STDs: A Comprehensive Clinical Review for Eye Care Providers

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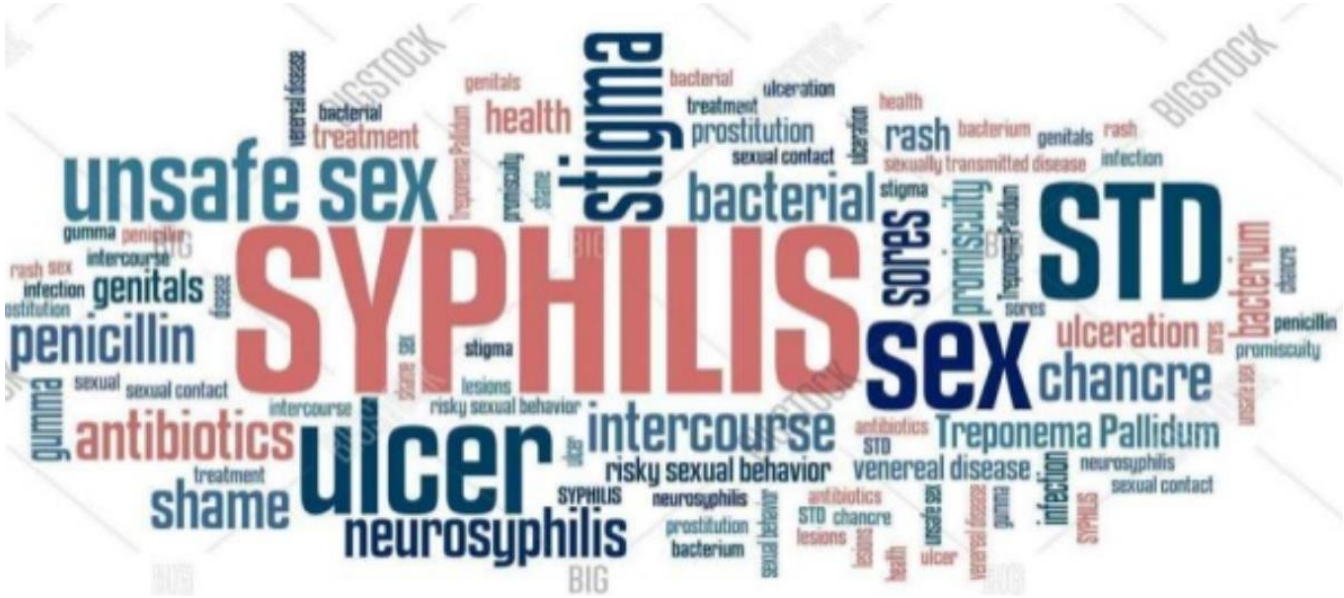

Disclosures

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Disclosures

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Expected Learning Objectives

At the end of the session, attendees should be able to:

1. Review background and demographic information regarding to STDs.
2. Explain proper evaluation including pertinent history and examination in patients suspected of an STD.
3. Recognize clinical characteristics, both ocular and systemic, of patients suspected of presenting with a STD.
4. Summarize proper examination including assessment of the findings and proper management and referrals of patient suspected of STD.
5. Recall appropriate principles of universal precautions when treating patients with STDs.

What is an STD?

The term **sexually transmitted disease (STD)** is used to refer to a condition passed from one person to another through *sexual contact*

An STD may also be called a sexually transmitted infection (STI) or venereal disease (VD)

You can contract an STD by having unprotected vaginal, anal, or oral sex with someone who has the STD

That doesn't mean sex is the only way STDs are transmitted

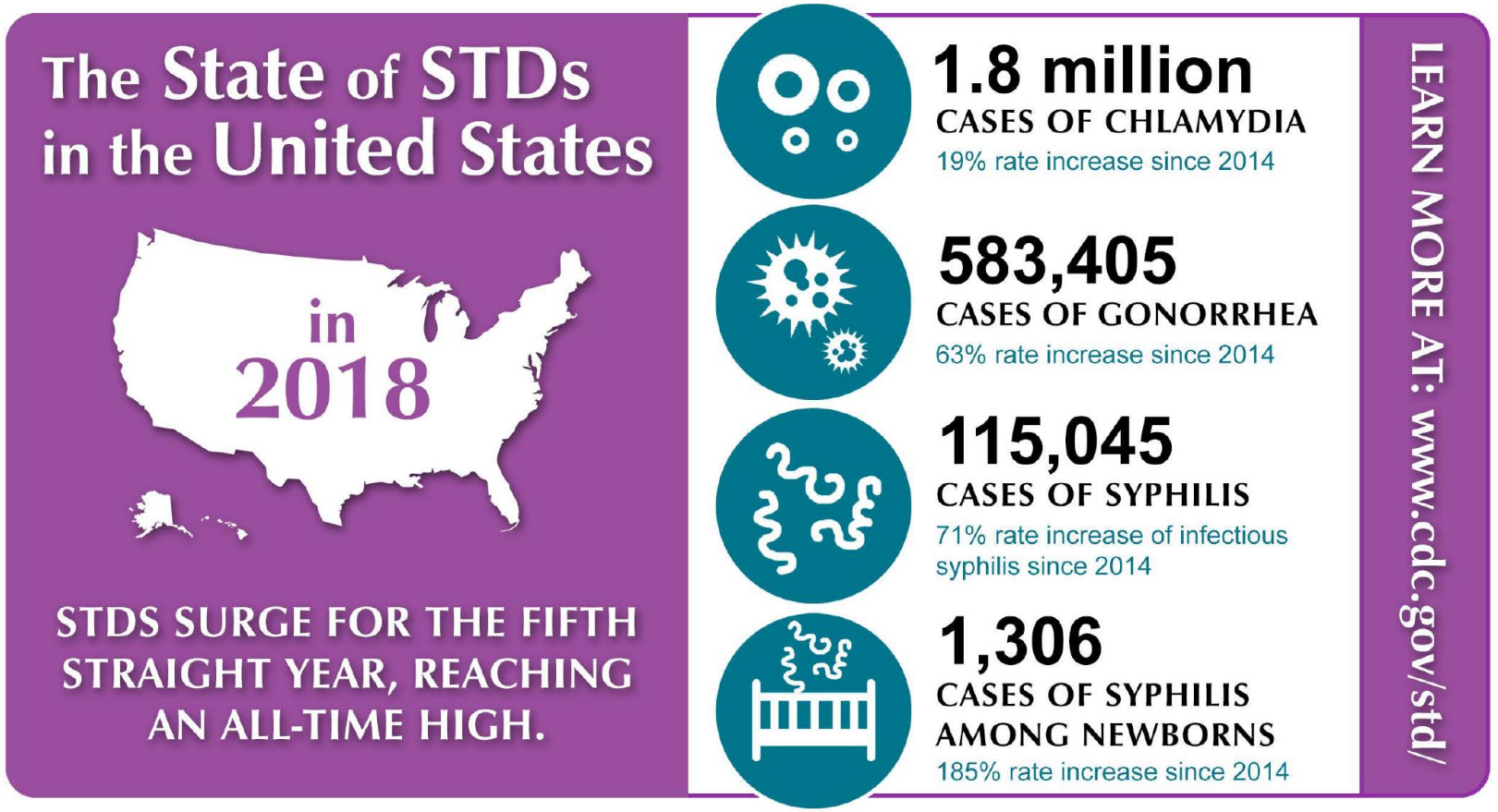
Depending on the specific STD, infections may also be transmitted through sharing needles, breastfeeding, etc.

What is an STD?

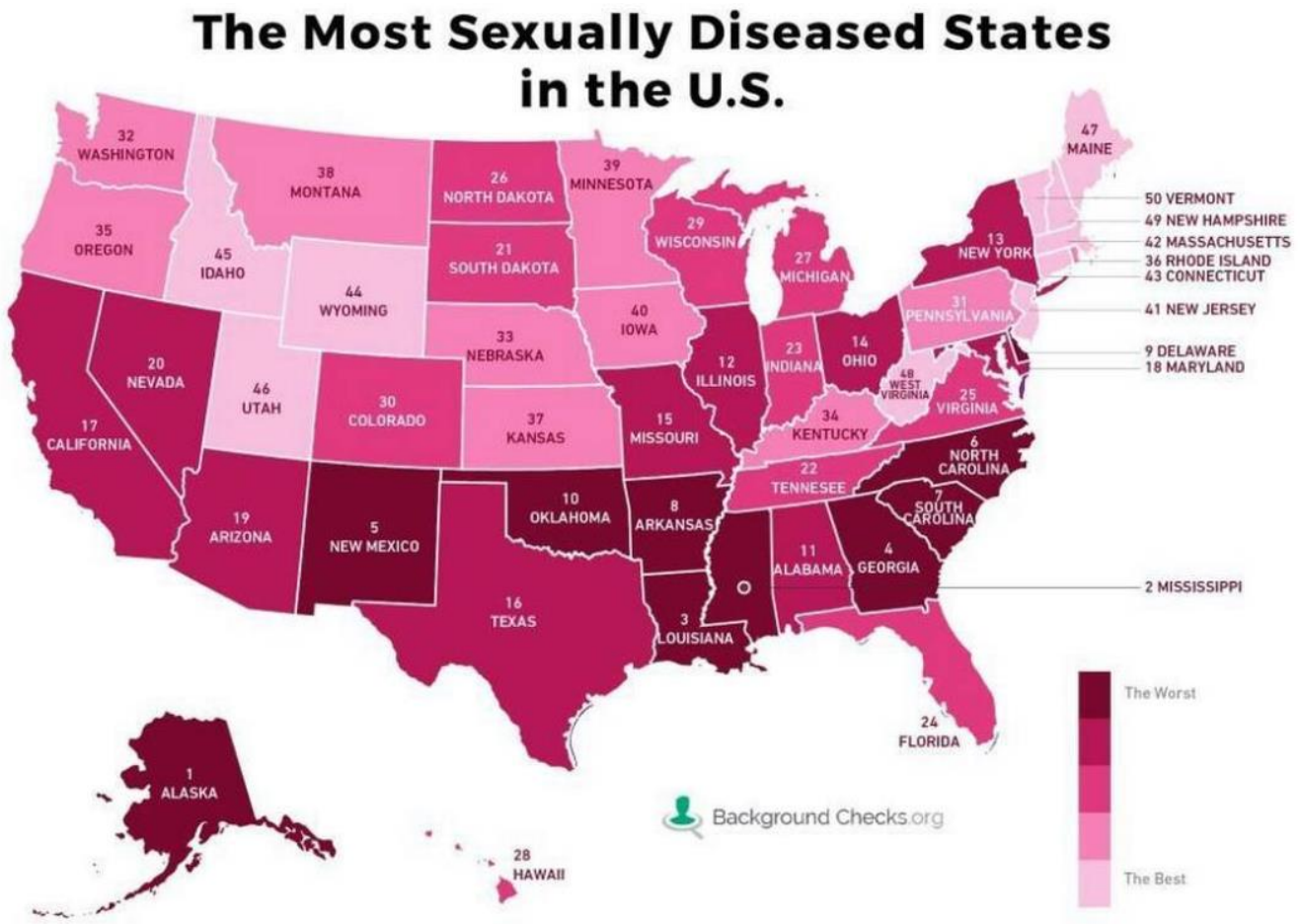
The causes of STDs are bacteria, parasites, and viruses

There are more than 20 types of STDs

STDs in the US: Current Statistics



STDs in the US: Current Statistics



STDs

In general, young people, especially in the age group **15-24 years**, bear the greatest burden of STDs and account for about 50% of all new cases

Most STDs affect both men and women, but in many cases their complications can be more severe for women

STDs and the Eye

The eye is a common site of infection

Nearly all STDs can have ocular involvement

Ocular infection can occur as direct or indirect infection

Ocular examination and proper investigations should be a part of the routine assessment of the patients seen with confirmed or suspected STDs to ensure prompt management of any further complications

STDs and the Eye

STDs with Ocular Manifestations

- Chlamydia
- Gonorrhea
- Syphilis
- Pediculosis
- Human Immunodeficiency Virus (HIV)
- Herpes Simplex Virus
- Hepatitis B & C Virus

Universal Precautions

Hand hygiene

Use of personal protective equipment

Safe use and disposal of sharps

Routine environmental cleaning

Reprocessing of reusable medical equipment and instruments

Respiratory hygiene and cough etiquette

Aseptic non-touch technique

Waste management

Universal Precautions

Hand Washing

- With soap and water after EACH patient
- Dry with FRESH towel

Gloves

- Used if open wound, weeping lesions, dermatitis or exposure to tears or mucous membranes
- Discard after EACH patient
- Double glove if risk of needle stick
- Double glove removes innoculum from needle

Gowns & Masks

- Unnecessary for routine exam
- Used only if splashing of blood or blood products anticipated (ER)

Universal Precautions

Instrumentation in Optometric Practice

- Single-use instruments and equipment should be used whenever possible
- All reusable instruments need to be cleaned immediately after use and then disinfected or sterilized, depending on intended use

Clinical Pearls

History

- May be difficult to elicit
  - Patient may not openly share information
    - Stigma
    - Not understanding pertinence to eye disease

Many patients need to be co-managed with infectious disease

- Detection of ocular complications in presence of known history of past or present STD
- Ocular findings leading to suspicions of past or present history of STD

Need to report to health agencies such as CDC a/o Health Dept

- Knowing who and how to report a patient

Chlamydia

Chlamydia trachomatis is the **most common** bacterial cause of sexually transmitted genital infections in both men and women

It can cause serious, permanent damage to a woman's reproductive system

And possible **sterility**

Chlamydia can also cause a potentially fatal ectopic pregnancy

Chlamydia

Mode of Transmission

- Through vaginal, anal, or oral sex with and infected person
- A previously successfully treated person, can be infected again through same modes of exposure
- Transmission is possible even in the absence of ejaculation
- An infected pregnant mother can pass on the infection to the baby during delivery via exposure in the birth canal

Chlamydia

Clinical Course

The incubation period of symptomatic disease ranges from 5 to 14 days following exposure

However, it is unclear how long those with asymptomatic disease may carry the infection

Chlamydia in the Eye

Ocular Findings: Chlamydial Inclusion Conjunctivitis

- Sexually transmitted, due to *Chlamydia trachomatis* serotypes D-K and typically found in young adults
- A history of vaginitis, cervicitis, or urethritis may be present

