disease processes?
2. How much is due to chronological aging?
3. How much is due to the toxicities of long-term treatment?

(I remember in the 1980s when I started seeing a practitioner of Traditional Chinese Medicine (TCM). He told me that in the TCM paradigm, HIV is considered to be a disease of "deep-seated heat" and that he would work with me to cool me down, using herbs, acupuncture and diet. Please remember this was at a time when we had absolutely no treatments in the pipeline.)

The development of HV associated co-morbidities has meant that we need to develop a better understanding of **frailty** in HIV. **Frailty** is defined as having 3 of the following: exhaustion, slowed walking speed, low activity, weakness, and weight loss. There are many similarities between the biology that underlies frailty and chronic HIV infection. Some HIV treatments appear to accelerate that biology.

It would therefore be useful to screen for biomarkers associated with frailty as a useful construct to identify HIV+ older patients who are most at risk for future study and for interventions. We know from the data that we are at increased risk of fracture, and while the data is still unclear about the level of that risk, I think we need to plan based on the expectation we will see more frailty, at an earlier age depending on length of time on treatment. We need not just to screen for frailty but also to learn from those working in the field of anti-aging medicine, which interventions will be useful in treating early frailty in HIV.

We need high quality research to begin to answer the following questions:

1. It remains unclear just how much or how many of these co-morbidities we are likely to see going forward. In other words, what is the real burden of disease going to look like?
2. Will we see higher rates of incidence and prevalence? Is this the tip of the iceberg?
3. It remains unclear to what degree predisposition and modifiable behaviours such as smoking, diet and exercise may play a role
4. It remains unclear to what degree HIV disease progression and / or toxicities of HAART play a role
5. Along with the collection and analysis of COHORT DATA, we need PROSPECTIVE trials designed quickly and soon in order to get a better understanding of accelerated aging in HIV
6. These trials must be designed taking into account gender and ethno-racial considerations (and be well controlled for genetic predisposition, diet, smoking, exercise)
7. We need to be able as community (meaning consumers/patients like me) to both influence the research agenda as well as advocate for access to early screening, diagnosis and therapeutic interventions where none yet exist.
8. Anti-aging doctors, specializing in geriatrics should be brought into the fold of HIV specialists to help screen, diagnose and treat age and HIV-related health conditions
9. We can and should start early screening for many of the age related problems we can now anticipate

Here is a short list of examples of screening for which we should probably develop guidelines that would help both doctors and patients:

- Dexa scan for bone density
- Anoscopy for anal cancer
- Baseline cognitive function testing
- Better assessment tools for CV risk (Framingham plus?)
- Regular glucose tolerance tests
- 24 hour urine tests
- Improved assessment tools for kidney disease
- Same for liver disease
- Screening for non AIDS related malignancies
- The SENIEUR Protocol to screen for underlying illness

To name a few. And it's not just a question of having the right set of diagnostic tools, it's a question of making them available across the country and to people who live in rural or remote settings.

Beyond the purely biomedical concerns about premature or accelerated aging in people living long term on treatment for HIV, we will also have to address the special care needs for this diverse population as we age. Like other chronic complex illnesses, the challenges to provide seamless and integrated care multiply in direct proportion to one's geographical proximity to specialists and clinic settings that can address multiple issues.

Further down the road, we must ensure that long term care is there for people who may need various degrees and levels of care sooner than in the general population and delivered in settings where people will feel safe and less likely to be judged.

We have yet to have a real debate in this country about the degree to which we continue to invest in nursing homes and other long term care facilities versus our investment in home care and respecting the wishes of many people to be able to stay in community. When my partner of 15 years died at our home in 1991, I felt it was the greatest gift I could give him at the time. So I guess you can figure out where I stand on this issue. That being said, it should always be about choice and ensuring we are able to offer a wide and comprehensive set of services to support us at the end of our lives.

We have pushed the envelope over the very recent history of HIV infection and made incredible progress. I expect that this new set of later in life challenges will again be useful in pushing the boundaries of research. My fervent hope is that there are among you in the room a number of experts in gerontology who will become interested in learning more about HIV. The benefits that may accrue will not just be for people with HIV but may extend to the general population as well.

Thank you for joining us today to learn more about this issue.