



## Infectious Retina

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No Disclosures

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1

### Disclosure Statement:

Nothing to disclose

## Common Posterior Segment Manifestations

- HIV Retinopathy
- Cytomegalovirus (CMV)
- Acute Retinal Necrosis (ARN)
- Progressive Outer Retinal Necrosis (PORN)
- Tuberculosis (TB)
- Toxoplasmosis
- Syphilis
- Cat Scratch Disease

## The Fight Against HIV/AIDS??

•Dr. Thomas R. Frieden, the director of the CDC, and Dr. Jonathan Mermin, the agency's chief of AIDS prevention, paint a bleak picture of the fight.

*"Hundreds of thousands of people with diagnosed H.I.V. infection are not receiving care or antiretroviral treatment," they wrote. "These people account for most new H.I.V. transmission."*

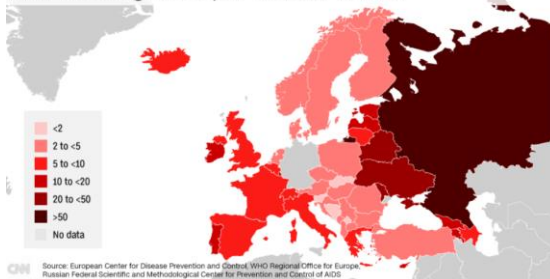
•Nearly 65 percent of the estimated 1.2 million Americans with H.I.V. are not on treatment; many disappear right after being tested.

•Budget cuts to PEPFAR (Presidents Emergency Plan for AIDS Relief)

**As things stand, the world is no longer on course to end the pandemic by 2030 - a target agreed by UN member states(The Lancet)**

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New HIV diagnoses per 100,000 in 2017



## HAART

•Highly Active Antiretroviral therapy (HAART) is the combination of several anti-retroviral medicines used to slow the rate at which HIV multiplies in the body.

•Use of three or more antiretroviral medicines referred to as an anti-HIV "cocktail"-currently the standard treatment for HIV infection

- Nucleoside/nucleotide reverse transcriptase inhibitors
- Nonnucleoside reverse transcriptase inhibitors
- Protease inhibitors
- Entry inhibitors
- Integrase inhibitors

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## HIV Retinopathy

- **Retinal Micro-vasculopathy**  
*Use to occur in 50-70% of patients*  
*Prevalence lowered by advent of HAART*
- **Symptoms:**  
*none*
- **Characterized by:**  
*dot blot hemes*  
*cotton wool spots*  
*roth spots*  
*retinal micro-aneurysms*
- **Thought to be due to increased plasma viscosity, immune complex deposits, and direct cytopathic effect of the virus on the blood vessel endothelial layer**



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## HIV Retinopathy Treatment

- Control viral load  
undetectable? Safe levels?
- Most findings resolve with time.
- Can be confused with diabetic retinopathy or hypertensive retinopathy.

## Cytomegalovirus (CMV)

- **Most common cause of intraocular infection in patients with AIDS.**
- **Part of the herpes family of viruses**  
*spreads from person to person through body fluids, such as blood, saliva, urine, semen and breast milk*
- **Seen in patients with a CD4 count less than 50 cells/uL**
- **Represents re-activation of latent CMV infection**
- *Necrosis through direct cell destruction, release of viral products from infected cells, and production of inflammatory molecules such as cytokines by virus infected and/or nearby cells*

## Signs and Symptoms

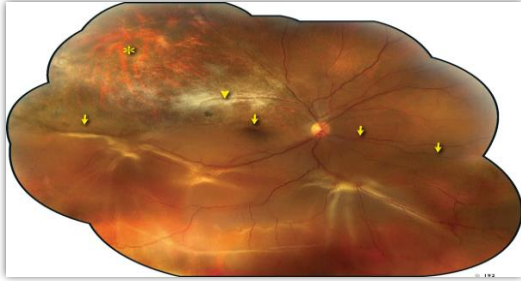
- **Symptoms**  
*Floaters*  
*Photopsias*  
*Decreased vision*  
*Pain( Minimal a/c reaction), photophobia*
- **Signs:**  
*Necrotizing retinitis (cheese)*  
*Hemorrhages (ketchup)*  
*Vascular sheathing*  
*Uveitis*  
*Retinal detachment*

