



# Ocular manifestations of HIV infection



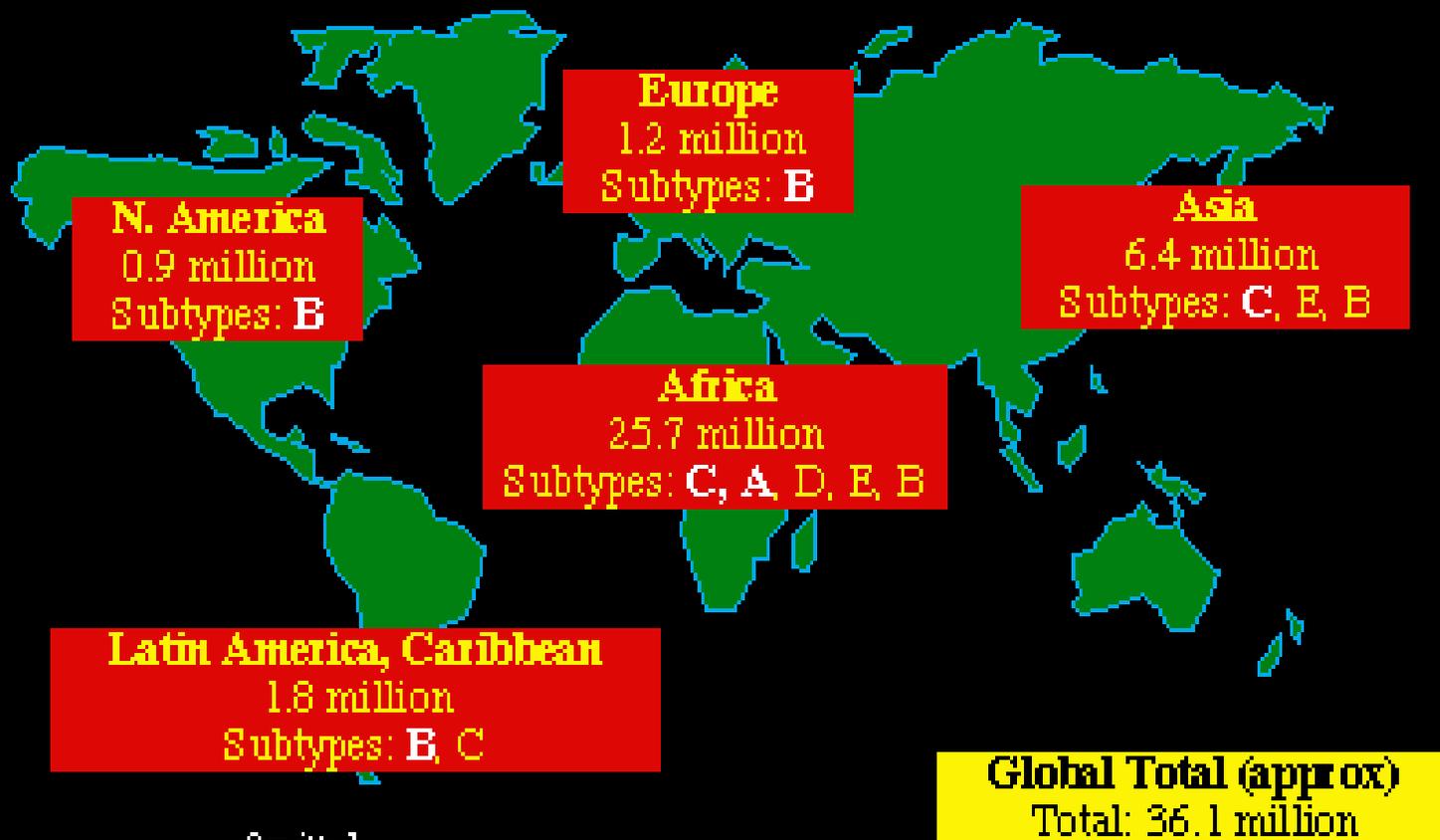
# Introduction

- AIDS is an infectious disease caused by the gradual decrease in CD4+ T lymphocytes causing subsequent opportunistic infections and neoplasia. It is a blood borne and sexually transmitted infection caused by the HIV (Human Immunodeficiency Virus)
- Approximately 36 million persons around the world are infected. Up to 70% of patients infected with HIV will develop some form of ocular involvement, ie: direct infection by HIV, opportunistic infections and neoplasia.
- HIV infection progresses through different phases