Chlamydia in the Eye

Chlamydial Inclusion Conjunctivitis

Signs

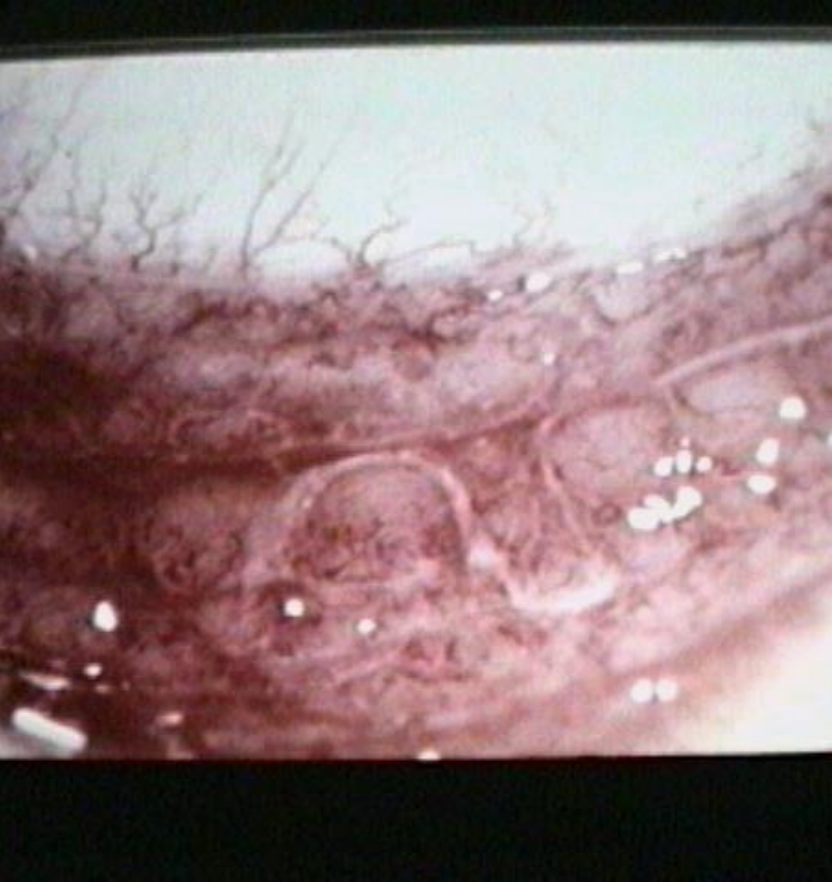
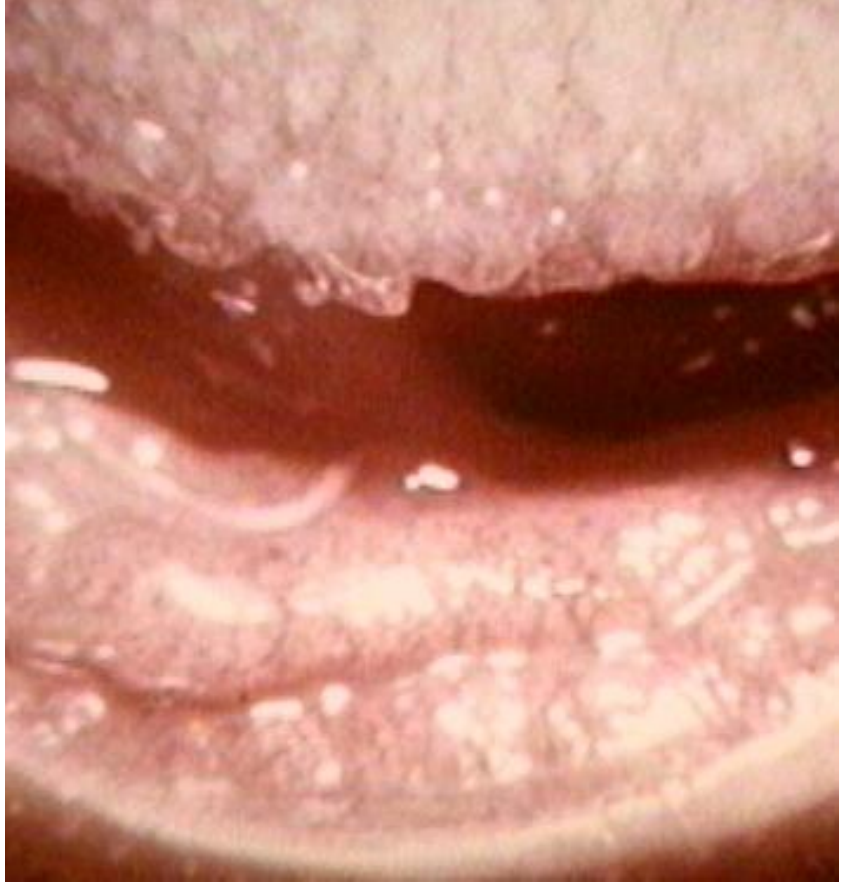
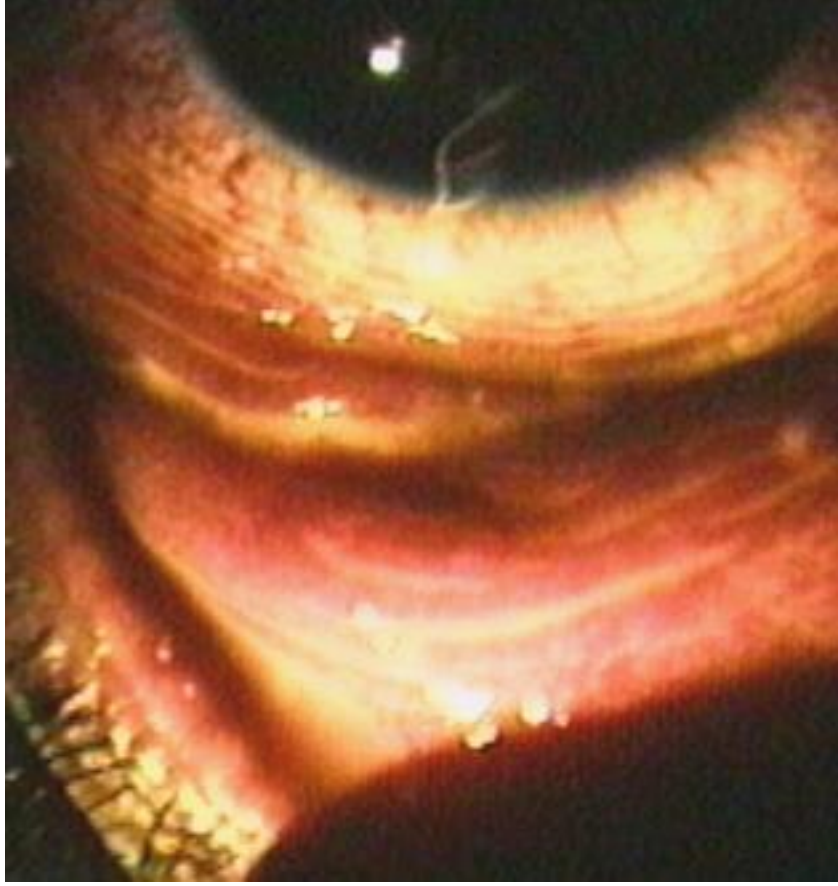
- Inferior tarsal or bulbar conjunctival follicles
- Superior corneal pannus
- Palpable preauricular node
- Peripheral sub-epithelial infiltrates (SEIs)
- A stringy, mucous discharge may be present

Chlamydia in the Eye

Chlamydial Inclusion Conjunctivitis

Workup

- History: Determine the duration of red eye, any prior treatment, concomitant vaginitis, cervicitis, or urethritis. Sexually active?
- Slit lamp examination
- In adults, direct chlamydial immunofluorescence test, DNA probe, chlamydial culture, or polymerase chain reaction of conjunctival sample
- Consider conjunctival scraping for Giemsa stain: Shows basophilic intracytoplasmic inclusion bodies in epithelial cells, polymorphonuclear leukocytes, and lymphocytes in newborns

Chlamydial Inclusion Conjunctivitis

Chlamydia in the Eye

Chlamydial Inclusion Conjunctivitis

Treatment

Azithromycin 1 g p.o. single dose, doxycycline 100 mg p.o. b.i.d., or erythromycin 500 mg p.o. q.i.d. for 7 days is given to the patient and his or her sexual partners	Topical erythromycin or tetracycline ointment b.i.d. to t.i.d. for 2 to 3 weeks

Chlamydia in the Eye

Chlamydial Inclusion Conjunctivitis

Follow-up

- In 2 to 3 weeks, depending on the severity
- The patient and sexual partners should be evaluated by their medical doctors for other sexually transmitted diseases
- Occasionally a 6-week course of doxycycline may be required

Gonorrhea

- Can infect both men and women
- It can cause infections in the genitals, rectum, and throat
- It is a very common infection, especially among young people ages 15-24 years
- Can be cured with appropriate treatment

Gonorrhea

Mode of Transmission

Through having vaginal, anal, or oral sex with someone who has gonorrhea	A pregnant woman with gonorrhea can give the infection to her baby during childbirth

Gonorrhea in the Eye

Ocular Findings: Gonococcal Conjunctivitis

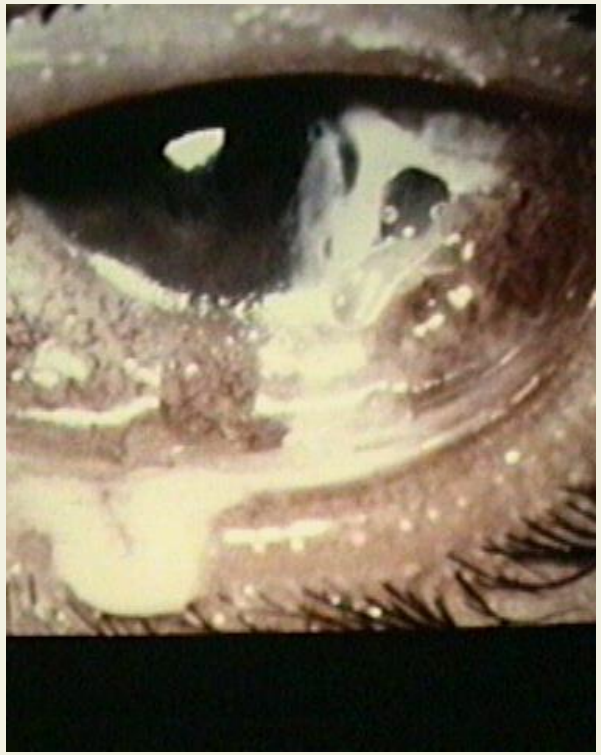
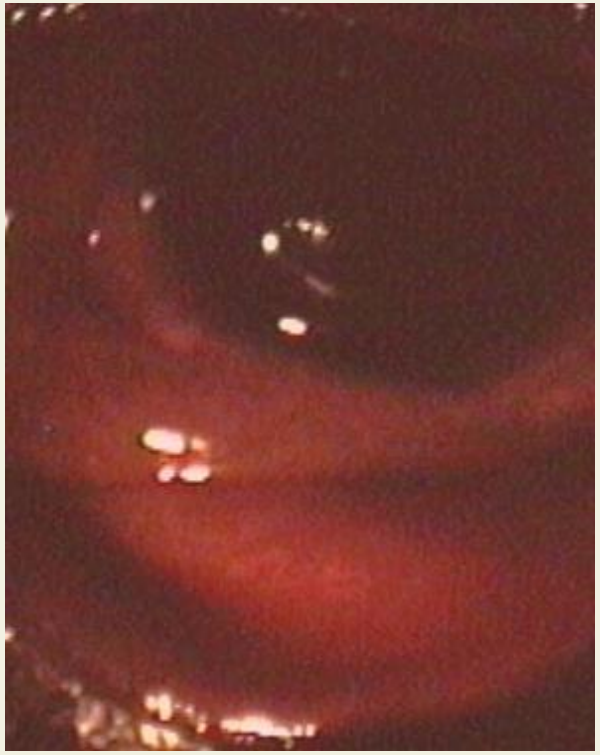
- **Signs**
  - Severe purulent discharge
  - Hyperacute onset (classically within 12 to 24 hours)
  - Conjunctival papillae
  - Marked chemosis
  - Preauricular adenopathy
  - Eyelid swelling

Gonorrhea in the Eye

Gonococcal Conjunctivitis

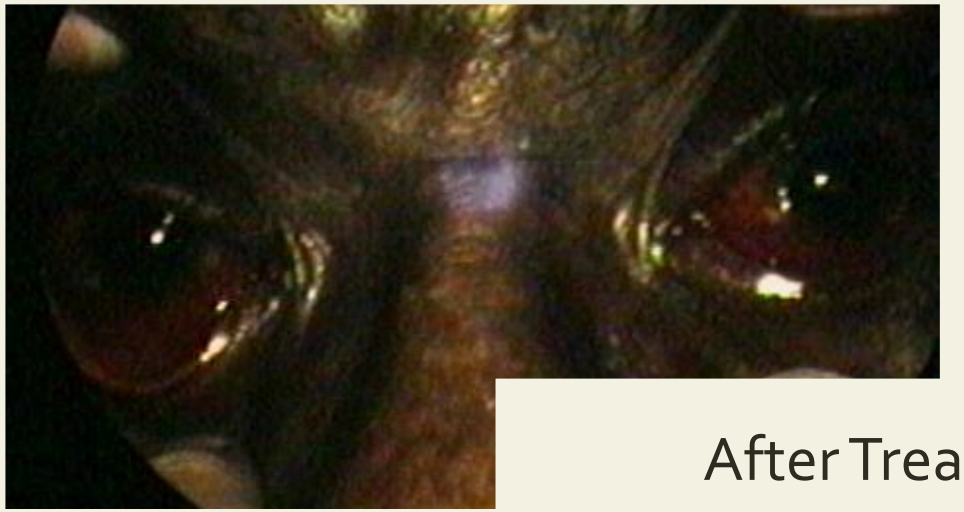
- **Work-Up**
  - Examine the entire cornea for peripheral ulcers (especially superiorly) because of the risk for rapid progression to perforation
  - Send conjunctival scrapings for immediate Gram stain and for culture and sensitivities (e.g., chocolate agar or Thayer–Martin agar)



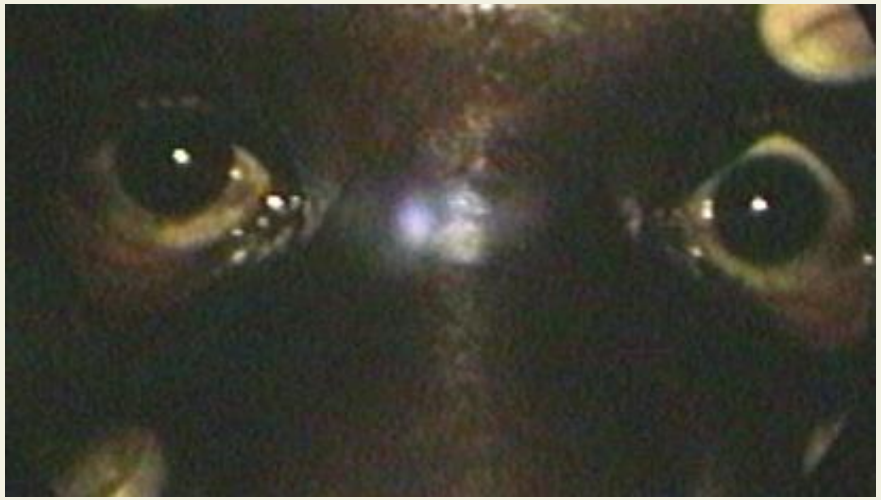



Gonococcal Conjunctivitis

Gonococcal Conjunctivitis



After Treatment



Gonorrhea in the Eye

Gonococcal Conjunctivitis

Treatment

Initiated if the Gram stain shows gram-negative intracellular diplococci or there is a high clinical suspicion of gonococcal conjunctivitis

A dual treatment regimen of ceftriaxone 1 g intramuscularly (i.m.) PLUS azithromycin 1 g p.o. both in a single dose is recommended

If corneal involvement exists, or cannot be excluded because of chemosis and eyelid swelling, hospitalize the patient and treat with ceftriaxone 1 g intravenously (IV) every 12 to 24 hours in place of IM ceftriaxone. The duration of treatment may depend on the clinical response.

Gonorrhea in the Eye

Gonococcal Conjunctivitis

- **Treatment** (***Continued***)
  - If ceftriaxone is not available or unable to be tolerated (e.g., cephalosporin-allergic patients), consider the following treatment regimens:
    - Gemifloxacin 320 mg p.o. in a single dose PLUS azithromycin 2 g p.o. in a single dose
    - Gentamicin 240 mg i.m. in a single dose PLUS azithromycin 2 g p.o. in a single dose

Gonorrhea in the Eye

Gonococcal Conjunctivitis

- **Treatment** ***(Continued)***
  - Topical fluoroquinolone ointment q.i.d. or fluoroquinolone drop q2h. If the cornea is involved, use a fluoroquinolone drop q1h (e.g., gatifloxacin, moxifloxacin, besifloxacin, levofloxacin, or ciprofloxacin)
  - Saline irrigation q.i.d. until the discharge resolves
  - Treat for possible chlamydial coinfection (e.g., azithromycin 1 g p.o. single dose or doxycycline 100 mg p.o. b.i.d. for 7 days)
  - Treat sexual partners with oral antibiotics for both gonorrhea and chlamydia as described

Gonorrhea in the Eye

Gonococcal Conjunctivitis

- **Follow-up**
  - Daily until consistent improvement is noted and then every 2 to 3 days until the condition resolves
  - The patient and sexual partners should be evaluated by their medical doctors for other sexually transmitted diseases

Syphilis

Syphilis is a bacterial infection usually spread by sexual contact

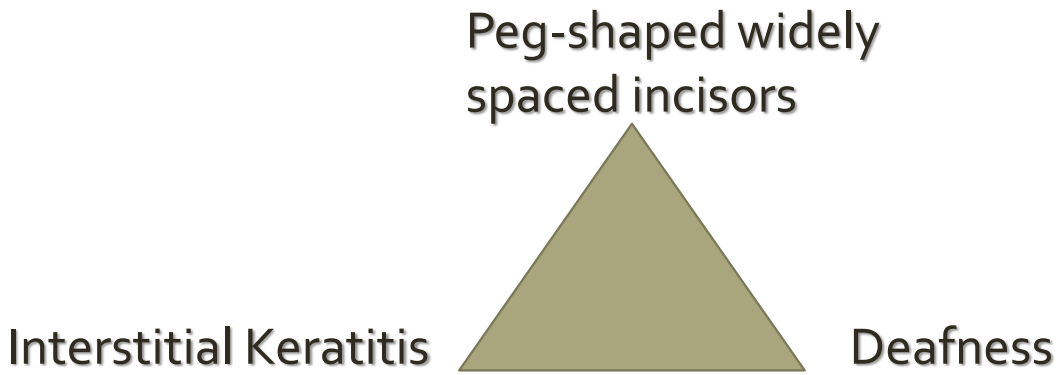
2 Types

Congenital	Acquired

Syphilis

Congenital Syphilis

- Hutchinson triad of congenital syphilis includes



Syphilis in the Eye

Congenital Syphilis

- Ocular signs include
  - Bilateral interstitial keratitis
  - Secondary cataracts
  - Salt-and-pepper chorioretinitis
  - Panuveitis

Syphilis

Acquired Syphilis

Systemic Signs

- Primary: Chancre (ulcerated, painless lesion), regional lymphadenopathy
- Secondary: Skin or mucous membrane lesions, generalized lymphadenopathy, constitutional symptoms (e.g., sore throat, fever), symptomatic or asymptomatic meningitis
- Latent: No clinical manifestations
- Tertiary: Cardiovascular disease (e.g., aortitis), CNS disease (e.g., meningovascular disease, general paresis, tabes dorsalis)