## Cytomegalovirus (CMV)

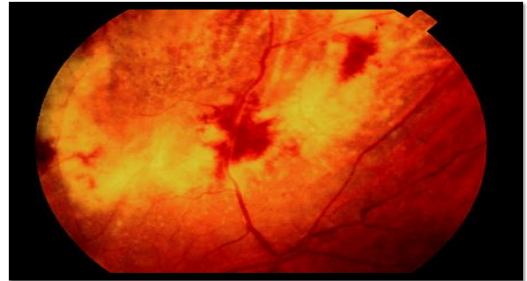
- **Types:**  
*Fulminant: Large areas of necrosis with hemes, found within the arcades*  
*Indolent: Retinal atrophy with minimal hemes in the periphery*  
*Perivascular: frosted appearance*
- **Progression can lead to papillitis, macular edema, retinal detachment**  
*Slow course, 250 um per week*

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## Cytomegalovirus (CMV)



## Cytomegalovirus (CMV)



## CMV Treatment Options

- **Intravenous ganciclovir, cidofovir, foscarnet**  
*Individually or in combination*
- **Oral ganciclovir or valganciclovir**
- **Intravitreal ganciclovir and foscarnet**
- **Ganciclovir implant-(discontinued)**  
*Systemic toxicity*  
*No indwelling catheter*  
*Useful if patient is intolerant of systemic ganciclovir or if progression continues despite intravenous treatment*

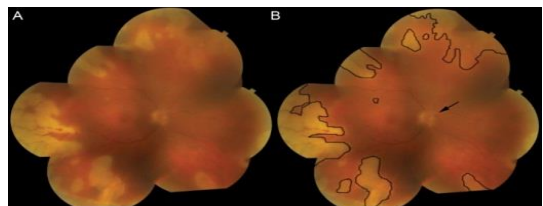
## Acute Retinal Necrosis (ARN)

- **Necrotizing retinitis that presents with:**  
*Varicella zoster virus (VZV)-more severe presentation*  
*Herpes Simplex Virus (HSV)*  
*Cytomegalovirus (CMV) (rare)*
- **Can occur in immunocompetent or immunocompromised patients**

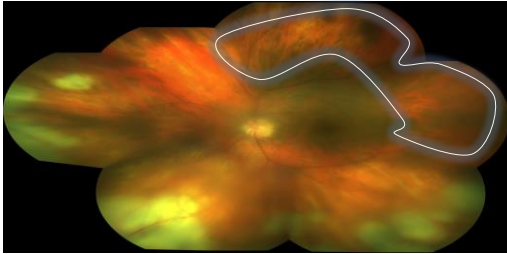
## Signs and symptoms

- **Symptoms:**  
*Eye pain, photophobia*  
*Decreased vision*  
*Floaters*
- **Signs:**  
*Necrotic lesions in periphery (with rapid progression)*  
*Hemorrhaging (minor)*  
*Retinitis/Vitritis/Uveitis*  
*Disc edema*  
*Retinal detachment*

## Acute Retinal Necrosis



## Acute Retinal Necrosis



### Treatment options

- Intravenous acyclovir/valacyclovir /famciclovir in conjunction with oral
- Intravitreals
- For anterior segment inflammation:
  - Cycloplegic with topical steroid
- Barricade laser
- Relapse is common, initiate initial therapy
- Systemic steroids??
- Vitrectomy?
  - Release of traction, cytokines?

