

# WHAT AGING WITH HIV MEANS IN THE YEAR 2019

Jules Levin<sup>1</sup> and Monty Montano<sup>2</sup>

1. National AIDS Treatment Advocacy Project
2. Harvard Medical School and Brigham and Women's Hospital

Running Title: HIV and Aging in 2019

KEYWORDS: Health disparities, HIV/AIDS pathogenesis, inflammation, aging

Corresponding author:

Monty Montano

221 Longwood Avenue

Boston, MA, 02446, USA

617-525-9046

[mmontano@bwh.harvard.edu](mailto:mmontano@bwh.harvard.edu)

*In Greek mythology, Tithonus was granted eternal life but not eternal youth. As time passes he withers, slowly losing his health and all that he knew, lamenting a cruel immortality (1).*

People with HIV are now living longer, but this has come at the cost of an ever increasing burden of comorbidities that reduce quality of life (2).

**Aging with HIV in 2019 means** becoming physically disabled and having difficulty walking, it means feeling abandoned, socially isolated & thus homebound; it means unable to shop myself for food; and increasingly it means cognitive impairment. Many of us face serious housing and financial hardships and have high rates of physical ailments - such as chronic pain, heart disease, diabetes, kidney disease, cancers, bone disease and fatigue - that diminish our quality of life (3-8). All of that's been known for several years. But services to meet our needs still fall short. Its time to recognize and adjust to the changing aging epidemiology in HIV, now 70% in many large cities are over 40 years old; in NYC 55% are over 50; in many of these cities 25% are over 65. It is estimated that soon 50% will be over 60, yet have we adjusted our thinking?

**While ART drugs are** life-saving, for many survivors, realizing we're going to live has opened a new chapter of emotional and physical challenges. In a recent survey: more than 60 percent suffer depression and about the same have serious anxiety. Seventy percent have symptoms of post-traumatic stress; nearly half have neuropathy which is untreatable, a form of nerve pain likely caused by HIV or the early drugs to treat it. Fifty-six percent have severe fatigue. On average, survey respondents reported at least six mental or physical ailments in addition to HIV infection; a quarter regularly don't have enough money to cover their expenses of daily living. Seven percent don't have a permanent home. Nearly half sometimes don't have enough to eat; more than one in four have no one to turn to if they become sick or disabled; fifteen percent say they have no one to count on for emotional support (9).

**Although the needs** of older people with HIV are becoming more widely recognized, services for health management have not kept up. Not all of the conditions we face are obviously tied to HIV. Many of us suffer post-traumatic stress from the extreme grief over the loss of so many friends and lovers to AIDS, and distanced from family the chronic

burden of fear that we too may lose our life. Problems like depression and loneliness also may be caused by the loss of so much of our community, and let's not forget the PTSD of surviving when so many of our peers have not. Complicating our care is that most older adults with HIV are used to seeing an infectious disease specialist for treatment — someone with expertise in HIV in particular. But those doctors are not geriatricians and do not necessarily know how to treat age and HIV-related heart disease or arthritis or diabetes, or the multimorbidity of all three at once (10, 11). As well, the healthcare infrastructure feels restricted and inadequate in general which for many has become a serious a problem in particular for older aging HIV+ individuals who need more attention to enable themselves to access available care, not less.

**The irony of HIV epidemic** is that those of us who were activists at the onset of the epidemic are now feeling too old and prematurely disease burdened to rally for the pressing necessity of HIV/AIDS research as a national priority. A further irony is that with its toll on human suffering, HIV has advanced our knowledge of medical science, from basic immunology to personalized medicine, and is now poised to advance our knowledge on the aging process itself. However, the NIH is at perilous risk of not leveraging this opportunity. People aging with HIV are burdened with greater numbers of multiple medical conditions that emerge at an earlier age and that are more commonly seen in older “normal” adults. Additionally, people aging with HIV are burdened with polypharmacy which means taking 8-15 daily medications (12). Studies now consistently indicate that the aging process is being hijacked and, for reasons that remain unclear, altered by HIV infection. As we struggle and all too often succumb, the science, to paraphrase Longfellow, grinds slowly and exceedingly small. We stand waiting.

