

Viruses in May: viral infection in the eye

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Viruses in May



Uveitis at just about any time

What we will cover:

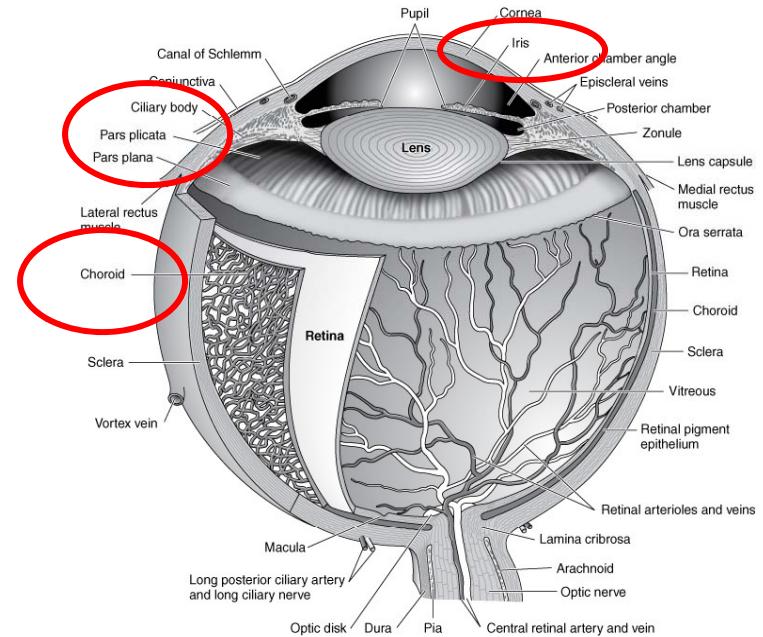
- classification of uveitis & scleritis
- what do we know about the pathogenesis of uveitis
- clinical features of viral infection & uveitis



Overview of Uveitis

What is uveitis?

- inflammation of the uveal tract
 - iris
 - ciliary body
 - choroid
- often spill over to involve adjacent structures
 - retina
 - vitreous
 - optic nerve head

