HIV-Associated Opportunistic Infections (OI): Part 3

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Disclosures of Financial Relationships with Relevant Commercial Interests

- None

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HIV Associated Opportunistic Infections: Part 3

- **Mucocutaneous Infections: Candida, VZV, HSV, EBV**
- **Fungal Infections (other than Cryptococcal Meningitis and Candida)**
- **Gastrointestinal (GI) Complications**
- **Cytomegalovirus (CMV)**

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Mucocutaneous Candidiasis in PWH

- Oropharyngeal and esophageal candidiasis common in people with HIV (PWH) who have CD4 cell counts <200
  - Esophageal candidiasis typically occurs at lower CD4 counts than oropharyngeal candidiasis
- Mostly due to *Candida albicans*
- Invasive candidiasis is **NOT** HIV related
  - Candida in blood should raise suspicion of catheter related blood stream infection or injection drug use

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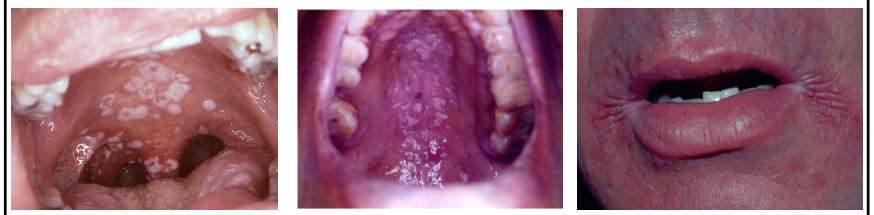
Oropharyngeal Candidiasis

Pseudomembranous | **Erythematous** | **Angular cheilosis**



Photograph from
David H. Spach, MD

https://www.hiv.uw.edu/go/basic-primary-care/oral-manifestations/core-concept/all
Also: Drs. Anisa Mosam, Richard Johnson. Patil S et al, Front Microb, 2015

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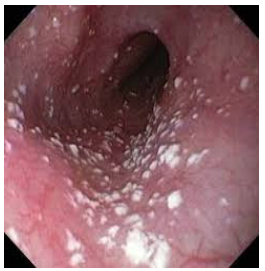
Esophageal Candidiasis



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Mucocutaneous Candidiasis in PWH: Management

- Fluconazole primary prophylaxis or chronic suppression NOT RECOMMENDED
- Treatment:
  - Oral candidiasis: oral fluconazole 100 to 200 mg daily (except during pregnancy); topical miconazole, clotrimazole troches, nystatin
  - Esophageal candidiasis: fluconazole, 14-21 days

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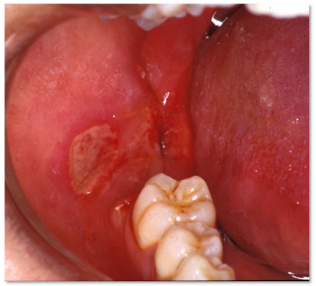
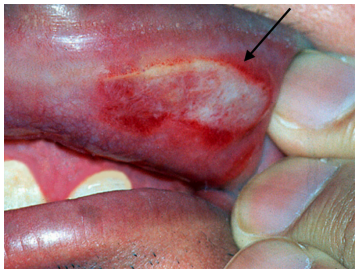
Aphthous Ulcers





Black arrow points to a large aphthous lesion on the lip.
Photograph from David H. Spach, MD

https://www.hiv.uw.edu/go/basic-primary-care/oral-manifestations/core-concept/all
Additional images courtesy of Drs. Anisa Mosam, Richard Johnson and Medscape

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Causes of Odynophagia in People with Advanced HIV

- Esophageal candidiasis
- Giant aphthous ulcers
- HSV esophagitis
- CMV esophagitis

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Herpes Zoster

- **Pre ART**
  - 15-fold higher incidence of zoster than general population!
- **Post ART**
  - Still increased risk even on suppressive ART
- **Localized (dermatomal)**
  - May occur at all CD4 cell counts
    - More frequent when CD4 cell count <200 or HIV RNA not suppressed
  - Risk of zoster increased in the months after ART initiation, possibly because of immune reconstitution inflammatory syndrome-related mechanism.