Syphilis in the Eye

Acquired Syphilis

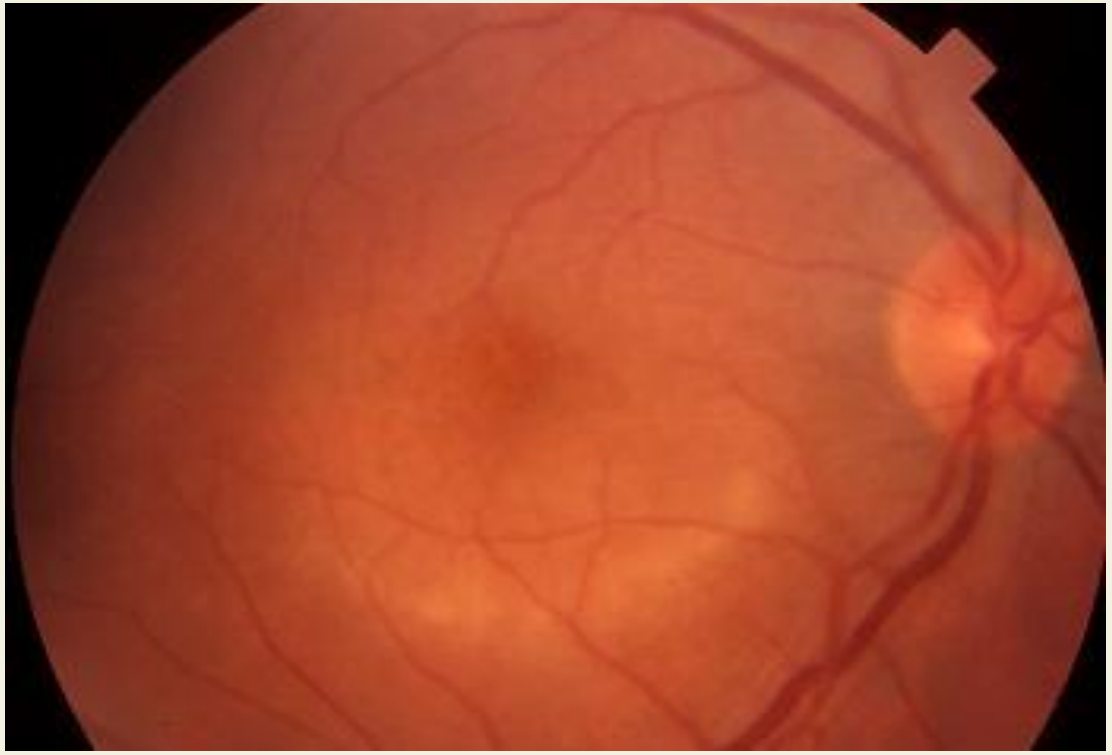
Ocular Signs

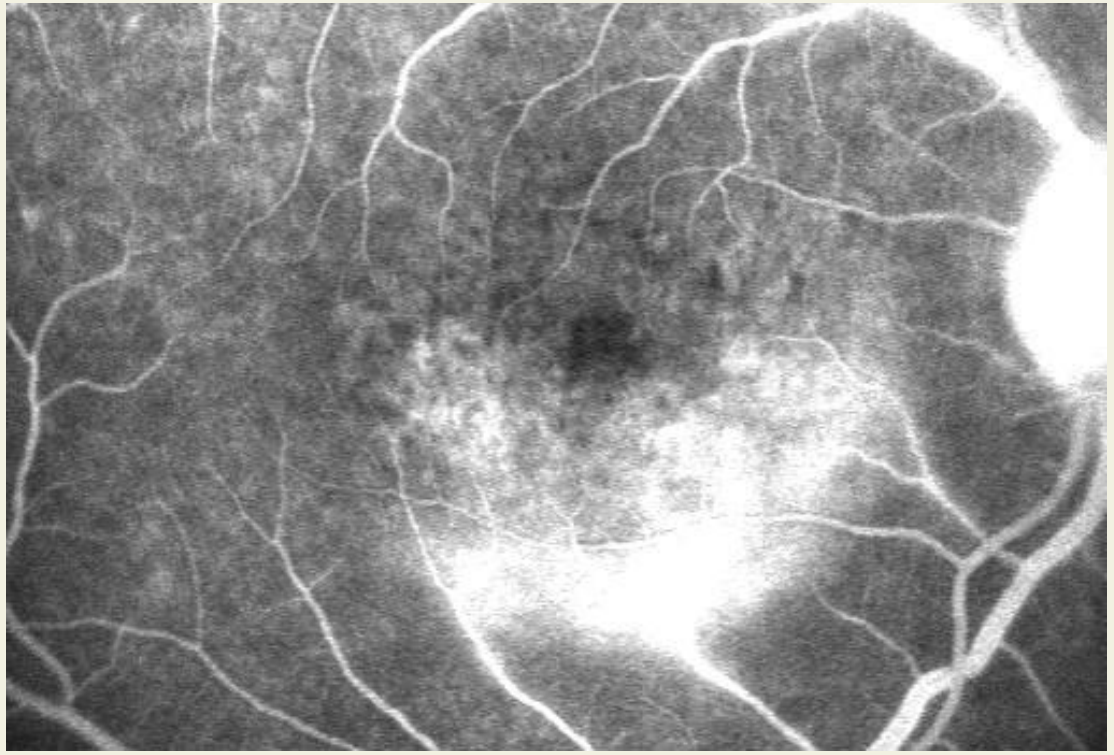
- Primary: A chancre may occur on the eyelid or conjunctiva
- Secondary: Uveitis (mixed anterior and intermediate most common), optic neuritis, active chorioretinitis, retinitis, retinal vasculitis, conjunctivitis, dacryoadenitis, dacryocystitis, episcleritis, scleritis, monocular interstitial keratitis, and others
- Tertiary: Optic atrophy, old chorioretinitis, interstitial keratitis, chronic iritis, Argyll Robertson pupil in addition to signs seen in secondary disease

Syphilis in the Eye

Differential Diagnosis

Anterior uveitis (iritis/iridocyclitis)	Posterior uveitis



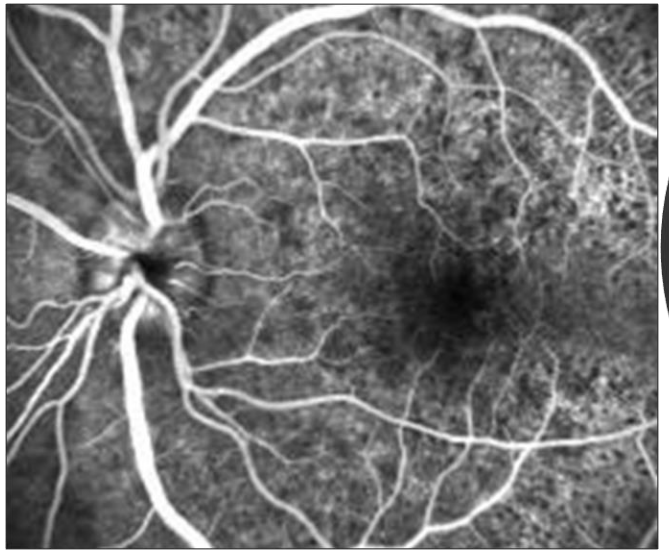


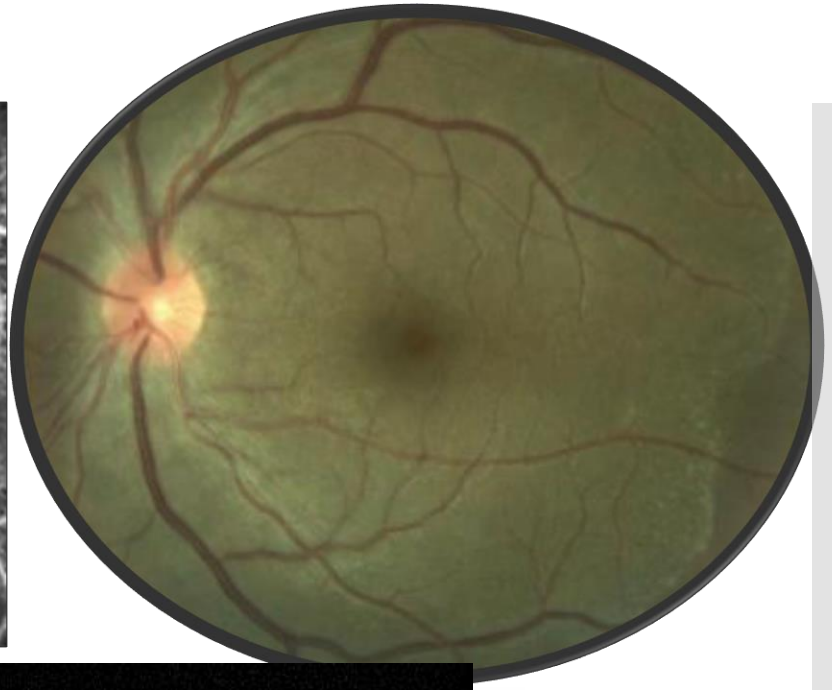
Syphilis: Multiple Presentations

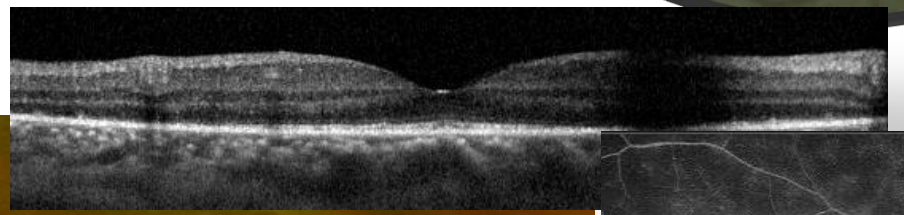
Test all patients with uveitic disease for syphilis

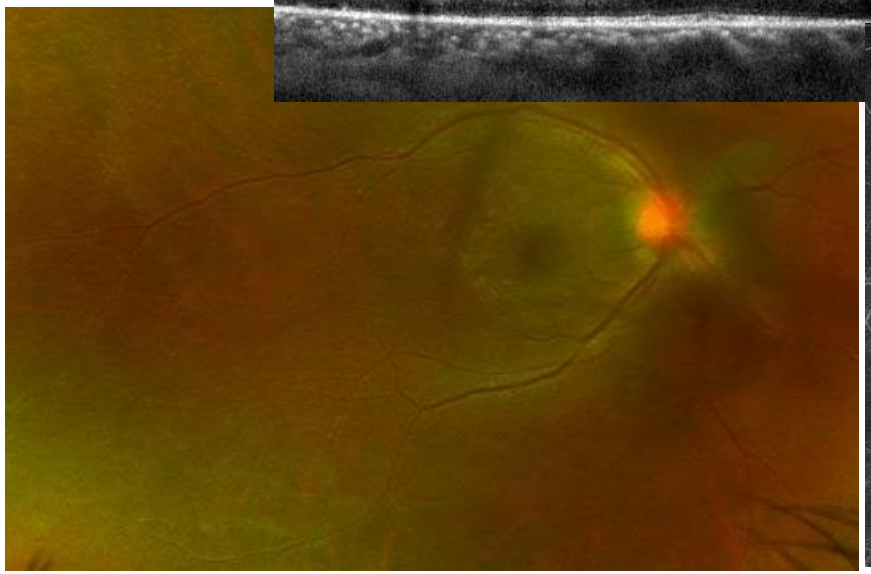
Syphilis: Various Presentations

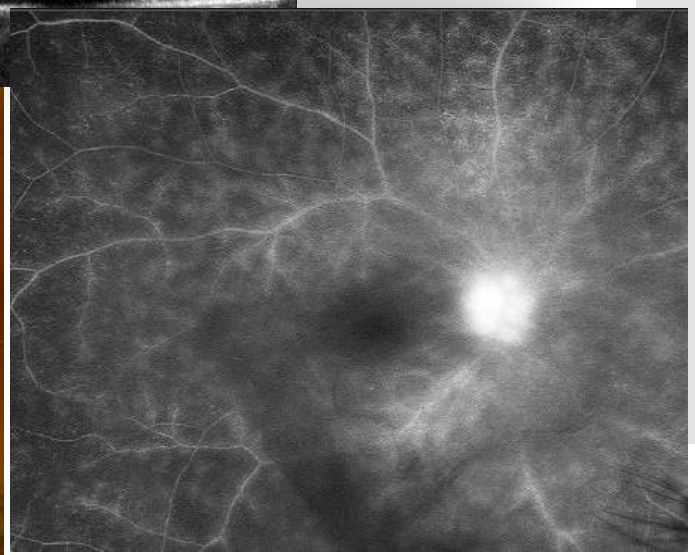
(Salt and pepper chorioretinitis)





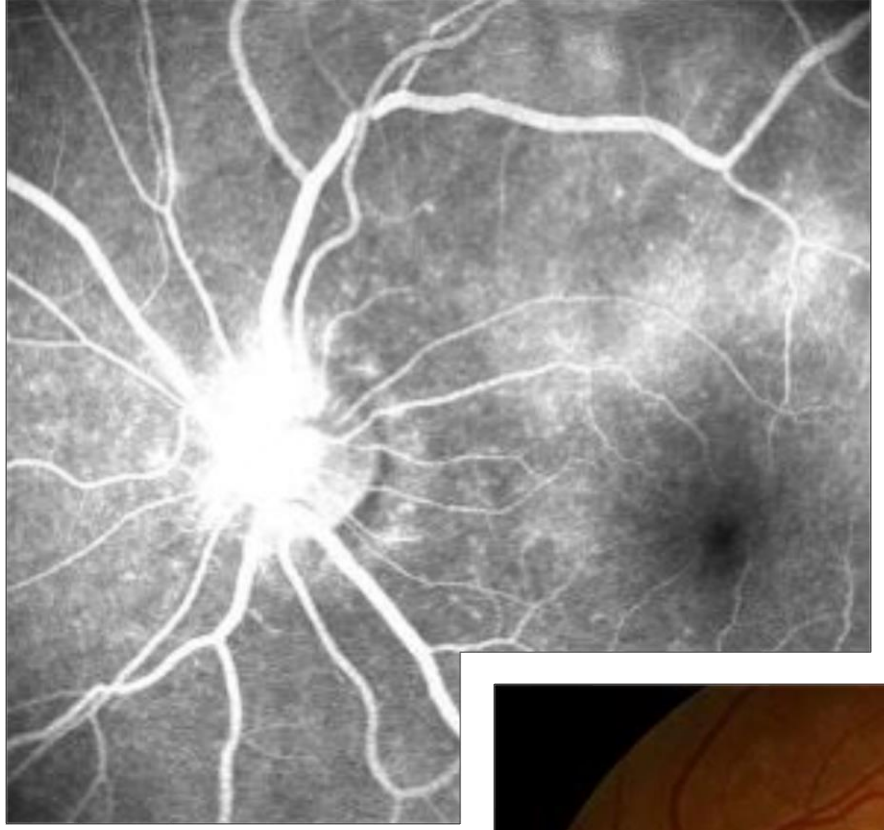


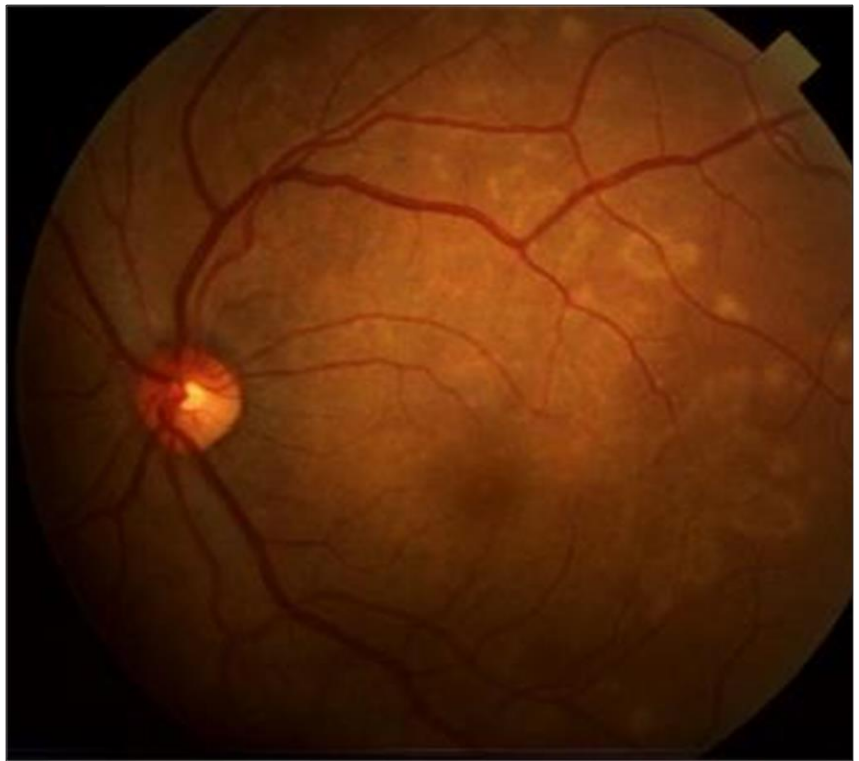




Syphilis: Various Presentations

(Acute syphilitic posterior placoid chorioretinitis)





Syphilis in the Eye

Work-up including laboratory testing

1. Complete ophthalmic examination, including DFE, and imaging is recommended
2. VDRL and RPR are often used for screening and for monitoring therapeutic response but many false-negative results can occur in early primary, latent, or late syphilis due to low sensitivity
3. FTA-ABS and a treponemal-specific assay such as *Treponema pallidum* microhemagglutination assay (MHA-TP) are very sensitive and specific in all stages of syphilis
    a. They are the **tests of choice** in suspected ocular syphilis
4. HIV testing is indicated in any patient with syphilis because of the relatively aggressive course in HIV-infected individuals as well as the frequency of co-infection
5. Patients should be evaluated for concomitant sexually transmitted diseases, with notification sent to the local health department when indicated
6. Consultation with infectious disease is recommended

