HIV and Aging

MEHUL TEJANI, MD, MPH
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Learning objectives

- Recognize the epidemiological pattern of aging with HIV in the United States and how it relates to testing and prevention
- Describe the population of older adults living with HIV consisting of recent seroconverts and long term survivors
- Identify variables such as polypharmacy and multisubstance use that affect the care and health of a person aging with HIV
- Identify the medical, psychological, and social challenges of older adults living with HIV
- Integrate geriatric concepts and key aging variables into HIV care
What comes to mind when you hear “HIV and aging”? 

HIV HAS NO AGE LIMIT.
Outline

- Epidemiology of older people living with HIV
- New HIV diagnosis in elderly
- Better adherence in elderly
- HIV and “accelerated aging”
- Similarities between HIV and aging in immunology
- Inflammation in HIV and aging
- HIV Associated Non-AIDS conditions (HANA)
- Geriatric syndromes, namely Frailty
- MACS and VACS?
- Mental health and social capital
- Advance directives
- Other resources
Epidemiology of older people living with HIV
Median Age at Death due to HIV Infection
United States, 1987–2010

Source: http://www.cdc.gov/nchs/deaths.htm
CDC estimates the percentage of HIV infected U.S. individuals older than 50 years in 2017 will be:

- a. 20%
- b. 25%
- c. 30%
- d. 40%
- e. > 50%
Estimated Diagnoses of HIV Infection, by Age
2011, United States

An aging HIV population

VA in 2003


Slide courtesy of Amy Justice
Case 1

- Mr. S is a 65 yo MSM who is HIV negative and has no other chronic medical conditions. He currently feels well.
- He is currently sexually active with multiple partners, uses condoms most of the time. He has never used any illicit drugs, never smoked tobacco, and rarely drinks alcohol. He has had STDs in distant past.
- He has been testing himself for HIV annually for decades, always on his birthday. His last negative was on his 65th birthday.
Case 1 question

• Should you recommend Mr. S get tested on his 66th birthday?

• Yes

• No
Mr. S actually did get himself tested on his 66\textsuperscript{th} birthday and was found to be HIV positive.

He is now in treatment

He is also very active in his local LGBT community as an activist and now an HIV spokesman
New HIV diagnoses in the elderly
Rate of new HIV diagnoses in >55 age group increased by 3.6% from 2009 to 2013.
Age at Diagnosis, 2013—United States
N = 47,165, Data from CDC surveillance
HIV Diagnosis in Older Adult

- Physicians are less likely to discuss HIV related risk factors with older adults
- HIV-associated symptoms and other illnesses
- Late presentation for diagnosis and care
- CDC recommendations which lead to...

- Patel D. Curr Inf Dis Rep 2011
- Lindau ST. NEJM 2007
- Gebo KA. Drugs Aging 2006
- MMWR Recomm Rep 2006
Late Diagnosis of HIV Infection

- Less common routine screening
- Poor awareness of the risk of HIV infection
- Poor awareness of safer sex practices
- Failure of physicians to consider HIV infection
- Confusion of symptoms between OIs and conditions associated with aging

- Grabar, S: JAC; Jan 2006
- Patel D. Curr Inf Dis Rep 2011
Myth: HIV over 50

- Seniors don’t have sex and therefore are not at risk for HIV
Sexual Activity in Older Americans (Male)

Sexual Activity in Older Americans (Female)

CASUAL SEX
ROMANTIC SEX
CURIOUS SEX
GAY SEX

IF YOU
HAVE SEX

AGE IS NOT A CONDOM

Learn more. Be safe. Get tested.
NYS 800-541-AIDS 800-541-2437
NYC 800-TALK-HIV 800-825-5448

WHEN IT COMES TO SEX...

AGE IS NOT A CONDOM

Talk to your doctor about your sex life.
Learn more. Be safe. Get tested.
NYS 800-541-AIDS 800-541-2437
NYC 800-TALK-HIV 800-825-5448
ageisnotacondom.org
But it’s not all bad: Adherence
COHERE Study: Baseline Virologic and Immunologic Profile by Age

Baseline HIV RNA

Baseline CD4 Count

COHERE Study:
Response by Baseline Age

Achieving CD4 Count
>200 Cells/mm³ at 12 Months

New AIDS Event
At 12 Months

COHERE Study:
Continuation of HAART by Baseline Age

- Similar rates of discontinuing or switching ≥1 antiretroviral agent during the first 12 months of HAART

- Complete treatment discontinuation was rare
  - Lower rates were observed among those ≥40 years of age

Discontinuation of All ARTs at 12 Months

\[ P < 0.0001 \text{ for trend} \]

Continuum cascade in older patients

HIV Continuum of Care for People ≥ 50 and older in the U.S.

