

# Sight- threatening Eye Infections

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# Ocular Infections

## Non-Sight-threatening Eye Infections

- I. Lid and Lacrimal System Infections
- II. Conjunctivitis

## Sight-threatening Eye Infections

- III. Microbial Keratitis
- IV. Endophthalmitis
  - I. Exogenous
  - II. Post-operative
  - III. Penetrating ocular trauma
  - IV. Endogenous
- V. Infectious Uveitis
- VI. Orbital Cellulitis (Eye/ENT)

# When can Bacterial Conjunctivitis become Sight- Threatening?

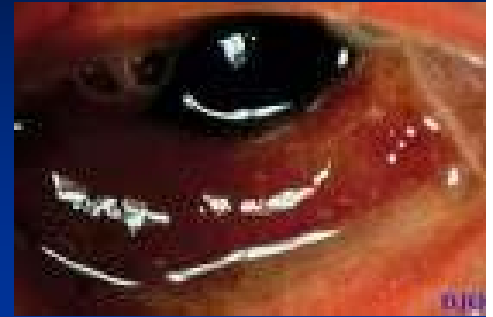


# Hyperacute Bacterial Conjunctivitis

*Neisseria gonorrhea* > *Neisseria meningitidis*;  
*C. diphtheriae*, *S. pneumoniae*, *S. pyogenes*

Direct Invasion/Toxins/Enzymes

“Wet Mucosal Surfaces” (Genital, Rectal, Pharyngeal)



Rapid progression (HOURS)

Marked Eyelid swelling and Conjunctival hyperemia

Corneal MELT (copious purulent exudate)

Involved side tender pre-auricular lymphadenopathy

40% progress to corneal ulceration ->

4% corneal perforation -> **LOSS OF VISION**

Intensive Systemic and Topical Treatment

Ceftriaxone 1gm IV/IM x 5 days (or Aq PCN 10mU/Day)

Penicillin GK 100,000U/mL q15min x 2hrs, then q30min-1hr.

*Co-STDs: Chlamydia trachomatis -30%; Syphilis*

# Chlamydial Conjunctivitis

## ■ Trachoma (Follicular Conjunctivitis)

- 84 million persons/worldwide
- **8 million are visually impaired; 3.4 million blind**
- Second most common cause of blindness
- Most common cause due to an infectious disease
- Confined to Africa, Asia, Middle East, and Aboriginal communities in Australia.
- Predilection for poverty and poor personal hygiene
- Transmission - towels, handkerchiefs, fingers, Flies (Bazaar fly, Australian bush fly)
- “Wet mucosal surfaces”
  - pharyngeal, rectum, (genital)



# Trachoma

**Follicular trachoma (Grade TF)** produces active follicles ( $>5 \times 0.5$  microns) on the upper tarsal conjunctiva. Young children

**Inflammatory trachoma (Grade TI)** causes thickening of the upper tarsal conjunctiva; more intense inflammation more scarring.

**Trachomatous scarring (Grade TS)** produces easily visible scarring in the upper tarsal conjunctiva.

**Trichiasis (Grade TT):** eyelashes touch the globe causing fibrosis and corneal opacification. Eyelid surgery to direct lashes away (Bilamellar tarsal rotation)

**Corneal opacity (Grade CO):** easily visible and obscures at least part of the pupillary margin- reflects the prevalence of vision loss and blindness.





# Trachoma: Management

- **NAAT (nucleic acid amplification testing)**
  - Best and most Expensive.
- **Direct fluorescein-labeled monoclonal antibody (DFA)** (sensitivity 70-100% and specificity 95%) - Most commonly used (Resource-limited). Consider confirmatory testing (NAAT). Two swabs on presentation; freeze NAAT swab.
- **Oral azithromycin 1 gm po x 1 or azithromycin (20mg/kg)**

**“There is a worm in my eye.  
Every time I try to show it, it  
disappears. People are  
starting to think I am crazy. I  
am beginning to wonder  
myself.”**

**When is Delusional Parasitemia NOT  
Delusional Parasitemia?**

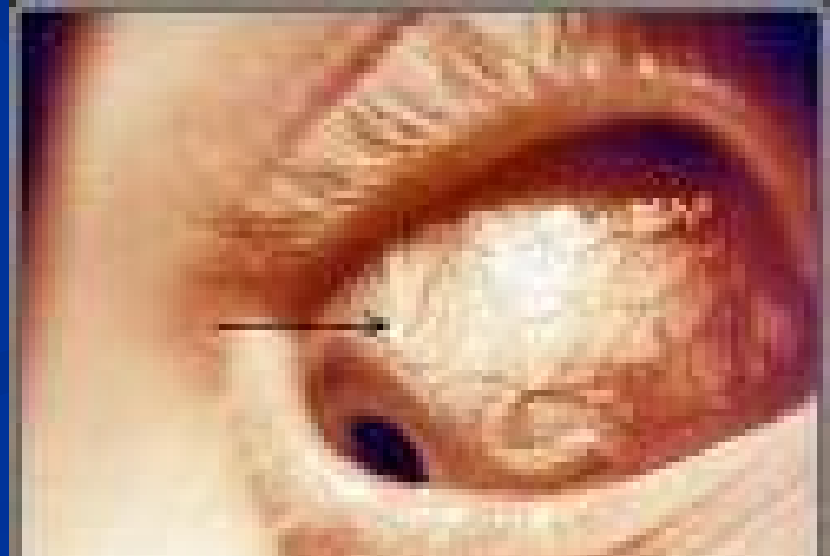


# Loa Loa

12-13 million infected

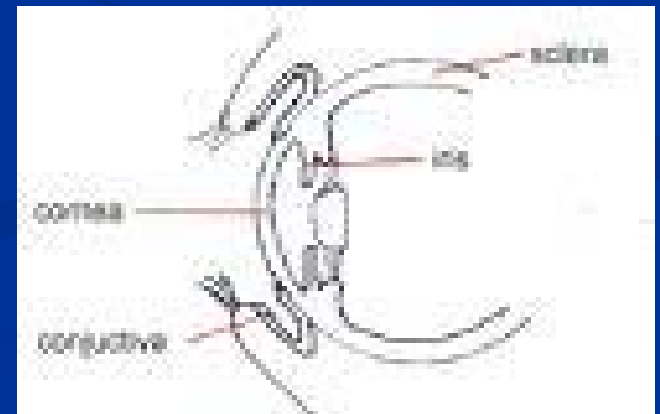
West and Central Africa rain forests (Cameroon and Ogowe River);

- Chrysops flies transmit; adult worm migrates in conjunctiva and aqueous.
- “Calabar swellings” in subcutaneous tissues
- Microfilariae in blood (Day)
- Tx: Diethylcarbamazine