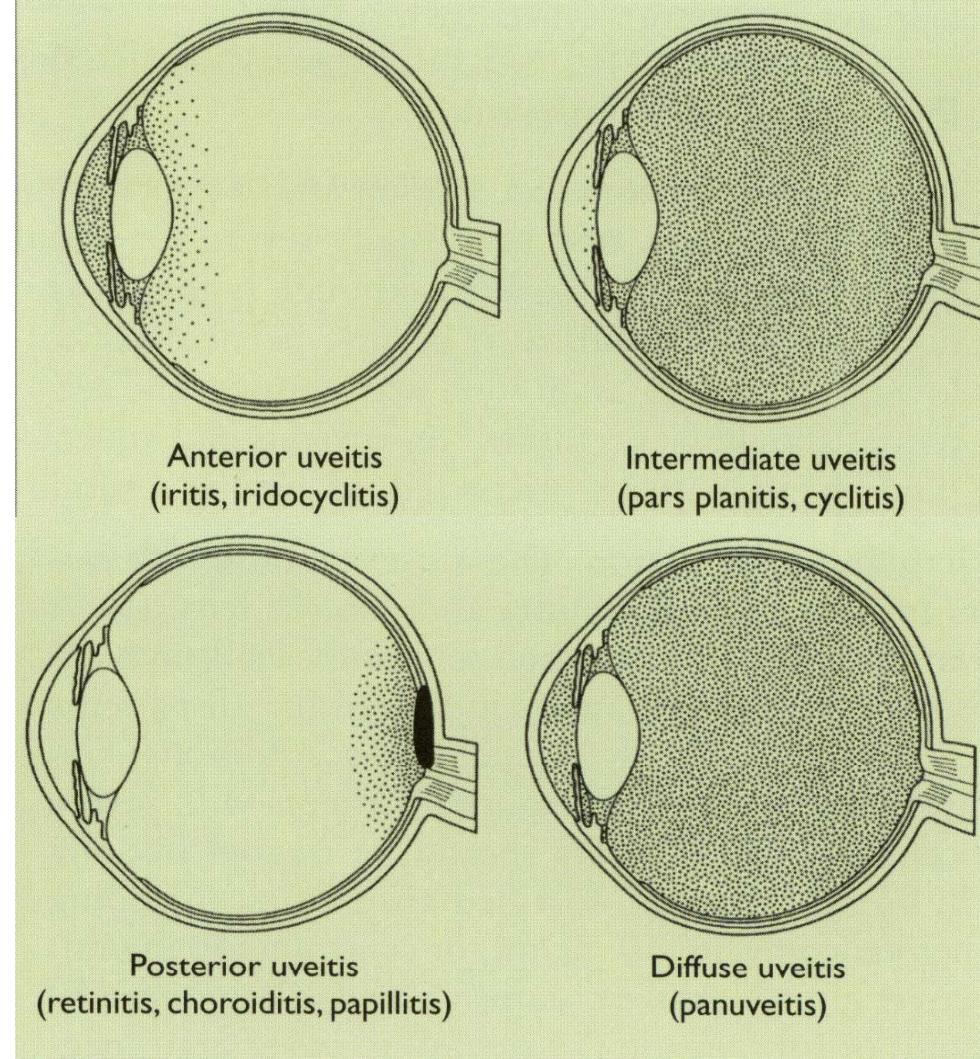




Uveitis Classification

- sudden or insidious onset
- limited duration or persistent

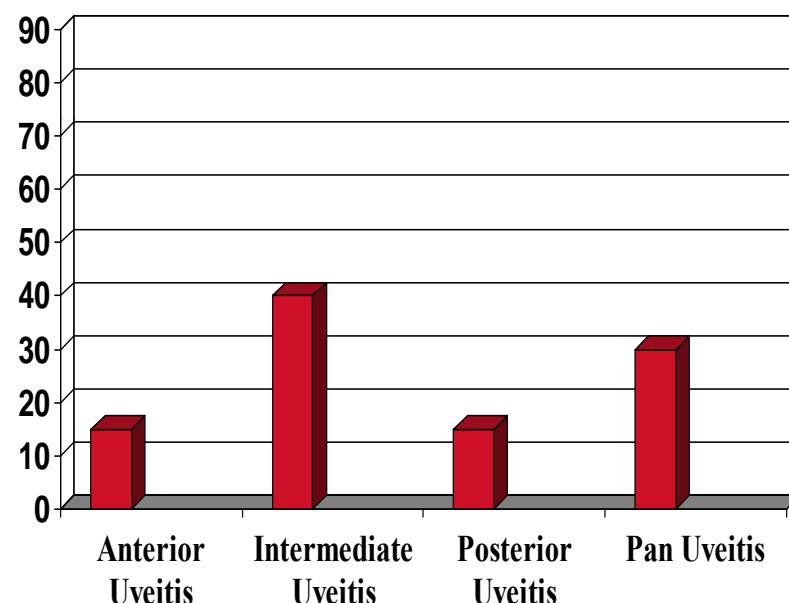
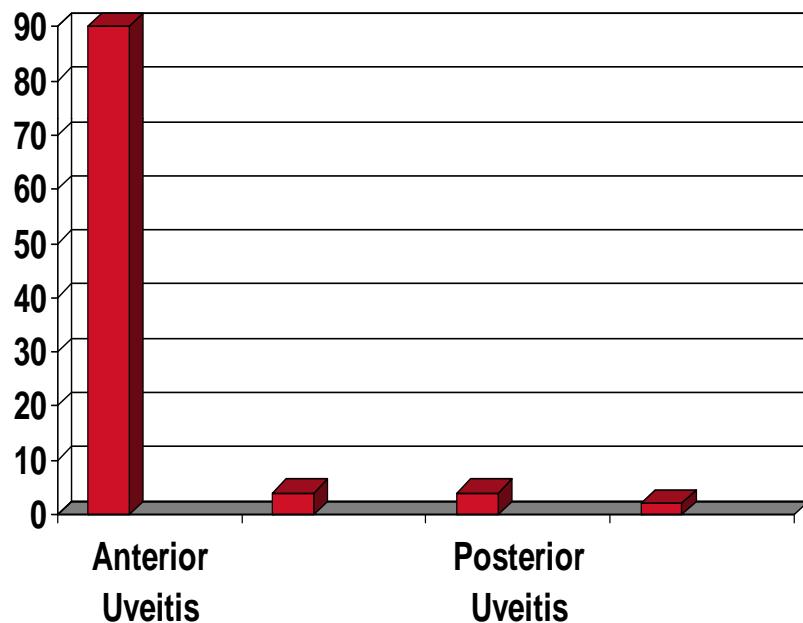
*International Uveitis Study Group
SUN group*





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Spectrum of Uveitis



Community Ophthalmologist

Tertiary Referral Uveitis Unit



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Causes of Uveitis

infection

endogenous inflammation

neoplasia

idiopathic

local Vs systemic disease process



Causes of Uveitis

infection **20%**

endogenous inflammation **40%**

neoplasia **<5%**

idiopathic **40%**

local Vs systemic disease process **60% Vs 40%**



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Common Causes of Uveitis

anterior

**HLA B27 related / herpetic
sarcoidosis**

intermediate

**Toxo / sarcoid / Behcet's disease /
VKHD / ocular syndrome**

posterior

“ocular mimics”

**syphilis, TB, sarcoidosis, herpetic
infection, lymphoma (& lyme disease)**



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Causes of Uveitis

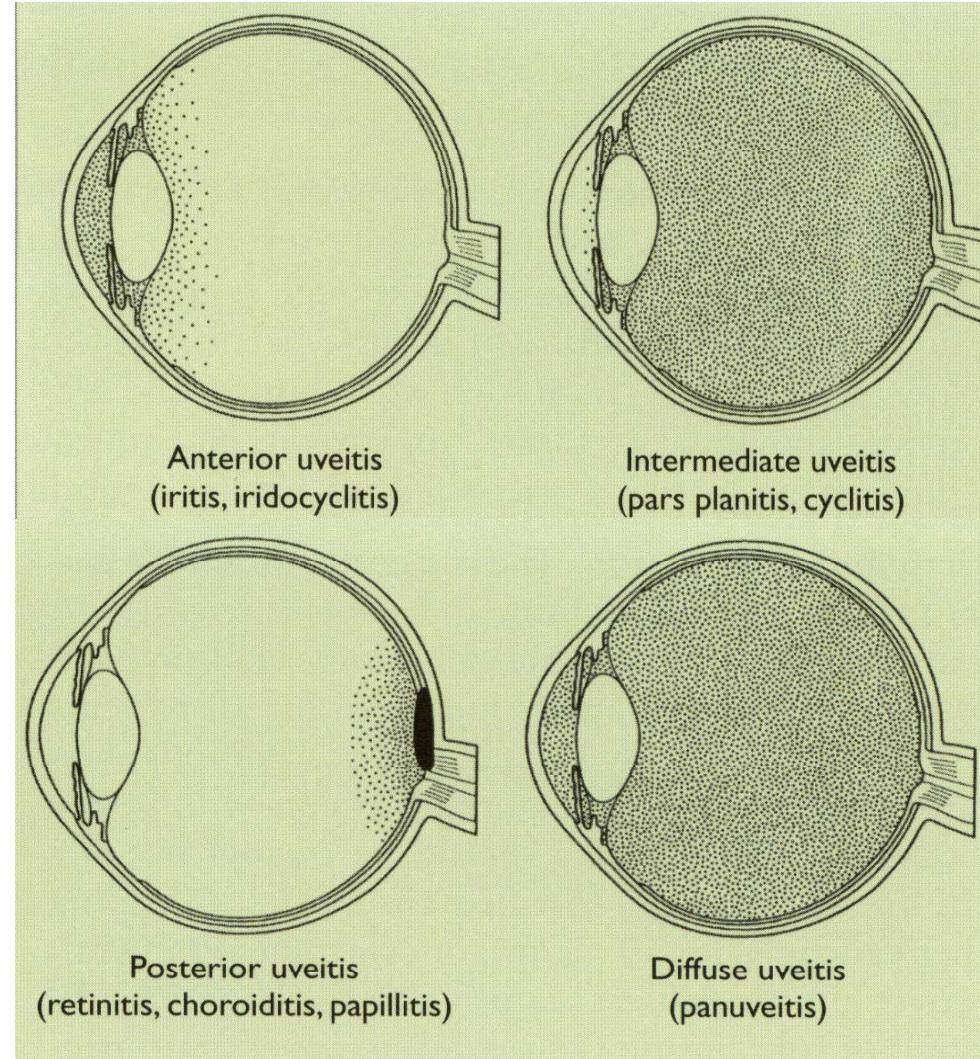
Denis to talk about pathology & immunology of uveitis