**We all hear about inflammation**, now recognized to be a critical factor – if not the critical factor - in multiple age-associated pathologies, including those of the heart, kidney, liver, bone, muscle, and now in neurocognitive function and indeed aging itself (*i.e.*, inflamm-aging) (13-16). What is less commonly appreciated is that the onset of the HIV epidemic drove key advances in the basic understanding of inflammation, notably in the discovery of the pivotal role for the molecule NF- $\kappa$ B as a major driver of inflammation and possibly even aging itself (17, 18).

**We also hear about personalized medicine** as an approach to managed care that is systematically replacing idealized one-size-fits-all approaches. What is less appreciated is that one of the earliest examples of clinical practice adapting drug regimens to an individual with a chronic disease is HIV disease management, with antiretroviral regimens continuously shifting to counter HIV drug resistance - possibly the earliest and best example of effective personalized medicine in action. As people with HIV live longer, we are experiencing more years burdened by increasing medical conditions (*i.e.*, multi-morbidity) and pharmacological treatment complications (*i.e.*, polypharmacy). Here, personalized medical management in the context of HIV is breaking new ground that will likely have relevance for everyone.

**The greying of America** is obvious, with the number of aging Americans chronically unwell growing and impinging on quality of life and straining health care resources. Welcome to my world where, unfortunately, multi-morbidity and polypharmacy are all too familiar, occurring in people aging with HIV at a younger age and often with more severity. In people aging with HIV all too often 65 is the new 75 as we see from several studies that HIV accelerates features of biological aging, in some cases by ten years or more. Indeed, perhaps the most egregious hallmarks of aging, the inexorable decline in physical and cognitive function (*i.e.*, frailty and dementia), also have an earlier onset in the HIV infected, often in middle-age (19-24).

**The challenge now in 2019** is to overcome critical gaps in knowledge that we believe can be directly addressed by the NIH. The first is addressing our gap in understanding mechanisms that drive decline in physical and cognitive function with aging, both of which occur more often and prematurely in people aging with HIV. Secondly, biobehavioral factors that limit access to comprehensive quality care and needed support services in aging Americans, including stigma, social isolation and reduced health literacy tools that cripple our ability to effectively engage the healthcare system, are all more prevalent and severely needed in people aging with HIV. Domestically the federal government spends \$5-10 billion a year on Medicaid and Medicare. The Ryan White Care Program budget is \$2 billion a year. For the 2019 fiscal year, the NIH budget is about \$37 billion with \$3 billion dedicated to HIV/AIDS research.

**We need to evolve our HIV healthcare system with a new infrastructure that incorporates geriatric consultation into care.** For me and a growing number of survivors, the problem of aging & HIV is now the #1 clinical issue. With this change and the aging of our population - as 50% are now over 50 and soon 70% will be over 50 – we need to adjust our HIV care system; we need a new paradigm that addresses the needs and provides the training and services that clinicians and HIV+ people need to optimize their healthspan (10, 11). We have an outdated care system. Up until now CD4, viral load and selecting an ART regimen were a major focus for many. However now for these PLWH the needs outlined in this special issue & the services needed have evolved with the epidemic. We have an aging population often with higher CD4 counts and undetectable viral load who now are facing a devastating problem and yet our care structure is not designed to adapt to this changing clinical picture in a comprehensive way. We need to evaluate people comprehensively and a priori for mental health and physical function, disabilities and emerging impairments to provide to care and services that they need, so we can intervene sooner in the arc of a patient's progression over time in the hope of preventing the worst of what we now see in many older frail PLWH. We need a seamless, connected and adaptive care infrastructure that links comorbidities specialists, the PLWH and the primary care physicians to assure PLWH get the proper care they deserve. We also need better patient education, as many PLWH today may not understand the context of their complex health condition besieged with comorbidities – in effect, all too often, they do not understand what is going on. We need a full complement of services in the clinic and community such as food security, in-home maintenance and care, virtual IT in-home medical visitations for those homebound or mobility challenged, having difficult in their activities of daily living; and how will we provide in-home care and future housing for those requiring institutionalization. Clinicians may not be trained to identify early signs of these changes, we need to discuss all this. Finally, reimbursement in healthcare in general has become more difficult to navigate, and is unlikely to optimally fit the needs of our patient population or the clinics.

**NIH reframed** with investment in programs spanning all NIH institutes (such as through an NIH Common Fund program on HIV and Aging) would fuel the next generation of innovations across diseases of multiple organ systems and reduce healthcare costs, now

This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

AIDS Research and Human Retroviruses  
 What Aging With HIV Means in the Year 2019 (DOI: 10.1089/AID.2019.0114)

estimated to be \$600 billion per year for Americans 65 years and older. This will require close collaboration between NIH institutes, HIV researchers and community-driven needs assessment. Doing so would optimize chances for improvements in healthspan and quality of life for all Americans as they age, with and without HIV infection.