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/varicella-zoster?view=full

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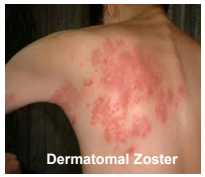
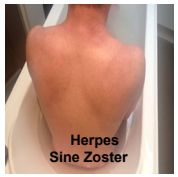
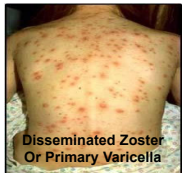
Localized and Disseminated Herpes Zoster







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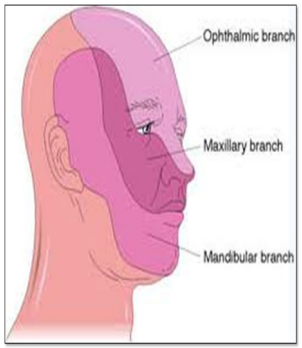
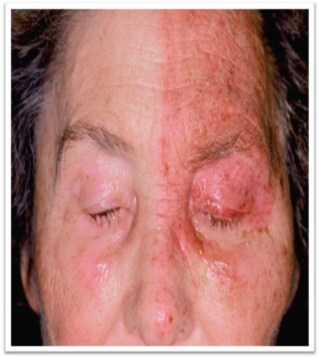
Zoster Ophthalmicus
Ophthalmic Branch CN V





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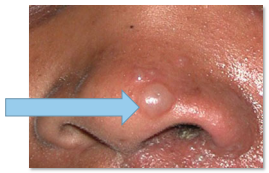
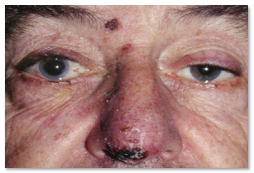
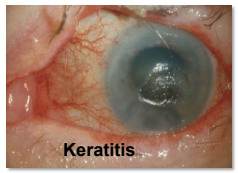
Hutchinson's Sign As Precursor to VZV Eye Disease

(Nasociliary Nerve of Ophthalmic Branch CN V)







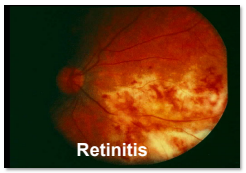


Image C. Stephen Foster, MD, Massachusetts Eye Research and Surgery Institute

- Vesicles on tip of nose, or vesicles on side of nose
- Accompanies development of ocular manifestations: keratitis, anterior uveitis

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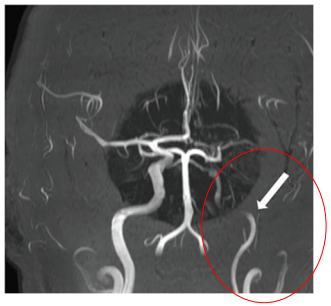
Zoster Ophthalmicus Related Stroke

- Vascular inflammation and occlusion
- Days or months post zoster (median 4 months)
- Occasionally cutaneous lesions absent (33%)
- Diagnosis: PCR of CSF or VZV antibody production in CSF



Fugate JE, January 2020, Practical Neurology

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Ramsay-Hunt Syndrome: Herpes Zoster Oticus

Geniculate Ganglion of Cranial Nerve VII
External Ear Vesicles and Facial Nerve Paralysis

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Prevention of Zoster

- Recombinant VZV glycoprotein E /adjuvant AS01B (RZV-Shingrix)
- Recommended in adults with HIV aged ≥18 years, regardless of CD4 cell count
- 2-dose series at 0 and then at 2 to 6 months
- RZV should not be given during an acute episode of herpes zoster

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/varicella-zoster?view=full

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Herpes Simplex

- Orolabial herpes: most common manifestation of HSV-1 infection
- Genital herpes: typically caused by HSV-2 but increasingly due to HSV-1 (recurrences and viral shedding less often with genital HSV-1)
- Proctitis in men who have sex with men; may not have external anal ulcers
- Dissemination: rare, even in severely immunosuppressed patients
- Other manifestations in PWH who have low CD4 counts (<100)
  - Esophagitis
  - Retinitis (acute retinal necrosis)
  - Chronic, extensive, deep genital ulcers, often acyclovir resistant

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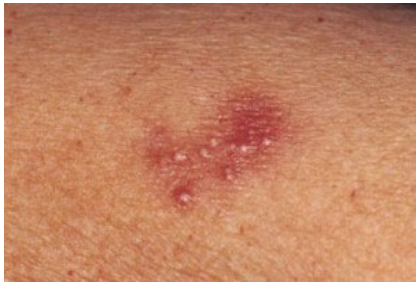
Localized Herpes Simplex