# Worldwide HIV-1 infections, Dec. 2000

Source: UNAIDS

[http://www.unaids.org/epidemic\\_update/report\\_dec00/index\\_dec.html](http://www.unaids.org/epidemic_update/report_dec00/index_dec.html)

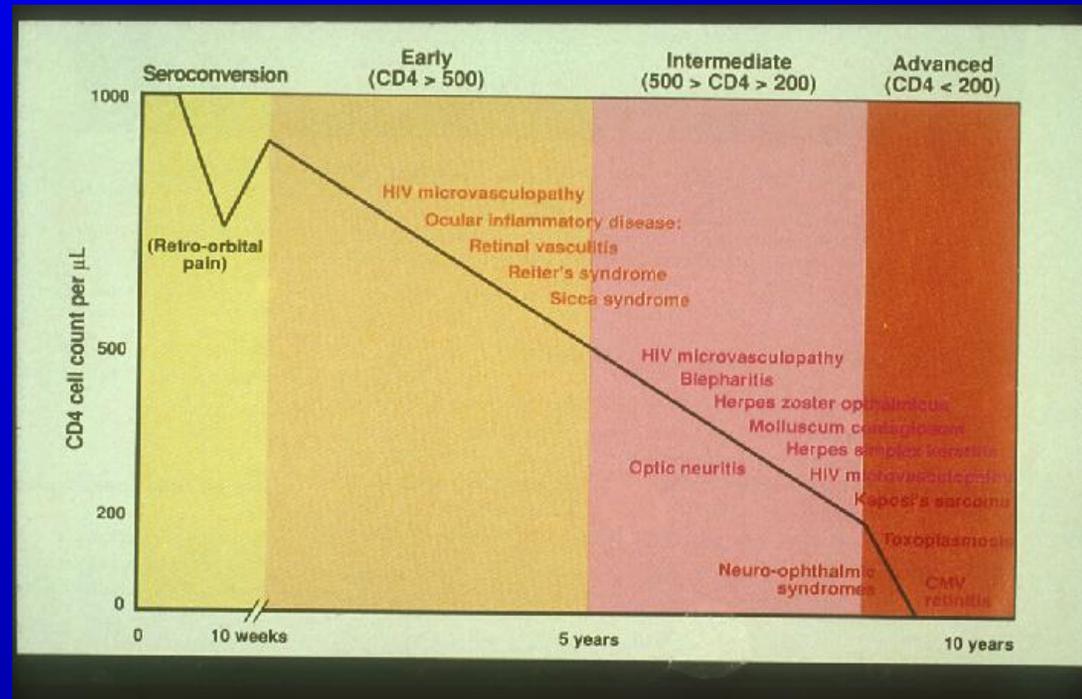


Omitted

subtypes F-J (rare); groups N, O

# Ocular manifestations correlating with immune status and stage of HIV infection

- When the CD4+ count deteriorates, the immune system fails and symptoms such as malaise, night sweats, fever and loss of weight develop as the infection progresses. Measuring the absolute CD4+ count is an essential part of the staging the disease.



Stage	CD4+	External eye	Anterior segment	Posterior segment	Neuro-ophthalmic
seroconversion	1000	Inflamed conjunctiva Dry eye			Headache Retro-orbital pain
Early HIV infection	500-1000	Allergic conjunctivitis	Reiter's syndrome Intermediate uveitis Retinal vasculitis	HIV retinopathy	Optic neuropathy
Intermediate infection	200-500	Dry eye Blepharitis Bacterial and follicular conjunctivitis Kaposi's sarcoma Molluscum contagiosum	Herpes zoster Herpes simplex	HIV retinopathy Tuberculous uveitis	Aspergillosis
Late	0-200	Opportunistic infections and tumours affecting all ocular structures			

Adapted from and with courtesy of PJ McCluskey: Overview of HIV infection and pre-AIDS ocular manifestations, HIV and the eye, S Lightman ED, Imperial College Press London, 2000