**JULES LEVIN, MS**

Founder and Executive Editor

National AIDS Treatment Advocacy Project (NATAP)

[www.natap.org](http://www.natap.org)

Email: [jules@natap.org](mailto:jules@natap.org)

**MONTY A MONTANO, PHD**

Principal Investigator, Harvard Medical School

Scientific Director, Boston Pepper Center

Office: 617-525-9046, Cell: 617-512-1352

Email: [mmontano@bwh.harvard.edu](mailto:mmontano@bwh.harvard.edu)

## REFERENCES

1. Lord Tennyson A. Tithonus. *Cornhill Magazine*. 1860.
2. Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. *The Lancet HIV*. 2017;4(8):e349-e56. Epub 2017/05/16. doi: 10.1016/s2352-3018(17)30066-8. PubMed PMID: 28501495; PMCID: PMC5555438.
3. Deeks SG, Tracy R, Douek DC. Systemic effects of inflammation on health during chronic HIV infection. *Immunity*. 2013;39(4):633-45. doi: 10.1016/j.immuni.2013.10.001. PubMed PMID: 24138880; PMCID: PMC4012895.
4. Erlandson KM, Allshouse AA, Jankowski CM, Mawhinney S, Kohrt WM, Campbell TB. Relationship of Physical Function and Quality of Life among Persons Aging with HIV Infection. *Aids*. 2014;28(13):1939-43. doi: 10.1097/qad.0000000000000384. PubMed PMID: 24992000; PMCID: PMC4380343.
5. Greene M, Covinsky K, Astemborski J, Piggott DA, Brown T, Leng S, Galai N, Mehta SH, Guralnik J, Patel KV, Kirk GD. The relationship of physical performance with HIV disease and mortality. *AIDS (London, England)*. 2014;28(18):2711-9. doi: 10.1097/QAD.0000000000000507. PubMed PMID: PMC4380225.
6. Mills EJ, Barnighausen T, Negin J. HIV and aging--preparing for the challenges ahead. *N Engl J Med*. 2012;366(14):1270-3. Epub 2012/04/06. doi: 10.1056/NEJMp1113643. PubMed PMID: 22475591.
7. Nixon DE, Landay AL. Biomarkers of immune dysfunction in HIV. *Current opinion in HIV and AIDS*. 2010;5(6):498-503. Epub 2010/10/28. doi: 10.1097/COH.0b013e32833ed6f4. PubMed PMID: 20978393; PMCID: PMC3032605.

8. Wada N, Jacobson LP, Cohen M, French A, Phair J, Munoz A. Cause-specific life expectancies after 35 years of age for human immunodeficiency syndrome-infected and human immunodeficiency syndrome-negative individuals followed simultaneously in long-term cohort studies, 1984-2008. *American journal of epidemiology*. 2013;177(2):116-25. Epub 2013/01/05. doi: 10.1093/aje/kws321. PubMed PMID: 23287403; PMCID: PMC3590031.
9. Levin J. 2019. Available from: [www.natap.org](http://www.natap.org).
10. Siegler EL, Burchett CO, Glesby MJ. Older people with HIV are an essential part of the continuum of HIV care. *J Int AIDS Soc*. 2018;21(10):e25188. Epub 2018/10/12. doi: 10.1002/jia2.25188. PubMed PMID: 30303293; PMCID: PMC6178281.
11. Singh HK, Del Carmen T, Freeman R, Glesby MJ, Siegler EL. From One Syndrome to Many: Incorporating Geriatric Consultation Into HIV Care. *Clin Infect Dis*. 2017;65(3):501-6. Epub 2017/04/08. doi: 10.1093/cid/cix311. PubMed PMID: 28387803.
12. Edelman EJ, Gordon KS, Glover J, McNicholl IR, Fiellin DA, Justice AC. The next therapeutic challenge in HIV: polypharmacy. *Drugs Aging*. 2013;30(8):613-28. doi: 10.1007/s40266-013-0093-9 [doi]. PubMed PMID: 23740523; PMCID: 3715685.
13. Bektas A, Schurman SH, Sen R, Ferrucci L. Aging, inflammation and the environment. *Exp Gerontol*. 2018;105:10-8. Epub 2017/12/25. doi: 10.1016/j.exger.2017.12.015. PubMed PMID: 29275161; PMCID: PMC5909704.
14. Franceschi C, Campisi J. Chronic inflammation (inflammaging) and its potential contribution to age-associated diseases. *J Gerontol A Biol Sci Med Sci*. 2014;69 Suppl 1:S4-9. Epub 2014/05/17. doi: 10.1093/gerona/glu057. PubMed PMID: 24833586.