Syphilis in the Eye

Treatment Indications

- In the presence of uveitis consistent with syphilis:
  1. FTA-ABS or MHA-TP negative: Syphilis unlikely, consider other causes
  2. FTA-ABS or MHA-TP positive and VDRL/RPR negative:
     a. If appropriate past treatment cannot be documented, treatment for syphilis is indicated
     b. If appropriate past treatment can be documented, treatment for syphilis is not indicated if another other cause is identified and the patient responds to therapy for that condition
  3. FTA-ABS or MHA-TP positive and VDRL/RPR positive:
     - Treat for syphilis

Syphilis in the Eye

Treatment Indications

- Neurosyphilis (positive FTA-ABS in the serum and either cell count >5 white blood cells/mm^3, protein >45 mg/dL, or positive CSF VDRL on lumbar puncture):
  - Aqueous crystalline penicillin G 2 to 4 million U i.v. q4h for 10 to 14 days, followed by benzathine penicillin 2.4 million U intramuscularly (i.m.) weekly for 3 weeks (1.2 million U in each buttock)
    - Many experts believe that any ocular involvement, especially retinal or optic nerve, should be considered as neurosyphilis and treated accordingly
- Anterior and/or intermediate syphilitic uveitis: Benzathine penicillin 2.4 million U i.m. weekly for 3 weeks
- If anterior segment inflammation is present, treatment with a cycloplegic (e.g., cyclopentolate 1% t.i.d.) and topical steroid (e.g., prednisolone acetate 1% q2h) may be beneficial

Syphilis

Management

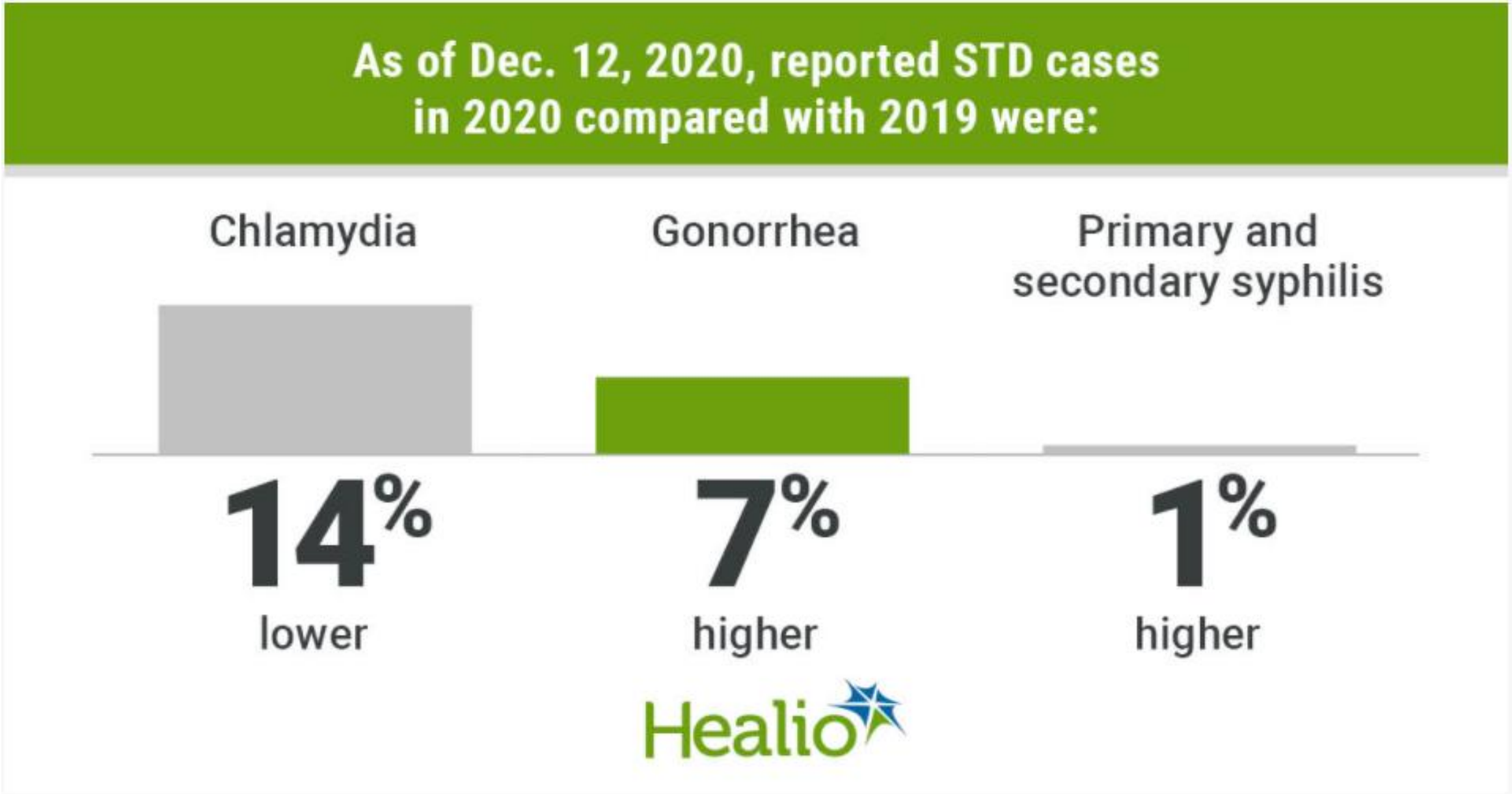
Follow-Up

- Neurosyphilis: Management by infectious disease specialist mandatory
- Repeat lumbar puncture every 6 months for 2 years, less frequently if the cell count returns to normal sooner
- The cell count should decrease to a normal level within this period, and the CSF VDRL titer should decrease fourfold within 6 to 12 months
- An increased CSF protein decreases more slowly
- If these indices do not decrease as expected, retreatment may be indicated

Syphilis

Management

- **Follow-Up**
  - Other forms of syphilis: Repeat the VDRL/RPR testing at 3 and 6 months after treatment
  - If a titer of 1:8 or more does not decline fourfold within 6 months, if the titer increases fourfold at any point, or if clinical symptoms or signs of syphilis persist or recur, lumbar puncture and retreatment are indicated
  - If a pretreatment VDRL/RPR titer is <1:8, retreatment is indicated only when the titer increases or when signs of syphilis recur (as in some patients treated with i.m. penicillin)



Source: Pagaoa M, et al. *Sex Trans Dis*. 2021;doi:10.1097/OLQ.0000000000001506.

Pediculosis (Lice, Crabs)

- **Mode of Transmission**
  - Typically develops from contact with pubic lice (usually sexually transmitted)

Pediculosis (Lice, Crabs)

Ocular Findings

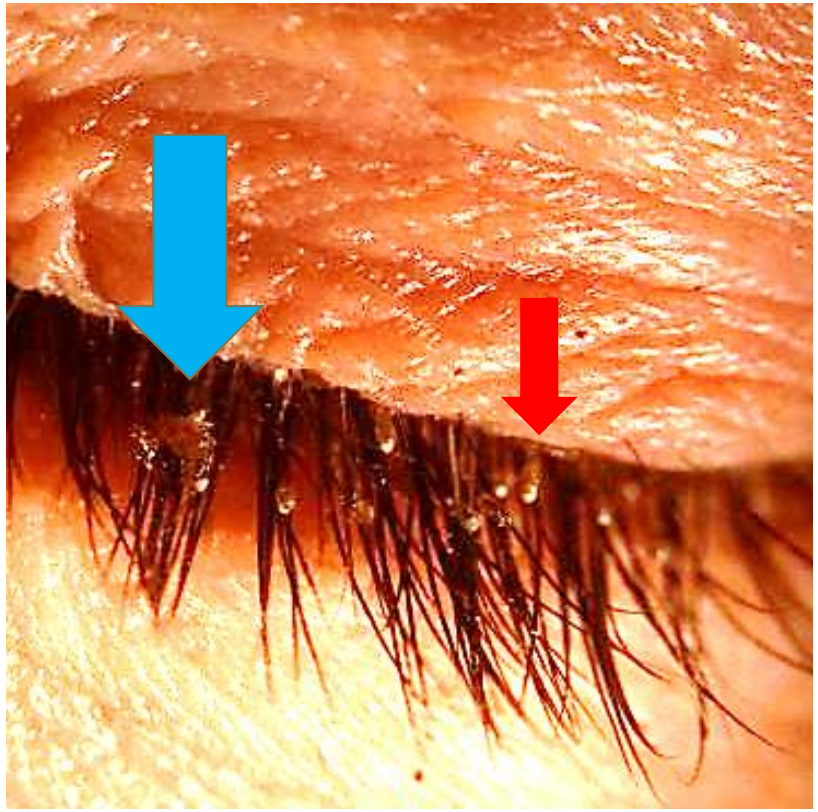
- **Symptoms**
  - Itching
  - Mild conjunctival injection
  - Can be unilateral or bilateral

Pediculosis (Lice, Crabs)

Ocular Findings

Signs

- Adult lice, nits, and blood-tinged debris on the eyelids and eyelashes
- Follicular conjunctivitis



Pediculosis

Pediculosis (Lice, Crabs)

- **Treatment**
  1. Mechanical removal of lice and eggs with jeweler's forceps
  2. Any bland ophthalmic ointment (e.g., erythromycin) to the eyelids t.i.d. for 10 days to smother the lice and nits
  3. 20% Fluorescein (for FA), and petroleum jelly, other modes
  4. Anti-lice lotion and shampoo as directed to nonocular areas for patient and close contacts
  5. Thoroughly wash and dry all clothes, towels, and linens

Human Immunodeficiency Virus (HIV)

HIV = human immunodeficiency virus

It is the virus that can lead to acquired immunodeficiency syndrome or AIDS if not treated

Unlike some other viruses, the human body can't get rid of HIV completely, even with treatment

So once you get HIV, you have it for life

- Note: Some patients believe that if their viral load is "undetectable", they no longer have the disease

HIV / AIDS

Mode of Transmission

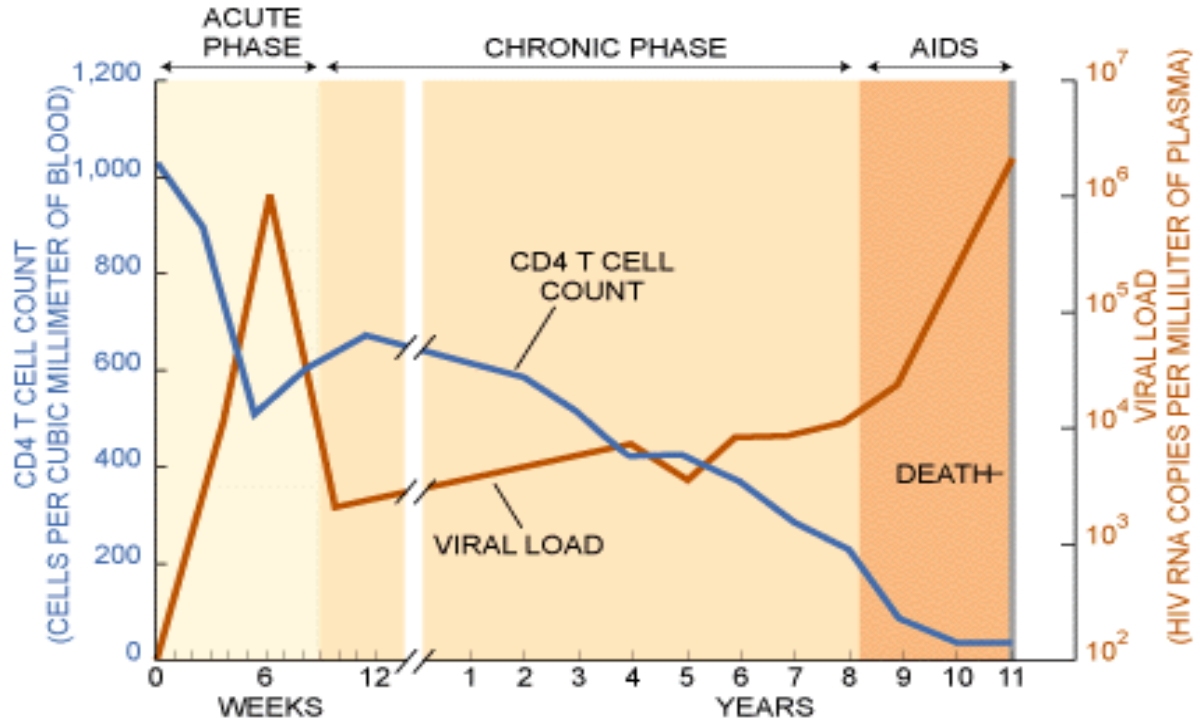
- HIV is a virus spread through **certain body fluids** that attacks the body's immune system, specifically the CD_4 cells, often called T cells

Clinical Course

- Over time, HIV can destroy so many of these cells resulting in immunodeficiency and inability of fighting infections and certain diseases
- Untreated, HIV reduces the number of CD_4 cells (T cells) in the body
- Opportunistic infections or cancers take advantage of a very weak immune system and signal that the person has AIDS

HIV / AIDS

- **Clinical Course**
  1. **Stage 1:** Acute HIV infection
  2. **Stage 2:** Clinical latency (HIV inactivity or dormancy)
  3. **Stage 3:** Acquired immunodeficiency syndrome (AIDS)



HIV / AIDS

Case History Specific Questions?

- When were you first diagnosed?
- Have you had or been treated for any opportunistic infections?
- What medications are you taking?
- Are you compliant with your medications?
- When was your last blood work done?
- What is your T-Cell or CD_4 count?
- What was is the viral load?

HIV / AIDS

If CD_4 count < 200:

- 1st year: 33% incidence of opportunistic infection
- 2nd year: 58% incidence of opportunistic infection

If CD_4 count < 100

- 1st year: 25% incidence of CMV retinitis

HIV:
Anterior Segment

K-Sicca

Infectious conjunctivitis and/or Keratitis

- HSV and HZV related
- Fungal Keratitis
- Microsporidlosis

Iridocyclitis

HIV: Posterior Segment

HIV Retinopathy

HIV-Related Retinitis and retinochoroditis

- Acute retinal necrosis or ARN (HZV, HSV)
- Progressive outer retinal necrosis or PORN (HZV)
- Cytomegalovirus or CMV retinitis

Other Associated

- Syphilis
- Tuberculosis
- Toxoplasmosis
- Histoplasmosis
- Neuro-ophthalmic manifestations

HIV in the Eye

Work-up

- History and complete ocular examination
- Serial fundus photographs to document stability should be taken at each visit
- Refer patient to an internist or infectious disease specialist for systemic evaluation and treatment
- Refer to Retina Specialist in presence of active posterior segment disease
- Complicated ant segment disease may require subspecialty referral

HIV in the Eye

Ocular Findings: Cytomegalovirus Retinitis (CMV)

- CMV is the most frequent ocular opportunistic infection in patients with AIDS
  - CMV is almost never seen unless the CD4+ count is <100 cells/mm^3
  - May also be seen in other immunocompromised states (e.g., leukemia and post-transplant):

HIV in the Eye

Ocular Findings: CMV

Symptoms

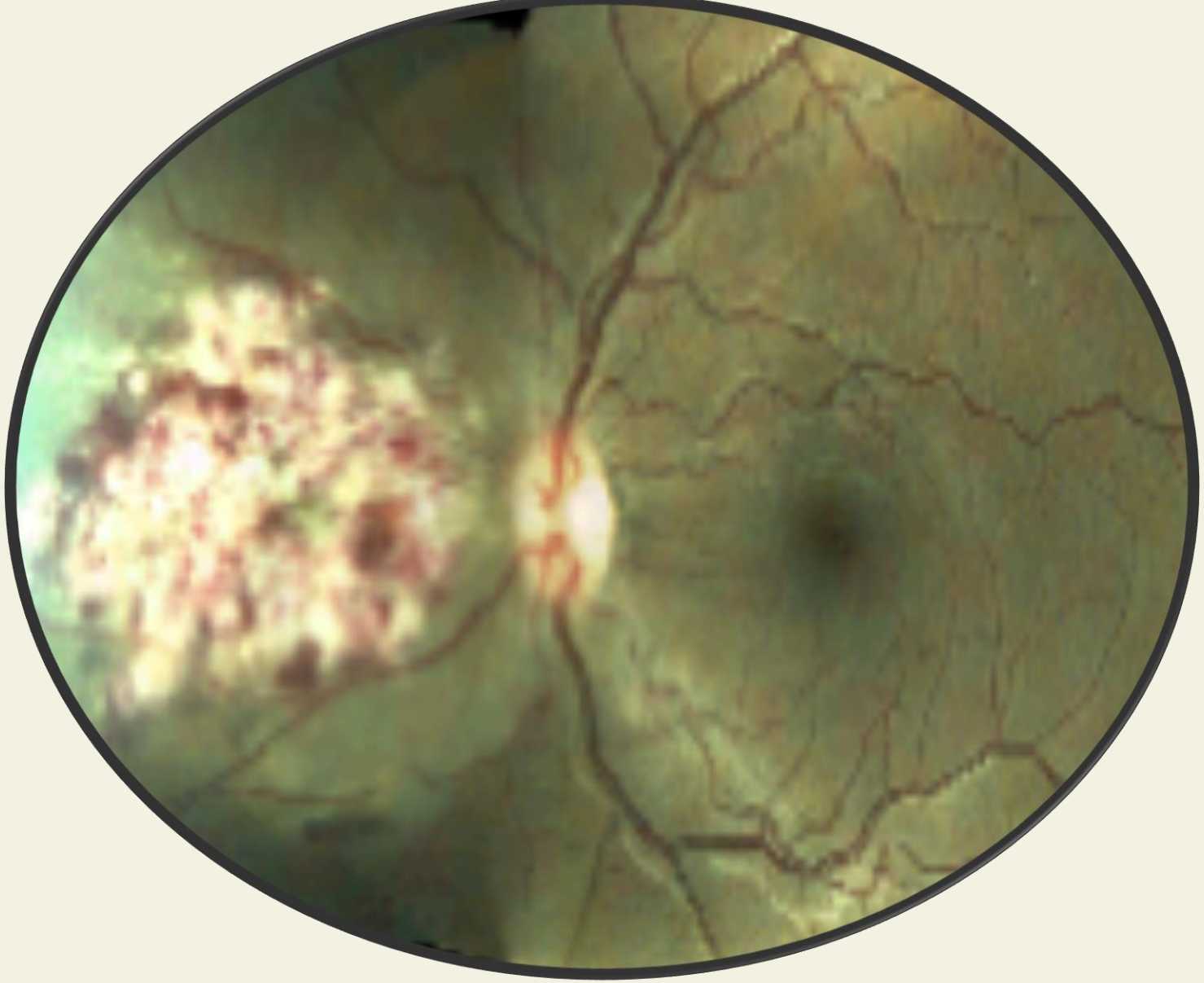
Scotoma or decreased vision in one or both eyes	Floaters or photopsias	Pain and photophobia are uncommon	Often asymptomatic