# Ophthalmic Manifestations of HIV Infection

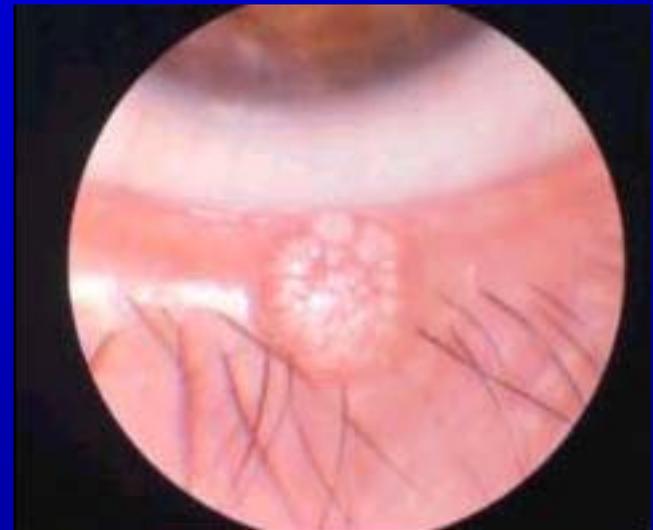
- AROUND THE EYE
  - Molluscum Contagiosum
  - Herpes Zoster Ophthalmicus
  - Kaposi's Sarcoma
  - Conjunctival Squamous Cell Carcinoma
  - Trichomegaly
- FRONT OF THE EYE
  - Dry Eye
  - Anterior Uveitis
- BACK OF THE EYE
  - Retinal Microvasculopathy
  - CMV Retinitis
  - Acute Retinal Necrosis
  - Progressive Outer Retinal Necrosis
  - Toxoplasmosis Retinochoroiditis
  - Syphilis Retinitis
  - Candida albicans endophthalmitis
- NEURO-OPHTHALMIC





# Molluscum Contagiosum

- Molluscum contagiosum is a viral infection of the skin.
- Affects up to 20% of symptomatic HIV infected patients.
- Clinically appears like painless, small, umbilicated nodules, which produce a waxy discharge when pressured.
- Treatment consists on excision of the lesion, curettage or cryotherapy





# Herpes Zoster Ophthalmicus

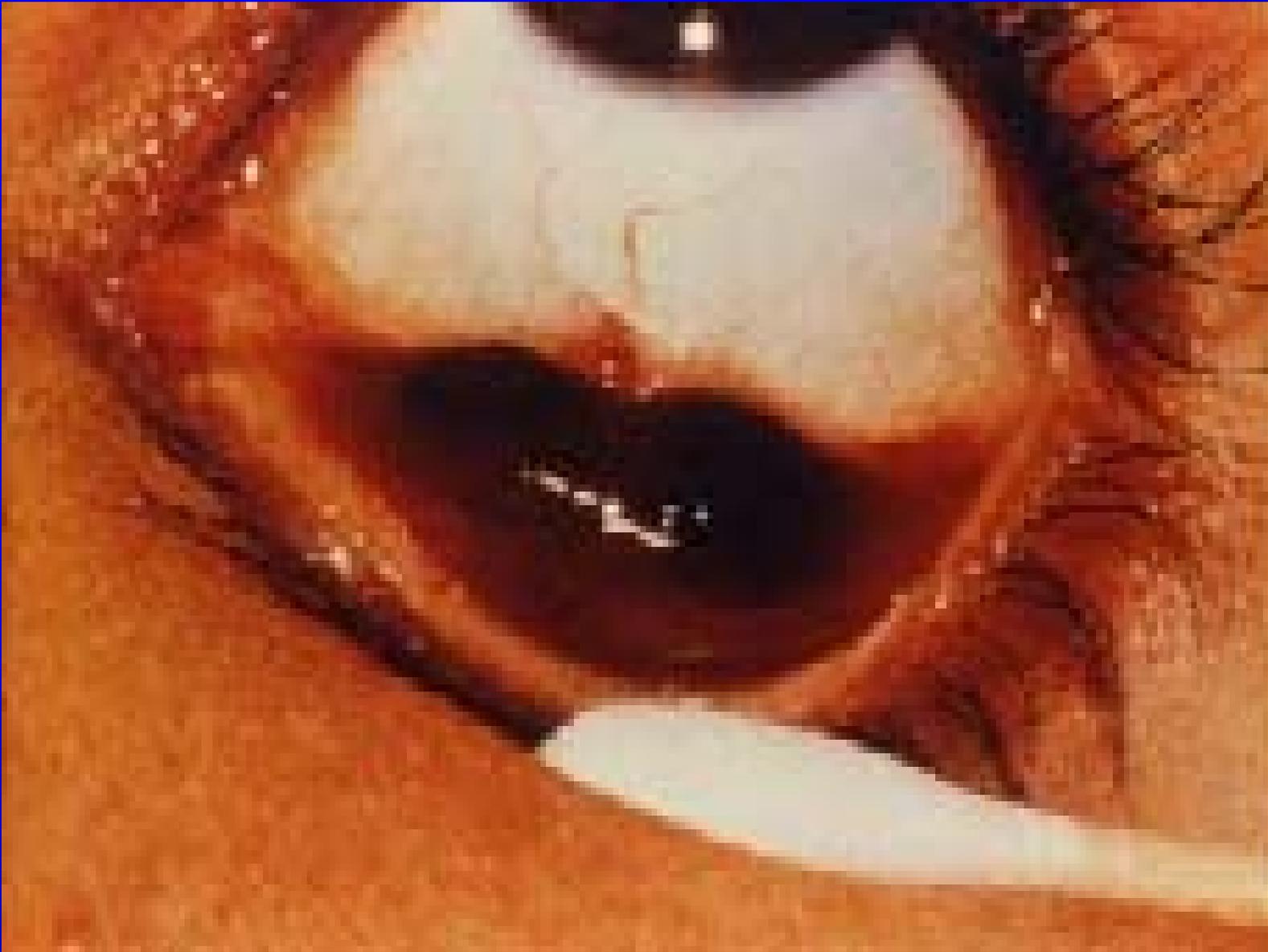
- Due to the reactivation of a latent infection by Varicella Zoster Virus in the dorsal root of trigeminal nerve ganglion.
- It manifests with a maculo-papulo-vesicular rash which often is preceded by pain. Usually involves the upper lid and does not cross the midline
- Treatment consists on oral Aciclovir 800mg 5 times /day. In immunocompromised patients Aciclovir is given intravenously for two weeks. Ocular manifestations such as anterior uveitis, are treated with topical steroids and mydriatics.