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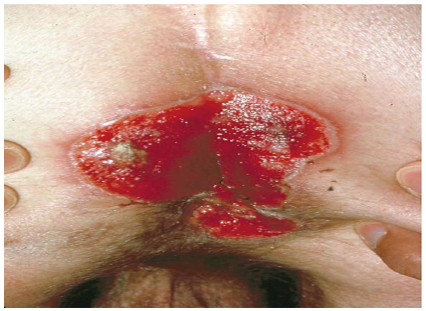
Chronic Extensive Perirectal HSV in PWH with Low CD4 Count



- Look for Acyclovir Resistance with Viral Culture and Phenotypic Testing
- Treatment for acyclovir-resistant HSV: iv foscarnet

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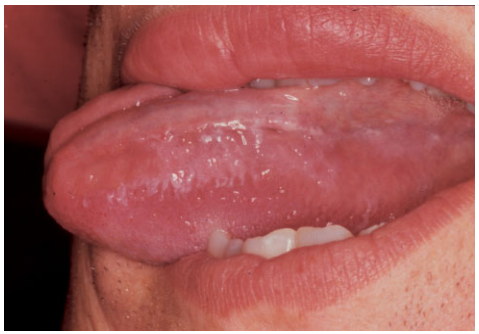
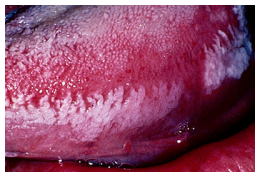
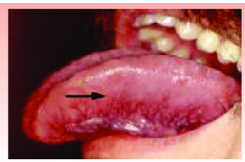
Oral Hairy Leukoplakia EBV Associated







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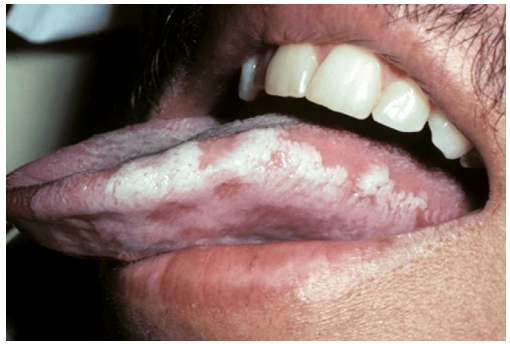
Oral Hairy Leukoplakia



Photograph from Mark Nichols, DDS, Dental Director, South Central AETC
https://www.hiv.uw.edu/go/basic-primary-care/oral-manifestations/core-concept/all

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HIV Diseases Associated with EBV

- Oral Hairy Leukoplakia
- Primary CNS Lymphoma

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Dermatologic Findings in PWH

Prurigo nodularis

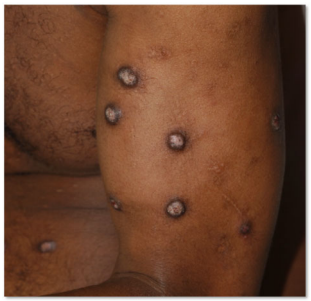
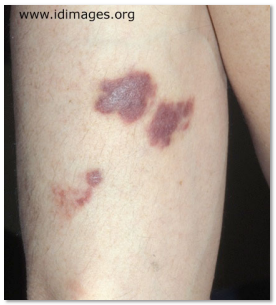


Image courtesy of Dr. Anisa Mosam

Kaposi Sarcoma (HHV-8 associated)



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HIV Associated Opportunistic Conditions: Part 3

Fungal Infections
(other than Cryptococcal Meningitis and Candida)

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Fungal Diseases (other than Cryptococcal Meningitis and Candida) in Persons Living with HIV

- Cryptococcus: cutaneous, prostate
- Talaromyces
- Histoplasmosis
- Coccidioidomycosis

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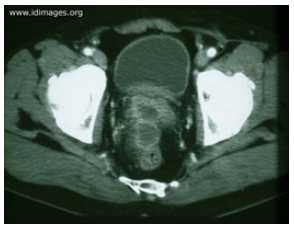
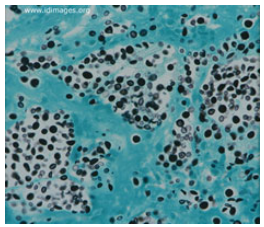
Cryptococcal Prostate Abscess

