

HIV / AIDS

OCULAR COMPLICATIONS

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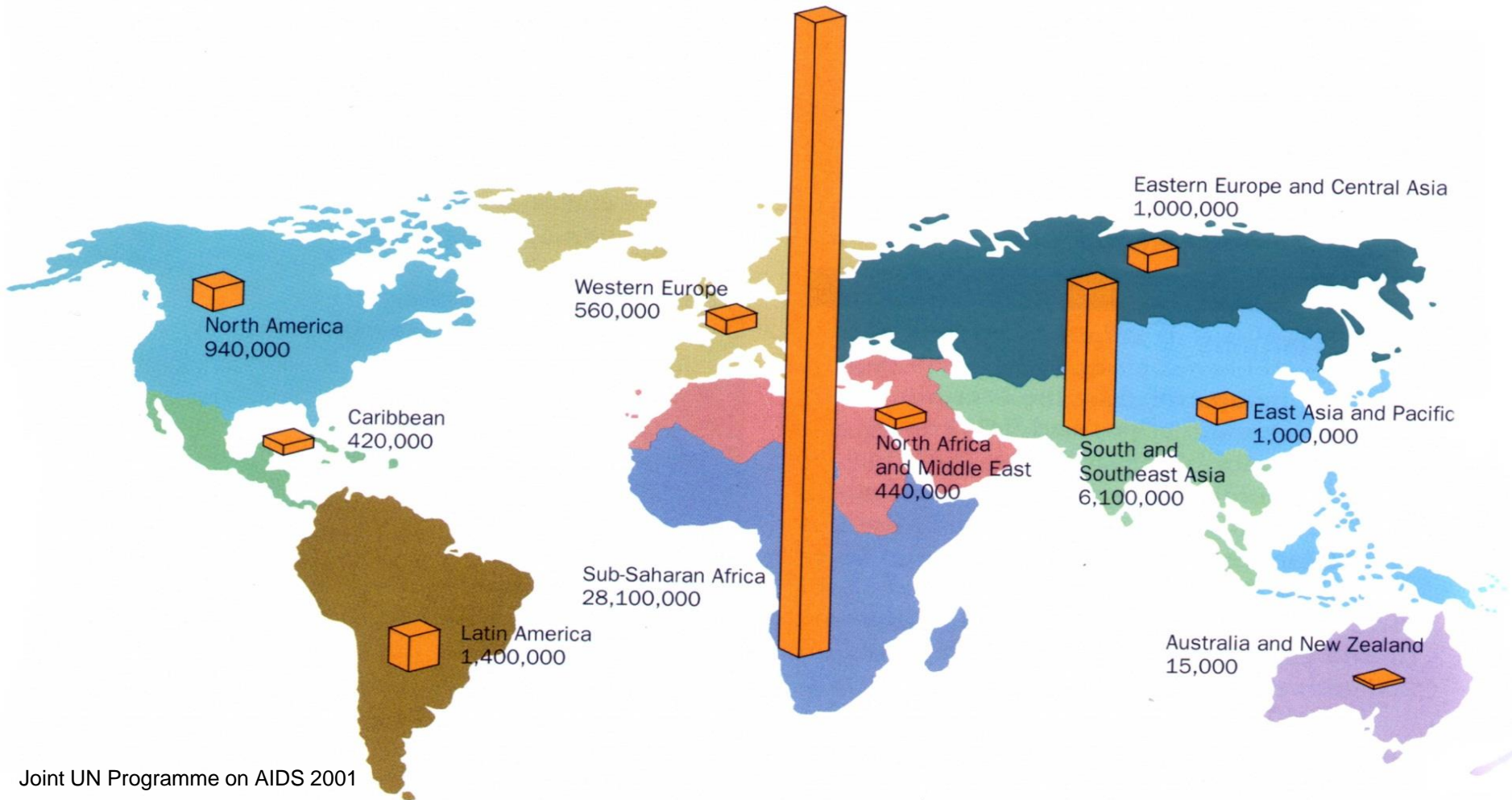
MB Ch B IV Lecture- 22nd February, 2016, University of Nairobi, LT III

Outline: HIV eye complications

- Epidemiology
- Ocular complications
 - Unusual Ocular-Adnexal tumours
 - Neuro-ophthalmic
 - Opportunistic Infection
- Summary