# Kaposi's Sarcoma

- Kaposi's sarcoma is a vascular neoplasm which is almost exclusively seen in patients with AIDS.
- KS is the commonest anterior segment lesion seen in AIDS; appears as a violaceous non-tender nodule on the eyelid or conjunctiva.
- Typically KS involves only the skin but when there is a reduced CD4 count it can progress rapidly to other sites such as the gastrointestinal tract and CNS
- Treatment of ocular adnexal KS may be necessary for cosmesis and to relieve functional difficulties. The mainstay of treatment is radiotherapy. Other options include cryotherapy or chemotherapy.





# Conjunctival Squamous Cell Carcinoma

- Squamous cell carcinoma (SCC) is the third most common neoplasm associated to HIV infection. This may be due to an interaction between HIV, sunlight and Human Papilloma Virus infection.
- SCC appears as a pink, gelatinous growth, usually in the interpalpebral area. Often an engorged blood vessel feeding the tumour is seen. It may extend onto the cornea, but deep invasion and metastasis are rare.
- The treatment of choice is local excision and cryotherapy but the presence of orbital invasion is an indication of exenteration





# Trichomegaly

- Trichomegaly or hypertrichosis is an exaggerated growth of the eye lashes found in the later stages of the disease
- The cause is not known
- When symptomatic or for cosmetic reasons the eyelashes can be trimmed or plucked





## Dry Eye

- Sicca syndrome is frequent among patients with HIV infection
- Patients complain of burning uncomfortable red eyes.
- There are several causes of dry eye in HIV infection from blepharitis to destruction of the lacrimal glands.
- Treatment is with tear supplements





- HIV related anterior uveitis can be:
  - Direct manifestation of the human immunodeficiency virus infection
  - autoimmune in origin
  - drug induced ie: rifabutin, secondary to direct toxic effect upon the non-pigmented epithelium of the ciliary body
  - Any of the different infections associated with AIDS, ie: Herpes Zoster Virus, Herpes Simplex Virus, Cytomegalovirus, Toxoplasma gondii, Syphilis

## Anterior Uveitis



# Rifabutin induced anterior uveitis





## Retinal microvasculitis

- Retinal microvasculopathy occurs in more than half of the patients with HIV
- It is seen as transient cotton wool spots (CWS), intra-retinal haemorrhages and microaneurysm, which occurs in 50-70% of patients. It is usually asymptomatic.
- It has an unclear pathogenesis, but it is thought to be HIV infection of retinal vascular cells.
- In an otherwise healthy individual the presence of CWS, should be differentiated from other forms of retinopathy, such as diabetic or hypertensive retinopathy. Serological test for HIV will confirm the diagnosis
- Treatment is based in delaying the progression of the disease associated with HIV

# Cotton Wool Spots





# CMV Retinitis

- **Introduction**

- CMV Retinitis is the commonest intraocular ocular opportunistic infection seen in patients with AIDS
- Antibodies are found in almost 95% of adults, causing a trivial illness in immunocompetent adults, however severe immunosuppression causes viral reactivation and tissue invasive disease

