PART IV
CLINICAL IMPLICATIONS
Background

• Biological link between HIV and aging paints a grim picture, however...

• The benefits of ART strongly outweigh the risks associated with ongoing immune activation and inflammation

• Key question:
  – Is the risk of aging-related diseases increased in PLWHIV vs. comparable HIV-negative individuals?
Background

• Answering question comes with challenges
  – Not clear what constitutes a comparable HIV-negative population
  – Not easy to adjust for confounders (hidden variables) between groups
    • Example: PLWHIV are much more likely to be smokers—a major risk factor for disease and death
    • Other confounders may be hard to identify

• Still, results from cohort studies have yielded important data
Italian Study

- Review of medical data between 2002 and 2009 comparing 2,854 ART-experienced PLWHIV with 8,562 controls
- Matched for:
  - Age, sex, race
- Compared rates of age-related diseases not caused by infections

Italian Study

- Greater likelihood of cardiovascular disease, high blood pressure, kidney failure, bone fracture, and diabetes among PLWHIV, particularly at younger ages.

Italian Study

- Greater likelihood of >1 age-related health complication (polypathology) among PLWHIV, particularly at younger ages

Dutch Study

- Cohort study comparing 489 PLWHIV with 452 comparable HIV-negative controls
- Like Italian study, evaluated rates of age-related diseases not caused by infections
- PLWHIV were somewhat older (53 vs. 52), current smokers, lower body mass index, less likely to be heavy daily drinkers, somewhat higher blood pressure

Dutch Study

- Greater likelihood of >1 age-related disease (60.4% HIV- vs. 74.4% HIV+)

Dutch Study

- Among HIV-positive, higher rates of:
  - High blood pressure
  - Heart attacks
  - Blood vessel problems
  - Reduced blood flow to brain
  - Liver disease
  - Kidney problems
  - Cancer

VACS Study

- Eight-city U.S.-based Veterans Aging Cohort Study
- Has enrolled more than 7,000 HIV-positive veterans and matching HIV-negative controls since 2002
- More than 150 analyses completed to date
- VACS has documented increased risks of:
  - Cardiovascular diseases
  - Pulmonary diseases
  - Decreased physical functioning
  - Fragility fractures (bone breaks from standing height)
  - Renal disease
  - Cancers
VACS Study

- Heart attacks and kidney disease did not occur at younger ages among HIV-positive veterans
- Non-AIDS cancers occur at younger ages, but only slightly
  – Difference of around 7 months compared with HIV-negative veterans

Althoff K, Wyatt C, Gibert C, et al. HIV+ adults are at greater risk for myocardial infarction, non-AIDS cancer, and end-stage renal disease, but events occur at similar ages compared to HIV– adults (Abstract 59). Paper presented at: 20th Conference on Retroviruses and Opportunistic Infections; 2013 March 3–6; Atlanta, GA.
Frailty Phenotype

- Originally pertained to older adults in general population
  - First described in 2001
- Modern-day equivalent of AIDS-related wasting syndrome among PLWHIV
  - Weight loss
  - Weakness
  - Poor endurance and energy
  - Low physical activity
  - Slow walking speed
MACS & Frailty Phenotype

• Frailty among PLWHIV a focus of Multicenter AIDS Cohort Study (MACS)
  – Cohort of HIV+ and HIV− men

• Has demonstrated that risk of frailty increases the further the CD4+ T-cell count falls below 400/mm$^3$

• Frailty can be reversed following start of ART, but symptoms can persist


Impaired Cognition

• HIV can enter brain, resulting in direct and inflammatory damage to central nervous system
  – Asymptomatic neurocognitive impairment
    • Formal tests show impairment, but no change in everyday function
  – Mild neurocognitive impairment
    • Mild-to-moderate impairment in activities
  – HIV-associated dementia
    • Moderate-to-severe impairment in activities
Impaired Cognition

- **MACS**: Higher incidence of diagnosed neurologic disease among PLWHIV

Impaired Cognition

- Hawaii Aging with HIV Cohort (HAHAC)
- 127 older (>50) and 110 younger (<40) PLWHIV, half with CD4+ T cells <200/mm³
  - Compared with matched HIV-negative controls
- Testing results found only marginal differences between the two groups
- Few data exploring duration of HIV infection and ART history on risk of impaired cognition in PLWHIV

Summary

• Generally speaking, data point to doubling of relative risk of age-related health problems in younger PLWHIV
  – Will greatly increase absolute risk of disease and death as PLWHIV continue to age
• More to learn about age-related health problems in PLWHIV with coinfections (e.g., hepatitis C)
• Better studies to understand risk factors in PLWHIV needed
Summary

• Many studies not included in the *Immune System, HIV, & Aging* report

• Lack of clarity regarding the extent to which risk may be increased in younger PLWHIV
  – Studies have not yet included detailed measures of immunologic aging, such as senescence and inflammation