## Progressive outer retinal necrosis (PORN)

- Caused by the varicella-zoster virus

*Double stranded DNA virus of the herpes group*

*Virus is spread through direct contact with the rash or by sneezing, coughing, and breathing*

*Virus remains latent in sensory ganglia*

**Reactivated during times of loss of T-cell regulatory control(AIDS)**

Necrosis through direct cell destruction, release of viral products from infected cells, and production of inflammatory molecules such as cytokines by virus infected and/or nearby cells

## PORN

- Facial rash/scars:

*Patients have an episode of cutaneous zoster a mean of two months before onset of visual symptoms.*

- Minimal intraocular inflammation

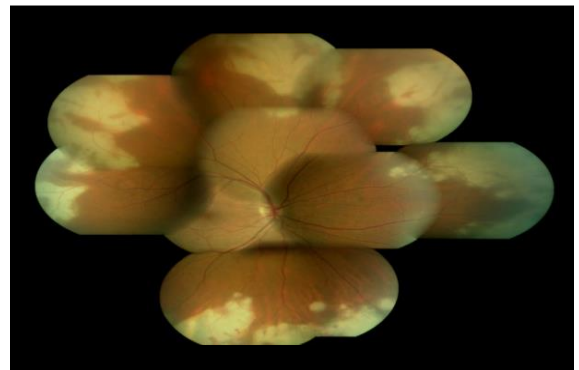
*CD4 count less than 21 in most studies*

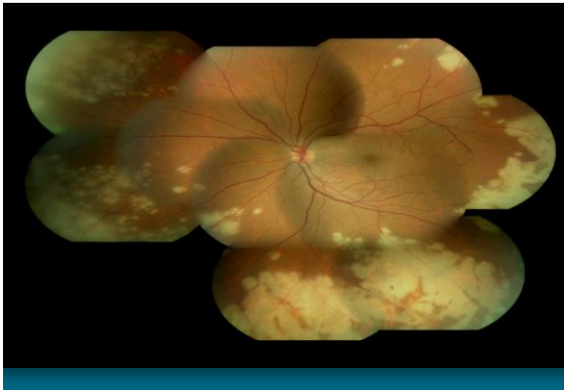
- Bilateral retinal necrosis involving the outer retinal layers with relative sparing of the inner retina and retinal vasculature.

- Lesions progress, and become confluent and full-thickness

## PORN

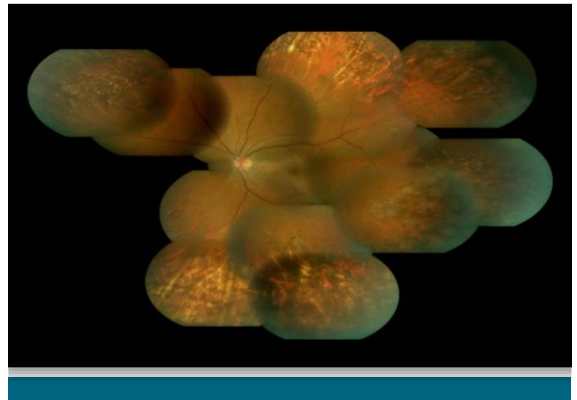
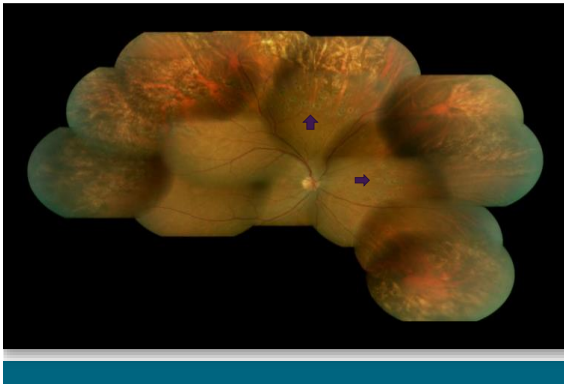
- Optic nerve involvement: edema, hyperemia, atrophy (17%)
- Rhegmatogenous retinal detachment secondary to atrophic, thin retina with multiple holes (70%)
  - Number one cause of vision loss





## PORN Treatment Options:

- Various combinations of intravenous, oral, and intravitreal antivirals.  
Ganciclovir, acyclovir, foscarnet
- Barricade laser
- Highly active antiretroviral therapy(HAART)
- Prognosis: guarded..