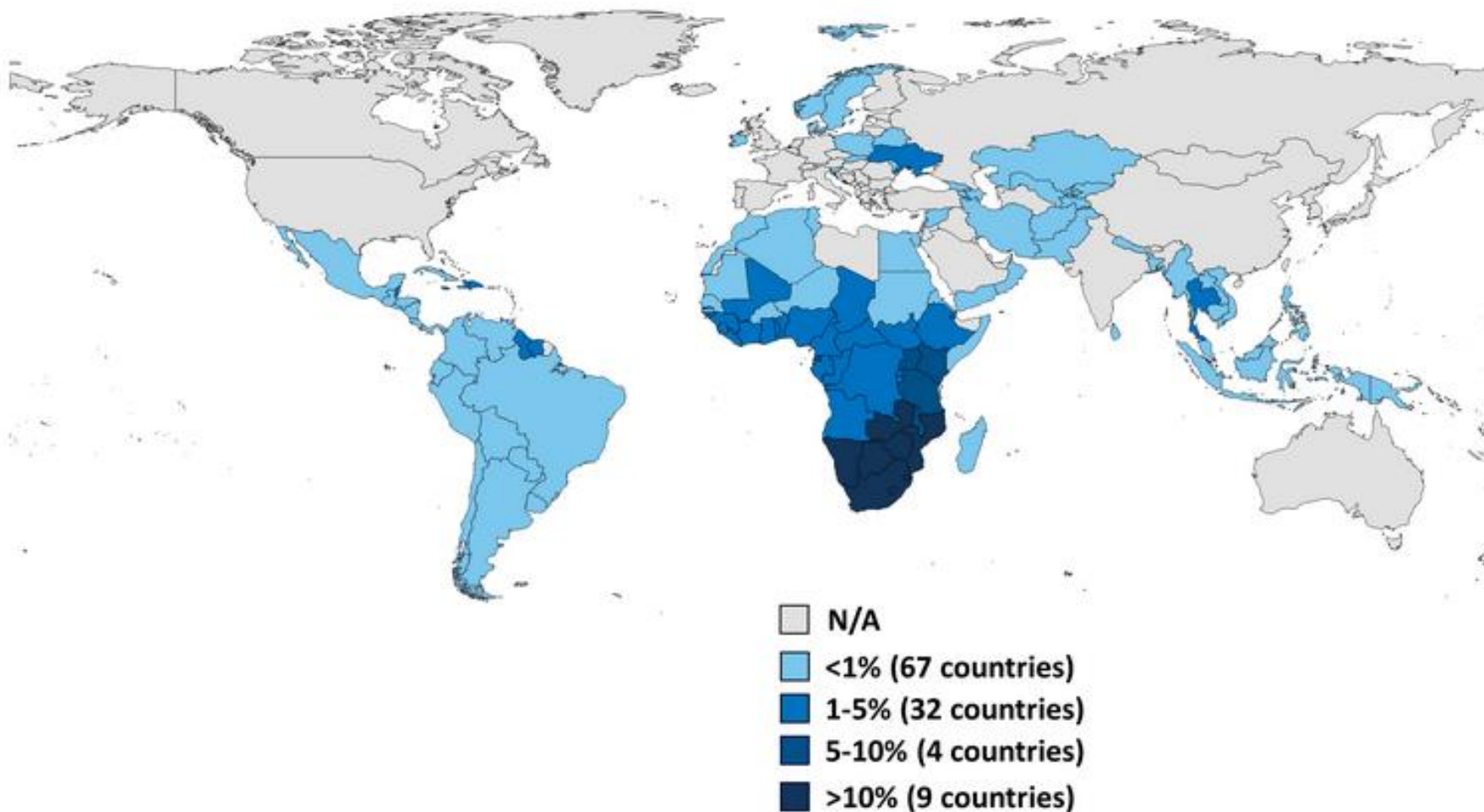
AIDS

(GLOBAL DISTRIBUTION - 2001)



Adult HIV Prevalence Rate, 2014

Global HIV/AIDS Prevalence Rate = 0.8%

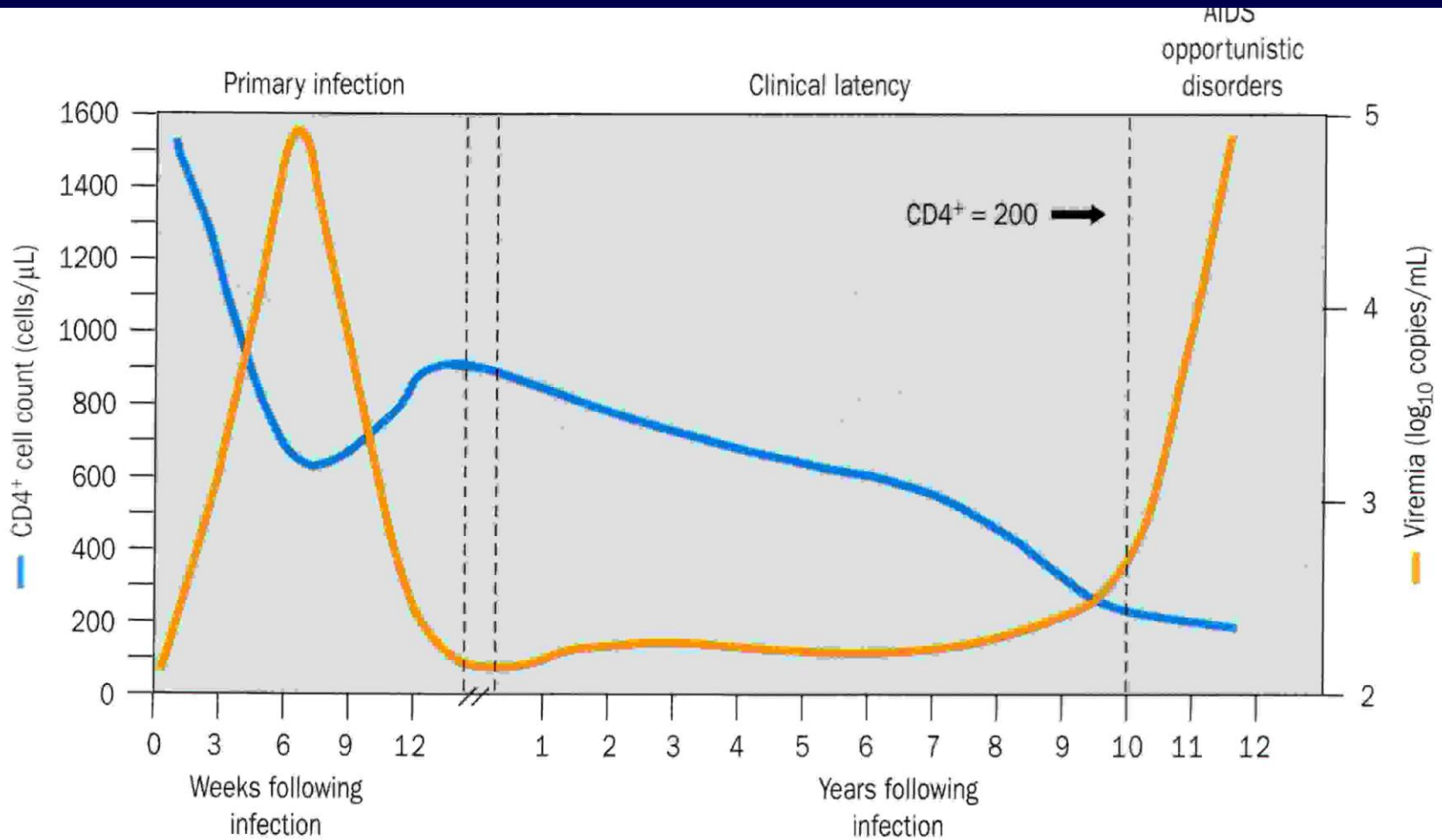


NOTES: Data are estimates. Prevalence rates include adults ages 15-49.

SOURCE: Kaiser Family Foundation, based on UNAIDS, How AIDS Changed Everything; 2015.

HIV

(NATURAL HISTORY)



