HIV/AIDS and the Eye: Epidemics, Endemics, and Syndemics
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I. What is HIV?
   a. The Human Immunodeficiency Virus (HIV-1) causes the disease AIDS (Acquired Immunodeficiency Syndrome)
   b. This retrovirus (that converts RNA to DNA) specifically attacks T cells (CD4+ cells)

II. HIV/AIDS in Cities Worldwide
   a. 33.4 million people living with HIV/AIDS in 2008 (down from 40.3 in 2005)
   b. 2.7 million people newly infected with HIV (down from 4.9 million in 2005)
   c. 60% of infections are in sub-Saharan Africa
   d. Women ~50% of all infections worldwide

III. HIV/AIDS in America (2010)
   a. As many as 1,000,000 people infected
   b. 20% are unaware
   c. 56,300 new infections per yr
   d. Over 18,000 die of AIDS each year in the US alone

IV. HIV/AIDS by County in US (2011)
   a. Leading killer of African-American males, age 25-44
   b. 7x more than whites
   c. 2/3 of AIDS cases in both women and children were among African-Americans

V. HIV Transmission
   a. Acute HIV Manifestations (weeks or months duration)
   b. Lymphadenopathy
   c. Fever
   d. Chills
   e. Night sweats
   f. Weight loss
   g. Diarrhea

VI. Chronic AIDS Manifestation: Dementia
   a. Characterized early by difficulty concentrating
   b. Decreased short-term memory
   c. Slowed mentation and movement disorders are seen
   d. Without treatment, expect progression to severe global dementia

VII. Symptoms of CMV ocular infection in AIDS patients
   a. Painless decrease in vision in one or both eyes
   b. Hazy vision
   c. Floaters/flashes
   d. Metamorphopsia
   e. VF defect
   f. May be asymptomatic

VIII. Early Signs of HIV/AIDS Retinopathy
   a. Cotton wool spots (CWS) may be initial ocular manifestation of AIDS
   b. While CWS present in 2/3 of patients with AIDS, they are nonspecific for AIDS
      i. DDX: Diabetic retinopathy, hypertension, severe anemia, lupus, leukemia
      ii. The eye may have higher susceptibility to CMV (cytomegalovirus) infection
   c. HIV/AIDS Retinal Hemorrhages
i. Incidence of 12-40% in patients with AIDS
ii. Flame-shaped
iii. Dot/blot
iv. Roth spot

IX. AIDS-Related Cytomegalovirus (CMV) Retinitis
   a. Infectious for humans of all ages
   b. Latent infections common
   c. Approximately 50 to 80% of US adults are CMV seropositive
   d. CMV Can occur as new infection or more commonly through reactivation of latent virus
   e. Prior to treatment of AIDS, CMV most common ocular opportunistic infection
      i. 12%-46% of all opportunistic infections
      ii. Leading cause of blindness in AIDS
   f. CMV Retinitis
      i. Necrotizing retinitis with or without hemorrhages is usual presentation
      ii. Patchy yellow-white areas with secondary hemorrhage along the edges
      iii. Occurs most frequently along the major vascular arcades or near the ONH
      iv. ALL retinal layers affected → full thickness retinal destruction
      v. Spread centrifugally - direct extension from diseased to healthy retina
   vi. Types of CMV Retinitis
      1. Hemorrhagic
      2. Brushfire
      3. Granular
   vii. Sequelae of CMV Retinitis
      1. Vessel attenuation
      2. Calcifications in atrophic retina
      3. Capillary nonperfusion
      4. Chorioretinal scarring
      5. Loss of VA (site specific)
      6. Optic atrophy
      7. Retinal detachment (24-50%)
   viii. Differential Diagnosis of CMV Retinitis
      1. HIV retinopathy (CWS and/or intraretinal hemorrhages)
      2. PORN (progressive outer retinal necrosis)
      3. HZV retinitis
      4. HSV retinitis
      5. Toxo retinochoroiditis
      6. Infectious multifocal choroiditis
   ix. Other CMV Ocular Complications
      1. Papillitis, Macular edema, Vasculitis, and Uveitis
      2. Immune recovery uveitis (IRU) – may occur when pt’s immune system recognizes/reacts to viral antigens in retina after successful HIV Tx
   g. CMV Retinitis Treatment Options
      i. HAART = Highly Active AntiRetroviral Therapy
         1. Ganciclovir ((Cytovene, Cymeveve)
            a. Inhibits viral DNA polymerase
            b. Nausea, vomiting, neutropenia, thrombocytopenia
         2. Foscarnet (Foscauvir)
            a. Inhibits viral DNA polymerase and reverse transcriptase
      ii. Pre-HAART (1995-98)
         1. CMV retinitis in 20-40%
         2. Survival 1985 → 12 months
      iii. HAART (1998-00)
         1. CMV retinitis decreased by 80%
         2. Survival 2005 → 30 months
      iv. "Typical" cocktail for CMV retinitis:
         1. IV cidofovir
2. vitreal implant ganciclovir
3. intravitreal injections of ganciclovir and/or foscarnet

v. Other CMV treatments:
1. Vitrasert – gancyclovir implant in those with active retinitis
   a. 4.5 mg sust. release, lasts 6-10 mo
2. Valganciclovir (Valcyte)
   a. oral 450mg tablets
3. Foscarnet (Foscavir)
4. Cidofovir (Vistide)
   a. vitreal injection 20 μg q5-6 weeks
5. Fomivirsen (Vitravene)
   a. vitreal injection 330μg on d1 and d15, then 1x/mo