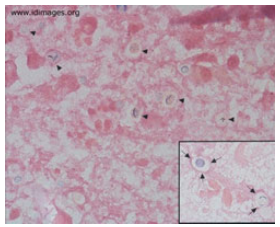
- Man with advanced HIV, CD4 cell count 40, HIV RNA 225,000 (not on ART) presented with 4 weeks of pain on defecation



Pelvic CT scan: Prostate Abscess



Silver stain of prostatic aspirate.



Hematoxylin and eosin stain.
www.idimages.org

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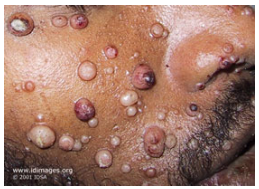
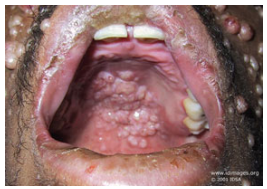
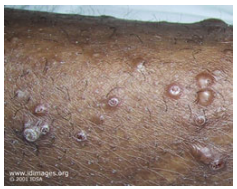
Mucocutaneous Cryptococcus

Man with advanced HIV, CD4 count <20 (not on ART) presented with fever, cough and skin lesions







www.idimages.org

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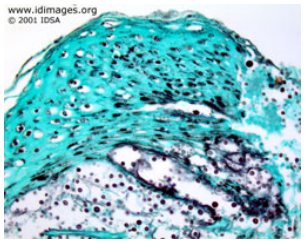
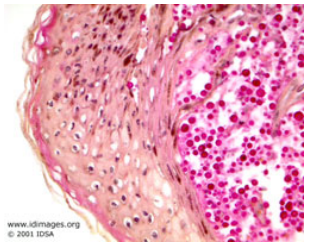
Mucocutaneous Cryptococcus

Man with advanced HIV, CD4 count <20 (not on ART) presented with fever, cough and skin lesions



Silver stain of skin biopsy



Mucicarmine stain of biopsy.

www.idimages.org

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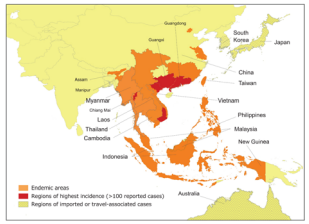
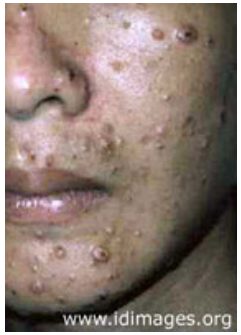
Talaromyces marneffei (formerly *Penicillium marneffei*)

- Dimorphic fungus endemic in SE Asia, East Asia, South Asia
- Advanced HIV is risk factor for severe disease
- Skin lesions: central-necrotic or umbilicated papules
- Pulmonary, GI involvement; hepatosplenomegaly





https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/talaromycosis?view=full

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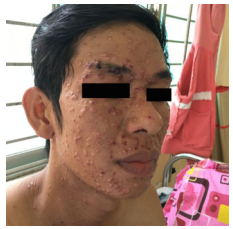
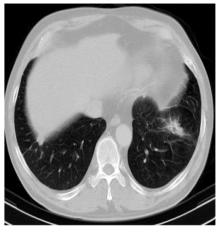
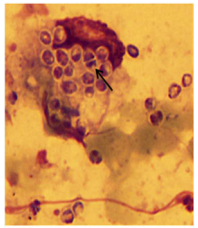
Talaromyces marneffei (formerly *Penicillium marneffei*)







Round-to-oval organisms,
3 to 6 µm in diameter.
Midline septum in a dividing yeast cell

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/talaromycosis?view=full

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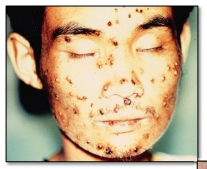
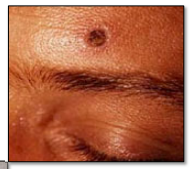
Skin Lesions for HIV Associated Endemic Mycoses May Be Difficult to Distinguish