# Microbial Keratitis: Risk Factors

- Healthy cornea normally resistant to infection
- Identifiable Risk factors (90%):
  - Corneal Injury or disruption of corneal epithelium
  - Protracted epithelial ulceration
  - *Herpes simplex* keratitis
  - Corticosteroid use in ocular surface disease
  - Extended Wear Soft Contact Lens Wear
    - 0.01% -> 0.2%; **20X** increase



# Microbial Keratitis:

## Suppurative and

## Nonsuppurative Keratitis

### ■ Suppurative Keratitis

- Risk factors:
  - Corneal injury, protracted epithelial ulceration, CL wear
- High Virulence
  - ***Staphylococcus aureus***
  - ***S. pneumoniae***
  - ***Pseudomonas aeruginosa***
  - Enterobacteriaceae
    - *Serratia*
    - *Proteus*
    - *Citrobacter*
    - *Enterobacter*
    - *Klebsiella*

### ■ Nonsuppurative Keratitis

- Risk factors:
  - Corneal injury, Contact Lens (CL) wear, penetrating keratoplasty, Intraocular lens (IOL), LASIK
- Low Virulence
  - **Coagulase-negative staphylococci**
  - Viridans group streptococci
  - *Moraxella*
  - *Haemophilus*
  - ***Mycobacteria* (atypical)**
  - *Nocardia*
  - **Yeast and Fungi**
  - ***Acanthamoeba***

# Keratitis: Regional Variation

	Staph	Strep	<i>Pseudo monas</i>	Other GNs	Fungi
New York	49%	9%	8%	22%	3%
South Florida	16%	8%	19%	9%	35%/ ++

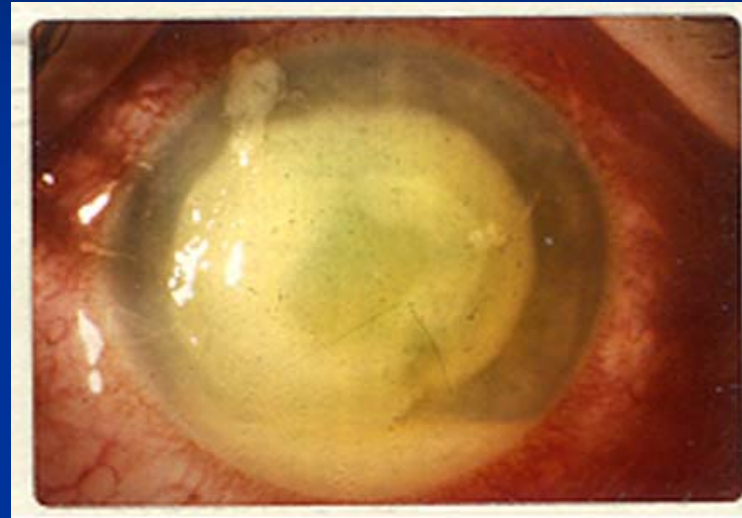
# Acute Suppurative Keratitis: *Pseudomonas aeruginosa* Keratitis



- Focal epithelial and stromal ulceration
- Dense, coagulative stromal suppuration
- Cellular infiltrate and edema in the adjacent stroma

# *Pseudomonas aeruginosa*

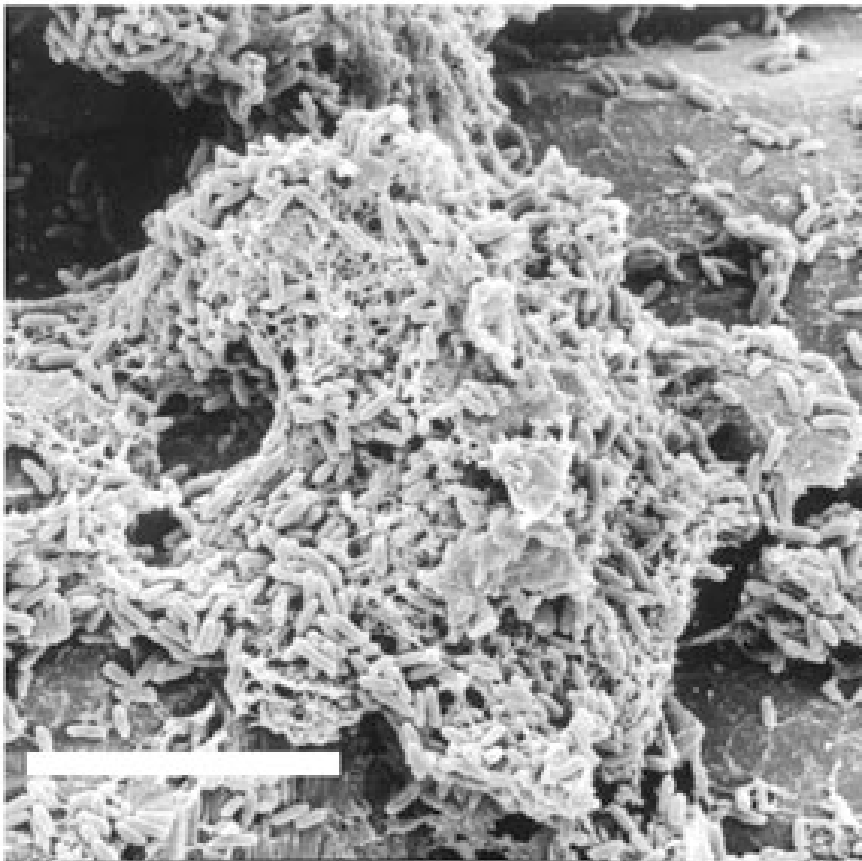
## Keratitis



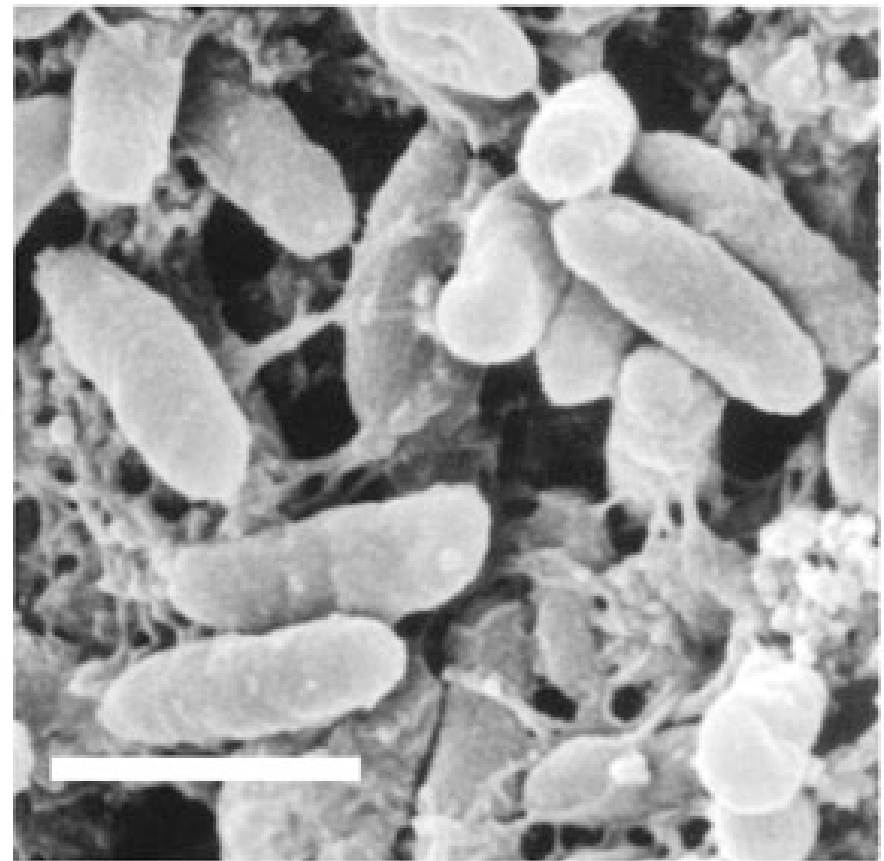
- Ubiquitous to environment, lives in water
- Nosocomial pathogen (ventilators, showers, water sources)
- Contact lenses and contact lens cases (70% of PsA; less with increasing use of antibacterial preservatives)

