PART V
ANTIRETROVIRALS & AGING
Background

- Potential effects of ART toxicity on aging process cannot be discounted
- ARV toxicity must be considered in context of immuno-aging effects of HIV
- The question isn’t whether it is HIV or ART that is associated with aging, but rather how they both contribute
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

• NRTIs can be toxic to the DNA in mitochondria, the energy powerhouses of cells

• Known consequences in PLWHIV
  – Peripheral neuropathy
  – Pancreatitis
  – Lactic acidosis
  – Lipoatrophy
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

• Also linked to muscle fibers deficient in the essential COX enzyme required for energy production
  – COX deficiency typically seen in the elderly
• Newcastle University study
  – HIV− and HIV+ not on ART had normal muscle fibers
  – NRTI-treated PLWHIV had increased frequency of COX-deficient muscle fibers

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

- Mitochondrial DNA dysfunction also linked to increased oxidative stress
  - Zidovudine and stavudine led to slowing of cell division, similar to aging
- Tenofovir can inhibit telomerase activity
  - Unclear if this results in more rapid shortening of telomere length or has any consequences on aging


Protease Inhibitors

- Ritonavir and ritonavir/lopinavir increased senescence markers, oxidative stress, and inflammation in artery cells in test tubes
- Senescence also increased in blood cells from PLWHV receiving PI-based regimens
  - Linked, in one study, to accumulation of prelamin A, which can cause genetic instability in cells
  - Second study did not confirm findings

Summary

- Though ART might have some aging-related effects, there is no evidence that these increase the risk of death.
- Potential for less robust CD4+ T-cell increases, in response to treatment, as PLWHIV age.
- Drug interactions may become increasingly complex as other medications are prescribed for age-related diseases.