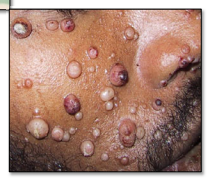
Talaromyces



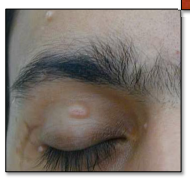
Histoplasmosis



Cryptococcosis



Molluscum



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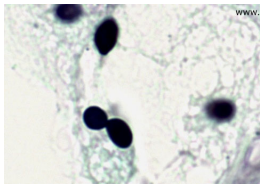
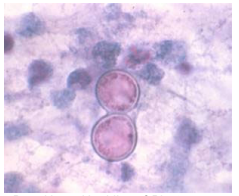
Other Fungal Diseases that are Covered Elsewhere in IDBR

- Look for questions on patients with HIV and….

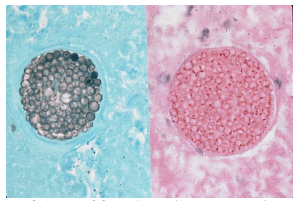
www.idimages.org



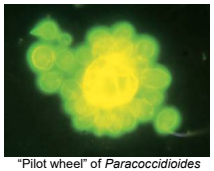
Narrow-based budding of *Histoplasma* (2-5 microns)



Broad based budding of *Blastomyces*
10-15 microns



Spherule of *Coccidioides* (25-100 microns)



"Pilot wheel" of *Paracoccidioides*
(10-20 microns)

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HIV Associated Opportunistic Conditions: Part 3

GI Complications

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Causes of Diarrhea in PWH

- **CMV Colitis**: bloody diarrhea, intestinal perforation in PWH with CD4 <100
- **Bacterial causes:** Salmonella, Shigella, Campylobacter, Enteroaggregative E coli; Clostridioides difficile; STIs/proctitis (LGV, GC, Syphilis); MAC (CD4 count <50: fevers, systemic symptoms)
- **Parasitic causes:** Microsporidia and Cryptospordia (CD4<100: chronic diarrhea, extra-intestinal manifestations); Cystoisospora (formerly Isospora); Cyclospora; Giardia; Amebiasis
- **Cancer:** Kaposi sarcoma, lymphoma
- **Medications:** antiretroviral therapy (particularly protease inhibitors), antibiotics

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/bacterial-enteric?view=full

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Evaluating Diarrhea in PWH

- Acute diarrhea: stool C and S, C difficile testing
- Chronic diarrhea: above plus stool O and P, cryptosporidia, microsporidia, isospora, cyclospora stains; giardia antigen; if proctitis, STI testing
- Diarrhea, fever, systemic symptoms in PWH and low CD4 cell count: AFB blood cultures, CMV DNA
- Endoscopy: if evaluation above is unrevealing

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Salmonella in PWH

- Bacteremia more common in PWH (especially those with low CD4 count) than people without HIV
- Bacteremia merits HIV testing
- Recurrence common unless effective ART given

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Update – CDC Recommendations for Managing and Reporting *Shigella* Infections with Possible Reduced Susceptibility to Ciprofloxacin

HAN HEALTH ALERT NETWORK
Distributed via the CDC Health Alert Network
June 7, 2018, 11:00 ET (11:00 AM ET)

This is an official CDC HEALTH UPDATE

June 7, 2018

Shigella

- Increasing number of Shigella isolates that test susceptible to ciprofloxacin (MIC 0.12 to 1 mcg/mL) but harbor resistance genes
- DHHS: consider treatment; may be withheld in PWH and CD4 >500 with mild symptoms or whose diarrhea is resolving before cultures return
- Counsel patients to wait to have sex for 1-2 weeks after diarrhea resolves

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/bacterial-enteric?view=full

Slide 37

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Increase in Extensively Drug-Resistant Shigellosis in the United States

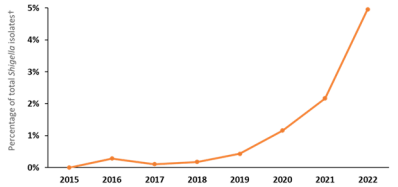
Print

HAN HEALTH ALERT NETWORK

This is an official CDC HEALTH ADVISORY

Feb 24, 2023

- ≃ 5% of Shigella now XDR: resistant to azithromycin, ampicillin, ciprofloxacin, ceftriaxone, TMP/SMX
- Men who have sex with men, people experiencing homelessness, international travelers, people with HIV



