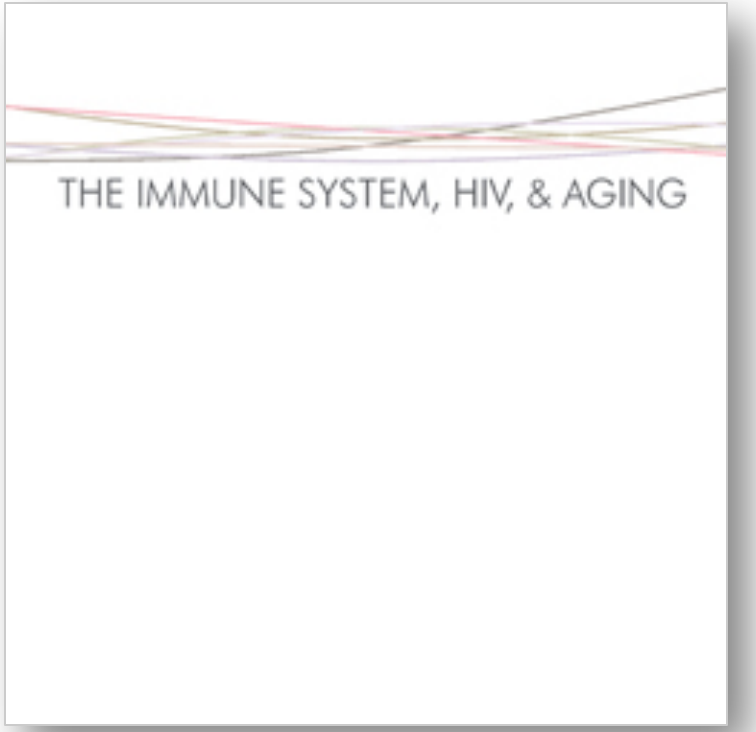


TAG

PART I
INTRODUCTION
AGING AND HIV PATHOGENESIS

INTRODUCTION

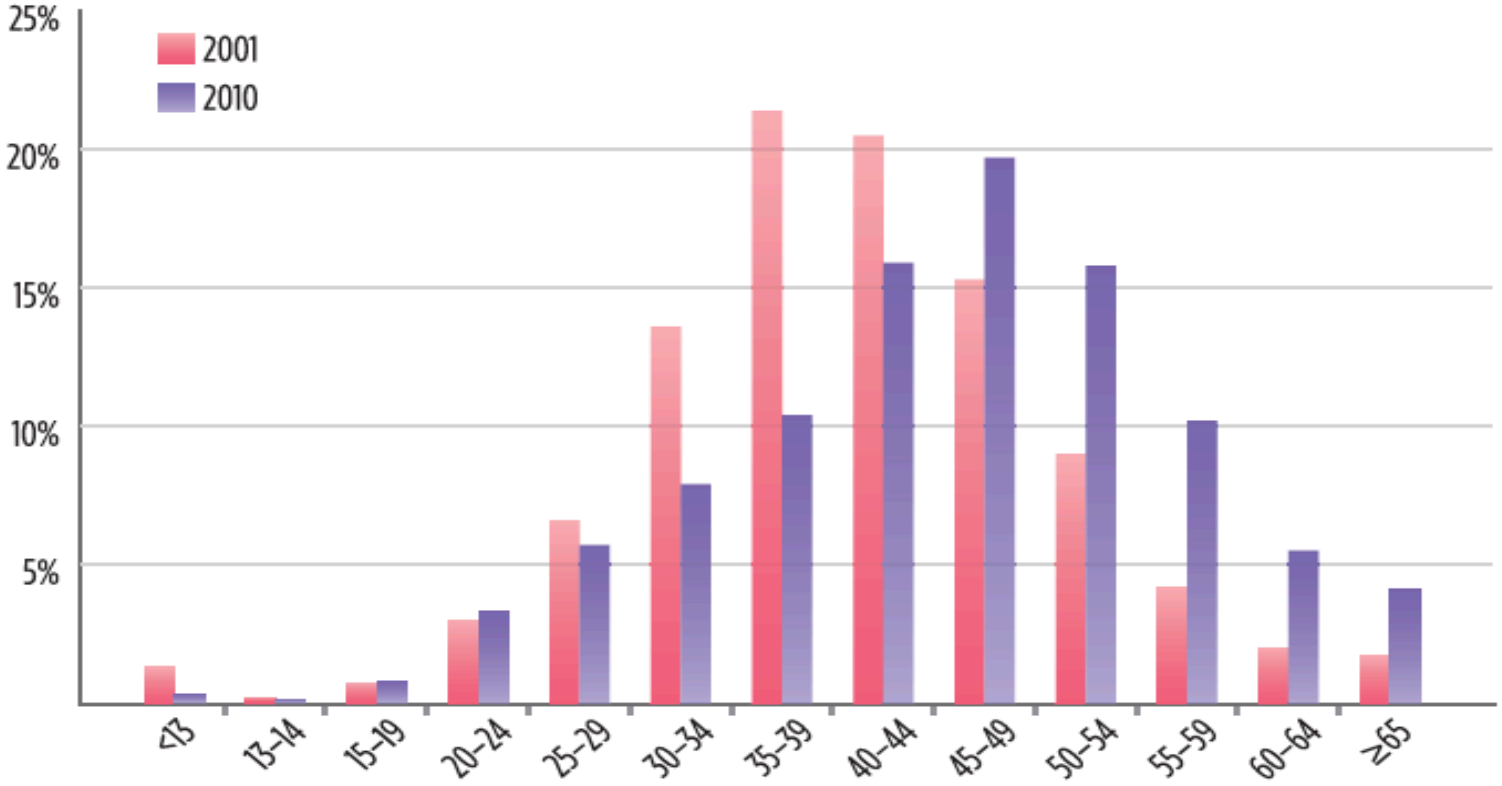
Background

- AIDS-related illness and death rates have plummeted everywhere ARV treatment is available
  - Survival of people living with HIV (PLWHIV) is approaching that of comparable HIV-negative people
- Attention has turned to non-AIDS-related illnesses
  - Risk of these illnesses is often elevated in PLWHIV

Background

- Of concern are illnesses typically associated with aging:
  - Cardiovascular, kidney, and liver disease
  - Bone loss and increased fracture risk
  - Frailty (weight loss, weakness, reduced activity)
  - Cognitive (mental) impairment
  - Cancer
- May be occurring at a younger age vs. comparable HIV-negative populations

Age Distribution of People Living with HIV: 2001 vs. 2010



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Aim

- Aim of TAG's *Immune System, HIV, & Aging* report and accompanying slide decks:
  - Review immunologic connections between HIV and aging
  - Highlight unresolved questions that are being addressed—or need to be addressed—by research

AGING AND HIV PATHOGENESIS

Background

- Early studies suggested that immune-system irregularities associated with HIV contributed to AIDS-related complications often seen in aging
  - Cognitive impairment, muscle wasting, and frailty