HIV in the Eye

Ocular Findings: CMV

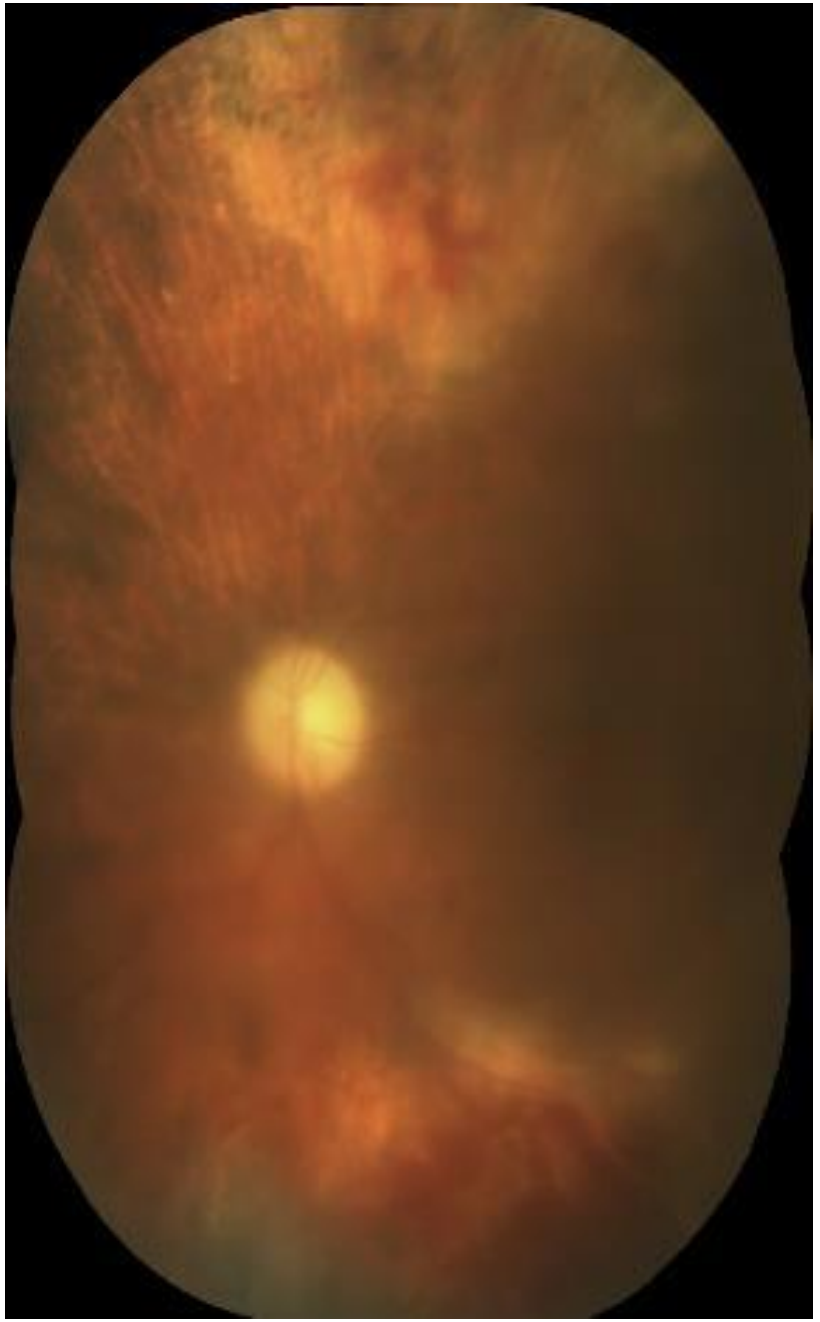
- **Signs**
- Indolent form: Peripheral granular opacities with occasional hemorrhage
- Fulminant form: Confluent areas of necrosis with prominent hemorrhage, starting along the major retinal vascular arcades. Progressive retinal atrophy may also indicate active CMV
- Anterior uveitis with nongranulomatous, stellate KP almost always present but mild
- Vitritis (mild to moderate, *the extent depends on the patient's immune status)*
- RPE atrophy and pigment clumping result once the active process resolves
- RRD occurs in approximately one-third of patients with CMV retinitis with increased risk when >25% of the retina is involved

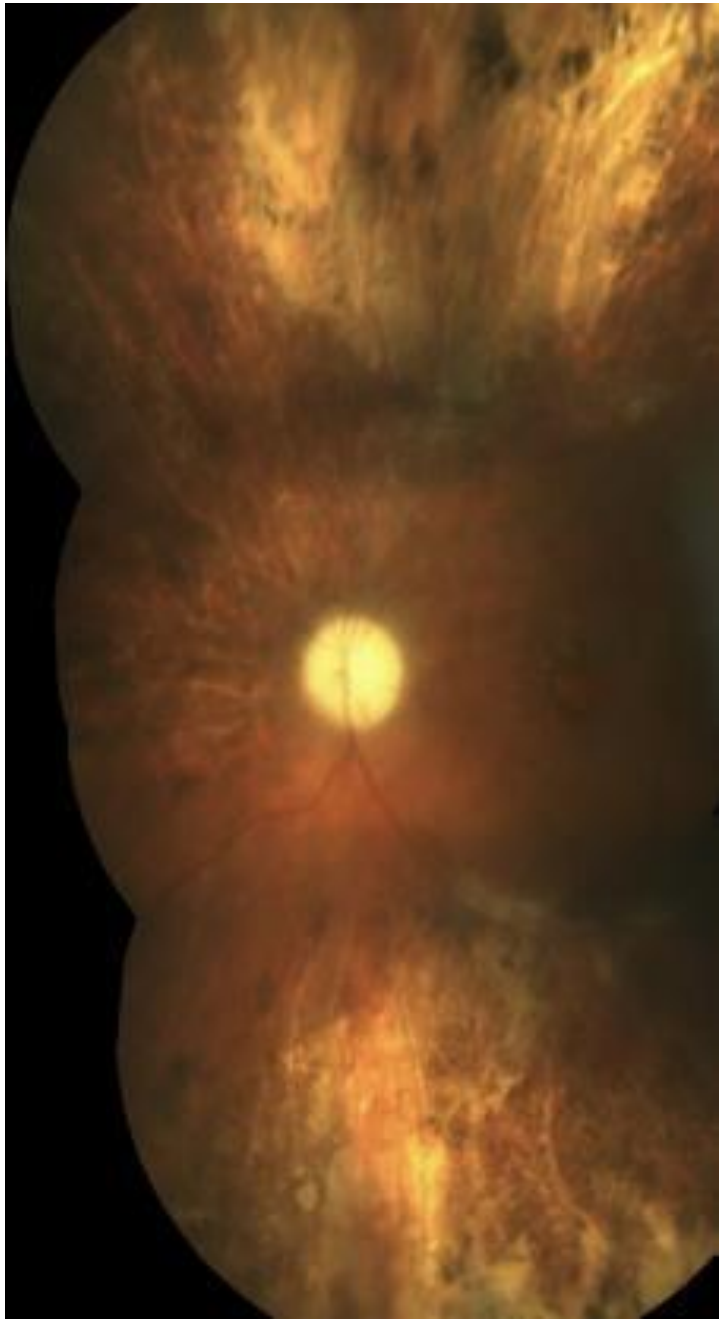
CMV Retinitis

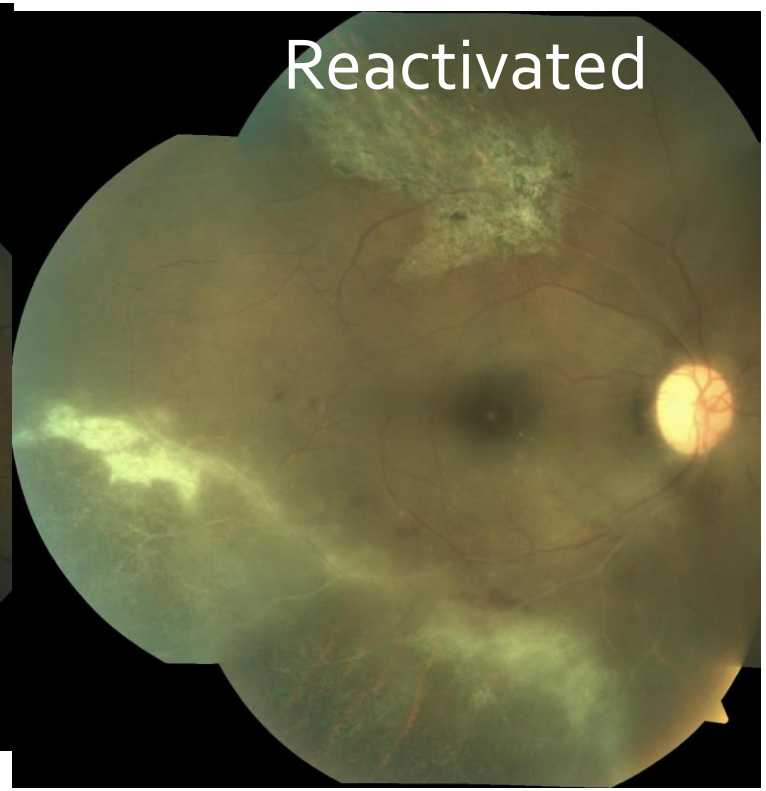


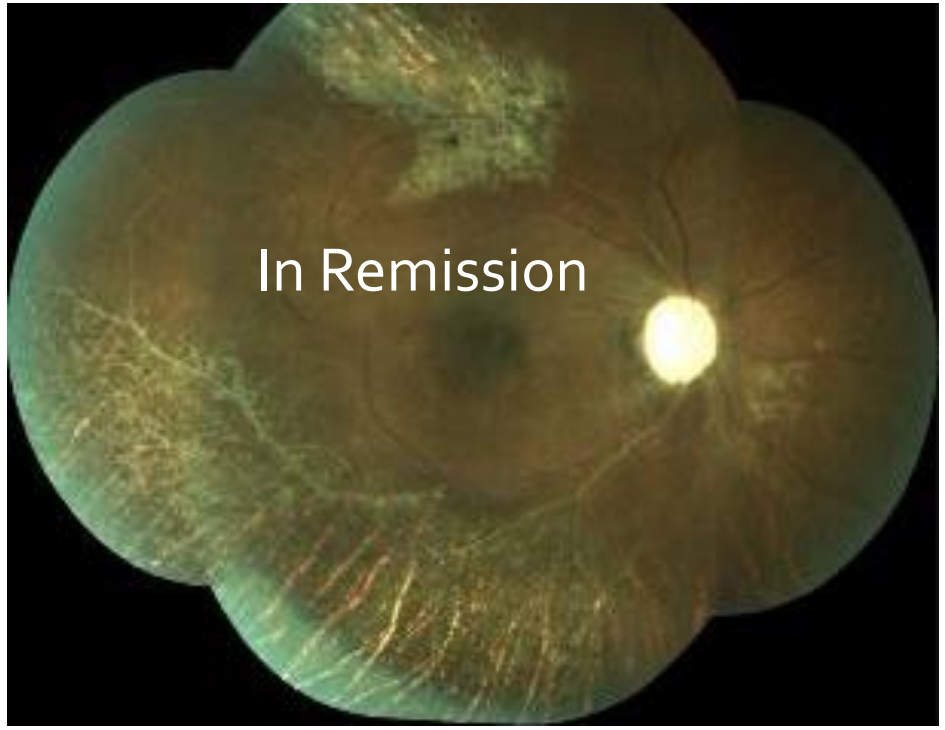
CMV Retinitis

(vitritis causing cloudy media in active phase)



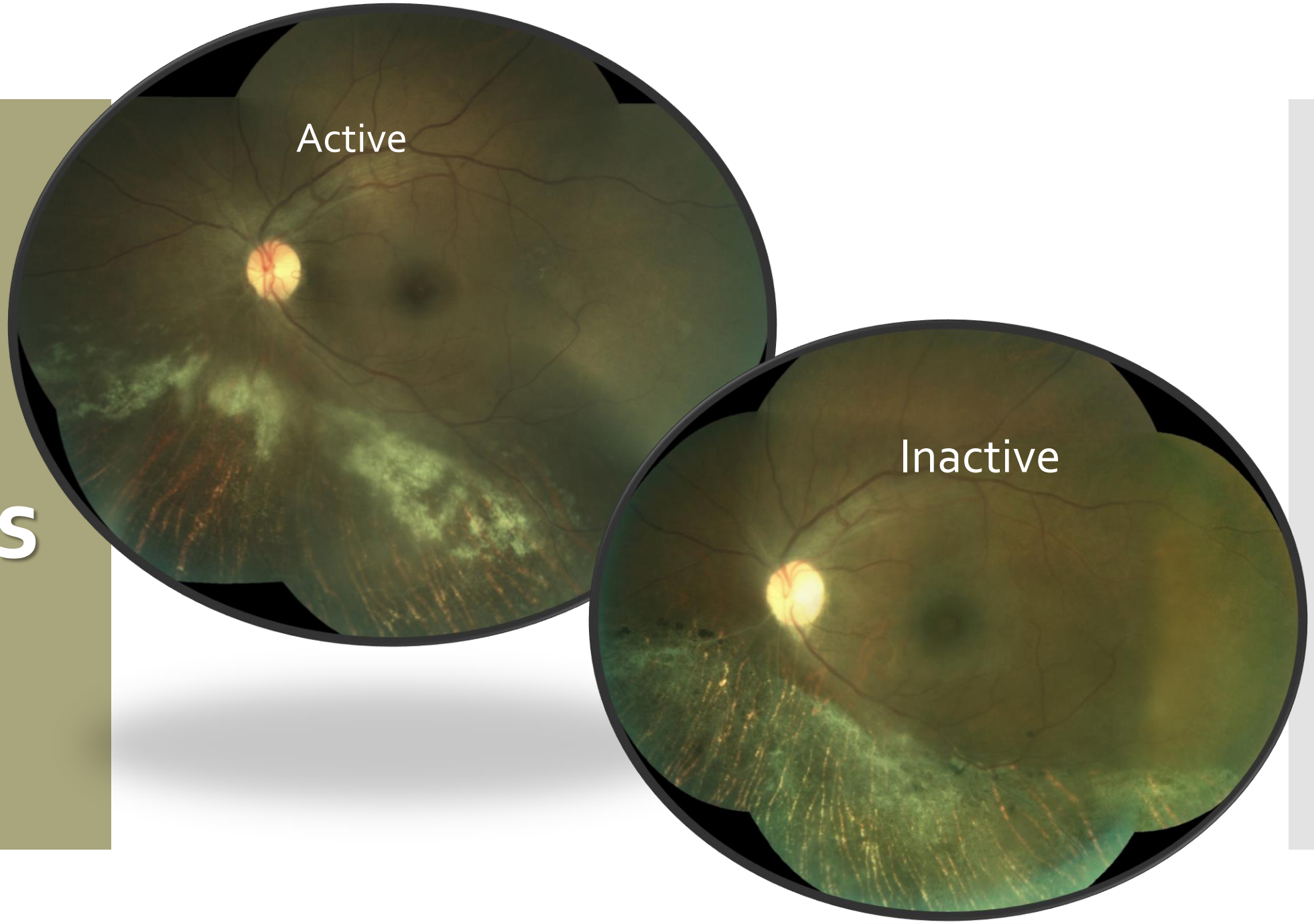






CMV Retinitis (waxing and waning)

CMV Retinitis



CMV Retinitis

Management

In the absence of mitigating history, refer to PCP for systemic disease

The Retinal disease need immediate treatment with oral and possible intravitreal antiviral therapy