# *Pseudomonas* Biofilm on Contact Lens

**a**

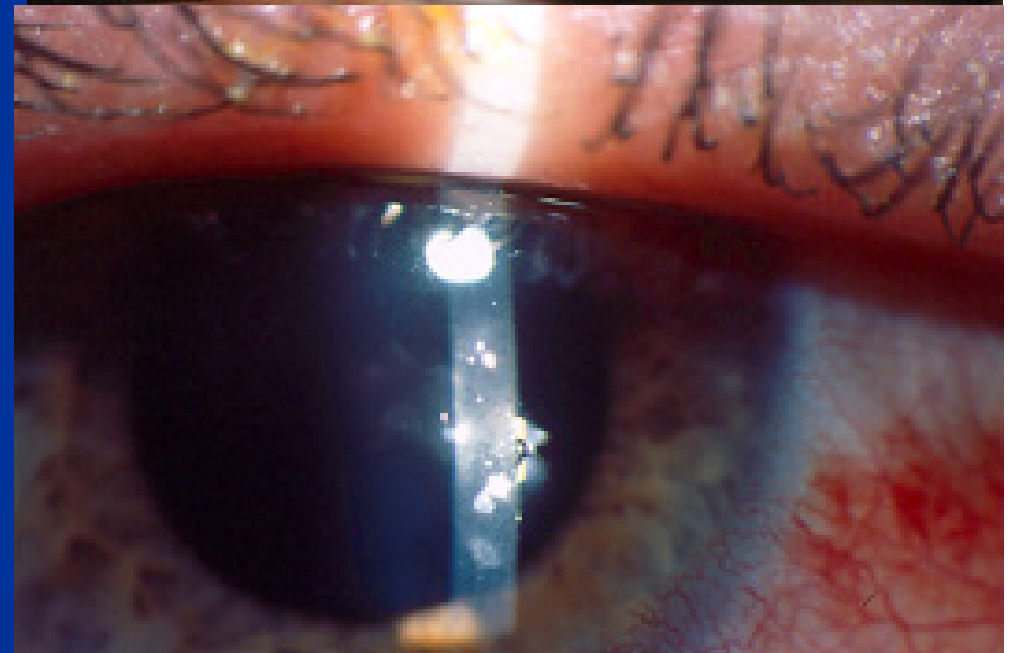
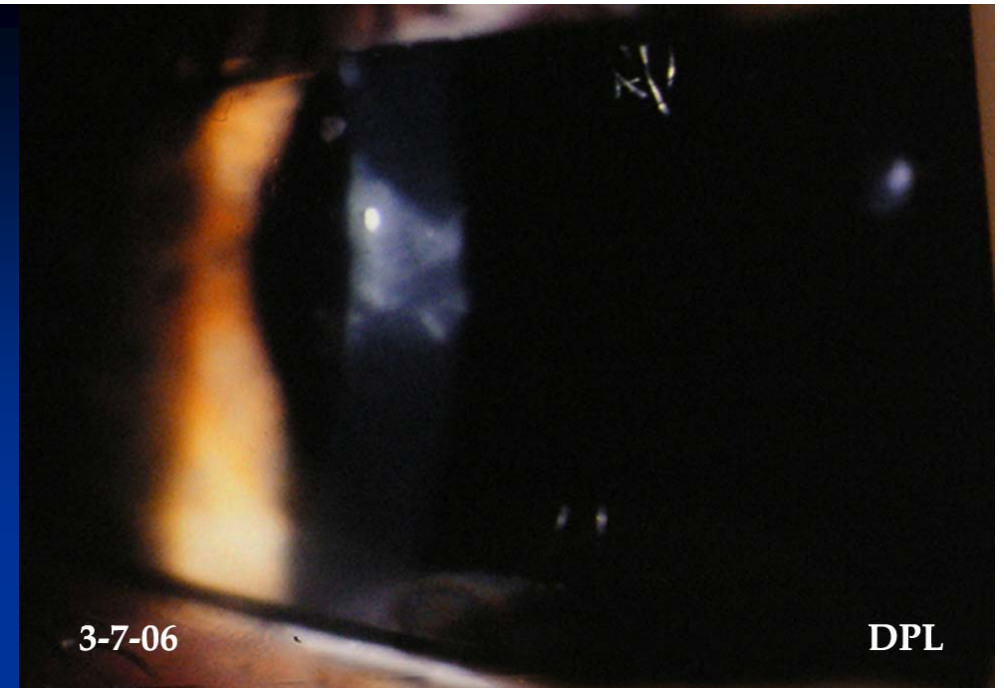


**b**



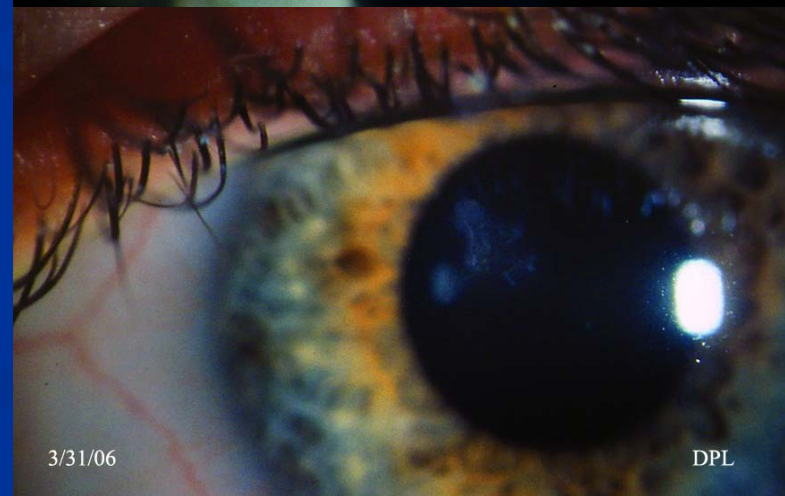


- 14 yo healthy F
- Soft contact lens wearer,
- ReNu with MoistureLoc
- Redness, photophobia
- 20/20