- **Pathogenesis**

- Reactivation from extraocular sites leads to seeding in other sites such as the retina

- **Epidemiology**

- The number of newly diagnosed cases of CMVR has decreased since the introduction of the HAART



# CMV Retinitis

- **Clinical manifestations**

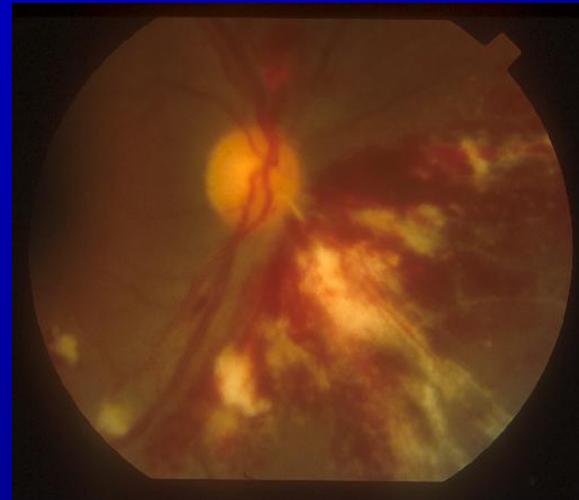
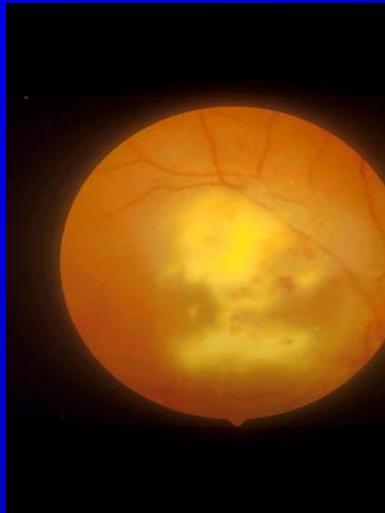
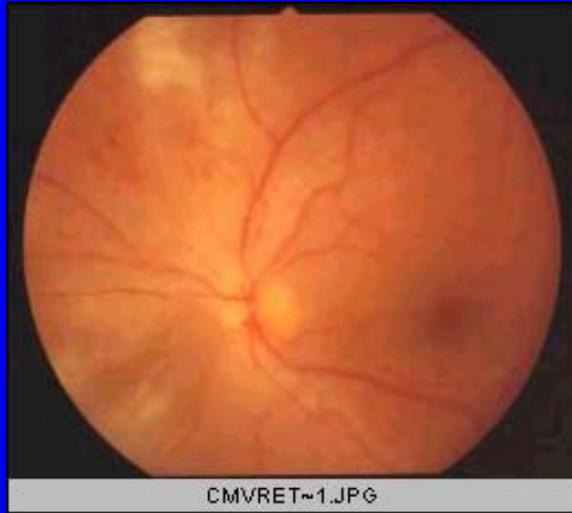
- Patients may complain of minor visual symptoms such as floaters, flashing lights or mild blurred vision, or be totally asymptomatic.
- It presents with a wide range of clinical appearances. From cotton wool spots which may look like HIV Retinopathy to confluent areas of full thickness retinal necrosis and vasculitis. CMVR can progress in a “brushfire” pattern from the active edge of an active lesion. The retinal vessels in an affected area show attenuation, becoming ghost vessels eventually.

- **Treatment**

- The treatment of CMVR in patients with AIDS requires the use of specific antiviral agents, ganciclovir, foscarnet or cidofovir in conjunction with HAART.
- These treatments can be administered orally, intravenously or intravitreally. Systemic treatment has the advantage of treating infection elsewhere in the body as well as the other eye but has the disadvantages of systemic side effects.
- Intravitreal implants release the drug over a six-month period, achieving prolonged high intravitreal levels of drug.