## Differentiating the Herpetic Retinopathies

	PORN	ARN	CMV
Symptoms	Floaters, VA loss, peripheral constriction, no pain	Hazy vision, peripheral constriction, pain	Mild or no change in VA, constricted fields, floaters, no to mild pain
Location	Peripheral	Peripheral	Arcades
Progression	+++	**	•
Optic Nerve Involvement	Possible	Possible	Possible
Etiology	VZV	VZV, HSV1,2	CMV
Inflammation	Minimal or none	Vitreol and/or AC	AC and ant. vitreous
Vascular Inflammation	None	Vasculitis	Vasculitis
HIV/AIDS	•	• or -	•

## Tuberculosis

- Caused by airborne transmission and infection with *Mycobacterium tuberculosis*, with main infection at the lungs
- **Can still get ocular tuberculosis**

Not everyone infected with TB bacteria becomes sick. As a result, two TB-related conditions exist: latent TB infection and TB disease.

TB bacteria overcome defenses of immune system and begin to multiply, resulting in progression from latent TB infection to TB disease.

Some people develop TB disease soon after infection, while others develop TB disease later when their immune system becomes weak.

## Latent

- Usually has a skin test or blood test result indicating TB infection
- Normal chest x-ray and a negative sputum test
- TB bacteria in body that are alive, but inactive
- Usually asymptomatic
- Cannot spread TB bacteria to others
- Still should get treated
- Can get latent TB with ocular involvement

## TB Disease

- Usually has a skin test or blood test result indicating TB infection
- May have an abnormal chest x-ray, or positive sputum smear or culture
- Active TB bacteria in body
- Feels sick and may have symptoms such as coughing, fever, and weight loss
- May spread TB bacteria to others
- Needs treatment to treat TB disease

## TB endemic areas

### Risk of TB higher in patients who are immune-compromised.

- *The risk of developing TB is estimated to be between 20-37x greater in those with HIV*
- leading killer of people with HIV
- *Skid row outbreak*
- *Rising Drug Costs*



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## TB Testing

- *Tuberculin Skin Test (TST)* -
  - induration of 5 or more mm** is considered positive in HIV-infected persons
  - induration of 10 or more mm** is considered positive in:
    - Injection drug users
    - Residents and employees of high-risk congregate settings
    - Mycobacteriology laboratory personnel
    - Persons with clinical conditions that place them at high risk
    - Children < 4 years of age
  - induration of 15 or more millimeters** is considered positive in any person, including persons with no known risk factors for TB

## TB Testing

- *TB blood tests (also called interferon-gamma release assays or IGRAs)*
  1. Quantiferon TB Gold: measure interferon released by sensitized T-cells, more specific
  2. T-SPOT
    - Less reader bias
    - Single visit
    - Access? Cost?

## Other Diagnostic Considerations

### Chest Radiograph

**AFB Smear and Culture**  
**Sputum examination is indicated for persons with positive test results for TB infection and either an abnormal chest radiograph or the presence of respiratory symptoms (even when the chest radiograph is normal).**

### Physical Examination and Medical History

## Tuberculosis

### Symptoms:

*Pain, decreased vision, floaters*

### Signs:

*Choroiditis  
Subretinal abscess, tubercles, and tuberculomas  
Vitreitis  
Anterior Uveitis  
Rare: Retinal involvement-vasculitis*

## Tuberculosis

• **Most commonly affects the choroid, due to high oxygen content and vascularization.**

• **Fundus findings in tuberculosis can be divided into four groups:**

#### *Choroidal tubercles:*

*small inflammatory nodule that forms when the immune system builds a wall around the TB*

#### **Choroidal tuberculoma:**

*Tubercles continue to grow into a larger mass*

*Sub-retinal abscess-necrotizing granulomas*

*Serpiginous like choroiditis*

## Tuberculosis



<http://www.retinalphysician.com/pentastaride.aspx?articleID=102293>



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## Tuberculosis

### •Treatment:

• **Depends if latent or active**

• **Latent: shorter courses**

### •Active:

*RIPE-Rifampin, Isoniazid, Pyrazinamide, **Ethambutol** for 6-9 months*

*Steroids can be used to control inflammation but only in conjunction with antibiotics*