Uveitis Classification

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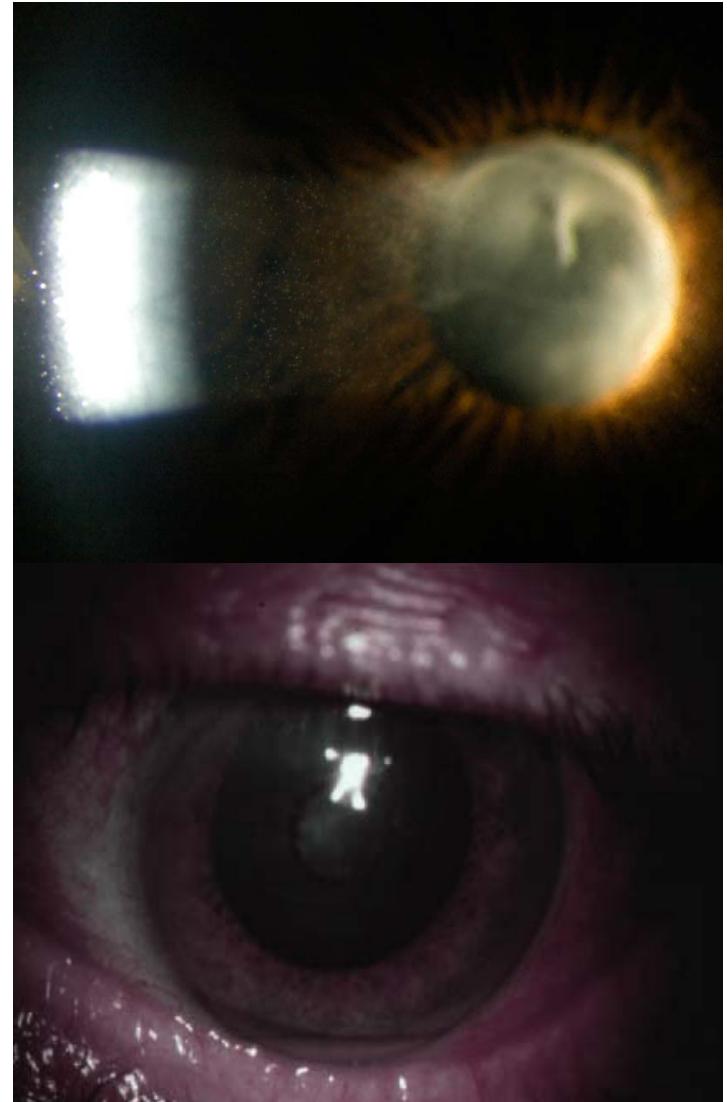
*International Uveitis Study Group
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Clinical Features

- sudden onset, limited duration
- red painful photophobic
- AC cells & KPs
- AC flare
- fibrin, synechiae, hypopyon
- cells anterior vitreous
- IOP normal/low
- fundus normal
- systemic: HLA B27 disease

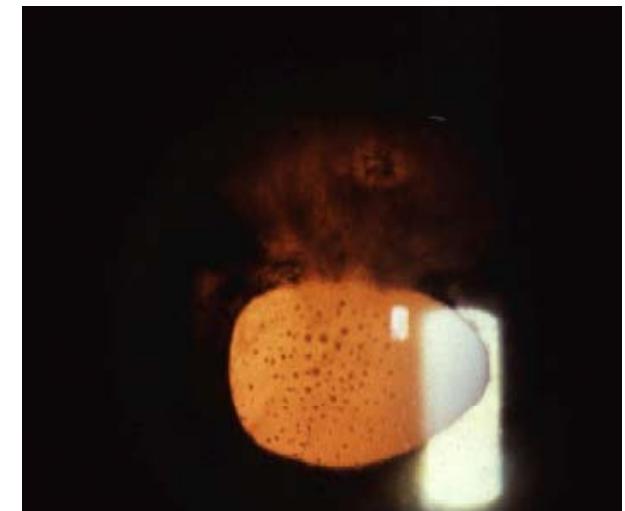
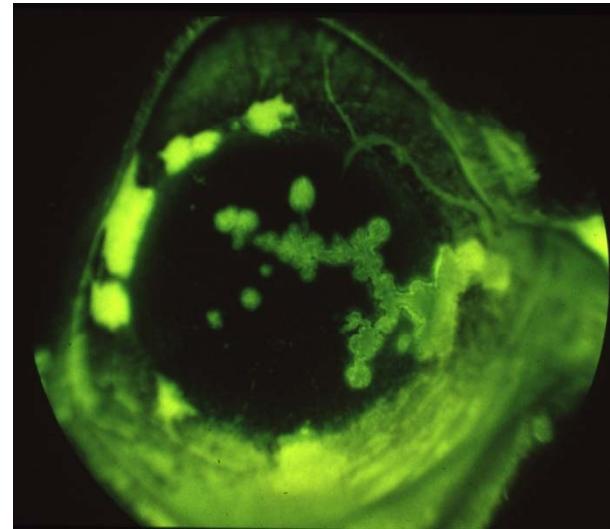




Acute Anterior Uveitis

Herpetic

- recurrent episodes
- after onset of corneal disease
- may occur in absence of corneal activity or disease
- iris changes common
- elevated IOP and cataract common
- recalcitrant in I/S and HIV patients



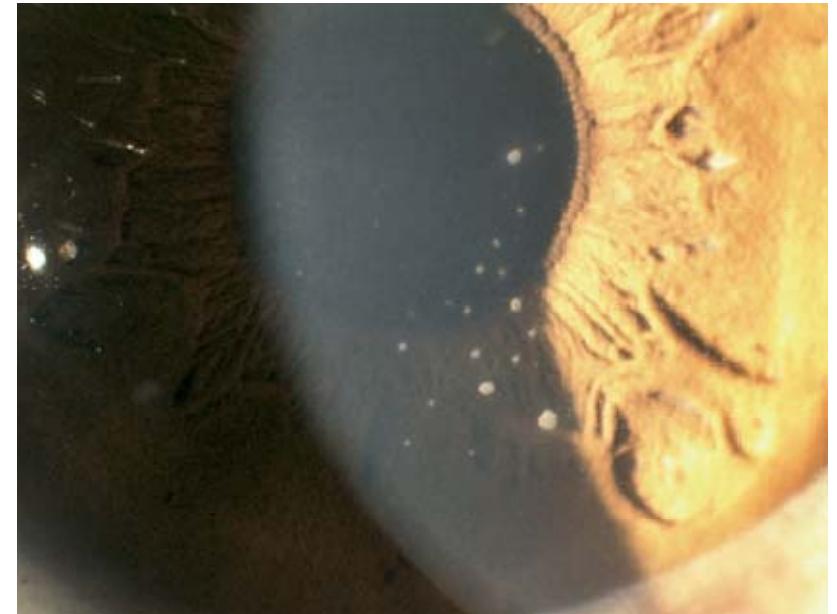


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Acute Anterior Uveitis

Posner-Schlossman Syndrome

- **uncommon**
- ↑ in Asian ethnicity
- transient mild recurrent uveitis
- inferior & peripheral KPs
- anterior iris stroma atrophy
- acute high IOP → severe IOP mediated damage
- ? related to CMV infection in up to 1/2 PSS