OCULAR COMPLICATIONS

4 Types:

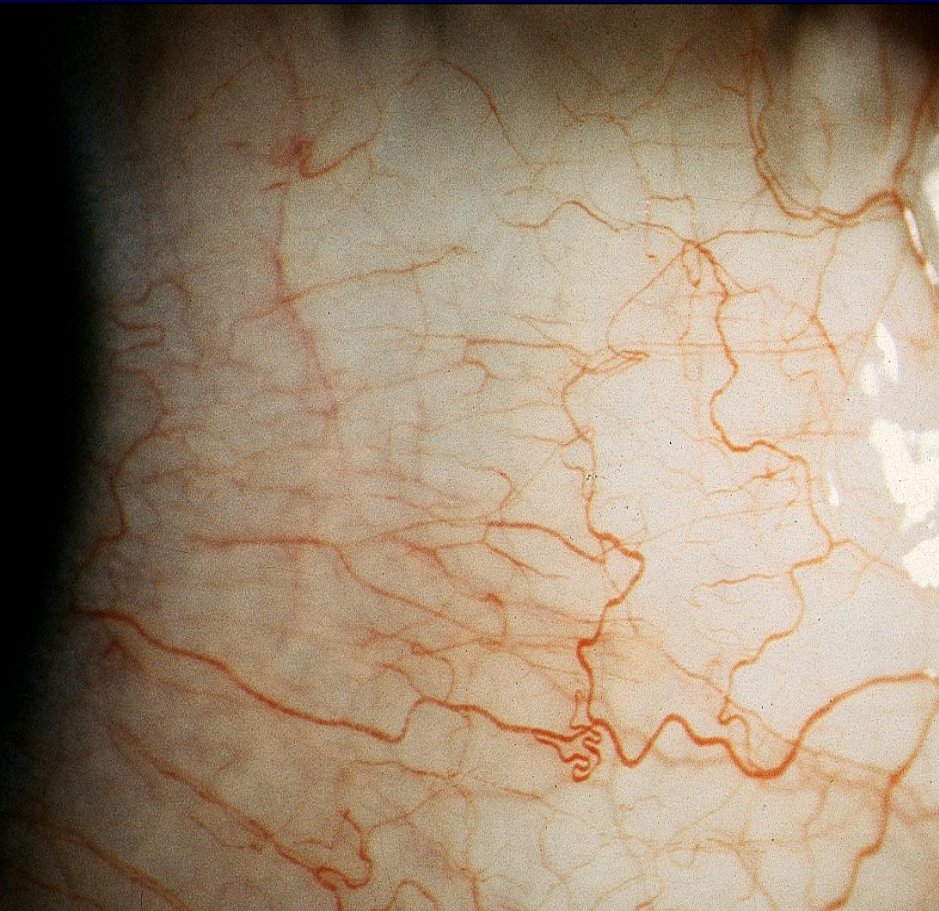
- VASCULAR diseases
- TUMOURS Ocular and adnexal
- NEURO-ophthalmological lesions
- INFECTIONS Opportunistic

OCULAR COMPLICATIONS

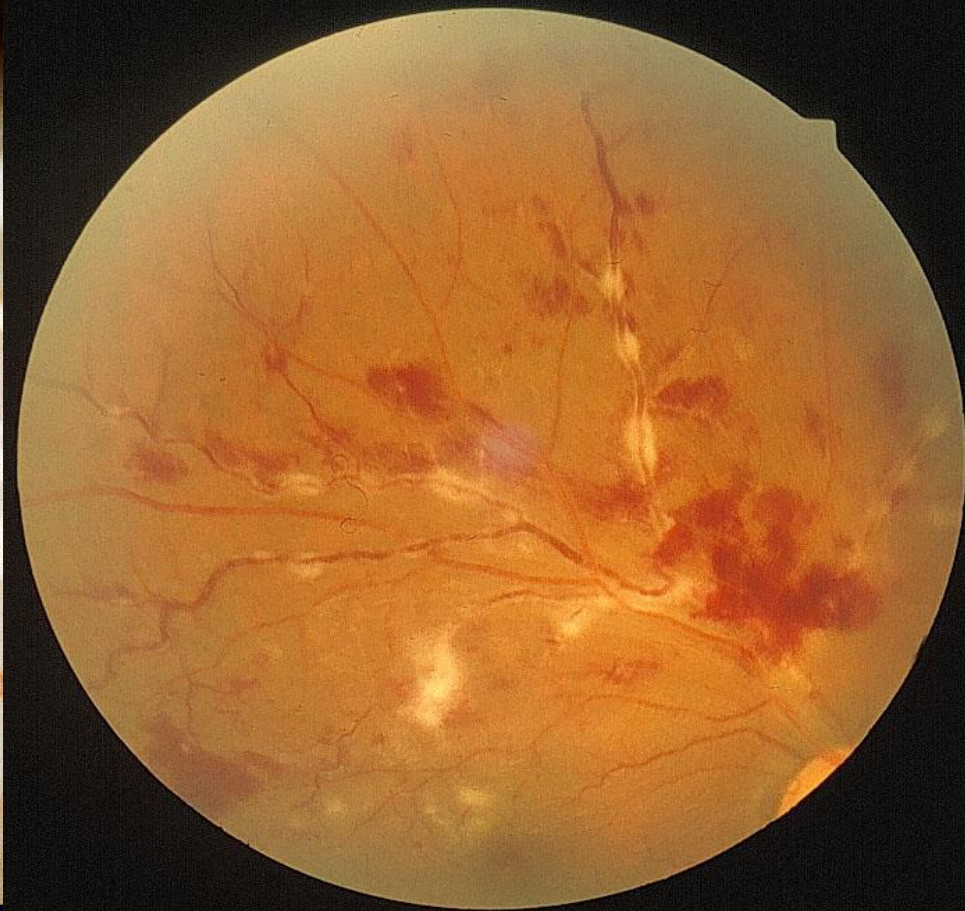
(IMMUNODEFICIENCY)

CD4+(c/ μ l)	VASCULAR	INFECTION	TUMOUR	NEURO
Any or uncertain	Vaso-occlusion (large vessels)	<ul style="list-style-type: none"> • Acute Retinal Necrosis • Molluscum contagiosum (disseminated) 	Squamous Cell Carcinoma (conjunctiva)	Direct (HIV)
≤ 500		<ul style="list-style-type: none"> • Herpes Zoster Ophthalmicus 	<ul style="list-style-type: none"> • Kaposi's sarcoma • Lymphoma 	
≤ 200		<ul style="list-style-type: none"> • Pneumocystis (choroid) • ocular TB • Mycosporidia (cornea / conjunctiva) 		Progressive Multifocal Leukoencephalo pathy (PML) – related
≤ 100	HIV – vasculopathy: <ul style="list-style-type: none"> • retina • conjunctiva 	<ul style="list-style-type: none"> • CMV retinitis • Toxoplasma chorio-retinitis • Progressive Outer Retinal Necrosis (PORN) • Mycobact Avium Complex (choroid) • Cryptococcus (choroid) 		Cryptococcal meningitis (e.g. optic neuropathy)

I. VASCULAR DISEASES



a) Micro-vasculopathy



b) Large Vessel Disease

LARGE VESSEL DISEASE (RETINA)