# Fungal Keratitis: Soft Contact Lens Wearer

- Cultures:
  - *Fusarium sp.* from contact lens
- Treatment: Topical Natamycin, Amphotericin B, 1% Voriconazole
  - +/- Voriconazole 200 mg po BID
  - Duration: Three months, no Surgery
- Reported: Boston Public Health Department



# Fungal Keratitis

- **Non-suppurative Keratitis**
- **Risk Factors:**
  - Cornea Injury
  - Organic and Vegetable Matter, Tree Branches
  - Host risks: Diabetes mellitus, steroids, HSV keratitis
  - Contact Lens Wear: Moisture-Loc =NO RUB
    - Moisture-Loc = “Fusarium-Loc”
    - ReNu removed from market April 14, 2006.
    - Is the risk gone?

**Fungal Keratitis in Boston area:  
1999-2002 compared to 2004-2007  
(47 months)**

- **Number of cases of yeast keratitis (mostly *Candida* sp.) unchanged**
- **Rise in Filamentous fungi associated keratitis (7 to 24 cases) exclusive of ReNu**
  - **Contact lens wear independent risk factor (exclusive of ReNu)**
  - **Topical Natamycin or Amphotericin B**
  - **The use of Oral Voriconazole did not prevent need for therapeutic penetrating keratoplasty**
  - **Contact lens wearers had better visual outcome (central area of involvement?)**

# Herpes Simplex Keratitis

Most common cause of blindness in  
Western Hemisphere

500,000 cases/yr in US

Tearing, pain, decreased  $V_A$ , thin dendritic  
(irregular) corneal ulcer

Dx- Elisa, corneal scrapings: Giemsa - red  
intranuclear inclusion bodies

Tx: Valacyclovir 1000mg TID or  
Famciclovir 500 mg BID-TID or  
Acyclovir 800mg 5x/day

Suppression: Acyclovir 400 mg BID or  
Valacyclovir 1000mg q D or Famciclovir  
500 mg q D

Recurrence rate: 95%, immune mediated



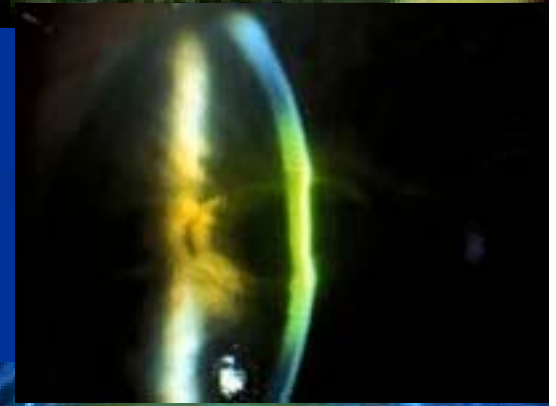
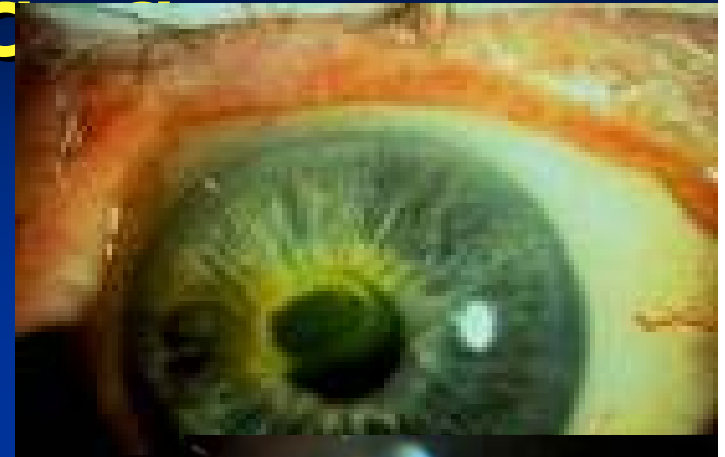
# Herpes Zoster

## Ophthalmic

Ophthalmic div trigeminal n.  
Nasociliary branch of ophthalmic  
n., lesion tip nose. Neuralgia.

Dx: Giemsa-inclusion bodies,  
titers, viral Cx

Tx: IV Acyclovir 10mg/kg q 8 hr x  
10-14 days (Severe or  
Immunosuppressed) Valacyclovir  
1000mg TID or  
Famciclovir 500 mg BID-TID or  
Acyclovir 800mg 5x/day





# Unilateral, Red, Painful Eye

- Patient with foreign body sensation, irritation, photophobia, and tearing OD. Slit lamp exam - superficial punctate keratitis OD. Treated with topical antibiotics
- RETURNS with worsening OD photophobia, redness, tearing, blurry vision, and pain. Corneal sensation was noted to be absent OD. Exam - corneal epithelial irregularity with small defect, mild corneal edema, keratic precipitates, and mild anterior chamber reaction.
- RETURNS -presumptively treated for HSV keratitis with po Acyclovir.
- RETURNS with worsening corneal edema. Topical Prednisolone was added with initial improvement.
- RETURNS- two weeks later, she developed worsening photophobia and severe pain.
- Previous ocular history: Myopia, Rigid gas permeable contact lenses x 40 years
- Past Medical History: Chicken pox during childhood
- DIAGNOSIS??



# "Unresponsive Keratitis"

## Diagnostic studies:

- - Bacterial cultures: negative
- - Viral cultures: negative
- - HSV PCR: negative
- - Fungal cultures: negative
- - Gram stain: PMNs, epithelial cells, no organisms
- - Calcofluor white stain: negative
- - Corneal biopsy: negative
- - *Acanthamoeba* culture: positive



# ***Acanthamoeba* Keratitis**

## **Risk factors:**

**Contact lens wear ( >80%)**

**All lenses soft, hard, gas-permeable, disposable, extended wear.**

**Homemade saline, jug of distilled water, or tap water as lens washing solutions**

**Exposure to contaminated water**

**Corneal trauma**

- **Inoculation occurs through corneal epithelial breaks. Early infection involves the epithelium only followed by spread to all layers of corneal as well as nerves.**
- **The trophozoite produces cytolytic enzymes that aid in tissue invasion, loss of keratocytes, and stromal necrosis**

# *Acanthamoeba* Keratitis

Mostly Unilateral, indolent,  
**ocular pain out of proportion to exam,**  
redness, decreased visual acuity,  
foreign body sensation, photophobia,  
and protracted progressive course  
no therapeutic response to topical  
antimicrobial agents.