# CMV Retinitis

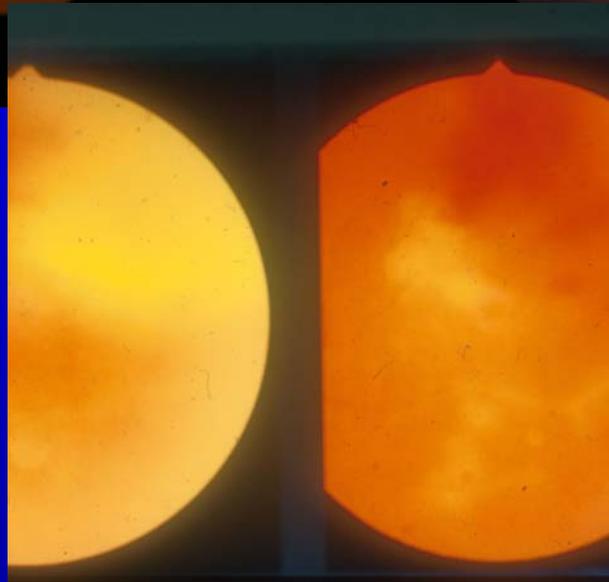
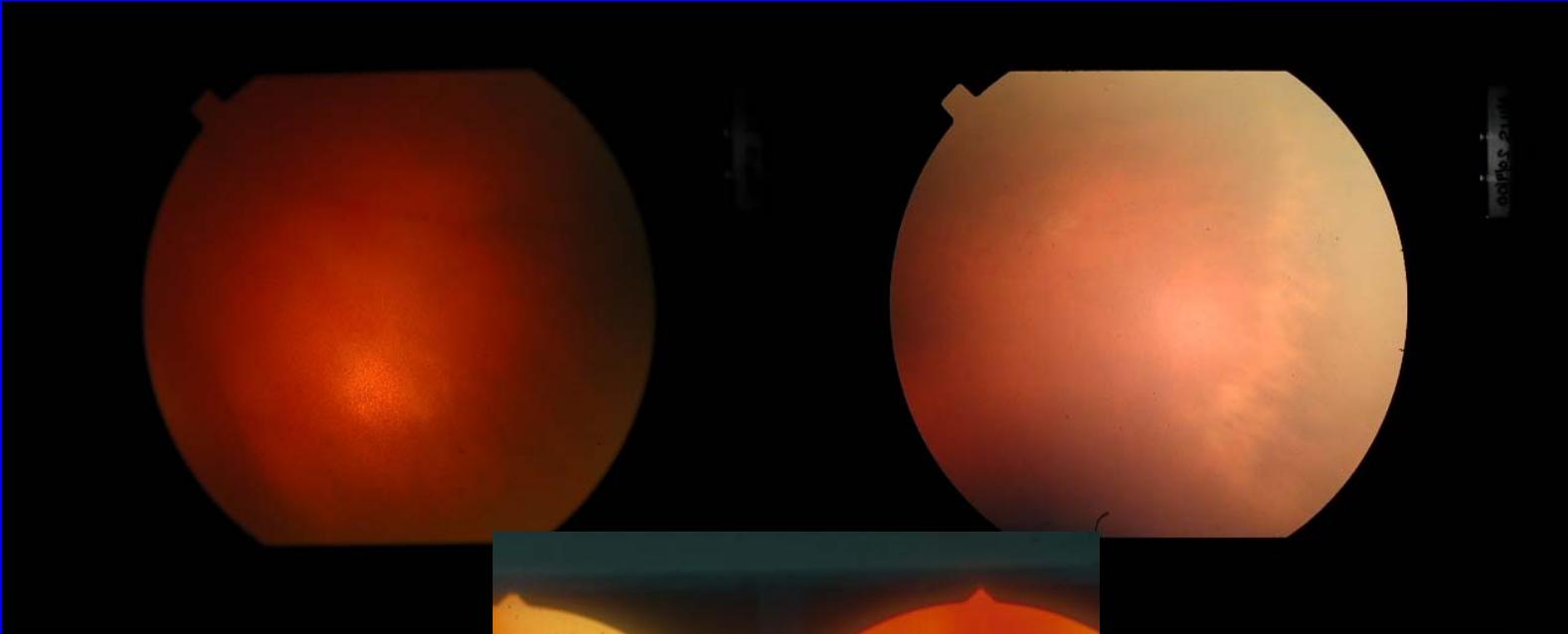




# Acute Retinal Necrosis

- ARN is a confluent peripheral whitening of the retina with marked vitritis and blood vessel closure. Optic neuritis and retinal detachment are frequent complications.
- ARN is usually due to Varicella-Zoster infection, but it can also be caused by Herpes Simplex virus or Cytomegalovirus.
- Initially described in the immunocompetent, it has also been described in the immunosuppressed.
- The diagnosis is mainly clinical and is confirmed by PCR assays on vitreous samples.
- Patients are treated with high doses of intravenous aciclovir or famciclovir, combined with laser treatment to prevent retinal detachment.