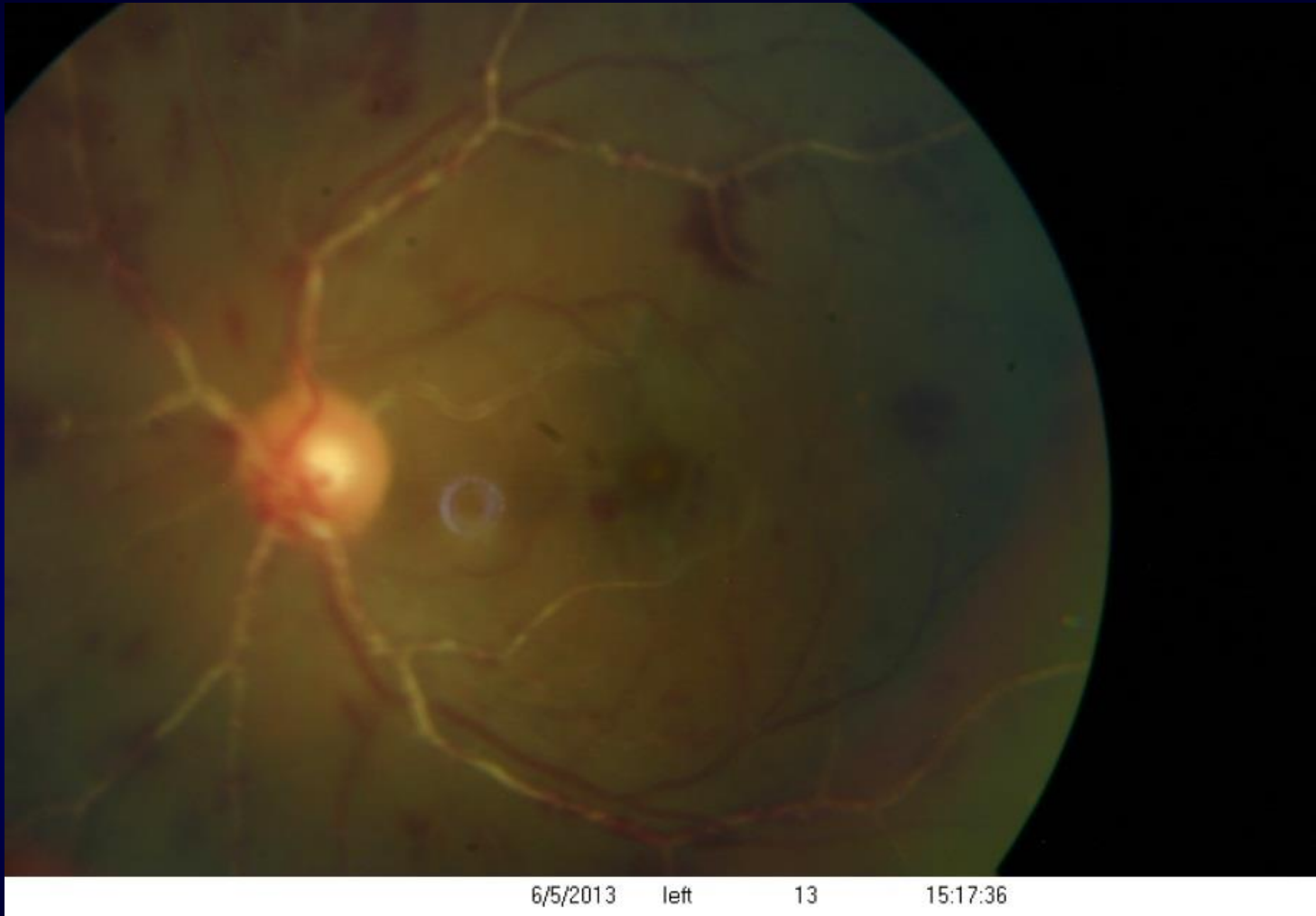


Unusual

Any stage (AIDS)?

- retinitis ...
- hyperviscosity ...
- Branch Retinal Artery occlusion
- Central & Branch Retinal Vein Occlusion
- Frosted Branch Vasculitis (CMV)

Frosted branch Angiitis- 2013



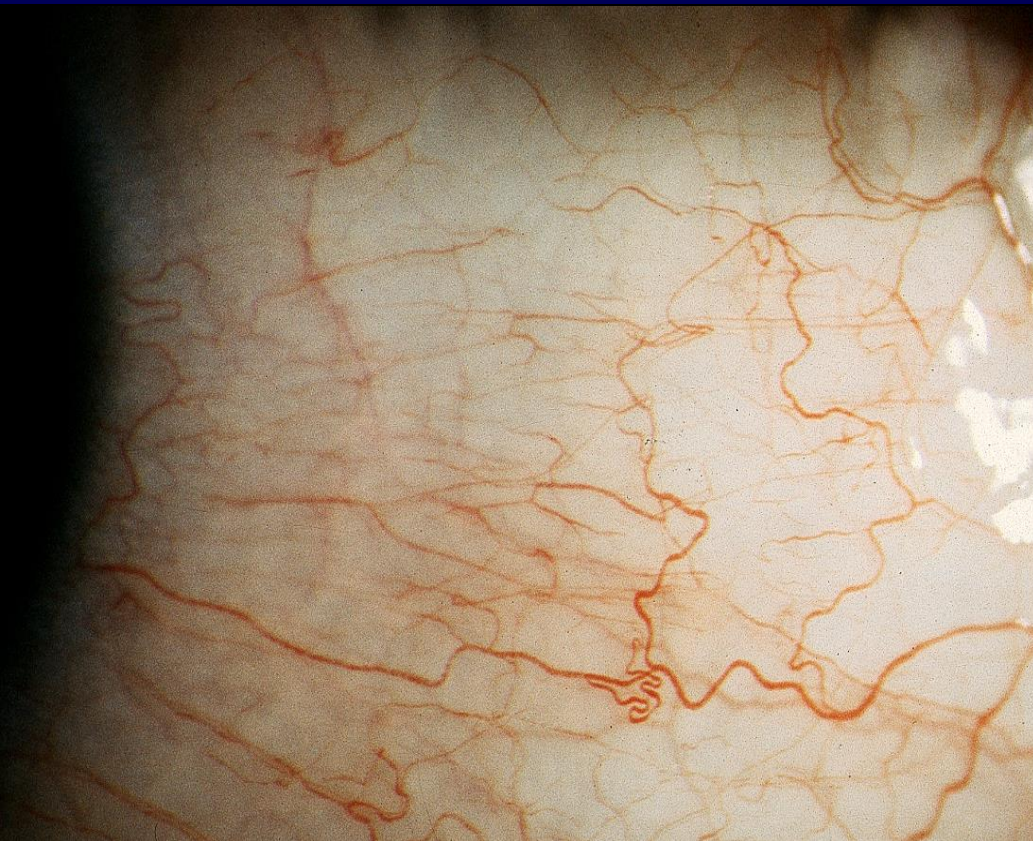
- Investigations: CD4, Cytomegalovirus(CMV)

MICRO-VASCULOPATHY

(CONJUNCTIVA - RETINA - OPTIC DISC)

- **Most common ocular manifestation (AIDS)**
- **Patho-mechanism:**
 - **deposition (HIV-related immune complexes)**
 - **direct infection (vascular endothelium)**
 - **increased plasma viscosity**
 - **combination?**
- **Marker for severely compromised immune status:**
 - **inversely related to CD4+ cell count**
($\approx 50\%$ of patients with **CD4+ ≤ 50 cells/ μ l**)
 - **risk of opportunistic infections, 3/12 follow up!**
- **HAART (chronic disease) » clinically relevant complications (like in DR)?**