Due to complexity most often patient is referred to retinal specialist

HIV in the Eye

Treatment: CMV

Oral therapy with valganciclovir 900 mg p.o. b.i.d. for induction (21 days), followed by 900 mg p.o. daily for maintenance

Alternatively, intravenous ganciclovir 5 mg/kg b.i.d. or foscarnet 90 mg/kg b.i.d. (adjusting for renal function) may be used, followed by oral therapy valganciclovir (900 mg p.o. b.i.d. to complete 3-week induction, then 900 mg p.o. daily)

The goal of treatment is quiescent retinitis: nonprogressive areas of RPE atrophy with a stable opacified border

Small, macula-sparing RRDs may be treated with laser demarcation. Pars plana vitrectomy with silicone oil is indicated for detachments involving the macula

CMV Retinitis

Therapy for CMV Retinitis

Drug	Dosing	Toxicities	Contraindications
Ganciclovir	Induction: 5 mg/kg i.v. b.i.d. for 14 days Maintenance: 5 mg/kg i.v. daily	Neutropenia, thrombocytopenia, anemia; Discontinue nursing	Absolute neutrophil count <500/mm^3, platelets <25,000/mm^3; Potentially embryotoxic
Valganciclovir	Induction: 900 mg p.o. b.i.d. for 21 days Maintenance: 900 mg p.o. daily	Neutropenia, thrombocytopenia, anemia; Discontinue nursing	Absolute neutrophil count <500/mm^3, platelets <25,000/mm^3; Potentially embryotoxic
Foscarnet	Induction: 90 mg/kg i.v. b.i.d. twice/wk Maintenance: 90–120 mg/kg i.v. daily (monitor creatinine and electrolytes; adjust dosing as needed)	Renal impairment neutropenia, anemia, electrolyte imbalances	Use caution with renal impairment or electrolyte imbalances
Cidofovir	Induction: 5 mg/kg i.v. weekly for 3 wks Maintenance: 3–5 mg/kg i.v. every two wks	Dose- and schedule-dependent nephrotoxicity, hypotony (necessitates discontinuation), iritis (steroid responsive); Must be given with probenecid	Recurrent uveitis, moderate to severe kidney disease, intolerance to probenecid

HIV in the Eye

Ocular Findings: Noninfectious Retinal Microvasculopathy / HIV Retinopathy

Noninfectious retinopathy is the **most common** ocular manifestation of HIV/AIDS

About 50% to 70% of patients with AIDS have this condition

HIV in the Eye

Ocular Findings: Noninfectious Retinal Microvasculopathy / HIV Retinopathy

Symptoms

Rarely symptomatic (focal scotoma, decreased contrast)

Signs

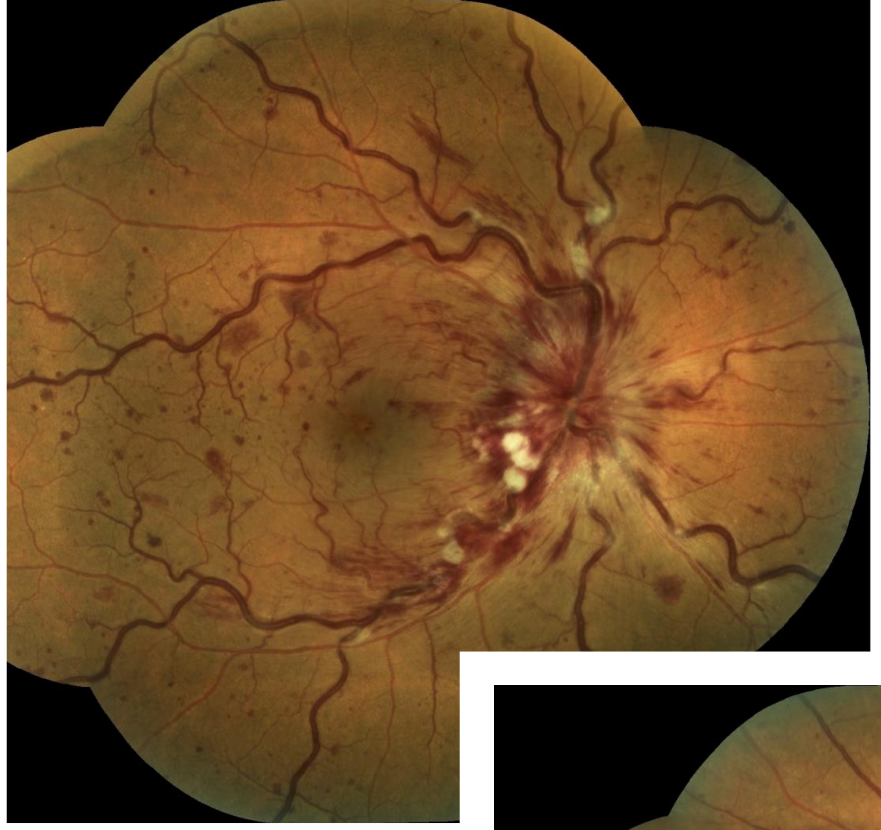
Cotton–wool spots

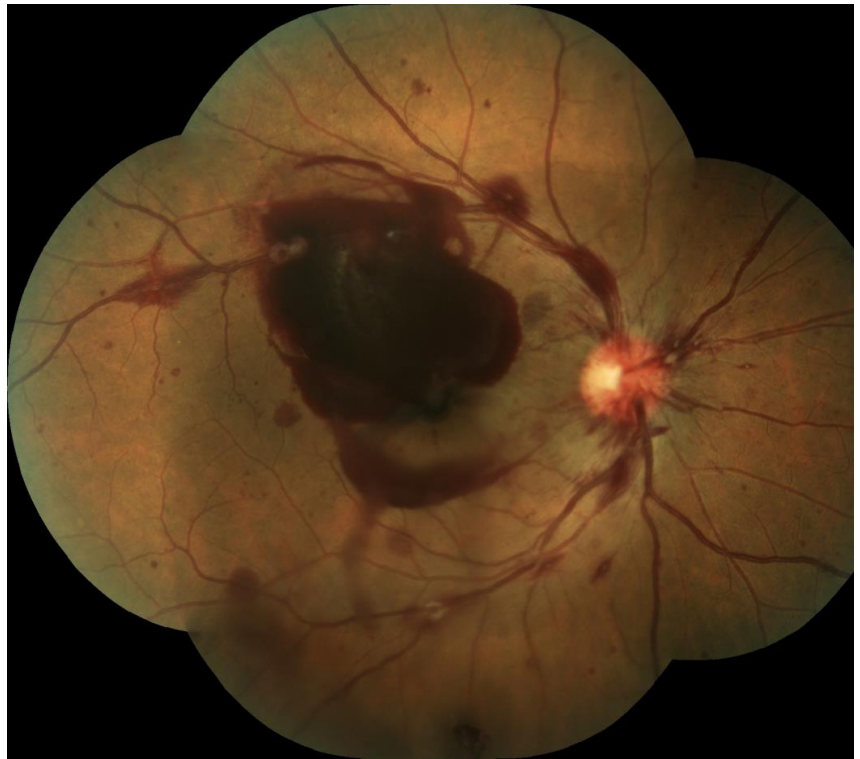
Intraretinal hemorrhages

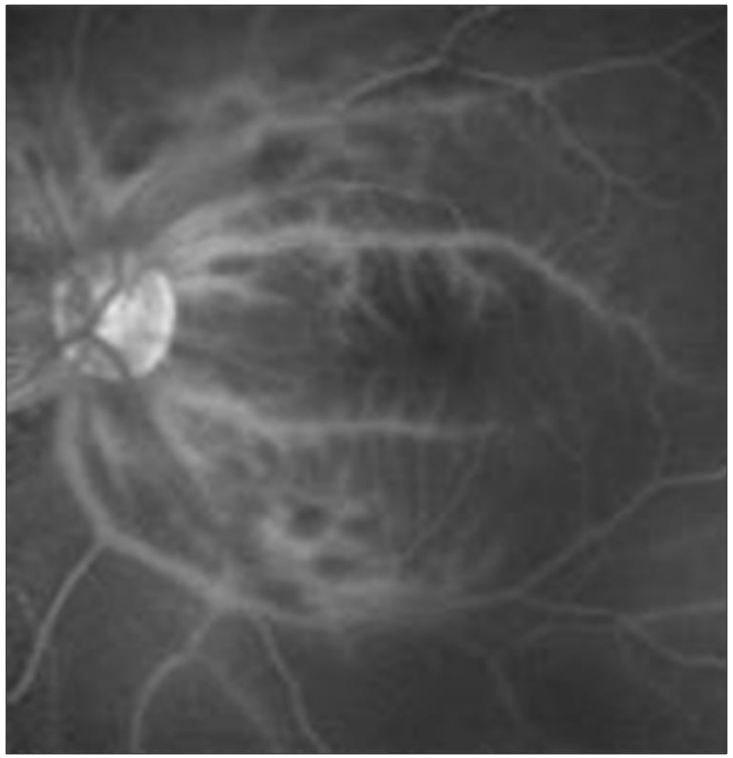
Microaneurysms

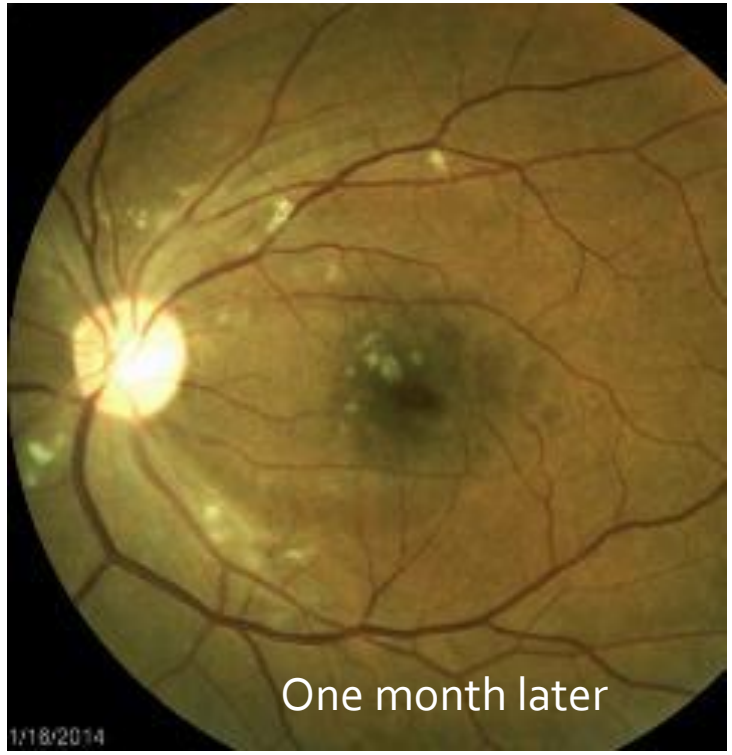
Arteriolar Occlusion

HIV Retinopathy









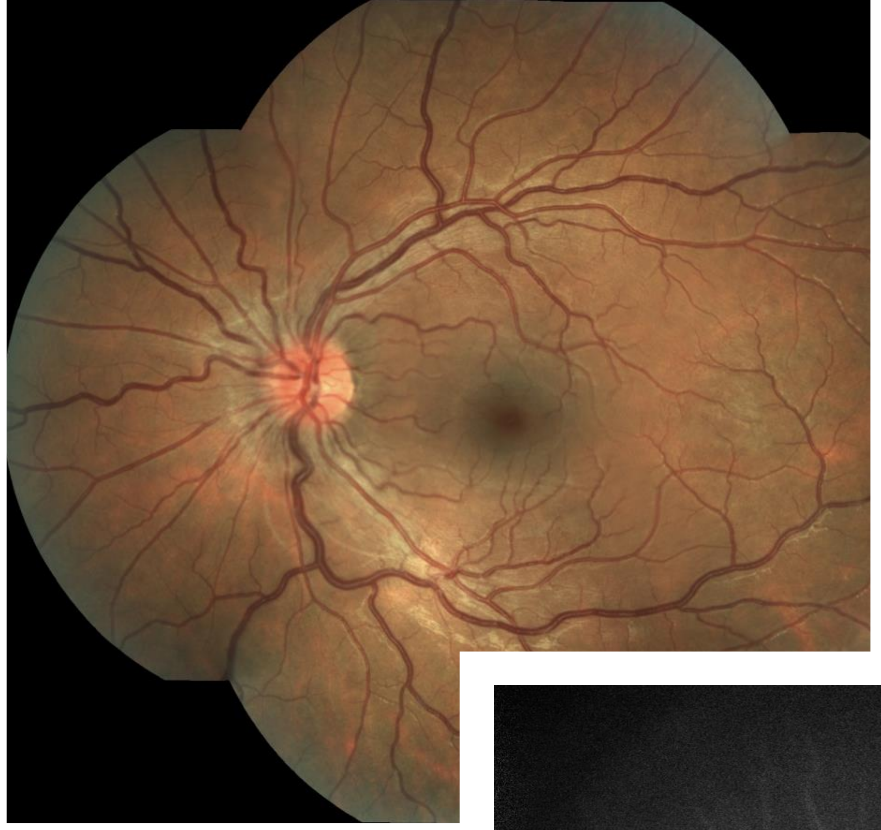
HIV

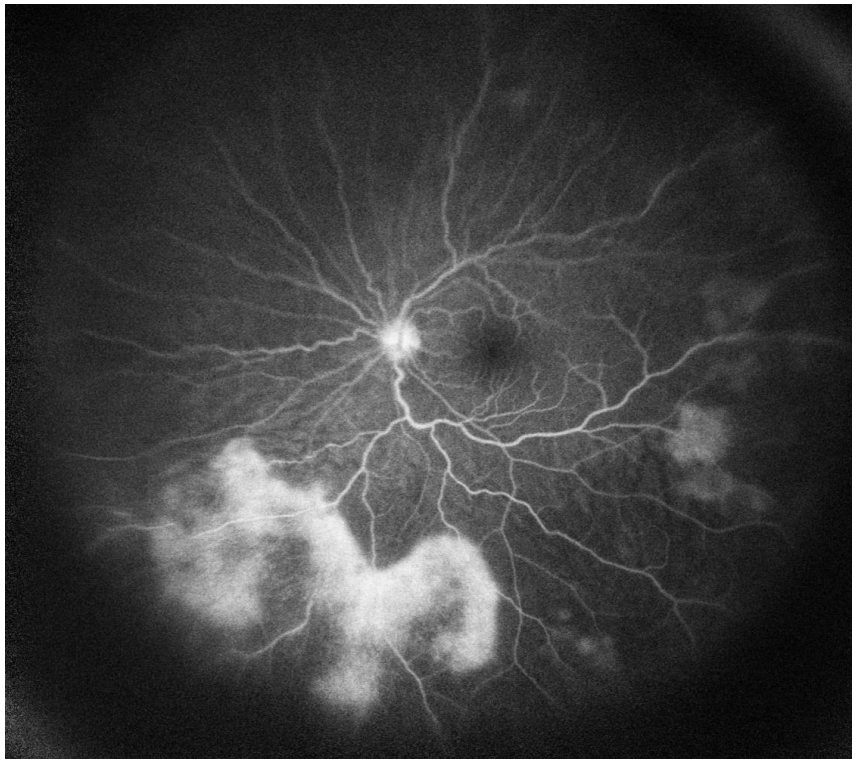
Cotton-Wool Spots

(HIV+ patient with concurrent syphilis)

HIV Retinal Vasculitis

May not be as evident clinically vs FA





HIV in the Eye

Work-up: Noninfectious Retinal Microvasculopathy / HIV Retinopathy

- HIV retinopathy is a marker of low CD_4+ counts
- Look for concomitant opportunistic infections
- Rule out the other causes for unexplained cotton–wool spots

HIV in the Eye

Treatment: Noninfectious Retinal Microvasculopathy/HIV Retinopathy

- No specific ocular treatment necessary, but resolves with HAART and increased CD_4+ counts

HIV in the Eye

Management: Noninfectious Retinal Microvasculopathy/HIV Retinopathy

- Patients with CD4+ counts <50 should be examined every 3 to 4 months

HIV in the Eye

Follow up for patients with **NO** retinal pathology:

- $CD_4 > 600$: Annually
- CD_4 599-300: 6 months
- CD_4 299-100: 3-4 months
- $CD_4 < 100$: 2-3 months
- Systemic CMV: 2-3 months

HIV in the Eye

Management

- Because **active retinitis is often asymptomatic**, patients with $CD4+$ counts <100 cells/mm^3 should be seen at least every 3 to 6 months

Herpes Simplex Virus (HSV)

There are two forms of Herpes Simplex

One is a common virus that causes skin and eye lesions, while the other is an STD

The herpes virus is known to mainly attack the cornea, but it can also damage the retina

HSV in the Eye

Ocular Findings: HSV

Symptoms

- Red eye
- Pain
- Foreign body sensation
- Photophobia
- Tearing
- Decreased vision
- Skin (e.g., eyelid) vesicular rash
- History of previous episodes
- Usually unilateral