# Acute Retinal Necrosis





# Progressive Outer Retinal Necrosis (Varicella-Zoster Retinitis)

- PORN is a devastating viral retinitis caused by Varicella-Zoster virus, without vitritis or retinal vasculitis.
- The retinitis can be located anywhere but it is common for the lesions to coalesce and spread posteriorly in a rapid fashion.
- The main symptom is rapid loss of vision. The retina shows typically a white lesion with no haemorrhages or exudates.
- Treatment is often unsatisfactory and usually requires combination of Ganciclovir and Aciclovir. The prognosis is very poor and retinal detachment is common. Resolution may leave a white plaque with the appearance of “cracked mud”.





# Toxoplasma Retinochoroiditis

- Toxoplasmosis retinochoroiditis is an uncommon infection of the eye in AIDS. Ocular toxoplasmosis in HIV positive patients is different in appearance from immunocompetent patients. Unlike in immunocompetent patients, HIV infected patients often have bilateral and multifocal disease associated with anterior uveitis and vitritis but unlike immunocompetent patients, in HIV infected patients often have with no pigmented scars adjacent to the areas of retinal necrosis. Toxoplasmosis in immunocompromised patients is not self-limiting as it is in immunocompetent patients.



# Toxoplasma Retinochoroiditis

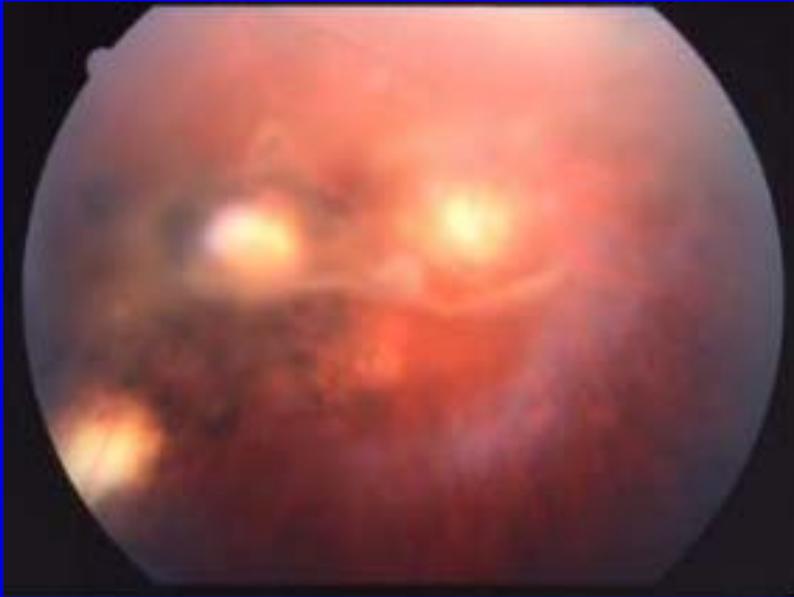
- When testing patients for antibodies to toxoplasmosis both IgG and IgM levels may be raised, but in immunocompromised patients these tests may be negative.
- Treatment in immunocompromised patients consists in the association of sulphadiazine or clindamycin, pyrimethamine and folinic acid (triple therapy).
- Long term maintenance treatment may be needed in order to prevent relapses.
- Often associated with toxoplasma lesions in the Central Nervous System.



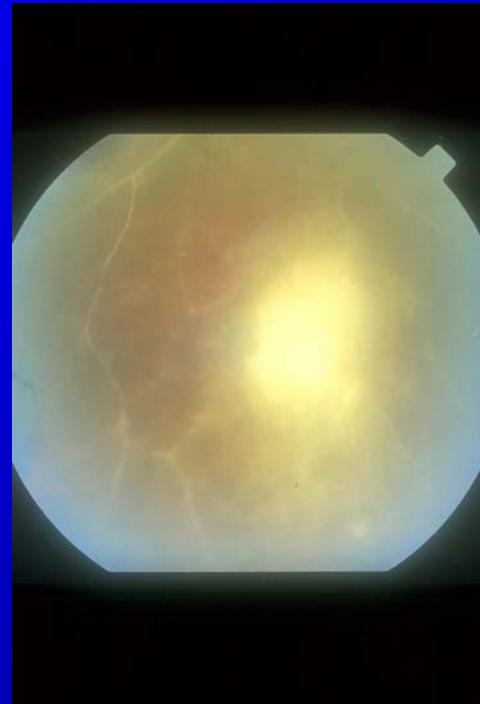
MRI T1 showing an uniformly enhancing lesion in the midbrain