MICRO-VASCULOPATHY **(CONJUNCTIVA)**



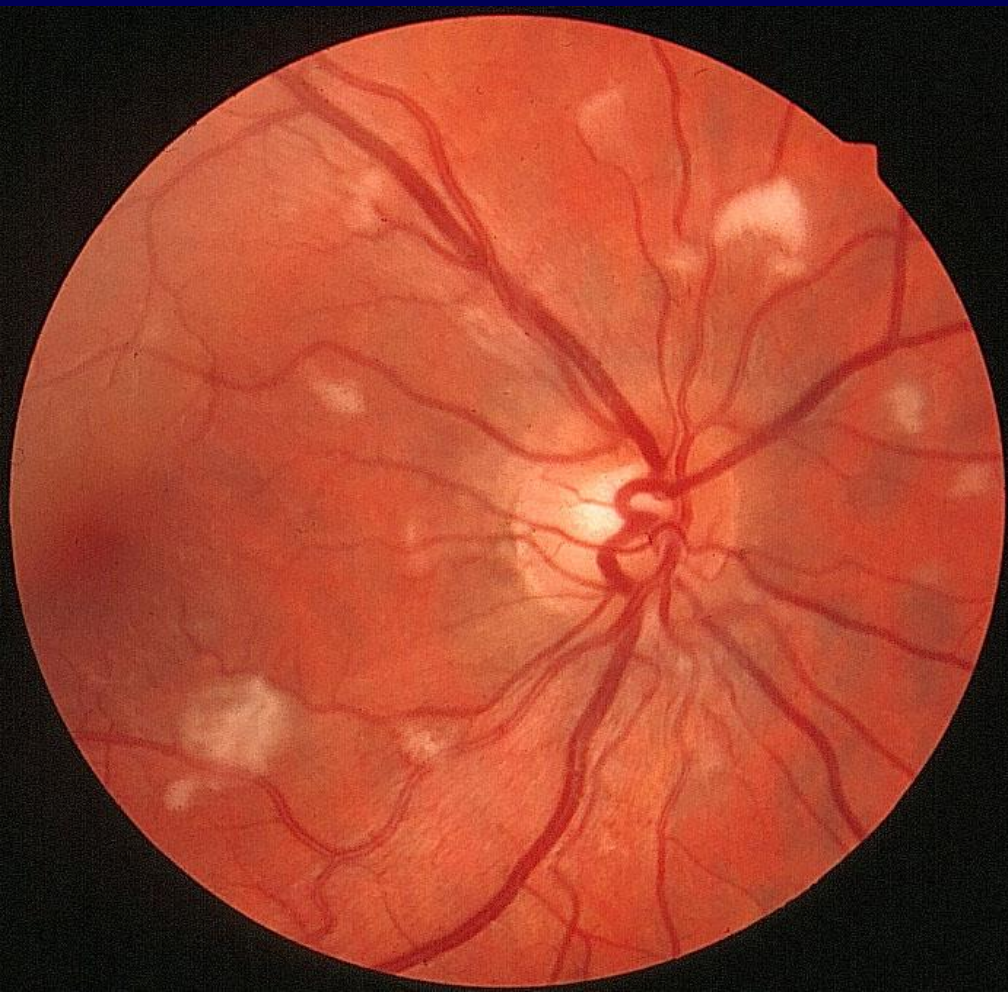
Common (HIV / AIDS)

No known adverse effects?

- **segmental dilation**
- **microaneurysms**
- **sludging**
- **comma-shaped fragments**

MICRO-VASCULOPATHY

(HIV - retinopathy)



Symptoms:

- asymptomatic (mostly)
- ischemic maculopathy (rare)

Clinical Findings:

- microaneurysms (FLA)
- multiple CWS (posterior pole)
- dot-blot haemorrhages

Histopathology:

- similar to DR:
 - Pericyte loss
 - Endothelial cell swelling
 - Basement membrane thickened

HAART

(achievements & consequences)

- **Incidence of HCMV-disease:**
 - ⇒ decreased by > 80% (USA & Europe)
- **Rare cases of HCMV-retinitis:**
 - ⇒ non-responders (HAART)
- **New clinical pictures:**
 - ⇒ Immune Reconstitution Uveitis / immune retinitis

II. UNUSUAL OCULAR & ADNEXAL TUMOURS

- **Kaposi's Sarcoma**
- **Squamous Cell Carcinoma of the Conjunctiva**
- **Lymphoma**

KAPOSI'S - SARCOMA

- Human Herpes Virus 8 (HHV 8)
- **Epidemiology:** - $CD4+ \leq 500$ c/ μ l
- rare with HAART
- **O/E:** vascular tumour; red-violet lesions (conjunctiva / eyelid); typically few & slowly progressing; may bleed, ulcerate and disseminate
- **Therapy:** excision; cryo; respond well to radiation



SQUAMOUS CELL CARCINOMA

- **Common in Africa (HIV - marker)**
⇒ “EPIDEMIC”

70% SCC ⇒ HIV+ (Malawi)

Any CD4+ count (lower counts)

- **Reflects high prevalence of Human Papilloma Virus (HPV)**
- **Therapy: excision**
 +/- 5FU / MMC

Prognosis?



NON-HODGKINS LYMPHOMA

- Epstein-Barr-Virus
- Systemic & CNS Lymphoma (important!)
- Ocular & Orbital Lymphoma
(very rare!)
- $CD4+ \leq 500 \text{ c}/\mu\text{l}$
- OE: necrotizing retinitis, multifocal choroiditis, retinal vasculitis, vitritis, subretinal mass, pseudo-hypopyon uveitis
- Opportunistic??
- Chemo-Therapy & Radiation



III. NEURO-OPHTHALMOLOGICAL LESIONS

≈ 6% of patients (AIDS > HIV: poor prognosis)

Optic nerve, Cranial nerves, Visual pathway

- **DIRECT neurological injury (HIV)**
- **Opportunistic INFECTIONS (CNS & meninges)**
- **Opportunistic TUMOURS (CNS & meninges)**

DIRECT NEUROLOGIC INJURY **(HIV)**

Subclinical Neuro-ophthalmological abnormalities

- abnormal saccades
- abnormal smooth pursuits

HIV-related Dementia

⇒ **any CD4+ count**

⇒ **Direct HIV-infection?**

CRYPTOCOCCAL MENINGITIS

≈ 50% of neuro-ophthalmological lesions (AIDS)
(CD4+ ≤ 100 c/μl)

- Papilloedema (raised intracranial pressure)
- Optic neuropathy & atrophy (direct invasion?)
- Cranial nerve palsy (6 th--- abducens)
- Cortical blindness
- Supranuclear eye movement disorders

Rx: Anti-fungals (e.g. Fluconazole, Amphotericin B?)