## Toxoplasmosis

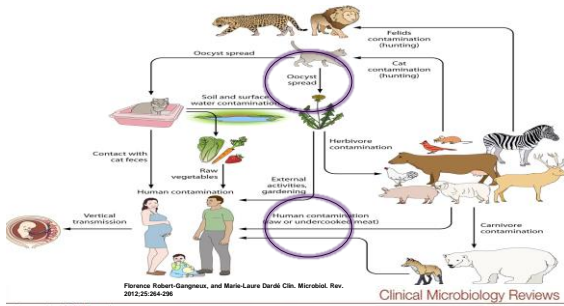
• Due to *Toxoplasma gondii*, protozoan parasite, which is transmitted by ingesting contaminated water and food (raw meats, raw eggs, unpasteurized milk), exposure to cats

• Two Types:  
*Acquired  
Congenital*

**Most common cause of posterior uveitis in any patient.**

### •Testing:

*Toxoplasmosis antibody titer (IgG an IgM)  
PCR*

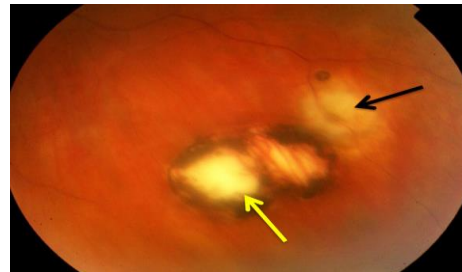


## Pathophysiology

**Tachyzoite:** active proliferating form that results from an oocyst: destructive immune response

Under pressure of the immune system, tachyzoites differentiate into **bradyzoites**, forming tissue cysts. *Latent form, may persist indefinitely in host tissues. Refractory to most currently available antiparasitic drugs* chronic *T. gondii* infection cannot be cured.

## Acquired toxoplasmosis



## Toxoplasmosis

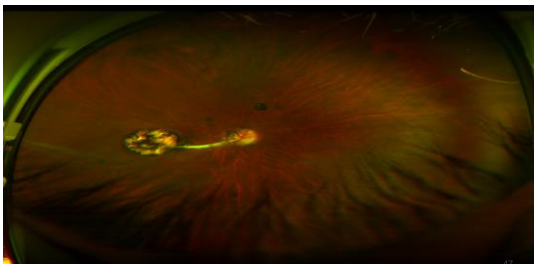
**Symptoms:**

- Decreased vision
- Floater
- Pain, if anterior chamber reaction

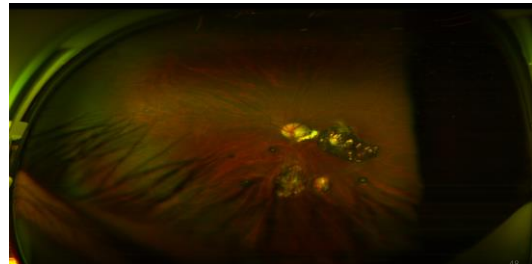
**Signs:**

- Necrotizing retinitis
- Vasculitis
- Vitritis (reduced compared to immuno-competent pt)
- Adjacent retinochoroidal scars not seen, suggesting that these represent recently acquired infections
- High association with CNS disease, MRI indicated

## Congenital toxoplasmosis



## Congenital toxoplasmosis





## Treatment

•**Main Factors Influencing Treatment Decision on Active Toxoplasmic Retinochoroiditis**

- Immune status of the individual*
- Location and size of the active lesion*
- Presence of macular and/or optic disc edema*
- Degree of vitritis and of decreased vision*
- Special situations (newborns, pregnant women, drug allergy)*
- Adverse effects of antiparasitic drugs and corticosteroids*