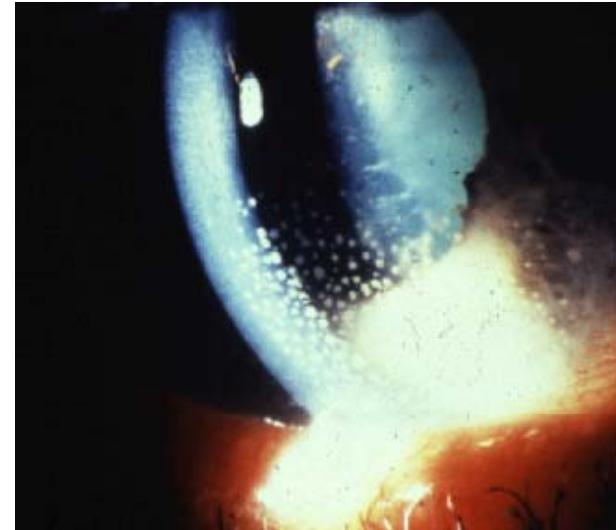


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Chronic Anterior Uveitis

Clinical Features

- **insidious onset, persistent**
- **blurred vision**
- **AC cells & KPs**
- **AC flare**
- **synechiae**
- **IOP low/normal/high**
- **fundus normal**
- **systemic: sarcoidosis**



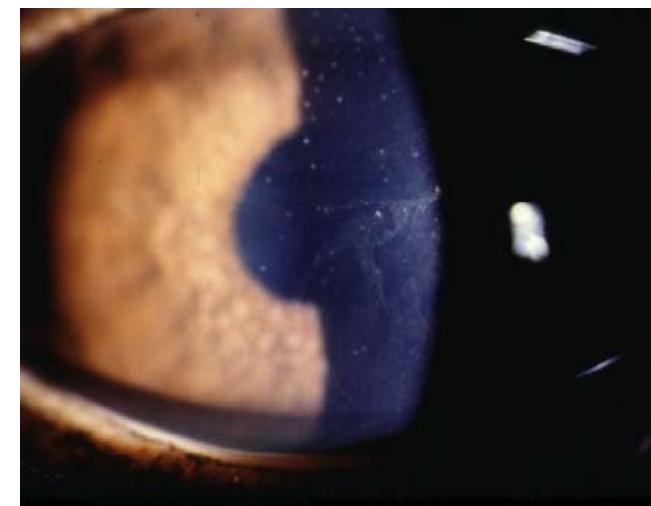
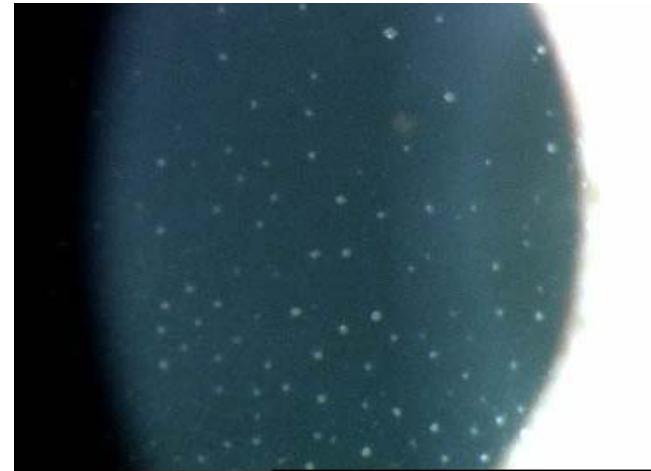


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Fuch's Heterochromic Cyclitis

Clinical Features

- typical KP - white, stellate
- “pan corneal”
- no response to topical steroids
- Rubella Virus:
 - intraocular antibody production
 - detectable on PCR
- ? ↓ with rubella immunisation





Chronic Anterior Uveitis

Varicella Zoster Uveitis

- uveitis in up to 40% of patients with HZO
- effect of anti-VZV therapy
- onset after rash and corneal disease
- florid severe chronic anterior uveitis
- elevated IOP and cataract common
- co-existing HIV infection

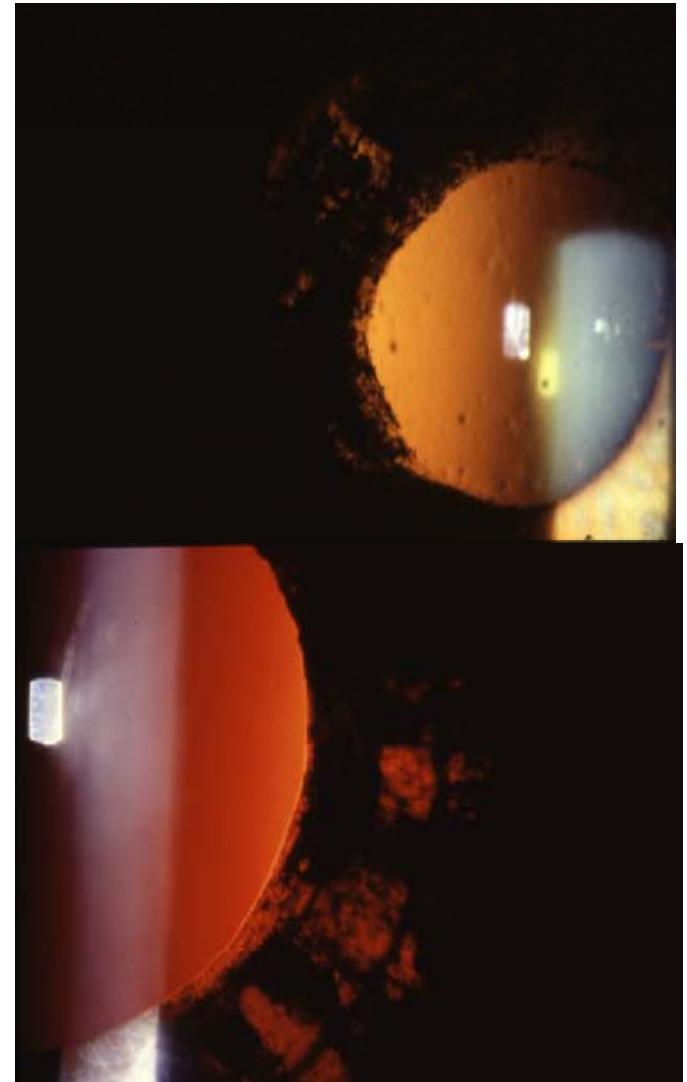




Chronic Anterior Uveitis

Varicella Zoster sine Herpete

- HZO of long posterior ciliary nerves
- trigeminal nerve pain
- decreased corneal sensation
- accomodation weakness
- pupil fixed and irregularly dilated
- acute onset, chronic severe anterior uveitis
- iris pigment defects