15. Franceschi C, Capri M, Monti D, Giunta S, Olivieri F, Sevini F, Panourgia MP, Invidia L, Celani L, Scurti M, Cevenini E, Castellani GC, Salvioli S. Inflammaging and anti-inflammaging: a systemic perspective on aging and longevity emerged from studies in humans. *Mech Ageing Dev.* 2007;128(1):92-105. Epub 2006/11/23. doi: S0047-6374(06)00249-1 [pii]

10.1016/j.mad.2006.11.016. PubMed PMID: 17116321.

16. Nasi M, De Biasi S, Gibellini L, Bianchini E, Pecorini S, Bacca V, Guaraldi G, Mussini C, Pinti M, Cossarizza A. Ageing and inflammation in patients with HIV infection. *Clinical and experimental immunology.* 2017;187(1):44-52. Epub 2016/10/22. doi: 10.1111/cei.12814. PubMed PMID: 27198731; PMCID: PMC5167025.

17. Baldwin AS, Jr. Series introduction: the transcription factor NF-kappaB and human disease. *J Clin Invest.* 2001;107(1):3-6. Epub 2001/01/03. doi: 10.1172/jci11891. PubMed PMID: 11134170; PMCID: PMC198555.

18. Bektas A, Schurman SH, Sen R, Ferrucci L. Human T cell immunosenescence and inflammation in aging. *J Leukoc Biol.* 2017;102(4):977-88. Epub 2017/07/25. doi: 10.1189/jlb.3RI0716-335R. PubMed PMID: 28733462; PMCID: PMC5597513.

19. Althoff KN, Jacobson LP, Cranston RD, Detels R, Phair JP, Li X, Margolick JB, Study ftMAC. Age, Comorbidities, and AIDS Predict a Frailty Phenotype in Men Who Have Sex With Men. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences.* 2014;69A(2):189-98. doi: 10.1093/gerona/glt148.

20. Desquilbet L, Jacobson LP, Fried LP, Phair JP, Jamieson BD, Holloway M, Margolick JB. HIV-1 infection is associated with an earlier occurrence of a phenotype related to frailty. *J Gerontol A Biol Sci Med Sci.* 2007;62(11):1279-86. Epub 2007/11/15. PubMed PMID: 18000149.

21. Erlandson K, Allshouse AA, Jankowski CM, Duong S, Mawhinney S, Kohrt W, Campbell T. Comparison of Functional Status Instruments in HIV-Infected Adults on Effective Antiretroviral Therapy. *Hiv Clinical Trials*. 2012;13(6):324-34. doi: 10.1310/hct1306-324.
22. Schrack AJ, Althoff NK, Jacobson PL, Erlandson MK, Jamieson DB, Koletar LS, Phair TJ, Ferrucci BL, Brown BT, Margolick BJ. Accelerated Longitudinal Gait Speed Decline in HIV-Infected Older Men. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2015;70(4):370-6. doi: 10.1097/qai.0000000000000731.
23. Schrack JA, Jacobson LP, Althoff KN, Erlandson KM, Jamieson BD, Koletar SL, Phair J, Brown TT, Margolick JB, Multicenter ACS. Effect of HIV-infection and cumulative viral load on age-related decline in grip strength. *AIDS*. 2016;30(17):2645-52. doi: 10.1097/QAD.0000000000001245. PubMed PMID: 27603294; PMCID: PMC5083134.
24. Tran T, Guardigni V, Pencina KM, Amato AA, Floyd M, Brawley B, Mozeleski B, McKinnon J, Woodbury E, Heckel E, Li Z, Storer T, Sax PE, Montano M. Atypical Skeletal Muscle Profiles in Human Immunodeficiency Virus-Infected Asymptomatic Middle-Aged Adults. *Clin Infect Dis*. 2018;66(12):1918-27. Epub 2018/01/03. doi: 10.1093/cid/cix1121. PubMed PMID: 29293942; PMCID: PMC5982799.