ASP-IDSA workshop
HIV and AGING

The Mucosal Immune System
Gut-Assocaited Lymphoid Tissue (GALT)

Effect of aging
Effect of HIV

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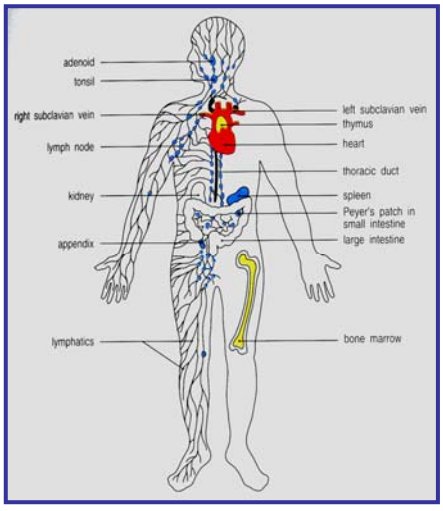
The mucosal immune system



Blood contains ~ 2% of total body lymphocytes

Gut is the site of high antigenic exposure

What do we know about the effect of aging on the human gut?

Data from mouse studies

- the gut immune changes appear at younger ages than those in the blood
- frequencies of CD4 T cells and dendritic cells in Peyer's patches decreases with age
- decreased responses to mucosal vaccines
- reduced responses to cholera toxin and E. coli enterotoxin
- decreased helper T cell and cytotoxic T cell activity

The gut and HIV: I

- Regardless of route of transmission, at initial infection, HIV selects CD4+ T cells that also express CCR5
- Most CCR5+ cells are in the gut
- Calculated # of lymphoid cells containing potentially replication-competent HIV-1 DNA
  PBMC 70,000; GALT 100,000
  (Poles et al. JAIDS, 2006)
- Different regions of gut have different "infectibility" (P. Anton, unpublished)

The gut and HIV: II

- even if treat early (during acute phase) and blood CD4+ T cells rebound normally, gut remains depleted (Markowitz and colleagues)
- After 3 yrs of therapy that fully suppressed HIV replication, most had only 50% of normal CD4+ T cell number in gut
- Once the infection has become chronic, the CD8+ T cell response in the gut is "too little, too late": <5% of that seen in any other lymphoid organ
- Long-term non-progressors: prolonged maintenance of mucosal T cells, enhanced virus-specific reponses

The gut and HIV: III

- Successful vaccine must stimulate mucosal immunity
- Mucosal tissue readout to evaluate vaccines
- HIV and colorectal cancer:
  present with more advanced case at younger age
  more adenomas found at younger age
- start screening at younger age

HIV and bone loss: are immune cells involved ?

- Activated T cells secrete factors that affect osteoclasts
- Immune activation associated with bone loss
- Osteoporotic fractures correlate with increased proportions of senescent CD8 T cells
- Oxidized LDL stimulate T cells