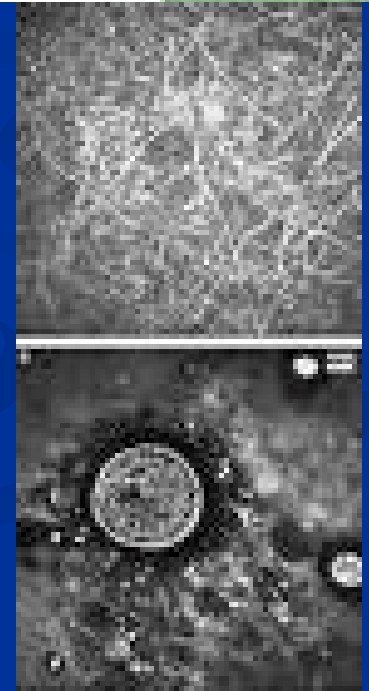
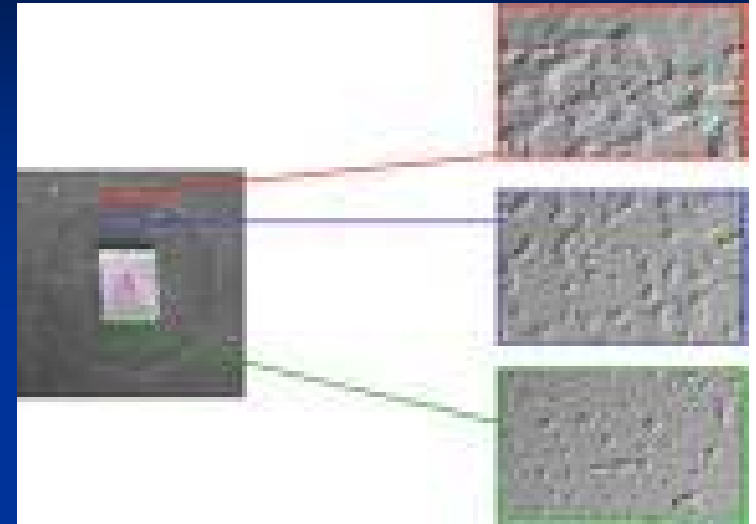


Many corneal manifestations may occur:

elevated epithelial lines that may form dendritic lesions,  
epithelial erosions, decreased corneal sensation, a  
gray-white ring infiltrate, nummular infiltrates, radial  
keratoneuritis, satellite lesions, disciform edema,  
thinning, and lack of neovascularization.

# *Acanthamoeba* Diagnosis

- Diagnostic modalities include:
- Ring infiltrate (6% early, 16% late finding)
- Culture (Neff's media)- non-nutrient agar with *E.coli* or *Enterobacter* (1-9, up 28 days)
- Giemsa Stain
- Corneal biopsy stained with Calcofluor White
- PCR
- In Vivo Confocal microscopy



# *Acanthamoeba* Keratitis

## Treatment

Early initiation of treatment is most effective and typically requires long-term therapy. Reported treatment modalities include:

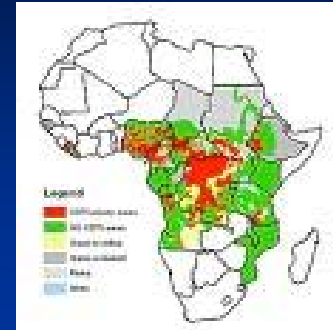
- Epithelial debridement AND three of the following
- PHMB, chlorhexidine diacetate AND
- Brolene (not available in US +/- OR
- Neosporin +/-OR
- imidazole derivatives (miconazole, clotrimazole, ketoconazole),
- Controversial: penetrating keratoplasty, steroids, and cryotherapy.

- As *Acanthamoeba* feeds upon bacteria, it accompanies bacterial ocular infections - Gram-negative bacteria, *L. pneumophila*, *Coxiella burnetii*, *P.aeruginosa*, *V. cholerae*, *H.pylori*, *Listeria monocytogenes* and *Mycobacterium avium*.



# Onchocerciasis (River Blindness)

- *Onchocerca volvulus*
- Black flies carry larvae -> bloodstream
- Mostly Africa; less Middle East & S. America
- 18 Million affected; 300,000 blind
- Progressive sclerosing keratitis, chorioretinitis, dermatitis, subcutaneous nodules
- Tx: IVERMECTIN -microfilaricidal -\$7/person.



## Intraocular infection

```
graph TD; A[Intraocular infection] --> B[Endophthalmitis]; A --> C[Uveitis];
```

### Endophthalmitis

Infection of the aqueous  
Bacteria or Fungi  
Not viruses or para

### Uveitis

Inflammation of Uvea  
Non-infectious (Autoi  
Infectious (50%)- A



# Endophthalmitis

## OPHTHALMIC AND ID EMERGENCY!

- Headache, eye pain, decreased  $V_A$
- Hyperemia, lid and corneal edema, anterior chamber and vitreous reaction, hypopyon (WBC in AC), vitreous opacification, absent red reflex.

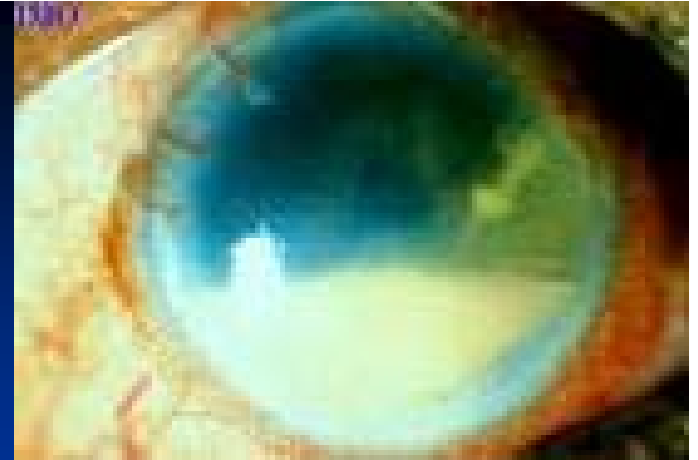
### Exogenous

Post-operative (acute, delayed)

Penetrating ocular trauma

### Endogenous (bacteremia)

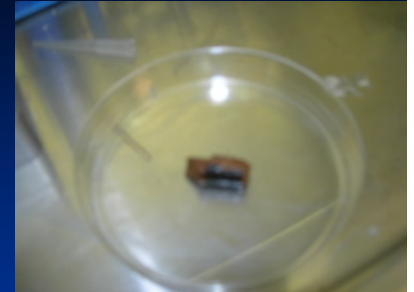
# Post-operative Endophthalmitis



- Post-cataract surgery:
  - most common, most dreaded
  - Incidence: 0.1% post-cataract surgery (unchanged)
  - Source: Lashes, lids, conjunctiva, lacrimal tissues
  - Coag-neg Staph (47%); *S. aureus*, streptococci (15%), rare GN, rare *P. acnes*.
- Chronic pseudophakic (intraocular lens)
  - Rare, indolent, months post-surgery.
  - 0.03 - 0.05% eye infection risk
  - coag-neg staphylococci, *S. aureus* (<4 days), *P. acnes*
- Bleb-related
  - Late onset - months to years post-surgery
  - Abrupt onset
  - *S. pneumoniae*, viridans streptococci (50%)