OTHER CAUSES of NEUROOPHTHALMOLOGICAL LESIONS (AIDS)

- **Toxoplasmosis (CNS)**
- **Lymphoma (CNS)**
- **Meningitis & Encephalitis (viral)**
- **Neuro-Syphilis**
- **Medication- (ON-lesions)**

OPTIC NEUROPATHY

(⇒ Infection of ON or CNS)

- **PERINEURITIS:**
(VA good; PR normal; enlarged blind spot)
 - **PAPILLOEDEMA:**
(LP: ICP elevated)
 - **OPTIC ATROPHY:**
- Syphilis
 - Cryptococcus
 - NHL
 - Syphilis
 - Necrotizing retinitis
 - AIDS-associated ON
 - Secondary OA

OPTIC NEUROPATHY

(⇒ Infection of ON)

- **PAPILLITIS:**

(poor VA, APD, VFD)

- Syphilis
- Toxoplasmosis
- CMV

- **RETROBULBAR NEURITIS:**

⇒ consider INFECTION until proven otherwise

⇒ systemic STERIODS contraindicated

- Cryptococcus
- Syphilis
- Histoplasmosis
- HZV
- Pneumocystis carinii

IV. OPPORTUNISTIC INFECTIONS (PRINCIPLE)

- **Opportunistic agents** (infection, reactivation)
virus, bacterium, fungus, protozoon ...
- **Immunosuppression** (iatrogenic, congenital, acquired)
AIDS, malignancy, immunosuppressive Rx, sepsis ...

OPPORTUNISTIC INFECTIONS (ROUTES)

EXTRAOCULAR:

- **Local invasion**
(conjunctivitis, keratitis)
- **Haematogenous**
(chorio-retinal)
- **Organ-specific**
(neuronal, e.g. Herpes-virus)

INTRAOCULAR:

- **Local reactivation**
(Toxoplasmosis)
- **Iatrogenic**
(intraocular surgery)

OPPORTUNISTIC INFECTIONS (ANTERIOR SEGMENT & ADNEXAE)

LID & CONJUNCTIVA

CORNEA

- Molluscum contagiosum
- Varizella Zoster virus (VZV)
- Herpes simplex virus (HSV)
- Varicella Zoster Virus (VZV)
- Herpes Simplex Virus (HSV)
- Microsporidiae
- Chlamydia
- Candida albicans

MOLUSCUM CONTAGIOSUM

Poxvirus (STD)

NORMALLY:

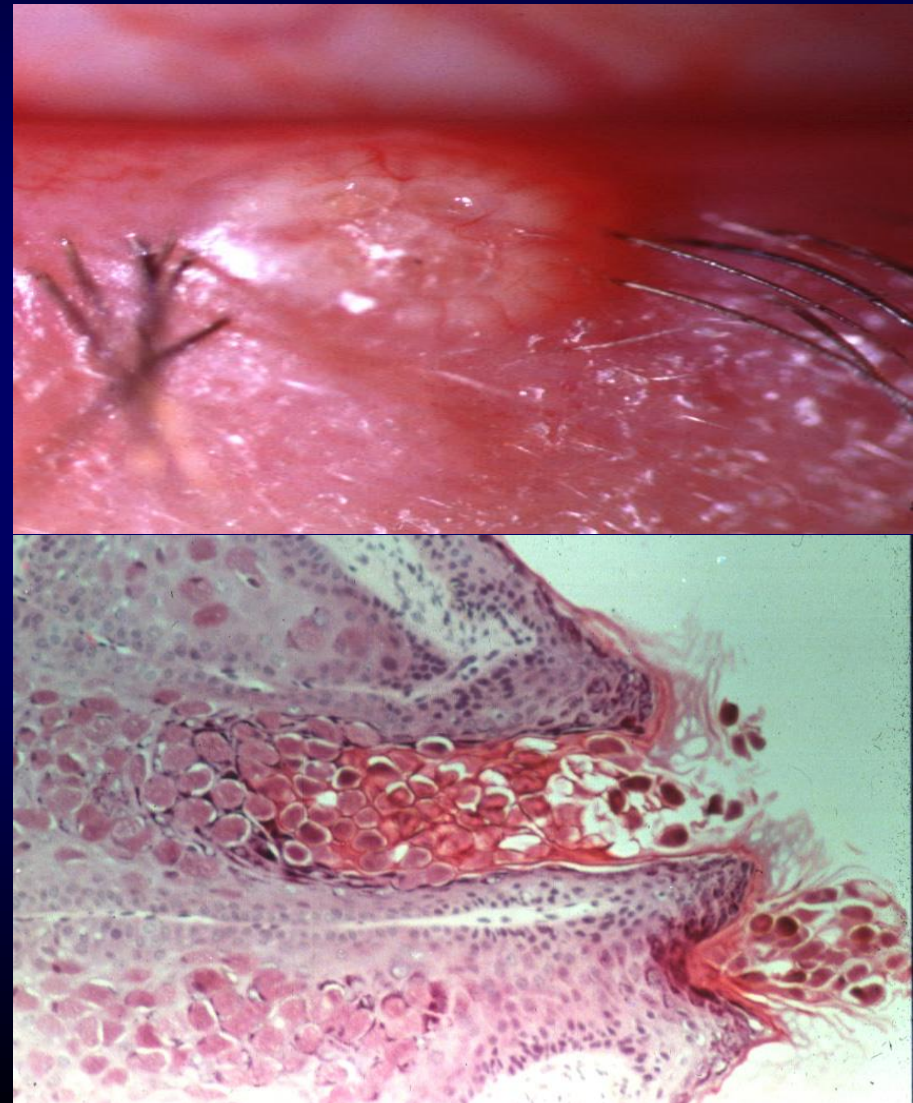
- few, small (2-4 mm)
- painless & white
- follicular conjunctivitis
- (superficial keratitis)

HIV:

- large
- disseminated
- any CD4+ count

Rx:

- Curettage, excision, cryo?
- Cidofovir (iv / topical)?



HERPES ZOSTER OPHTHALMICUS

Varizella zoster virus (VZV)

- Herpesviridae (subclass α)
- reproduce quickly » destructive!
- latency (nerve ganglia)
- Chickenpox » 20% HZO
- 1st division of Trigeminal Nerve (V1)
- nasociliaris (uveitis / IOP) **Hutchinson sign+**

HIV:

- **3 – 4% (HIV / AIDS)**
- **leading ocular complication!**
- **CD4+ \geq 200 c/ μ l (early!)**
- **opportunistic?**
- **50 – 70% ocular complications**
- **post-herpetic neuralgia (less frequent)**

RX: **Acyclovir, Valacyclovir, Famcyclovir**



INFECTIOUS KERATOCONJUNCTIVITIS

Herpes Simplex virus (HSV)

- HIV:**
- no higher frequency
 - severe / atypical
 - CD4+ \leq 500 c/ μ l?