- Virally Suppressed
- Prescribed ART
- Retained in Care
- Linked to Care
- Diagnosed


Disclaimer: The original version of this bar graph was taken from the CDC website and modified to display data for the 45 years and older population only.

The good news is that this is slightly better than the general population.
HIV and accelerated aging?
Mr. D is a 78 year old male with HIV, DM, HTN, possible stroke, CKD, hearing loss

- Stroke was reported by family after he suffered sudden loss of function of right leg while at a nursing facility, but was never evaluated as patient refused transfer

- In addition, he also has a history of right 3rd toe amputation 9 years ago

- HIV VL is suppressed on raltegravir, abacavir/lamivudine, last known CD4 of 163

- Other medications include insulin 70/30, amlodipine, rosuvastatin, aspirin, gabapentin
Case 2, question 1

Which of the following puts him at greatest risk of falling?

- Possibility HIV associated osteoporosis
- Diabetic neuropathy
- Prior amputation
- Prior fall
- Multiple medications
Case 2, question 2

- Is Mr. D at an increased risk of prostate cancer compared to an HIV negative 78 year old man with similar comorbidities?
  - Yes
  - No
  - Maybe

- What about an 88 year old man?
Accelerated Aging in Patients With HIV

- Drug toxicity (e.g., with older HIV treatments)
- Persistent immune dysfunction and inflammation
- Normal aging
- HIV virus itself
- Cognitive/functional decline
- Lifestyle risk factors (e.g., drug/alcohol abuse)
- Coinfection with HBV/HCV

Premature aging
Premature aging in HIV patients?

- Premature aging would imply that same events happen at an earlier age, as in bottom panels

- But seems more likely that events happen at similar ages with increased frequency, as in top panels
Age distribution in the AIDS and general populations. Follow-up time at risk for cancer in both the AIDS and general populations, by age, for regions covered by the HIV/AIDS Cancer Match Study (1996 to 2007).


©2010 by American College of Physicians
Possible arguments in favor of aging

- **Epigenetics**
  - In a small study, the genetic profiles of the DNA of PLWH seemed to be 14 years older than their chronologic age based on genetic profiles of HIV negative controls

- **Comorbidities seem to occur at an earlier age**
Poly-pathology is more common in HIV+ patients and increases with age.

Polypathology (Pp) prevalence among HIV+ cases and HIV-uninfected controls, by age categories.

- **Cases**
  - ≤ 40 yrs: 1%, 3%, 3%, 1% (Pp prevalence 3.9%)
  - 41 to 50 yrs: 1%, 8%, 6%, 4% (Pp prevalence 9.0%)
  - 51 to 60 yrs: 1%, 17%, 15%, 9% (Pp prevalence 20.0%)
  - > 60 yrs: 1%, 15%, 21%, 9% (Pp prevalence 46.9%)

- **Controls**
  - ≤ 40 yrs: 1%, 9%, 31%, 9% (Pp prevalence 10.0%)
  - 41 to 50 yrs: 2%, 17%, 29%, 17% (Pp prevalence 46.9%)
  - 51 to 60 yrs: 1%, 28%, 31%, 28% (Pp prevalence 65.0%)
  - > 60 yrs: 0.25%, 42%, 42%, 42% (Pp prevalence 18.7%)

- **Co-morbidities included:** hypertension, diabetes mellitus, hypothyroidism, cardiovascular disease, bone fractures.