# Endophthalmitis



- Post-traumatic
  - *Bacillus* sp., *S. aureus*, streptococci and GNs; anaerobes
  - Organic contamination: Molds
  - Vancomycin for *Bacillus*; Clindamycin for anaerobes
- Endogenous bacterial endophthalmitis
  - **1/3 present to non-ophthalmologist**
  - Source: Endocarditis (40%), GI (30%), other (catheter-related, meningitis, UTI, organ abscess, cellulitis)
  - Streptococci (30%), *S.aureus* (25%), GNR (30%)
  - **Intravitreal** and Intravenous Antimicrobials
- Use of Steroids-controversial
  - Organism defined (Gram stain, culture); Control of infection; Decrease inflammation leading to destruction.
  - Intravitreal Dexamethasone (400 micrograms/0.1mL)

# Fungal

## Endophthalmitis



### ■ Yeast

- Most common in temperate climates
- Usually endogenous (9% Candidemia); cryptococcus
- Distinguish between chorioretinitis vs endophthalmitis
  - Chorioretinitis- clear vitreous; white lesions in retina
    - Systemic treatment only; untreated may -> endophthalmitis
  - Endophthalmitis
    - Cloudy vitreous+++; Fluff white balls in vitreous
    - Need vitrectomy and intra-vitreal amphotericin

### ■ Filamentous Fungal

- More common in tropical climates
- Usually exogenous; *Aspergillus* (50-90%)
  - Risks:
    - IVDU
    - Immunocompromised (Transplant)

# Endophthalmitis: Diagnosis

## Vitreous aspiration vs. Vitrectomy

If fulminant, toxin-mediated- (any strep, *S.aureus*, GNR), V<sub>A</sub> is only LP -> Vitrectomy

Vitreous aspirate: 27 gauge needle aspirate 0.2 mL (office, topical anesthesia)

Vitrectomy: 20 gauge vitrector debrides the vitreous, drains abscess (OR, local anesthesia)

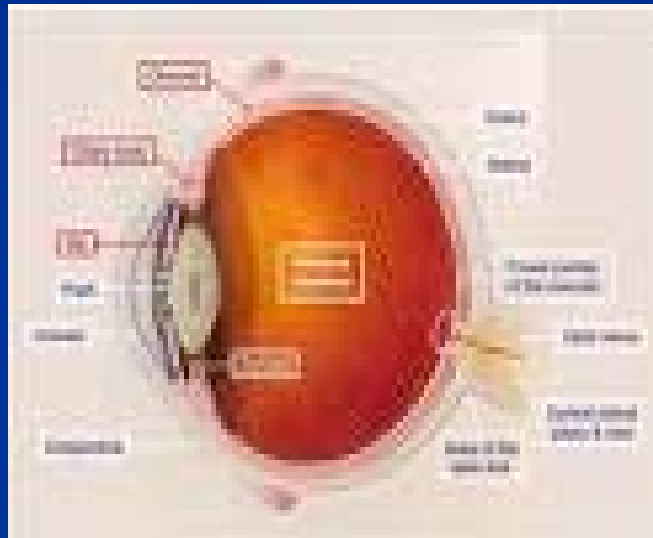
Stat Gram stain +/- Calcofluor white

Intravitreal injection of antibiotics immediately

Processing of specimen: Vitreous aspirate directly on plates; For vitreous washing, the use of a filter (0.45 micron membrane) recommended and then plated.

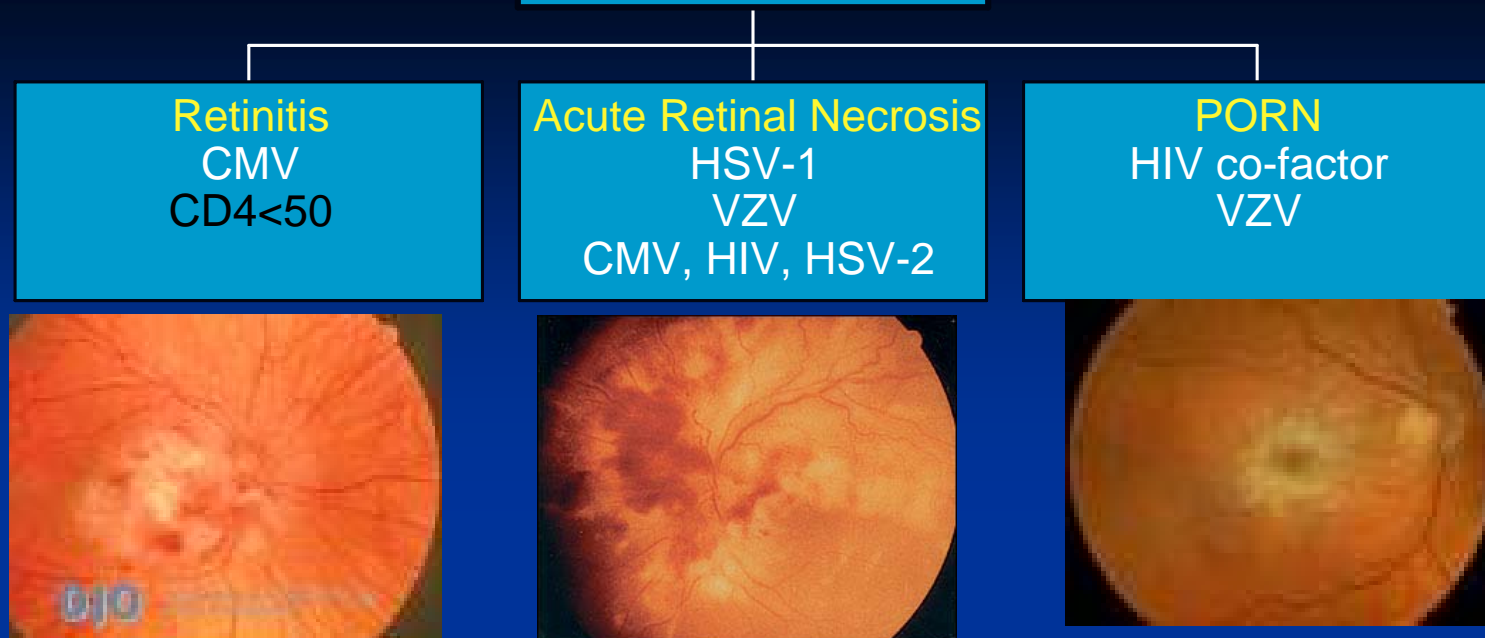
# Infectious Uveitis

- 2.3 million/US; prevalence 38/100,00
  - Third leading cause of blindness in US (10-15%)