## Toxoplasmosis Treatment:

- **Pyrimethamine** and either sulfadiazine (allergy) or clindamycin in standard dosages with oral pred 24 hrs after antibiotics begin  
Goodrx with a coupon....
- Trimethoprim/sulfamethoxazole: reoccurrences
- Folinic acid to minimize bone marrow toxicity
- Anterior chamber reaction: cycloplegic and steroid

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## Syphilis

•**Syphilis is a chronic venereal disease caused by the spirochete *Treponema pallidum*.**

•**In the United States, the rates of syphilis have been increasing since 2000, particularly in HIV-positive patients and homosexual men**

- *Men, women, seniors...*
- *Proper education, huge budget cuts*

•**The Great Masquerader.....**

External adnexa	Dacryocystitis, dacryoadenitis, lymphadenopathy
Conjunctiva/sclera	Chancro, conjunctivitis, scleritis
Cornea	Interstitial keratitis (more common in congenital syphilis)
Pupil	Light near dissociation, Horner's syndrome
Mobility	Internuclear ophthalmoplegia
Lens	Cataract
Uveal tract	Iris nodules, iritis, vitritis, multifocal chorioiditis
Optic nerve	Papillitis, disc edema
Retina	Retinitis, neuroretinitis (especially in HIV+ patients), exudative retinal detachment

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CALIFORNIA **#1** IN SYPHILIS CASES

AHR

freeSTDcheck.org

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## Syphilis Staging

- Primary syphilis:**  
*painless chancre that develops at the site of infection an average of three weeks after exposure.*
- Secondary syphilis:**  
*The most common features are fever, lymphadenopathy, diffuse rash, and genital or perineal condyloma latum ( papules at muco-cutaneous junctions)*
- Latent stage:**  
*patients are asymptomatic. Serologic tests are positive for T. pallidum.*
- Tertiary:**  
*Infection can involve any organ system.*

## Syphilis Staging

### Special Circumstance:

*Neuro-syphilis is a distinct category affecting the CNS and can occur at any time during the course of the disease*

## Types

### •Two Types:

1. *Acquired*
2. *Congenital*

Widely spaced, centrally notched anterior incisors (Hutchinson's teeth) and the abnormal facies (saddle nose). Congenital syphilis may present with interstitial keratitis, uveitis, optic neuritis, glaucoma, cataract, and/or retinal vasculitis.

Hutchinson Triad: deafness, Hutchinson's teeth, interstitial keratitis



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## Syphilis testing

•Two types of antibody tests: non-treponemal and treponemal

•**Non-treponemal** : RPR & VDRL detect antibodies directed against host antigens, advantage of quantifiability, **reflect both disease activity and response to therapy**, and can be used to test for reinfection. Limited sensitivity-as low as 70%.

•**Treponemal** : FTA-ABS & MHA-TP tests, measure serum antibodies directed specifically against *T. Pallidum*, highly sensitive.

*Not reliable in gauging response to treatment*

*False positive with: collagen vascular disease, advanced age and HIV infection.*

**positive for life even despite treatment**

## Syphilis

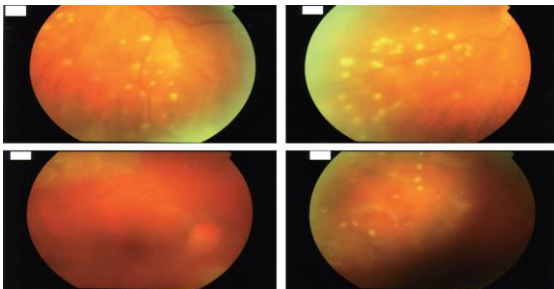
### Symptoms:

- *Decreased vision*
- *Floaters*
- *Pain*
- *Photophobia*

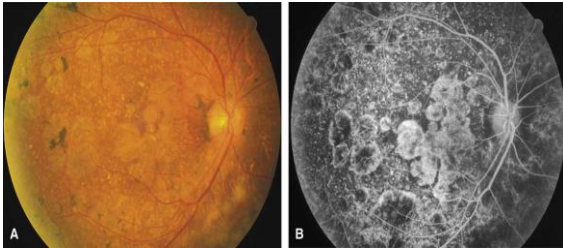
### Signs: (no sign is pathognomonic)