One week later, the lesion showing ring enhancement



Immunocompetent

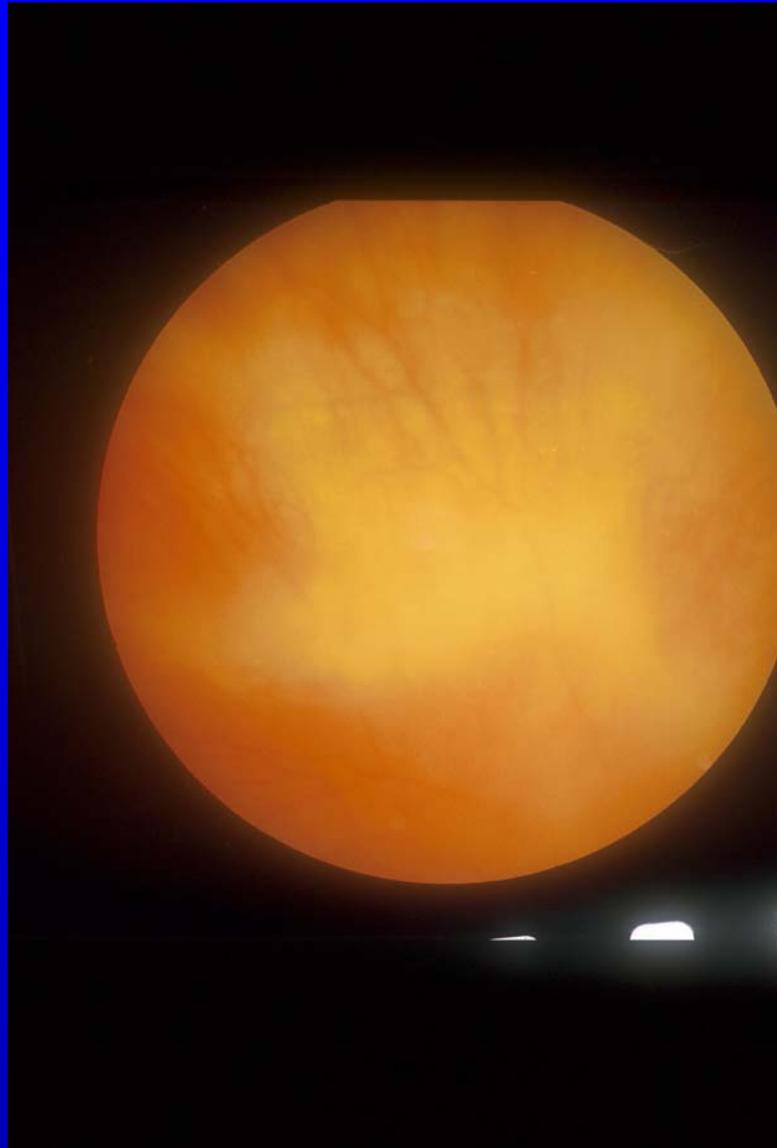


Immunocompromised



# Syphilis Retinitis

- There is a strong association between syphilis and HIV infection.
- It can manifest as a retinitis with dense vitritis, retinal vasculitis, serous retinal detachment or neuroretinitis, as well as other types of ocular involvement such as, conjunctivitis, anterior uveitis, cranial nerve palsies and optic neuritis.
- Treatment consists in high dose of intravenous Penicillin for 2 weeks.





# Candida albicans endophthalmitis

- Infection with candida albicans is rare. Candida albicans is the commonest cause of fungal endophthalmitis
- Affected patients usually have a history of drug abuse or indwelling central lines
- In the initial stages, floaters are the main symptom. As the condition progresses, whitish “puff-balls” and vitreous strands develop. Later, similar infiltrates appear in the choroid and retina
- The treatment depends on the severity of the ocular involvement and systemic disease. The original foci should be removed. The drugs of choice are Amphotericine B and Fluconazol

# Candida albicans endophthalmitis





## Glossary

- **CD4:** Director of the immune response. When activated it releases cytokines which in turn will activate the immune system
- **Cotton Wool Spots:** Light-coloured deposits in the retina secondary to infarcts of the nerve fibre layer
- **HAART:** Highly Active Antiretroviral Therapy
- **Immunoglobulin:** Protein in charge of fighting foreign substances in our body. **IgG** is the commonest type of immunoglobulin and **IgM** is the earliest class of immunoglobulin.
- **PCR:** Polymerase Chain Reaction is a technique used to make numerous copies of a specific portion of DNA
- **VDRL:** Venereal Disease Research Laboratory. The test becomes negative after successful treatment of the disease.