HSV in the Eye

Ocular Findings

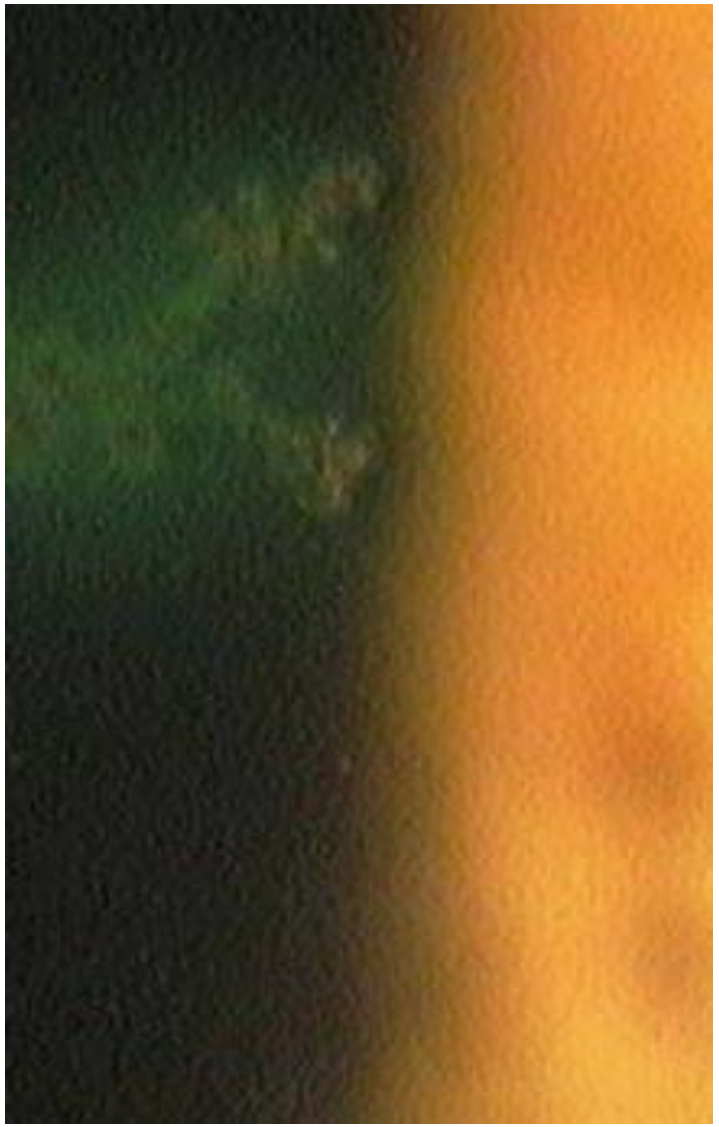
- **Signs**
  - Eyelid/Skin Involvement
    - Clear vesicles on an erythematous base that progress to crusting, heal without scarring, cross dermatomes, but are typically unilateral (only 10% of primary HSV dermatitis is bilateral)
  - Conjunctivitis
    - Patients may have a history of perioral cold sores
    - Manifests with acute unilateral (sometimes recurrent) follicular conjunctivitis, with or without conjunctival dendrites or geographic ulceration
    - Palpable preauricular node
    - Occasionally, concurrent herpetic skin vesicles along the eyelid margin or periocular skin

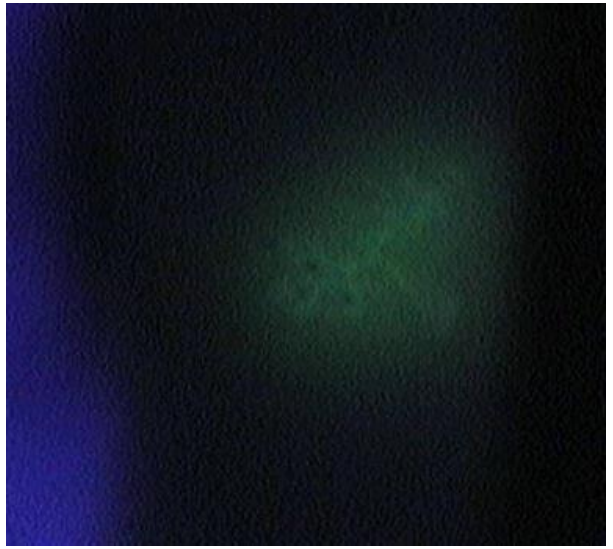
HSV in the Eye

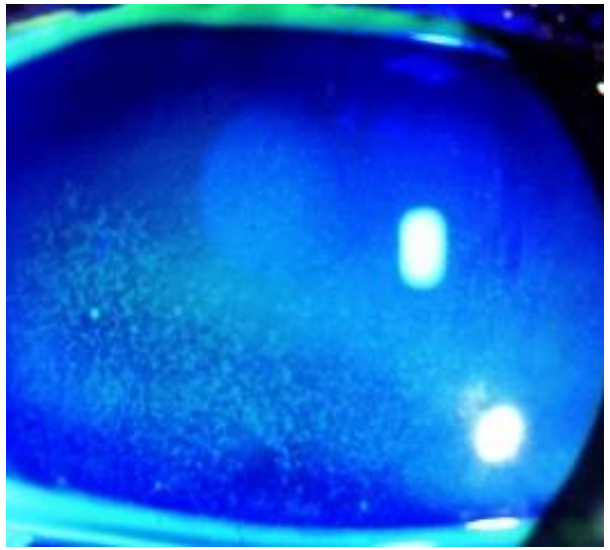
Ocular Findings

- **Signs**
  - Corneal Epithelial Disease may be seen as
    - Macropunctate keratitis
    - Dendritic keratitis (a thin, linear, branching epithelial ulceration with club-shaped terminal bulbs at the end of each branch)
    - Or a geographic ulcer (a large, amoeba-shaped corneal ulcer with a dendritic edge)

HSV in the Eye





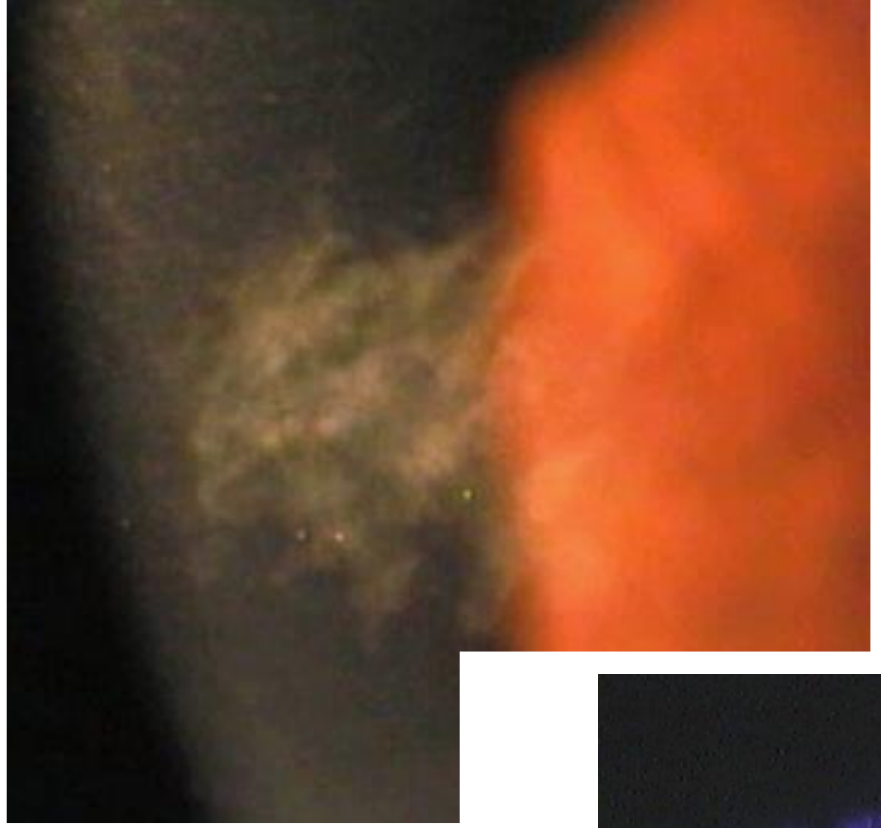


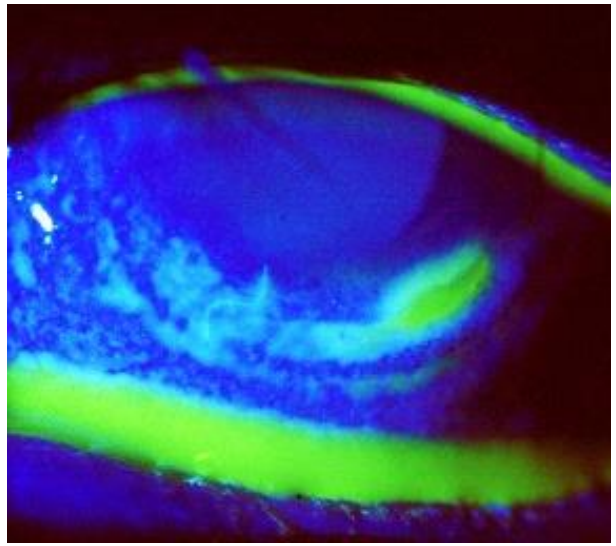
HSV in the Eye

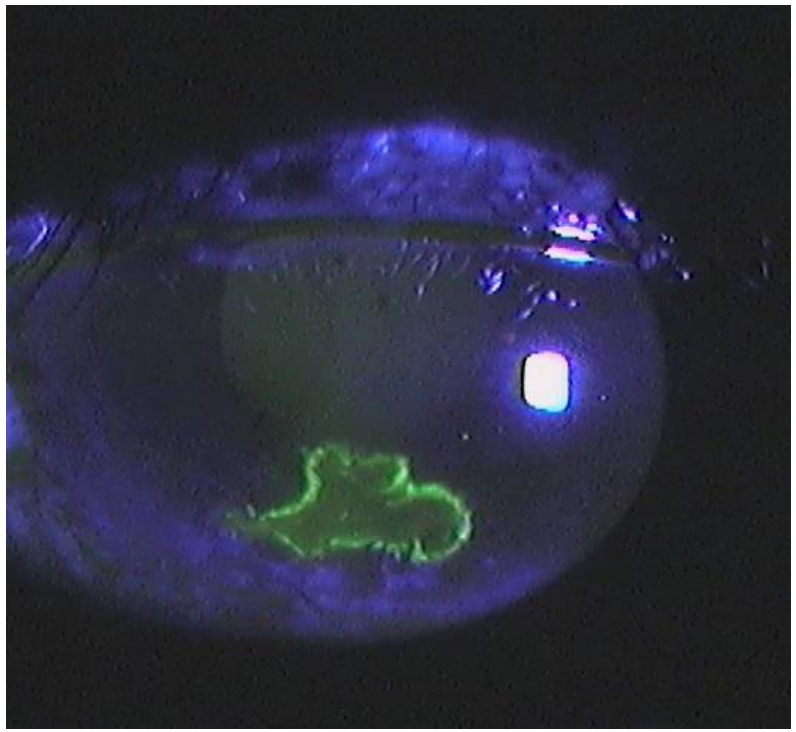
Ocular Findings

- **Signs**
  - Corneal Stromal Disease
    - Disciform keratitis (nonnecrotizing keratitis): Disc-shaped stromal edema with an intact epithelium
    - A mild iritis with localized granulomatous keratic precipitates is typical, and increased IOP may be present
    - No necrosis or corneal neovascularization is present
    - Necrotizing interstitial keratitis (IK) (uncommon)
    - Appearance of multiple or diffuse, whitish corneal stromal infiltrates with or without an epithelial defect, often accompanied by stromal inflammation, thinning, and neovascularization
    - Concomitant iritis, hypopyon, or glaucoma may be present
    - Microbial (bacterial and fungal) superinfection should be ruled out

HSV Keratitis





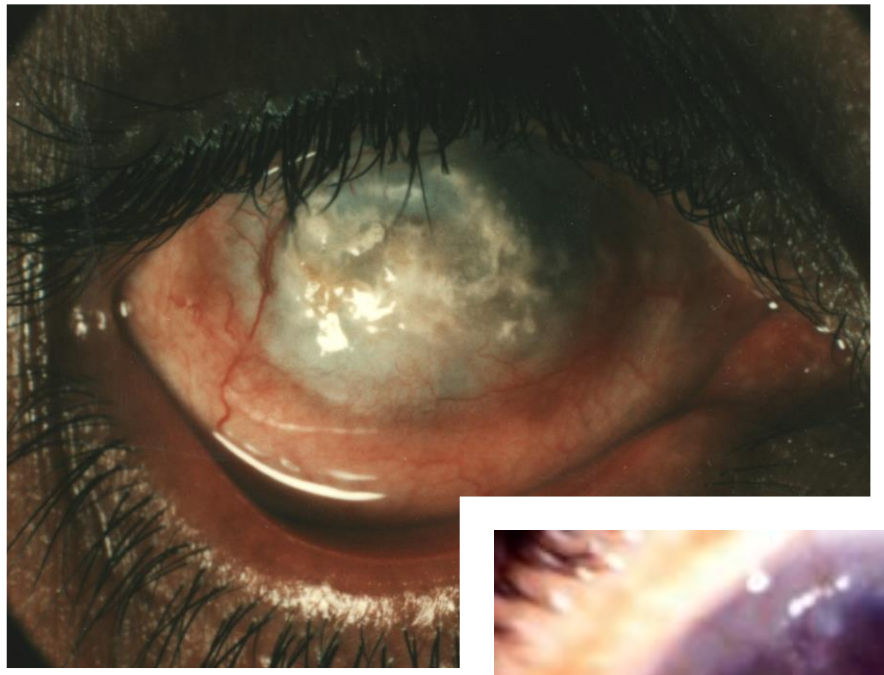


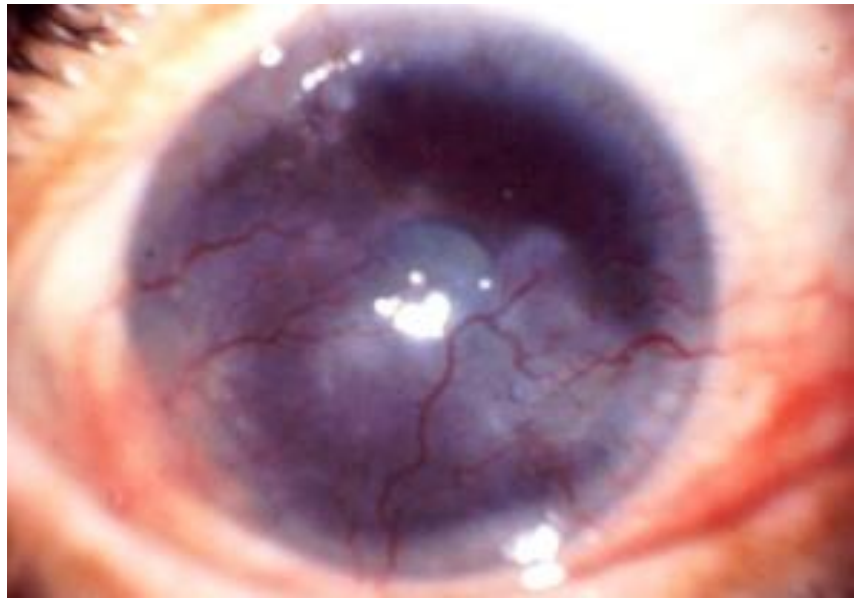
HSV in the Eye

Ocular Findings

- **Signs**
  - Neurotrophic Ulcer
    - A sterile ulcer with smooth epithelial margins over an area of interpalpebral stromal disease that persists or worsens despite antiviral therapy
    - May be associated with stromal melting and perforation