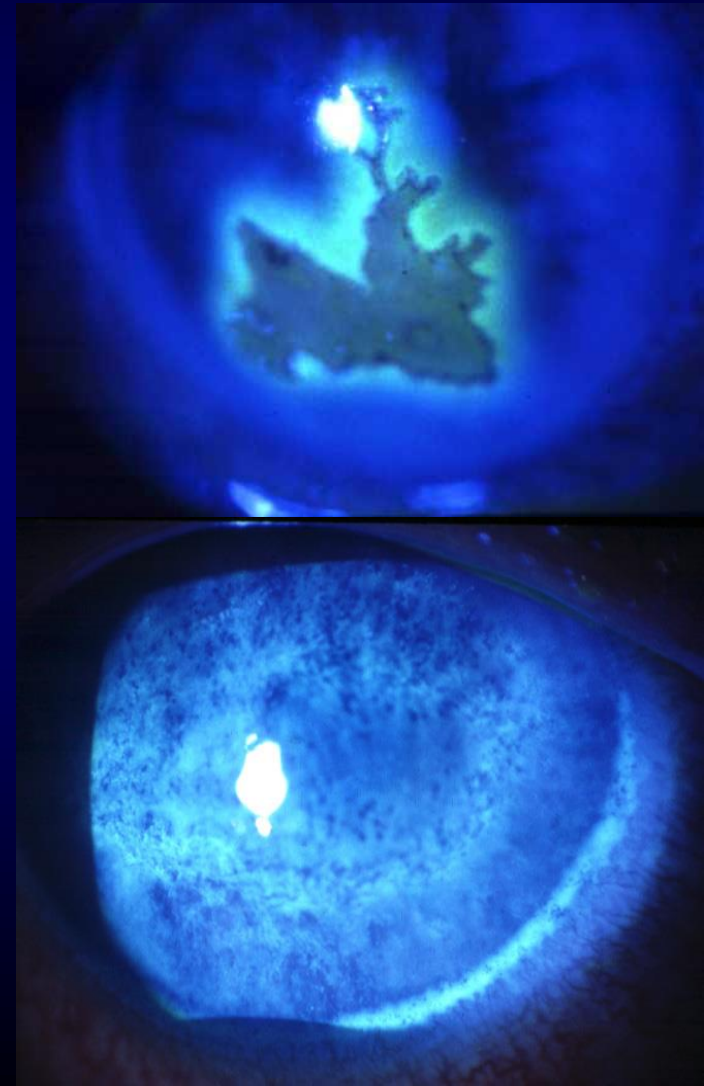
RX: - Acyclovir, Valacyclovir, Famcyclovir

Microsporidia (obligate intracellular protozoon)

- HIV:**
- unusual
 - clears with HAART
 - CD4+ \leq 200 c/ μ l

Rx:

- corneal debridement
- oral Itraconazole
- topical Fumigillin,
Propamidine, Albendazole?



OPPORTUNISTIC INFECTIONS (POSTERIOR SEGMENT)

FUNDAMENTAL PRINCIPLES

- **DISSEMINATION** - Systemic infection
- **SYSTEMIC Rx** +/- Ocular treatment?
- **2 PHASES (Rx)**
 - Induction (high dose)
 - Maintenance (toxicity, cost, life)
- **HAART** - Immune Recovery?
- **2 CLINICAL PATTERN**
 - Necrotizing Retinitis
 - Multifocal Choroiditis
- **INFLAMMATION**
 - Red Eye » higher CD4+ count
 - Quiet Eye » lower CD4+ count

OPPORTUNISTIC INFECTIONS (RETINA)

- **Cytomegalovirus** (HCMV retinitis)
- **Herpes simplex virus** (ARN)
- **Varizella zoster virus** (ARN, PORN)
- **Treponema pallidum** (chorio-retinitis)
- **Candida albicans** (endophthalmitis)
- **Staph. aureus ...** (endophthalmitis)

OPPORTUNISTIC INFECTIONS

CHOROID:

- *Cryptococcus neoformans*
- *Mycobacterium avium intracellulare*
- *Histoplasma capsulatum*
- *Pneumocystis carinii*

RETINA & CHOROID:

- *Toxoplasma Gondii*
- *Aspergillus*

TOXOPLASMIC RETINO-CHOROIODITIS

- **Epidemiology:** < 1% of AIDS patients in USA (more common in Brazil)
- **CD4+ ≤ 200 c/ μ l**
- **Aetiology:** *toxoplasma gondii*
- **AIDS:** bilateral & multifocal; no association with chorioretinal scar
 \Rightarrow PRIMARY INFECTION?
- **Simultaneous CNS-disease?**



HIV - RETINITIS

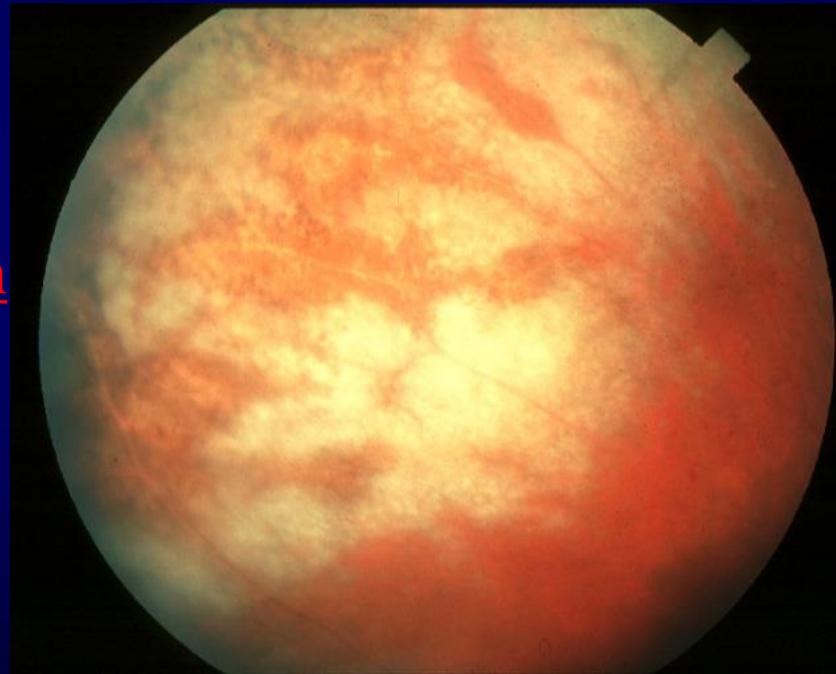
- **Clinical picture:** peripheral multifocal retinitis, low-grade vitritis, retinal vasculitis

⇒ stationary / very slow progression
(**DD:** CMV / Syphilis)

- **CD4+ < 120 c/μl**

- **Aetiology:**

- **HIV?** (responds to **ARV**)
- **Syphilis?** (must be r/o)



HCMV – RETINITIS

(MAIN OCULAR PROBLEM IN AIDS)