“A central definition of frailty in geriatric medicine is that it is a clinical state of vulnerability to stressors, […] resulting from aging-associated declines in resiliency and physiologic reserves and a progressive decline in the ability to maintain a stable homeostasis.” [1]

Frailty is a predictor of poor outcomes
- Falls
- Hospitalization
- Institutionalization
- Disability
- Mortality [2]

Similarities between HIV and aging in immunology
Similarities between HIV Infection and Aging

- **At the biological level**
  - T-lymphopenia, decreased cellular immunity
  - Replicative senescence of T-lymphocytes
  - \( \uparrow \) pro-inflammatory markers (IL-6, TNF-\( \alpha \), IFN-\( \gamma \))

- **At the clinical level**
  - Sarcopenia (loss of muscle mass), weight loss, wasting
  - Cognitive disorders, dementia
  - Rheumatologic disorders, decrease in bone mineral density
  - Frailty-like clinical presentation, disability, and death
  - (treated) Apparent earlier onset of chronic diseases associated with aging
Haematopoietic stem cells experience functional decline with aging

Sahin and DePinho, *Nature* 2010
## Age- and HIV-Associated Changes of Immune Response (B cells)

<table>
<thead>
<tr>
<th>Adaptive immune response</th>
<th>Change in HIV-infected compared to age-matched control</th>
<th>Change in aging persons, compared with young adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naïve cell number</td>
<td>Normal to low</td>
<td>Normal to low</td>
</tr>
<tr>
<td>Memory cell number</td>
<td>Increased</td>
<td>Increased</td>
</tr>
<tr>
<td>Resting activation</td>
<td>Increase</td>
<td>Normal</td>
</tr>
<tr>
<td>Cytokine production (unstimulated)</td>
<td>Increased</td>
<td>Normal</td>
</tr>
<tr>
<td>CD86 (costimulatory ligand) expression</td>
<td>Increased</td>
<td>Normal</td>
</tr>
<tr>
<td>Total IgG and IgA level</td>
<td>Polyclonal increase</td>
<td>Normal</td>
</tr>
<tr>
<td>$V_H$ gene use (naïve B cells)</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>$V_H$ gene mutation frequency</td>
<td>Few data</td>
<td>Normal</td>
</tr>
<tr>
<td>Primary responses</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Memory responses</td>
<td>Low to normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>

High, KP CID Aug 2008
## Age- and HIV-Associated Changes of Immune Response (T cells)

<table>
<thead>
<tr>
<th>Adaptive immune response</th>
<th>Change in HIV-infected compared to age-matched group</th>
<th>Change in aging persons, compared to young adults</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CD4 cells</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naïve cell number</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Memory cell number</td>
<td>Low</td>
<td>Normal to high</td>
</tr>
<tr>
<td>Resting activation</td>
<td>Highly increased</td>
<td>Increased</td>
</tr>
<tr>
<td>Cytokine production</td>
<td>Low</td>
<td>Low to normal</td>
</tr>
<tr>
<td><strong>CD8 cells</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naïve cell number</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Memory cell number</td>
<td>Low</td>
<td>Normal to high</td>
</tr>
<tr>
<td>Resting activation</td>
<td>Highly increased</td>
<td>Increased</td>
</tr>
<tr>
<td>Cytokine production</td>
<td>Low</td>
<td>Normal to high</td>
</tr>
<tr>
<td>Senescent phenotype</td>
<td>Very high</td>
<td>High</td>
</tr>
</tbody>
</table>

High, KP CID Aug 2008
## T Cell Immunosenescence in Advanced Age Versus Long-Term HAART

<table>
<thead>
<tr>
<th>Biological Parameter</th>
<th>Aging (&gt; 70 years)</th>
<th>Long-term treated HIV Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low CD4/CD8 ratio</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Low naïve T cell %</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Low T cell proliferation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Increased T cell activation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Expansion of CMV-specific T cells</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Reduced T cell repertoire</td>
<td>Yes</td>
<td>Probable</td>
</tr>
<tr>
<td>Reduced T cell telomeres/telomerase</td>
<td>Yes</td>
<td>Unknown</td>
</tr>
<tr>
<td>Reduced regenerative potential (HSM, thymus)</td>
<td>Yes</td>
<td>Probably</td>
</tr>
</tbody>
</table>

Desai S. Curr HIV/AIDS Rep 2010
Inflammation in HIV and Aging
Inflammation predicts disease in treated HIV infection, as it does in the general population

- **Cardiovascular Disease** (Baker, CROI 2013)
- **Lymphoma** (Breen, Cancer Epi Bio Prev, 2010)
- **Venous Thromboembolism** (Musselwhite, AIDS, 2011)
- **Type II Diabetes** (Brown, Diabetes Care, 2010)
- **Cognitive Dysfunction** (Burdo AIDS 2012)
- **Frailty** (Erlandson, JID 2013)
HIV, Aging, and the Heart