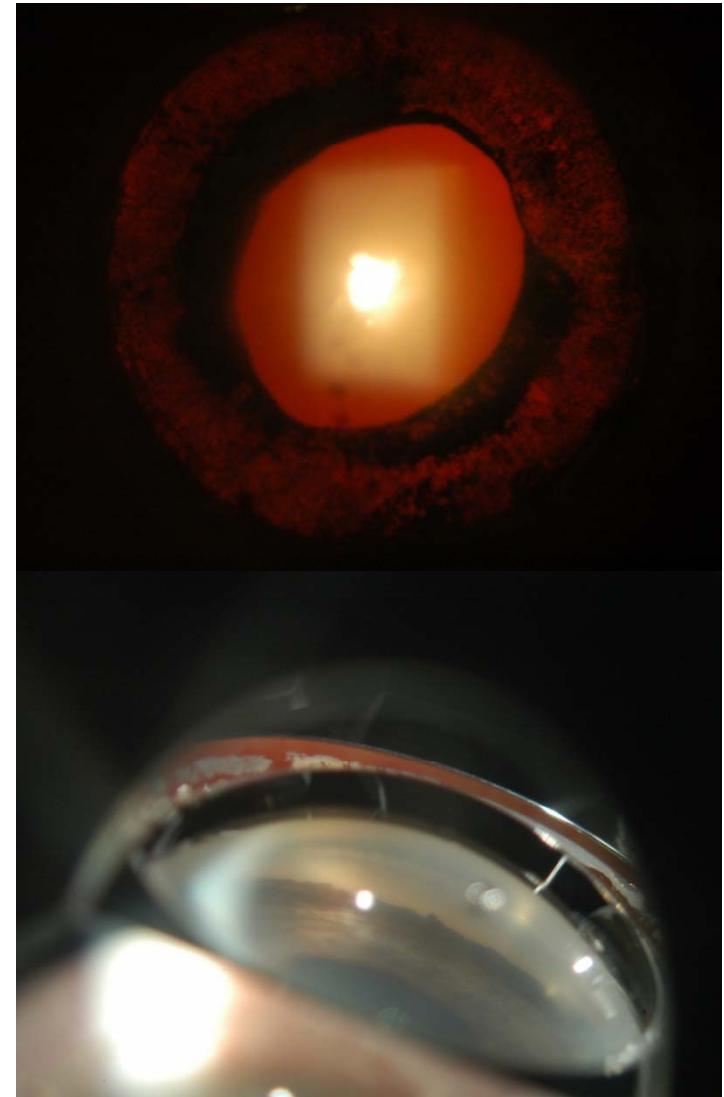


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Chronic Anterior Uveitis

Varicella Zoster sine Herpete

- **severe iris changes**
 - pupil dilation and loss of function
 - sectorial iris atrophy
 - widespread pigment loss
- **chronic relapsing recalcitrant course**
- **elevated IOP – pigmentary glaucoma**
- **cataract**





Viral Anterior Uveitis

Diagnosis

- clinical often sufficient
- VZV need positive diagnosis for systemic Rx
- critically important in I/S patient
- diagnosis → AC tap for PCR





Treatment

HSV & VZV

- topical acyclovir
- judicious topical steroids
- treatment course valacyclovir
- suppressive dose valacyclovir if I/S
- specific Rx for cataract & ↑IOP



CMV

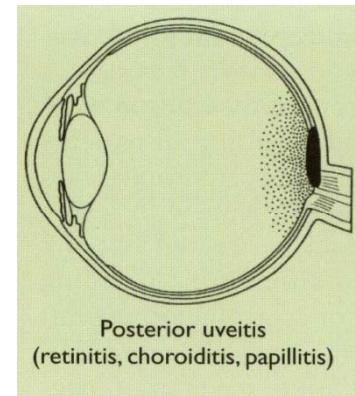
- topical steroids
- control ↑IOP – medical ± surgery
- ??? valganciclovir – role uncertain



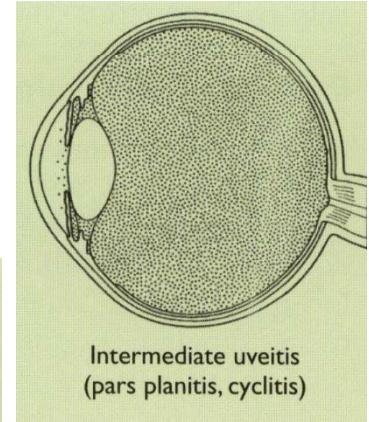


Posterior Uveitis

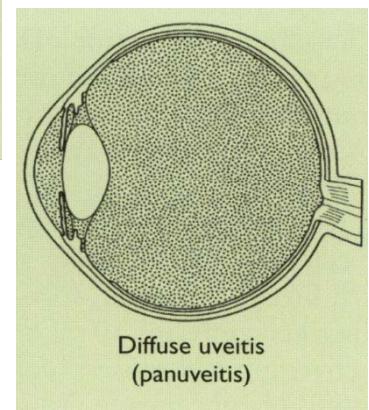
- **range of clinical presentations**
 - **emergent** – “*the Friday night special*”
 - **sudden onset**
 - **insidious onset**
 - **often defined by clinical features**
 - **ocular examination critical**
 - **sight threatening complications**



Posterior uveitis
(retinitis, choroiditis, papillitis)



Intermediate uveitis
(pars planitis, cyclitis)



Diffuse uveitis
(panuveitis)