- **CMV: Herpesviridae (subfamily β)**
- **ubiquitous worldwide (40 – 100%)**
- **Systemic infection**
- **Most common ocular opportunistic infection!**

- **CD4+ < 50 - 100 c/ μ l**

- **Haematogenous**
- **Retina / optic nerve**
- **Latency (persists in infected host)**

- **O/E (Types):**
 - a) granular lesions
 - b) hemorrhagic
 - c) perivascular infiltrates



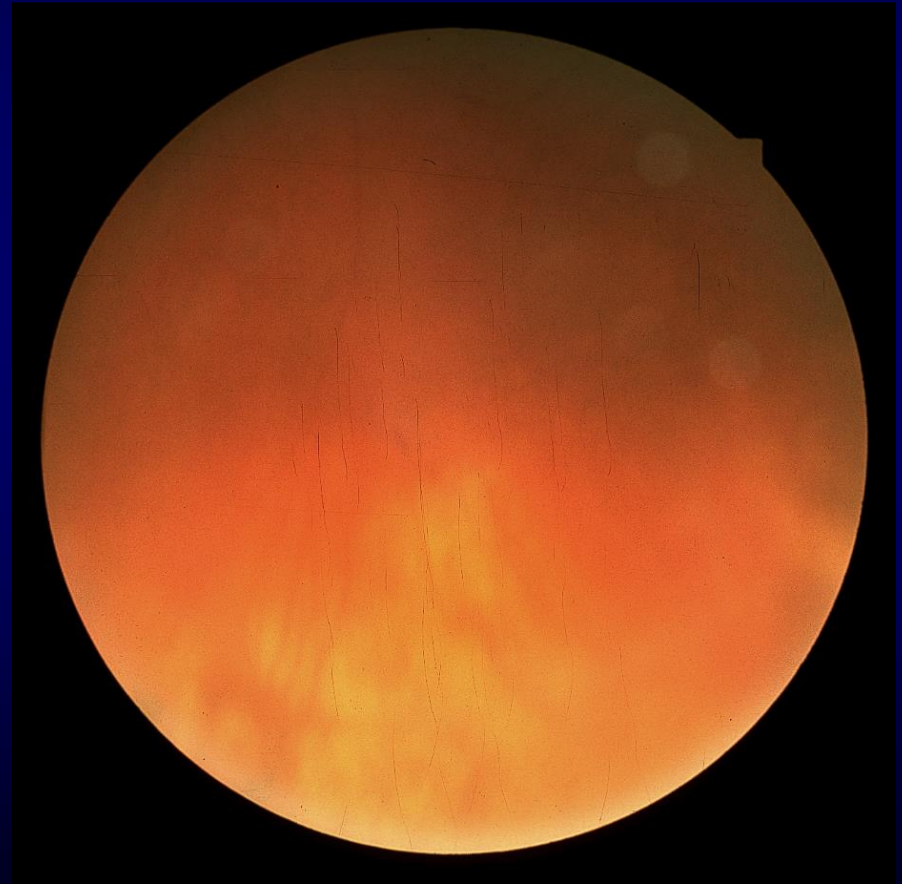
HCMV (overview)

- up to **40% of untreated HIV patients**
- usually **no antiretroviral therapy (HAART)**
- **CD4+ < 50 - 100 c/μl**
- **SSA ↓**
 - CMV seroprevalence?
 - death (e.g. TB) at higher CD4+?
- **3 monthly Screening (CD4+ < 50 c/μl)**
 - 15% asymptomatic
 - only floaters / gradual visual field loss
 - 52% bilateral
 - poor prognosis (VA)

HERPES ZOSTER (VHV)

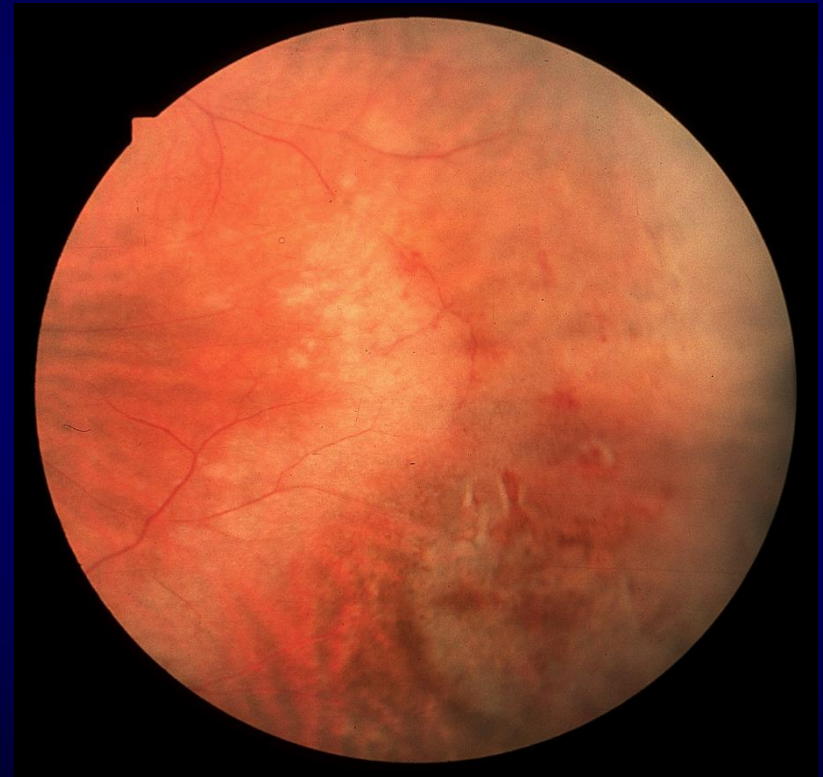
RETINITIS

- **CD4+ < 200 c/μl**
- **spreads along nerves**
- continuous spectrum:
 - **ARN** (immunresponse ↑)
 - **PORN** (immunresponse ↓)
- **Painful, occlusive necrotizing retinitis, vitritis**
- **retinal detachment (atrophic holes)**
- **Rx: Antivirals + ppVitreotomy**
Laser demarcation?



HERPES SIMPLEX (HSV) RETINITIS

- **CD4+ < 200 c/μl**
- continuous spectrum:
 - **ARN** (immunresponse ↑)
 - **PORN** (immunresponse ↓)
- **necrotizing retinitis / extensive vascular disease / vitritis**
- **rapid progression!**
- **bilateral (30%)**
- **retinal detachment (>70%)**
- **Rx: Aciclovir, Foscarnet, Brivudin + ppV**
Laser demarcation?



PERSPECTIVES

(HAART & EYES)

Appropriate HAART:

- » **sustained immune recovery**
- » **reduced risk (ocular complications ↓)**
- » **“Honey Moon” (resistance)?**

Improved Clinical Management (without HAART):

- » **improved survival but poor immunity**
- » **increased risk (ocular complications ↑)**