- Only recently have studies explored immunologic links between HIV-related disease and aging

The Immune System and Aging

- Chronic infections (pathogens controlled rather than cleared from the body) appear to contribute to decline in immune system competence over time
  - Cytomegalovirus (CMV), possibly Epstein-Barr Virus (EBV)
- Decline in immune system competence is associated with chronic inflammation, or “inflamm-aging”

Immune System in Aging and HIV

- Many similarities between the elderly and PLWHIV
  - Higher CD8 cell count relative to CD4 cell count (inverted CD4:CD8 ratio)
  - Decreased healthy T-cell proliferation
  - Increased senescent (worn out) cells (CD8+CD28- T cells)
  - Elevated levels of inflammatory cytokines (e.g., IL-6, TNF-alpha, and alpha interferon)
  - Decreased T-cell diversity (repertoire)

Drivers of Aging-Associated Disease Risk

- Immune-system alterations in HIV suggest virus is a major driver of aging-associated disease risk
- Other potential contributors
  - ARV toxicities
  - Obesity
  - Insulin resistance
  - Substance use disorders
  - Smoking
  - Stress/depression
  - Sleep disturbances

Summary

- Diseases of aging a growing concern for PLWHIV
- Chronic infections can impair immune system in several ways and lead to chronic inflammation
- Immune profiles in PLWHIV are similar to those seen in elderly
- Immune-system alterations in HIV just one possible driver of aging