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Management of Uveitis

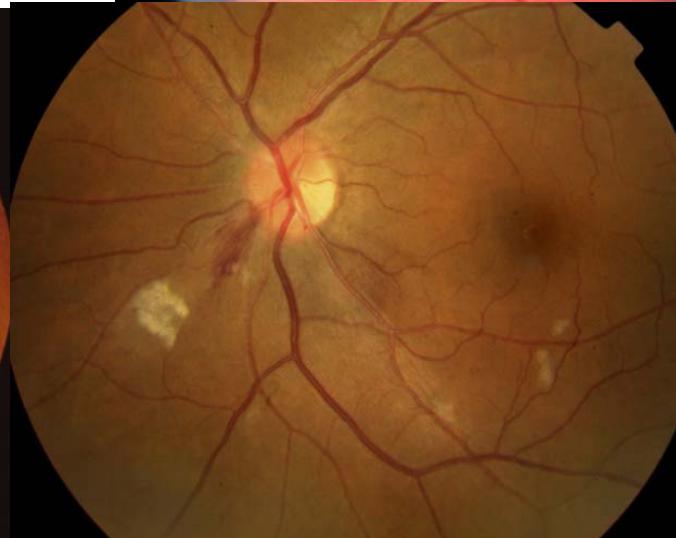
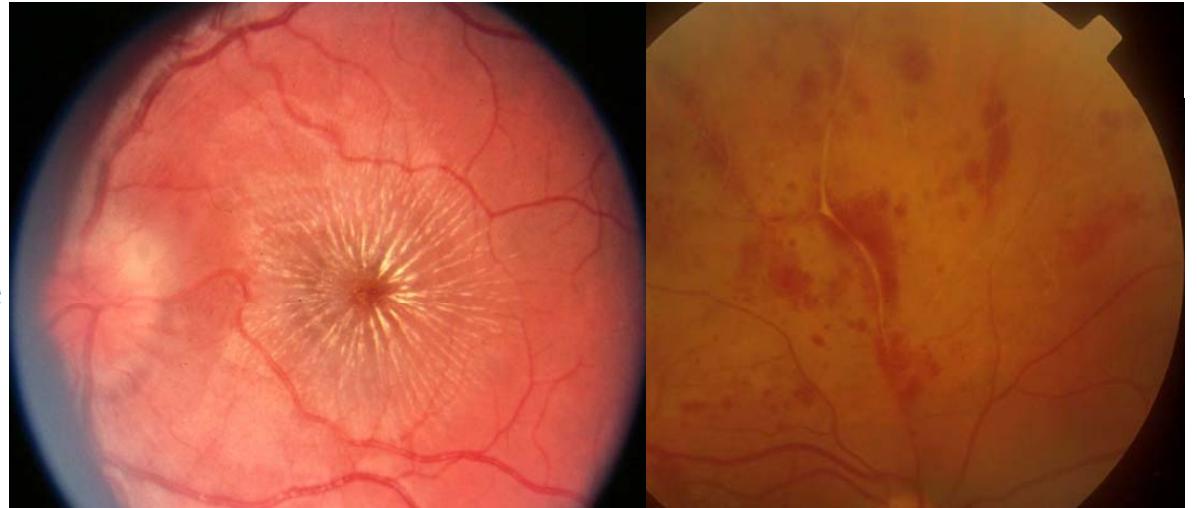
Management Algorithm

- **clinical assessment of uveitis**
 - **review of systems**
 - **pattern recognition**
 - **likely differential diagnosis**
- **ascertain the cause of visual loss**
- **selective investigations to help define a diagnosis**
- **plan treatment**



Posterior Uveitis: Signs of vasculitis

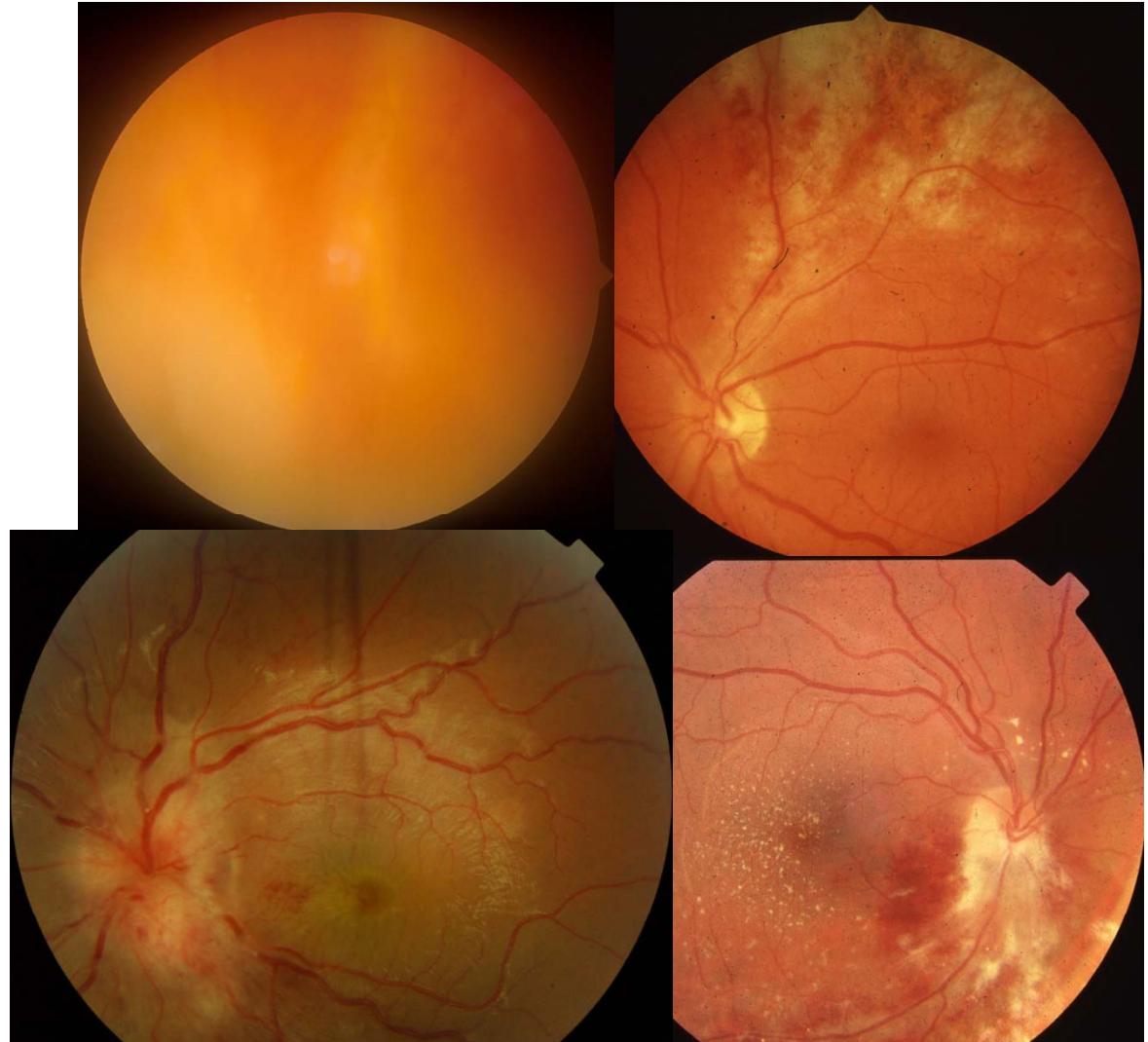
- **vascular sheathing**
- **leakage ± exudate**
- **retinal haemorrhage**
- **vessel occlusion**