- Uveitis: Inflammation or infection of the:
  - Iris (iritis)
  - Ciliary Body (cyclitis, iridicyclitis)
  - Choroid (choroiditis)
  - Retina (retinitis)

## Uveitis- Viral



### ■ Retinitis

- Hemorrhage and yellow-white irregular borders
- Usually no anterior chamber reaction; painless loss of vision
- Not in immunocompetent; 10-30% pre-HAART era; CMV

### ■ Acute Retinal Necrosis (ARN)

- Necrotizing retinitis and vasculitis with hemorrhages (cheese PIZZA)
- Immunocompetent (most HSV, some VZV, rare CMV)

### ■ Progressive Outer Retinal Necrosis (PORN)

- Fulminant posterior chorioretinitis in HIV (VZV)



# Uveitis - Viral: Diagnostics

- Serology (blood)
  - HSV-1, HSV-2, VZV, CMV, HIV antibody
  - HIV viral load (RNA)
  - CMV antigenemia Viral culture (Gold Standard) - Eye
  - Culture: HSV, VZV, and CMV shell vial
    - Best pre-treatment; detects Acyclovir-resistant HSV.
- Viral PCR (high sensitivity/specificity)  
Vitreous fluid (CSF equivalent tests)

Vitreous biopsy/ vitreous fluid best yield over the AC tap.

# **Uveitis - Viral:**

## **Treatment**

- Presumptive treatment with Acyclovir 10-12.5 mg/kg/ q 8 hours
- No response or progresses.
- ?Resistant HSV or CMV or not viral.
- Diagnostic tap for viral and other entities, and therapeutic instillation of Intravitreal Foscarnet  
Change to Ganciclovir 5 mg/kg IV q 12h OR  
Foscarnet 90 mg/kg q 12h x 14-21 days.
  - S.E. GCV: bone marrow toxicity (Use GM-CSF)
  - S.E. FOS: nephrotoxicity and hypercalcemia

# Viral Retinitis Therapy

- In HIV+, increase CD4 with HAART.
  - 33-62% who respond to HAART (>60 CD4 cells/ml) develop:
    - IMMUNE RECOVERY VITREITIS
      - $V_A$  decreases and floaters, with posterior segment inflammation -vitritis, papillitis, & macular changes; occurs approx 43 weeks after Rx (JID 179: 697, 1999; AIDS 14:1163, 2000; CID 36:1063, 2003).
      - Corticosteroids decrease inflammation rxn of the immune recovery without reactivation CMV retinitis (5th CRV, Abstr. 75)

# **Bacterial Uveitis:**

## **Endogenous Endophthalmitis**

- **Endogenous Endophthalmitis**
  - ACUTE onset of pain, sudden loss of vision.
  - Hypopyon, vitritis
  - May be bilateral
  - Common sites of infection: septicemia, infected IV line, endocarditis, kidney or liver abscess, and dental abscess
- **Culture suspected Sites; blood cultures x 3**
- **Anterior Chamber and vitreous cultures PRIOR to therapy; Gram Stain STAT and culture**
- **Therapeutic vitrectomy- send tissue for culture!**
- **SPEED is CRITICAL.**

# Uveitis - Bacterial Ocular Bartonellosi

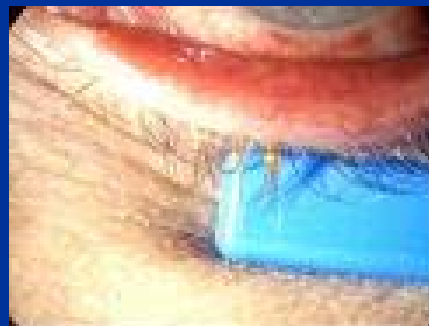


## Cat Scratch Disease/Ocular Bartonellosis

- Regional lymphadenopathy (22,000 cases/yr/US; 6.6/100,000); most children with young cat contacts
- 13% Eye: Parinaud's oculoglandular syndrome (granulomatous conjunctivitis with pre-auricular lymphadenopathy, neuroretinitis, focal chorioretinitis).
- Ocular Bartonellosis: Unilateral (majority) macular star (lipid exudates seen as subretinal fluid resolves) with optic disc swelling;
- enlarging blind spot
- *Bartonella hensalae* serology

Tx: most get better;

- one-month course



U of Iowa, 2004



## **Syphilitic Uveitis: Chorioretinitis**



- Usually Late (tertiary), so RPR may be low (TPPA always positive)
- May be secondary and may have fulminant course (HIV).
- 6 weeks to 6 months after primary disease
- Pain, redness, photophobia, blurring
- Anterior uveitis +/- iris nodules
- Focal or multifocal choroiditis +/- arteritis and periarteritis
- Late stage gliosis, atrophy, pigment proliferation
- Late stage chorioretinitis indicates neurosyphilis.

# Syphilitic Uveitis

## Treatment

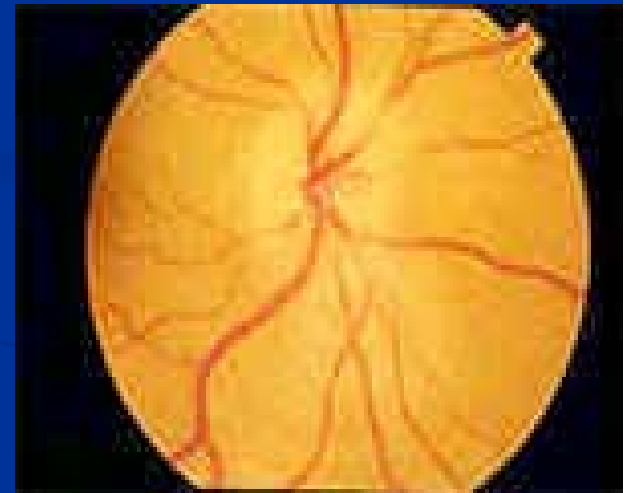
- Topical:
  - Corticosteroids for anterior segment inflammation
- Systemic:
  - Late (CNS/Ocular): Penicillin G 24 mU IV/day x 14 days.
  - If vision threatened, may need high-dose systemic steroids (Jarisch-Herxheimer reaction)
  - If Penicillin allergic
    - Desensitize to PCN
    - Ceftriaxone 2 gm IV/IM x 14 days (23 % relapse rate)

# Uveitis - Spirochetal: Lyme Disease

- *Borrelia burgdorferi*
- Erythema chronicum migrans
- Arthritis
- CNS
- Cardiovascular
- Vitritis and Optic Neuritis