X. Other anterior segment manifestations of AIDS
a. Molluscum contagiosum
   i. Umbilicated center
   ii. Shed viral particles
b. Herpes Zoster Ophthalmicus
c. Conjunctival vascular changes (75%)
d. Dry eye (10-15%)
   i. SPK
   ii. Microsporidia (parasitic protozoan) is cause
   iii. Mild conjunctivitis
   iv. CD4 below 50 cells/ml³
e. Kaposi’s Sarcoma
   i. Rare dermatologic neoplasm in immunocompromised pts
   ii. Endemic in Africa
   iii. One of the more common cancers in AIDS
   iv. Lymph nodes 80%
v. GI tract 80%
vi. Pulmonary involvement 10%
vii. Conjunctival and/or lid involvement in 17%-24% of AIDS patients
viii. Kaposi’s Sarcoma Treatment
   1. Radiation (brachytherapy, beam irradiation)
   2. Chemotherapy (antineoplastic drugs)
   3. Excision/destruction (cryo/thermal)

XI. Untreated HIV Time Course
a. Acute HIV syndrome within 3-9 weeks of infection
b. Clinical latency between 9 weeks and 9 years
c. AIDS symptoms to death between 9-11 years

XII. HIV Tests
a. Enzyme-Linked Immunosorbent Assay (ELISA)
b. Western Blot
c. Rapid Antibody Tests
d. OraQuick® In-Home HIV Test

XIII. Optometric co-management of patients with HIV/AIDS
a. Early diagnosis
b. Screening exam every few months:
   i. With retinal specialist
   ii. With primary care physician
   iii. With infectious disease specialist
   iv. With immunologist
   v. Low vision devices
c. Consultation/referral to medical physician skilled in treating HIV-infected patients
d. No separate treatment of the eyes may be necessary
e. Always ask about helper T cell (CD4) count and viral load
   i. Normal CD4 = 1,000 cells/mm³
   ii. Average decline of 85 cells/year
   iii. Retinitis develops at ~ 50-75 cells/mm³
   iv. Return to clinic based on CD4 count
      1. CD4 > 400: RTC q1 year
         a. If normal retinas or solitary IRH and/or CWS
   v. There is no ‘normal’ viral load
   vi. CD4 count is more important than viral load
   vii. US Federal guidelines recommend treatment when CD4 count < 350 cells/mm³

XIV. Anti-HIV Therapy
   a. Combination of NRTI with two NNRTIs
      i. “Triple Therapy”, “Highly Active Antiretroviral Therapy” (HAART), “Cocktail”
      ii. 3 or more drugs used for best outcomes (usually from 2 or more classes)
   b. Nucleoside Reverse Transcriptase Inhibitors (NRTIs)
      i. Many can cause peripheral neuropathy
      ii. Zidovudine (ZDV, AZT)
         1. Thymidine analog; first approved for HIV
         2. Incorporates into cell and viral DNA
         3. Useful for AIDS dementia
         4. Can reduce mother-to-infant HIV transmission from 25% to 8%
         5. Myelosuppression risk
      iii. Didanosine
          1. Pancreatitis risk
      iv. Zalcitabine
   c. Non-Nucleoside Reverse Transcriptase Inhibitors
      i. Binds/inactivates reverse transcriptase
      ii. Inhibits HIV-1 (but not HIV-2 or other retroviruses)
      iii. Nevirapine
          1. Can reduce mother-infant transmission by 40%
      iv. Delavirdine
      v. Efavirenz
         1. Unique neurotoxic effects (abnormal dreams)
   d. Protease Inhibitors
      i. Binds to viral proteases, preventing viral assembly; no I-C activation needed
      ii. Saquinavir
         1. First protease inhibitor (1995); not used much
      iii. Ritonavir
      iv. Indinavir
      v. Amprenavir
      vi. Nelfinavir
      vii. Ganciclovir (Foscarnet)
   e. Antiretroviral Fusion Inhibitor
      i. Prevents fusion of HIV with host cell outer membrane, preventing cell infection
      ii. Enfuvirtide (Fuzeon, T20)
         1. Subcutaneous injection
   f. Combination HIV/AIDS Medications

XV. Summary

XVI. References