- *Uveitis-strong predictor of HIV co-infection*
- *Optic neuritis*
- *Retinitis*
- *Choroiditis*
- *Vasculitis*

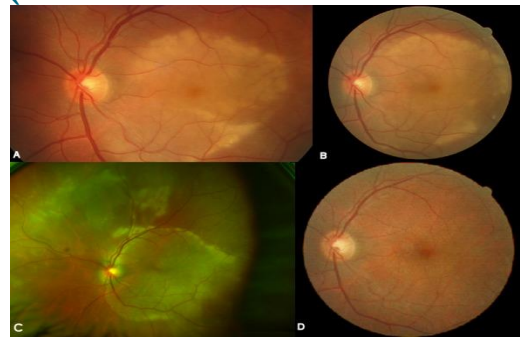
## Syphilis



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## Treatment Options

### •IV Penicillin

•Patients with ocular syphilis should undergo CSF testing and, regardless of findings, be treated as neurosyphilis with 10 to 14 days of high-dose intravenous followed by three weekly injections of IM penicillin

Allergy: ceftriaxone (CR), azithromycin and doxy (not as good)

penicillin desensitization

•Uveitis: cycloplegics with topical steroids

•Tell the CDC!

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## Cat Scratch Disease

•Cause: *Bartonella henselae*

### •Etiology and Pathology:

Fleas (*Ctenocephalides felis*) carry *B. henselae* and can transmit the bacterium from cat to cat.

Exposure to kittens is a greater risk factor than exposure to adult cats.

*B. henselae* can be transmitted to humans following contact with cats (scratches, bites) and possibly following contact with cat fleas.

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## Cat Scratch Disease

•22,000 cases yearly in the U.S. (about 6.6 cases per 100,000)

•no racial nor gender predilection

•majority of cases are in pediatric patients with cat exposure

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## Cat Scratch Disease

### •Testing:

*Indirect fluorescent assay specific for antibodies directed against B. henselae.*

This test has a sensitivity and specificity above 90 percent

*Enzyme-linked immunoassay for both IgG and IgM anti-B. henselae antibodies.*

*PCR-based techniques*

Very sensitive and can differentiate between *Bartonella* species

Harder to obtain

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## Cat Scratch Disease

### Signs:

- *granulomatous conjunctivitis with pre-auricular lymphadenopathy*
- *systemic lymphadenopathy*
- **optic nerve edema**
- **subretinal fluid, exudates, or a macular star**
- **focal chorioretinitis**
- *positive skin test or serum titer for Bartonella H.*

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## Cat Scratch Disease

### Symptoms:

systemic symptoms of disease may resemble a flu-like illness (malaise/weakness, low-grade fever, headache, and joint or muscle pains)

patients may also notice enlarged regional lymph nodes in the axillae, groin, neck, or head

decreased/blurry vision, usually in one eye

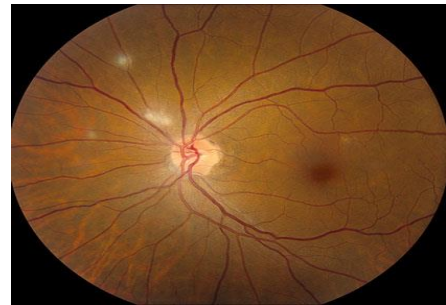
red eye

patients may notice decreased visual field

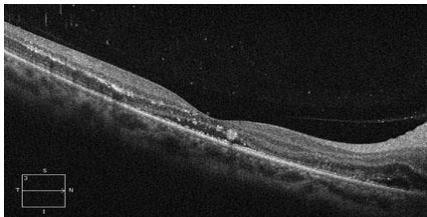
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## Treatment:

- *Controversial*
- *Documented that patients will almost always get better on their own*  
final visual acuity is 20/40 or better in 93% of patients
- *Treatments include doxycycline (don't give to kids), erythromycin, rifampin, azithromycin, ciprofloxacin*

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