Dx: Lyme PCR of vitreous fluid  
Serology

Tx: Ceftriaxone 2 gm IV x 3-4 weeks

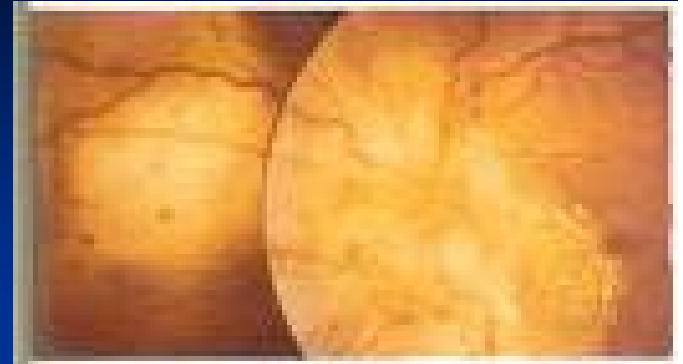




# Uveitis - Mycobacteria

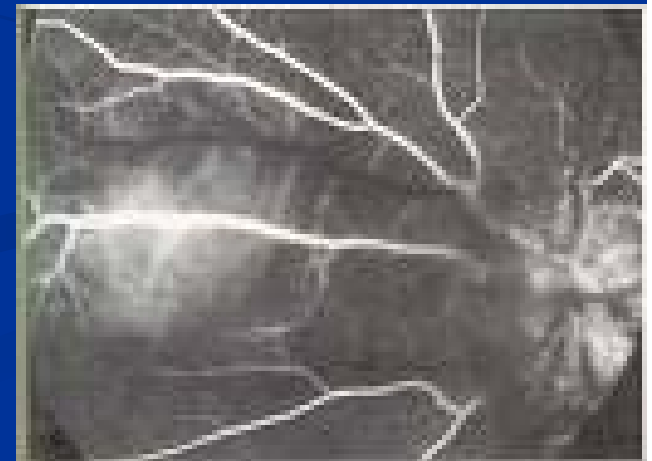
## ■ Ocular TB

- Rare in pre-antibiotic era; HIV
- CXR normal in 50% with ocular TB
- Vitreous culture/PCR neg
- Multifocal choroiditis -most common
- Chronic anterior granulomatous uveitis
- As TB meningitis- long course with steroids



## ■ Leprosy

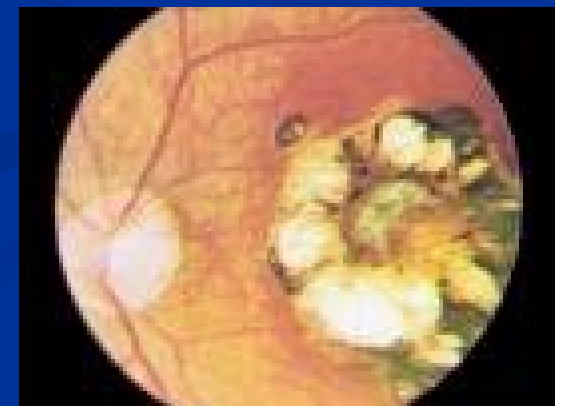
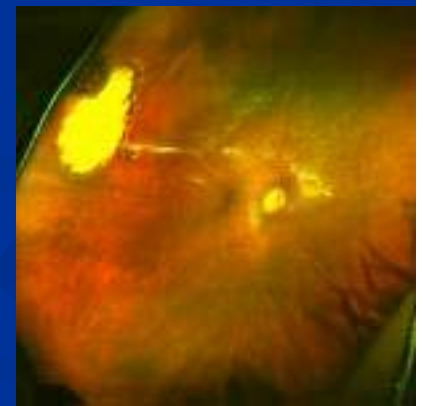
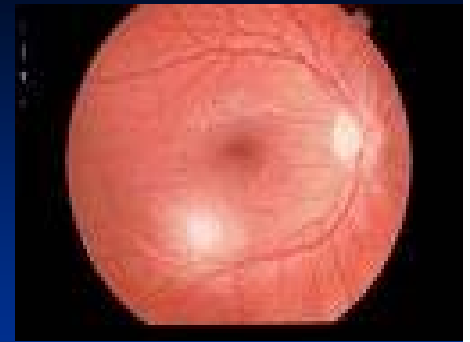
## ■ *Mycobacterium avium-intracellulare* choroiditis



# Uveitis - Protozoan Toxoplasmosis

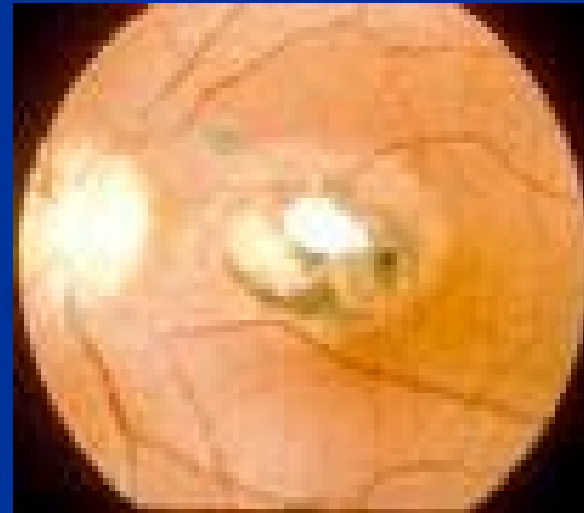
## ■ *Toxoplasma gondii*

- 30-40% of all posterior uveitis (highest -France, Brazil) Exudative focal retinitis, progresses to focal necrotizing chorioretinitis
- Unilateral Floaters and blurred vision
- Vitreous opacities usually present
- “Headlight in Fog” appearance
- Whitish-yellow, raised, fuzzy fundus lesion usually in posterior pole.
- Usually adjacent to chorioretinal scar



# Uveitis - Protozoan Toxoplasmosis

- *Toxoplasma gondii* serology and PCR
- Reported up to 30% of patients with chorioretinitis will have CNS lesions



# Sight-Threatening Eye Infections

- Virulence of Pathogen
- Host Risk factors (Contact Lens, Surgery, Trauma, Immunocompromised)
- Endophthalmitis and Uveitis -Emergencies
- Diagnostic testing: Culture of corneal tissue and vitreous best. Same PCR diagnostics as CSF.
- Put the drug where the infection is: Topical or Intravitreal.
- Antimicrobial penetration similar CSF; greater toxicities in the eye
- Prevention

# Ultraviolet Keratitis (Snow Blindness)



- Sunburn of the cornea and conjunctiva
- UV increases 4%/1000 ft
- Sunglasses with maximum UV absorption with side shields
- Lost Sunglass Emergency- dark fabric or tape folded on itself/Blacken skin underneath with charcoal
- Inuit Caribou Antler Goggles;
- Henry Larson (1929-1948)