Posterior Uveitis: Signs of inflammation

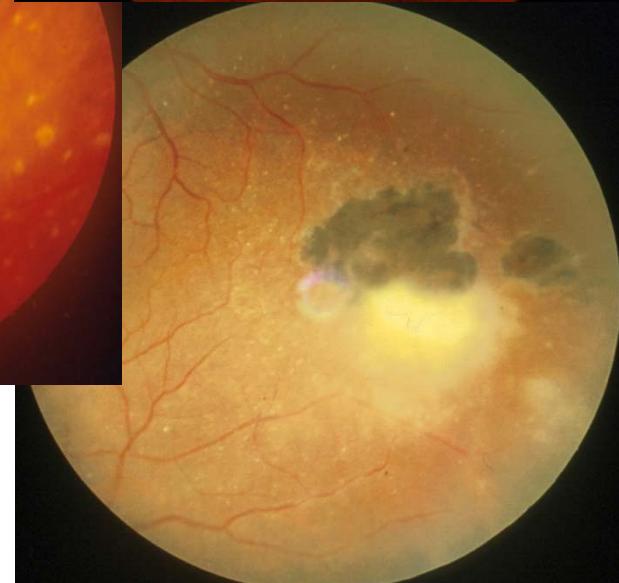
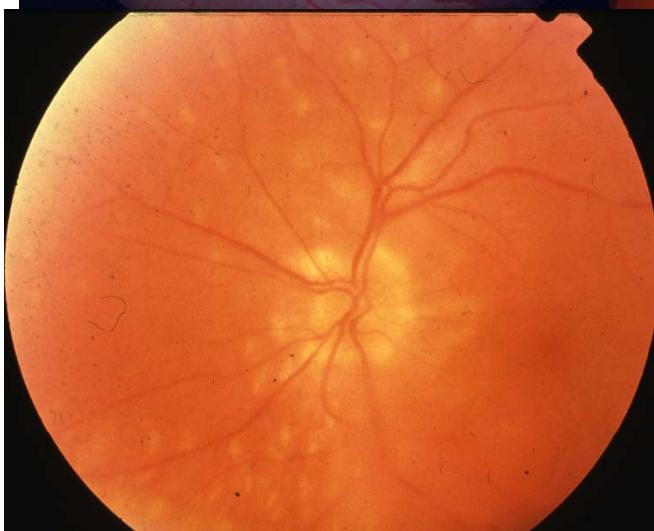
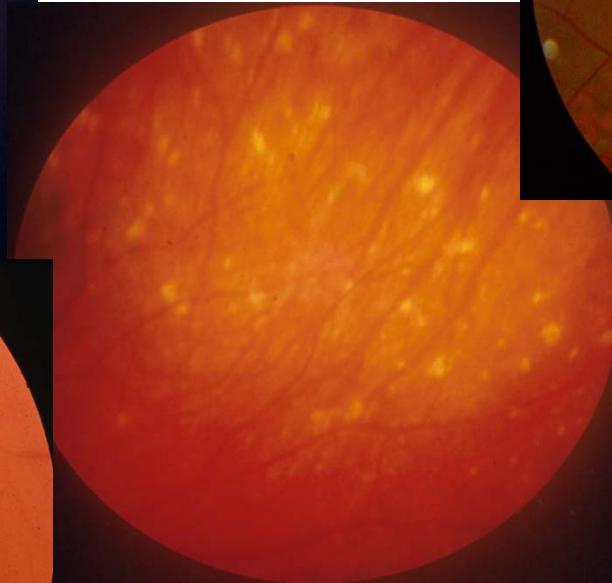
- **vitritis**
- **retinitis**
- **macular oedema**
- **optic disc swelling**
- **neovascularisation**





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Posterior Uveitis: Spots & Scars





Spectrum of Viral Retinitis

EBV

- no clearly defined clinical syndrome
- high ocular expression in HIV related CNS lymphoma

Dengue

- maculopathy
- covered by Denis

Coxsackie Virus

- unilateral acute idiopathic maculopathy (UAIM)

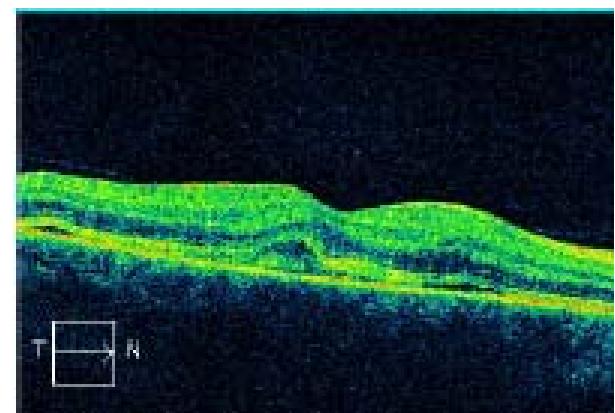
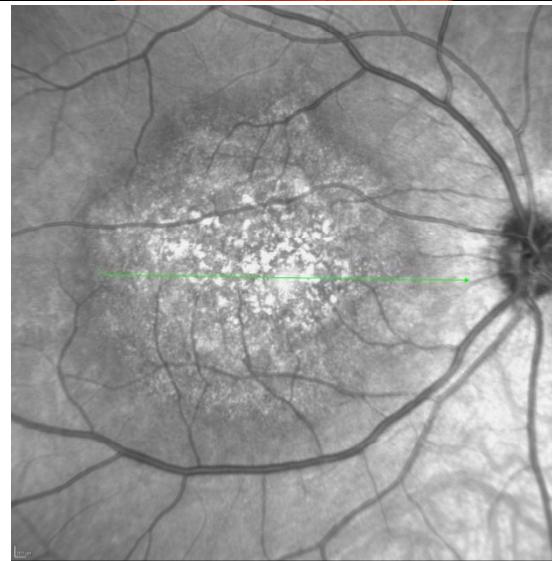
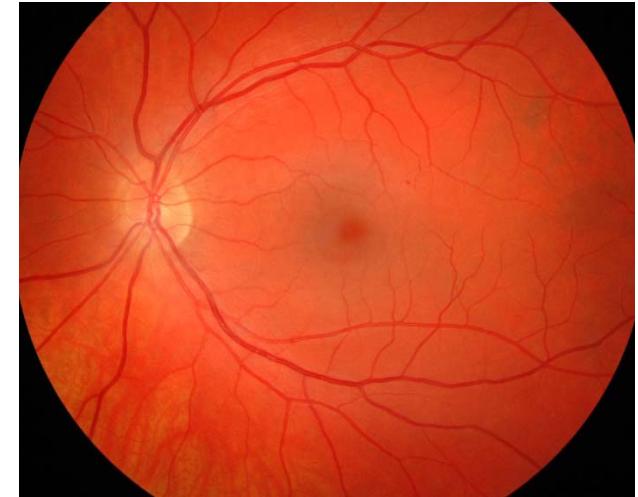
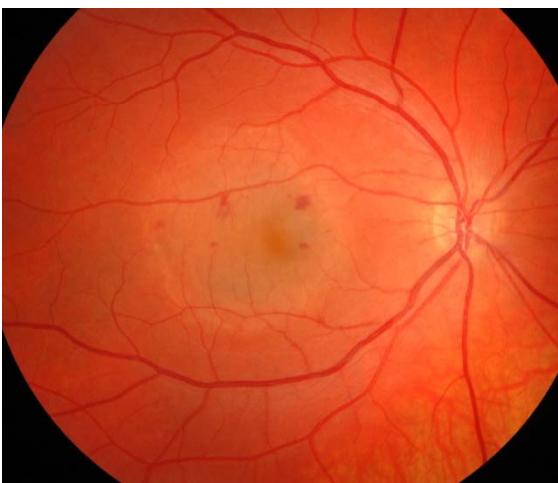
HIV retinopathy