Corneal Ulcer and Opacification



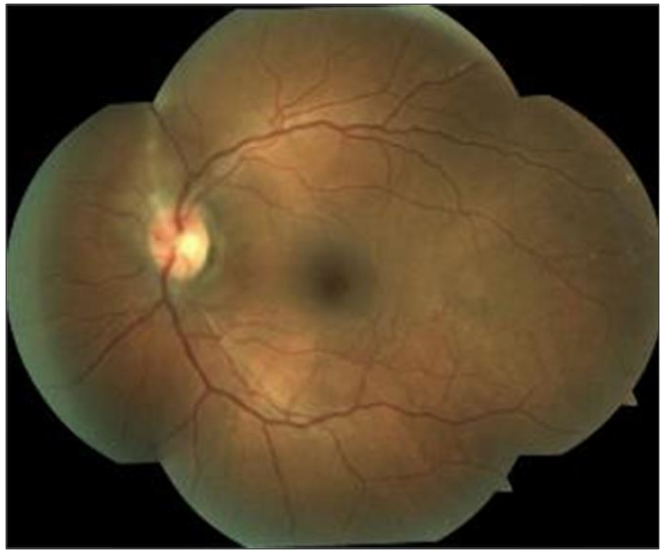


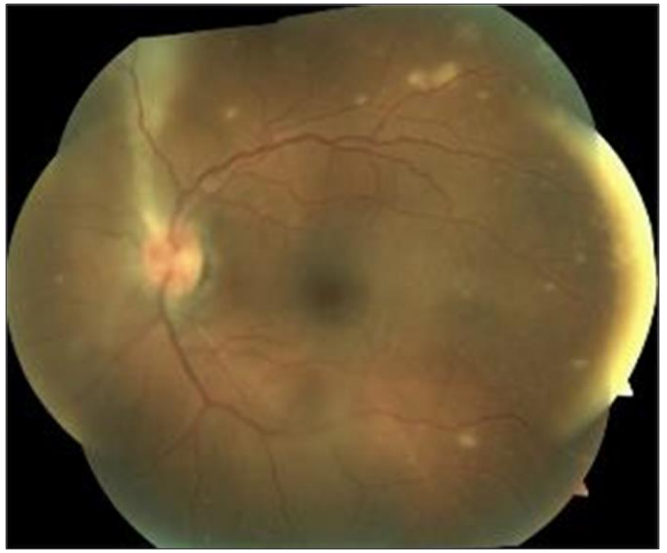
HSV in the Eye

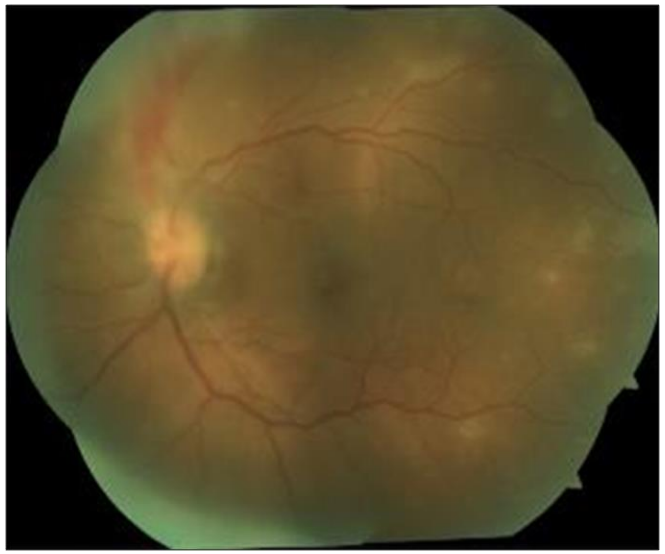
Ocular Findings

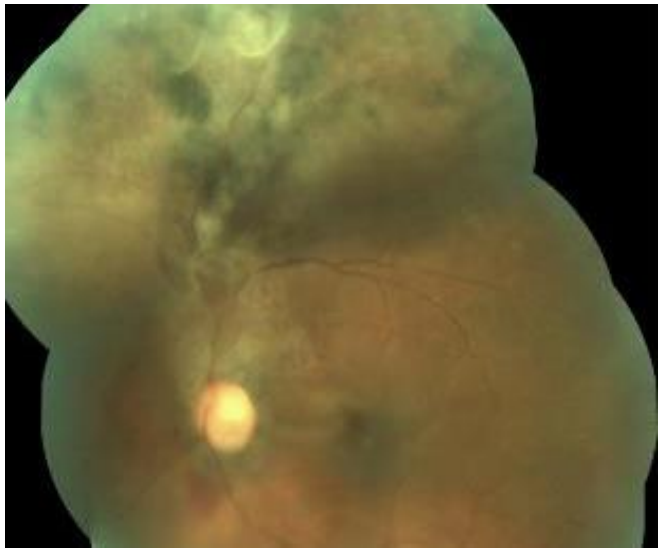
- **Signs**
  - Uveitis
    - An anterior chamber reaction may develop during corneal stromal disease
    - An anterior chamber reaction and granulomatous keratic precipitates may also develop independent of active corneal disease and may be associated with elevated IOP, pigmented anterior chamber cells, or progressive iris atrophy
  - Retinitis
    - ARN (HSV vs HZV)
    - Rare

Herpes ARN and PORN Rapidly Progressive Retinal Necrotizing Conditions









HSV in the Eye

Work-Up

History: Previous episodes? History of corneal abrasion; contact lens wear; or previous nasal or oral sores? Recent topical or systemic steroids? Immune deficiency state? Recent fever or sun/UV exposure? History of shingles?

External examination: Note the distribution of skin vesicles if present. The lesions are more suggestive of HSV than VZV if concentrated around the eye without extension onto forehead, scalp, and tip of nose. HSV often involves both the upper and lower eyelids.

Slit lamp examination with IOP measurement

Check corneal sensation (before instillation of topical anesthetic), which may be decreased in HSV and VZV

Herpes Simplex Virus

Work-Up: Laboratory Testing

Herpes simplex is usually diagnosed clinically and requires no confirmatory laboratory tests. If the diagnosis is in doubt, any of the following tests may be helpful:

- Scrapings of a corneal or skin lesion (scrape the edge of a corneal ulcer or the base of a skin lesion) for Giemsa stain, which shows multinucleated giant cells (this will not help differentiate HSV from other herpes family viruses). Enzyme-linked immunosorbent assay testing specific to HSV also is available.
- Viral culture: A sterile, cotton-tipped applicator is used to swab the cornea, conjunctiva, or skin (after unroofing vesicles with a sterile needle) and is placed in the viral transport medium.
- HSV antibody titers are frequently present in patients. They rise after primary but not recurrent infection. The absence of HSV1 antibodies helps rule out HSV as a cause of stromal keratitis. Positive titer is nonspecific as HSV is ubiquitous and exposure rates in the general population are extremely high.

HSV in the Eye

Treatment

Eyelid/Skin Involvement

- Topical acyclovir ointment, five times per day, is an option, although it has not been proven effective
- Any dermatologic and nonocular preparation of acyclovir ointment should be used on the skin only
- Erythromycin or bacitracin ophthalmic ointment is often used b.i.d. for bacterial prophylaxis
- Ganciclovir 0.15% ophthalmic gel five times per day may also be effective.
- Warm or cool soaks to skin lesions t.i.d. or p.r.n.

Eyelid margin involvement

- Add ganciclovir 0.15% ophthalmic gel or trifluridine 1% drops, five times per day, to the eye
- These medications are continued for 7 to 14 days until resolution of the symptoms.

HSV in the Eye

Treatment

Conjunctivitis

- Treat with antiviral therapy
  - Trifluridine 1% drops eight times per day
  - Ganciclovir 0.05% gel five times per day
  - Or oral agents such as acyclovir 400 mg five times a day
  - Warm compresses
  - Steroids are contraindicated
  - Discontinue the antiviral agent after 7 to 14 days;
  - If the conjunctivitis has failed to improve, reevaluation is recommended

HSV in the Eye

Treatment

- **Corneal Epithelial Disease**
  - Ganciclovir 0.15% ophthalmic gel five times per day, trifluridine 1% drops nine times per day, or vidarabine 3% ointment five times per day
    - Topical ganciclovir gel appears to have a lower incidence of corneal toxicity than trifluridine
  - Oral antiviral agents (e.g., acyclovir 400 mg p.o. five times per day, valacyclovir 500 mg p.o. t.i.d., or famciclovir 250 mg p.o. t.i.d. for 7 to 10 days) are effective alternatives to topical antiviral agents and can be used when topical medications cannot be given due to compliance problems, especially in children
  - Consider cycloplegic agent (e.g., cyclopentolate 1% t.i.d.) if an anterior chamber reaction or photophobia is present
  - Patients taking topical steroids should have them tapered rapidly

HSV in the Eye

Treatment

- **Corneal Epithelial Disease**
  - Limited debridement of infected epithelium can be used as an adjunct to antiviral agents
    - Technique: After topical anesthetic instillation, a sterile, moistened cotton-tipped applicator or semisharp instrument is used carefully to peel off the lesions at the slit lamp. After debridement, antiviral treatment should be instituted or continued as described earlier
  - For epithelial defects that do not resolve after 1 to 2 weeks, bacterial coinfection or Acanthamoeba keratitis should be suspected
  - Noncompliance and topical antiviral toxicity should also be considered
  - At that point, the topical antiviral agent should be discontinued, and a nonpreserved artificial tear ointment or an antibiotic ointment (e.g., erythromycin) should be used four to eight times per day for several days with careful follow-up
  - Smears for Acanthamoeba should be performed whenever the diagnosis is suspected

HSV in the Eye

Treatment

Corneal Stromal Disease

Disciform keratitis

- *Mild*. Consider treatment with cycloplegic (e.g., cyclopentolate 1% t.i.d.) in conjunction with antiviral prophylaxis
- *Moderate to severe or central (i.e., vision is reduced)*
  - Cycloplegic, as described previously
  - Topical steroid (e.g., prednisolone acetate 1% or loteprednol 0.5% q.i.d. to q2h)
    - If an epithelial lesion is present, it should be treated before starting high frequency corticosteroids.
  - Antiviral prophylaxis: Ganciclovir 0.15% ophthalmic gel three to five times a day, trifluridine 1% t.i.d. to q.i.d., acyclovir 400 mg p.o. b.i.d., valacyclovir 500 mg p.o. one to two times a day.
- Adjunctive medications which may be used include:
  - Topical antibiotic (e.g., erythromycin ointment q.h.s.) in the presence of epithelial defects
  - Aqueous suppressants for increased IOP. Avoid prostaglandin analogues due to association with recurrent HSV infections and uveitis

HSV in the Eye

Treatment

Corneal Stromal Disease

Necrotizing Interstitial Keratitis

- Treated as severe disciform keratitis.
- The first priority is to diagnose and treat any associated overlying epithelial defect and bacterial superinfection with antibiotic drops or ointment
- Tissue adhesive or corneal transplantation may be required if the cornea perforates (this is more common with neurotrophic keratitis)
- Oral antiviral treatment may be beneficial in the treatment of herpetic uveitis
- Rarely, a systemic steroid (e.g., prednisone 40 to 60 mg p.o. daily tapered rapidly) is given to patients with severe stromal disease accompanied by an epithelial defect and hypopyon
- Cultures should be done to rule out a superinfection
- The persistence of an ulcer with stromal keratitis is commonly due to the underlying inflammation (requiring cautious steroid therapy); however, it may be due to antiviral toxicity or active HSV epithelial infection
  - When an ulcer deepens, a new infiltrate develops, or the anterior chamber reaction increases, smears and cultures should be taken for bacteria and fungi

HSV in the Eye

Follow-Up

Patients are reexamined in 2 to 7 days to evaluate the response to treatment and then every 1 to 2 weeks, depending on the clinical findings

The following clinical parameters are evaluated:

- The size of the epithelial defect and ulcer
- Corneal thickness and the depth of corneal involvement
- Anterior chamber reaction
- IOP
- Patients with necrotizing keratitis need to be followed daily or admitted if there is threat of perforation.

Topical antiviral medications for corneal dendrites and geographic ulcers should be continued five times (for ganciclovir and vidarabine ophthalmic gel) to nine times (for trifluridine drops) per day for 7 to 14 days until healed, then two to four times per day respectively for 4 to 7 days, then stopped

HSV in the Eye

Follow-Up

Topical steroids used for corneal stromal disease are tapered slowly (often over months to years)

The initial concentration of the steroid (e.g., prednisolone acetate 1%) is eventually reduced (e.g., loteprednol 0.5% or prednisolone acetate 0.125%)

Extended taper includes dosing q.o.d., twice weekly, once weekly, etc., especially with a history of flare-ups when steroids are stopped

Prophylactic systemic agents (e.g., acyclovir 400 mg b.i.d.) or less commonly, topical antiviral agents (e.g., ganciclovir 0.15% or trifluridine 1% t.i.d.), are used until steroids are used once daily or less

Corneal transplantation may eventually be necessary if inactive postherpetic scars significantly affect vision, though an RGP lens and maximization of the ocular surface with aggressive lubrication should be tried first

Recommend long-term oral antiviral prophylaxis (e.g., acyclovir 400 mg b.i.d.) if a patient has had multiple episodes of epithelial disease or stromal disease

Hepatitis B Virus (HBV)

Hepatitis B virus (HBV) is the most common cause of liver cancer in the world

Currently, of the two billion people infected with HBV worldwide, 600,000 deaths are anticipated to result annually—either secondary to HBV complications or hepatocellular carcinoma

Hepatitis B Virus (HBV)

- **Mode of Transmission**
  - Sexual contact
  - Needle sharing
  - Blood transfusion
  - Transplacental passage from mother to neonate

Hepatitis B Virus (HBV)

Clinical Course

Acute HBV infection is associated with general malaise, fever, loss of appetite, vomiting and jaundice

Fulminant presentation of infection involves liver failure accompanied by tissue necrosis

The virus is able to inject itself into the host cell to replicate with a resulting immunological response, causing hepatocellular injury

Hepatitis B Virus in the Eye

Ocular Findings

- Ischemic retinopathy
- Pupil sparing third nerve palsy
- Optic neuritis
- Uveitis
- Retinal Vasculitis

Hepatitis B Virus in the Eye

Work-Up

- Slit-lamp examination and DFE
- Serial fundus photographs to document progression should be taken at each visit
- Refer patient to an internist or infectious disease specialist for systemic evaluation and treatment

Hepatitis B Virus (HBV)

Work-Up

ELISA testing is essential for detecting circulating hepatitis viral proteins

A complete blood count with platelets is also useful for detecting other concurrent systemic diseases

Additionally, prothrombin time (PT) is helpful to assess the coagulability of the blood, and may indicate liver damage.

Liver function tests (LFT) are useful to determine the extent of liver damage

Hepatitis B Virus in the Eye

Work-Up

In the case of optic neuritis and uveitis secondary to immune complex deposition, be sure to test for:
- Titrated levels of IgG, IgA, IgM, C_3 and C_4 on commercial plates
- Complement haemolytic activity (CH_{50})
- C1q binding (C1qBA) and conglutinin binding competition (KgB-CA, CIC) assay

If vasculitis is observed, order additional tests

- Erythrocyte sedimentation rate (ESR)
- C-reactive protein (CRP)
- Urine tests
- Imaging (X-ray, CT and MRI) of larger vessels
- Angiogram
- Biopsy

Hepatitis B Virus (HBV)

Treatment for HBV

- Interferon therapy is administered subcutaneously
- Nucleotide analogs reduce HBV replication by mimicking and inserting themselves as a base upon the viral DNA, effectively halting HBV replication
- Vaccination has dramatically reduced the prevalence of HBV around the globe

Hepatitis B Virus in the Eye

Management for HBV

- Side effects of interferon therapy include headache, myalgia, alopecia and fatigue
- The most common ocular complication associated with interferon therapy is **retinal ischemia**, which is characterized
  - CWS
  - Microvascular abnormalities
  - Hemorrhages

Hepatitis B Virus in the Eye

Management for HBV

Patients placed on the medication should be monitored **every 3-4 months** for

- Fundus changes
- Visual field abnormalities
- Retinal nerve fiber layer (RNFL) thickness alterations

Increased RNFL thickness warrants close observation, and any patient who manifests CWS should cease therapy immediately

Other, less common conditions associated with interferon use include:

- Subconjunctival hemorrhage
- Retinal detachment
- Optic neuropathy
- Elevated intraocular pressure

Ocular signs typically present from two weeks to six months following therapy initiation

Hepatitis B Virus in the Eye

HBV Vaccination

- Has dramatically reduced the prevalence of HBV around the globe
  - Is an effective agent that is safe for administration at birth
- Potential Ocular Side Effects:
  - Uveitis
    - Posterior Uveitis: Multiple Evanescent White Dot Syndrome (MEWDS)
    - Disc edema
    - Central vein occlusion
    - Optic neuritis

Hepatitis C Virus (HCV)

- Approximately 3.6 million persons in the US are infected with the hepatitis C virus (HCV), a condition with both hepatic and extrahepatic sequelae
- Although no pathognomonic manifestation of HCV infection in the eye has been demonstrated, associations between HCV infection and various ocular syndromes have been reported in small case series and individual patients
- At this time, the ocular manifestations of HCV infections best supported by the literature include:
  - Dry eye syndrome similar to Sjögren syndrome
  - Ischemic retinopathy caused by either an HCV-induced vasculitis or treatment with interferon

Hepatitis C Virus (HCV)

- Patients with diabetes seem to be more susceptible to interferon retinopathy and to subsequent permanent visual loss
- There have been no cases of HCV transmission via corneal transplantation, suggesting that current cadaveric screening protocols are effective in preventing this route of transmission
- Screening for HCV should be considered in patients with risk factors for HCV infection who suffer from unexplained ischemic retinopathy or dry eyes

Pediatrics

Ophthalmia Neonatorum (Newborn Conjunctivitis)

Etiology

- Pregnant women with active STDs can transmit the disease to their babies in the birth canal during delivery

Pediatrics

Ophthalmia Neonatorum (Newborn Conjunctivitis)

Signs

- Purulent, mucopurulent, or mucoid discharge from one or both eyes in the first month of life
- Diffuse conjunctival injection
- Eyelid edema
- Chemosis

Pediatrics

Ophthalmia Neonatorum (Newborn Conjunctivitis)

Treatment

- Newborns are universally treatment with erythromycin ointment in the delivery room to prevent this
- However, the newborn may present with symptoms of these after being discharged from hospital

Pediatrics

Ophthalmia Neonatorum (Newborn Conjunctivitis)

Differential Diagnosis

Dacryocystitis: Swelling and erythema just below the inner canthus	Nasolacrimal duct obstruction	Congenital glaucoma

Prevention: Patient Education

How to help prevent eye complications from sexually transmitted infections?

- Wash your hands often
- Do not touch or rub your eyes unless your hands are clean
- Never share eye makeup or cosmetics with anyone
- When you have conjunctivitis, throw out all eye makeup you have been using
- Do not share towels, washcloths, or pillowcases with others
- If just one of your eyes has an infection, use a separate towel for each eye
- Use appropriate protection during sexual activities

Sources

- Wajda & Bagheri. *The Wills eye manual: office and emergency room diagnosis and treatment of eye disease.* Wolters Kluwer/Lippincott Williams & Wilkins, 2017
- Centers for Disease Control and Prevention. https://www.cdc.gov