- Cumulative toxicity from ARV
  - Use of PI, NRTI
- Proatherogenic state induced by chronic immune activation
  - “cytokine storm”
- Lifestyle factors
- Increased vascular age

Incident rate ratio for acute MI by age

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Rate Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39</td>
<td>2.2</td>
</tr>
<tr>
<td>40-49</td>
<td>1.3</td>
</tr>
<tr>
<td>50-59</td>
<td>1.8</td>
</tr>
<tr>
<td>60-69</td>
<td>1.5</td>
</tr>
<tr>
<td>70-79</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Models adjusted for recognized risk factors

Impact of HIV on risk comparable to traditional risk factors including HTN, DM and hyperlipidemia
HIV, Aging, and the Brain

- More than half will have some impairment
  - Asymptomatic neurocognitive impairment
  - HIV-associated mild neurocognitive disorder
  - HIV-associated dementia
- HAND accelerates in aging
- Chronic inflammation and cerebral flow

Geriatric Syndromes
The Aging Phenotype and the Genesis of Geriatric Syndromes

Aging Phenotypes
- Changes in Body Comp
- Discrepancy Energy Production/Utilization
- Homeostatic Dysregulation
- Neurodegeneration

Disease Susceptibility
- Reduced Functional Reserve
- Reduced Healing Capacity
- Unstable Health
- Failure to Thrive

Geriatric Syndromes
- Gait Disorders
- Falls
- Disability
- Sarcopenia
- Urinary Incontinence
- Decubitus Ulcers
- Cognitive Impairment
- Delirium
- Sleep Disorders
HIV-infected adults have many traditional risk factors for frailty and other geriatric syndromes, raising concerns that the real burden of disease will only become apparent late in life.

Chang et al., Archives of Gerontology and Geriatrics, 2012
MACS: Frailty Phenotype in HIV-Positive MSMs 50 to 70 Years of Age

- Prospective cohort of MSMs (2009-2010)
  - 2850 person-visits
  - HIV positive on HAART (n=1451)
  - HIV negative (n=92)
- Ages 50 to 70 years
  - Frailty phenotype more common in HIV-positive men versus HIV-negative men
    - May be effect of HIV infection, HAART, or both
- Further longitudinal studies are needed

VACS Index Highly Predictive of Long Term (5 Year) All Cause Mortality

\[ y = 0.0091x - 0.0318 \]

\[ R^2 = 0.9916 \]

VACS Index in OPTIMA

Regression of Percent Mortality by Baseline VACS Risk Index Score with Scores by 10

\[ \text{PctN}_{10} = -5.8783 + 0.9856 \times \text{HIVProgScoreV2} \]

Social and mental health factors in HIV and aging
HIV, aging, and depression

- Well established that depression, substance abuse, and the combination are more prevalent in HIV positive patients than in non-HIV infected patients
- Research outside HIV infection shows that depression increases likelihood that minor cognitive impairment will subsequently evolve into dementia
- Though not yet known, feared that HIV will only worsen this likelihood
Elderly patients face several societal barriers, HIV compounds that

- Ageism
- Racism
- Sexism
- Discrimination against sexual preference
- Stigma, especially among age cohort
Social isolation

- Not purely a problem in HIV populations
- But many HIV patients have lost connections
  - To death
  - To lost family ties
  - To lost friends
- This can be difficult because these may all potentially worsen depression, but may also be signs of depression
Advance care planning
Advance planning

- End-of-life discussions, advance directives, and power-of-attorney decisions are important for all older patients.
- Important in HIV patients, especially those with any degree of cognitive or functional impairment.
- Power of attorney especially important if patient does not want closest blood relative to serve as default surrogate decision maker.
- This is a process, not a one-time decision.
Case of Mr. D

- Mr. D was suffering loss of appetite, frequently became hypoglycemic as he was not able to adjust his own insulin doses with decreased intake
- During admission for hypoglycemia, had worsening delirium and was not able to communicate with team, but listed as full code
- Eventually recovered, and during outpatient conversation with him and his wife, whom he formally designated to make decisions, opted for no resuscitation or intubation
The HIV and Aging Consensus Project

Recommended Treatment Strategies for Clinicians Managing Older Patients with HIV

Sponsored by
American Academy of HIV Medicine
AIDS Community Research Initiative of America
Supporting Partner:
American Geriatrics Society
AETC HIV and Aging Toolkit

- http://aidsetc.org/toolkit/aging/home