- No current treatment recommendations
  - In UK, oral Pivmecillinam and Fosfomycin or IV carbapenem and colistin (hospitalized)

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HIV Associated Opportunistic Conditions: Part 3

CMV

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CMV in PWH: Highlights

- Cause of end-organ disease in PWH who have CD4 count <50 and are not receiving ART
- End-organ disease:
  - Retinitis
  - Colitis
  - Esophagitis: odynophagia, retrosternal or mid-epigastric pain
  - Neurologic disease
  - Pneumonitis: rare in people with HIV; when CMV found in bronchoalveolar lavage, frequently a bystander

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/cytomegalovirus?view=full

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Prevention of CMV Disease in PWH

- Antiretroviral therapy to maintain CD4 count >100
- Valganciclovir prophylaxis is NOT recommended

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/cytomegalovirus?view=full

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Diagnosis of HIV Related CMV Disease

- **Serology**
  - Disease unlikely if IgG seronegative
- **Cytology**
  - Rarely useful
- **Biopsy**
  - Helpful if many inclusions and substantial inflammation
- **PCR**
  - Correlates with low CD4 Count
  - "Less than ideal" sensitivity and specificity for clinical disease

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/cytomegalovirus?view=full

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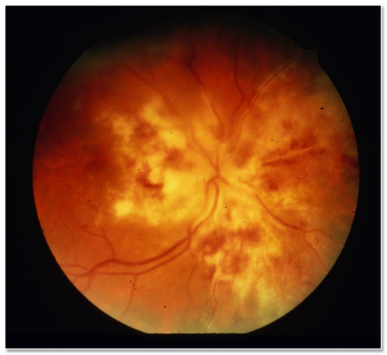
CMV Retinitis

- **Visual changes, decreased visual acuity**
- **Funduscopic exam**
  - Bilateral disease in 1/3
  - Mustard and Ketchup
  - Necrosis of retina
  - Little vitreal inflammation
- **PCR of blood not useful: 70% sensitive, but non-specific**
- **Vitreal taps for diagnosis with PCR rarely necessary**
  - Tap positive in 80% of cases



https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/cytomegalovirus?view=full

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Therapy for CMV Retinitis

- **Immediate sight-threatening lesions**
  - ART
  - IV Ganciclovir or Valganciclovir 900 mg PO (twice daily x 14–21 days), then daily for at least 3-6 months plus
  - Intravitreal ganciclovir weekly over several weeks until lesion inactivity
  - Ganciclovir implant no longer manufactured
- **Small peripheral lesions**
  - ART
  - Oral valganciclovir for at least 3-6 months and immune reconstitution
  - +/- intravitreal ganciclovir

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/cytomegalovirus?view=full

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CMV Colitis

- **Clinical Presentation**
  - Fever, anorexia, abdominal pain, diarrhea
  - May cause perforation, hemorrhage
  - CT may show colonic thickening or mass
- **Diagnosis**
  - Colonoscopy with cytology or biopsy: mucosal ulcerations, intranuclear and intracytoplasmic inclusions, immunohistochemistry
  - PCR non-specific
- **Therapy:** Ganciclovir, Valganciclovir. Alternative: Foscarnet

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/cytomegalovirus?view=full

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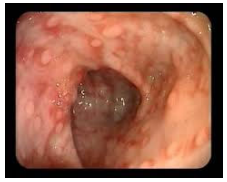
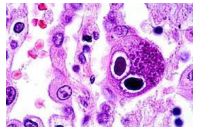
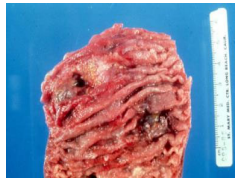
CMV Colitis

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CMV Neurologic Disease

- **Encephalitis**
- **Ventriculoencephalitis**
  - Focal neurologic signs, rapid progression
  - Peri-ventricular enhancement on MRI or CT imaging
- **Polyradiculomyelopathy or transverse myelitis**
  - Radicular back pain, urinary retention, bilateral leg weakness
  - Spastic myelopathy, sacral paresthesia
  - CSF: neutrophilic pleocytosis (100-200), low glucose, elevated protein

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/cytomegalovirus?view=full

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Thank you

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