- microvasculopathy



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Viral retinitis – UAIM

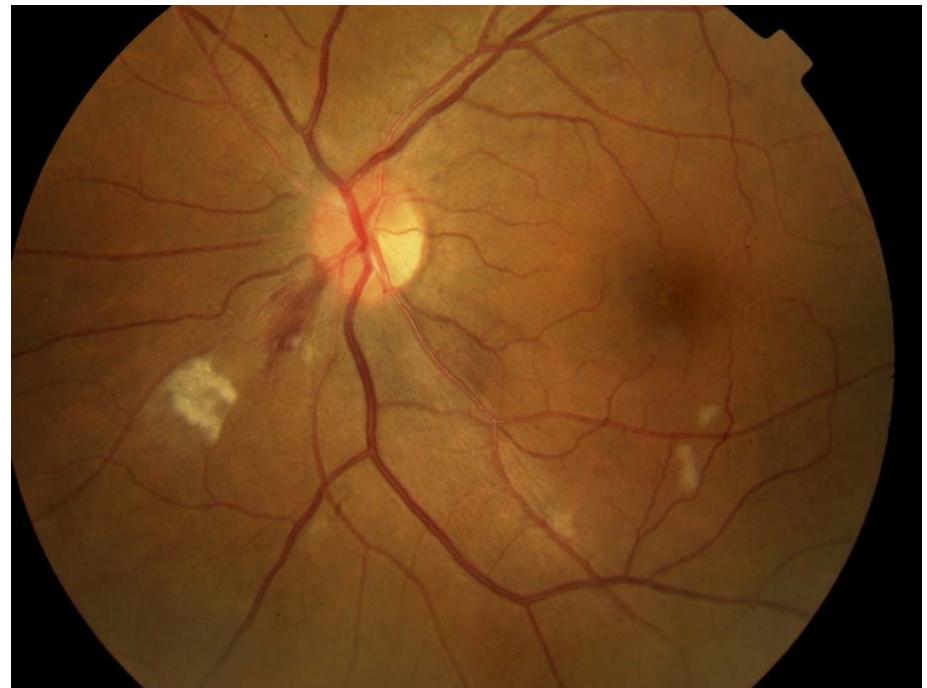




Viral retinitis – HIV microvasculopathy

Clinical Features

- commonest ocular finding
- microvasculopathy
- cotton wool spots
- haemorrhages, IRMAs & microaneurysms
- wax and wane
- high viral load
- very rarely → visual loss

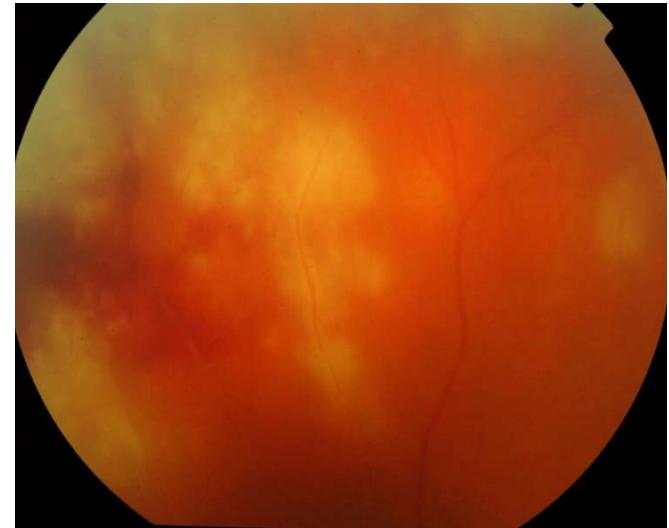




Spectrum of Herpetic Retinitis

HSV & VZV

- **clinical presentations**
 - acute retinal necrosis (ARN)
 - progressive outer retinal necrosis (PORN)
- **normal and immunocompromised**
 - organ transplant recipients
 - HIV infection



CMV

- **only in immunocompromised patients**
 - HIV infection
 - organ transplant recipients





Viral retinitis

Pathogenesis

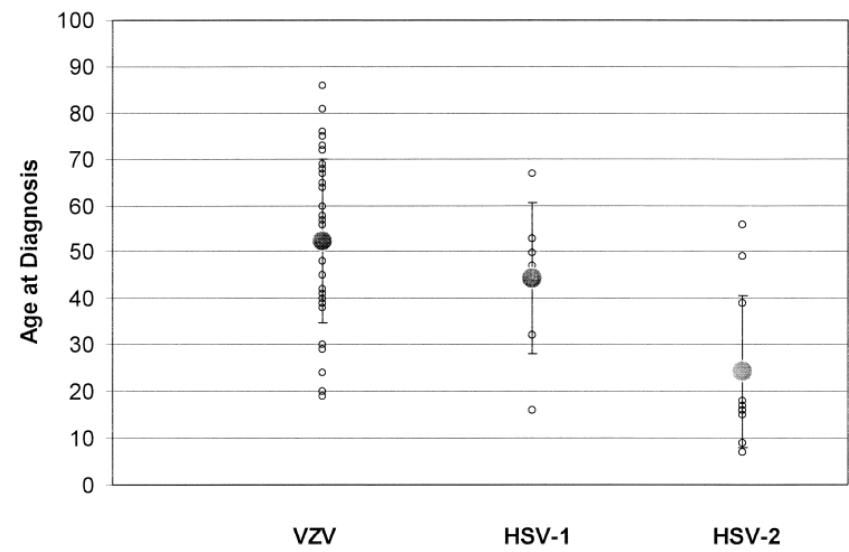
HSV & VZV

- reactivation of latent CNS virus
- triggers unclear in most patients
- ? related to recent re-exposure

CMV

- damaged blood eye barrier
 - CWS from HIV infection
- CMV viraemia
- neurotropic virus

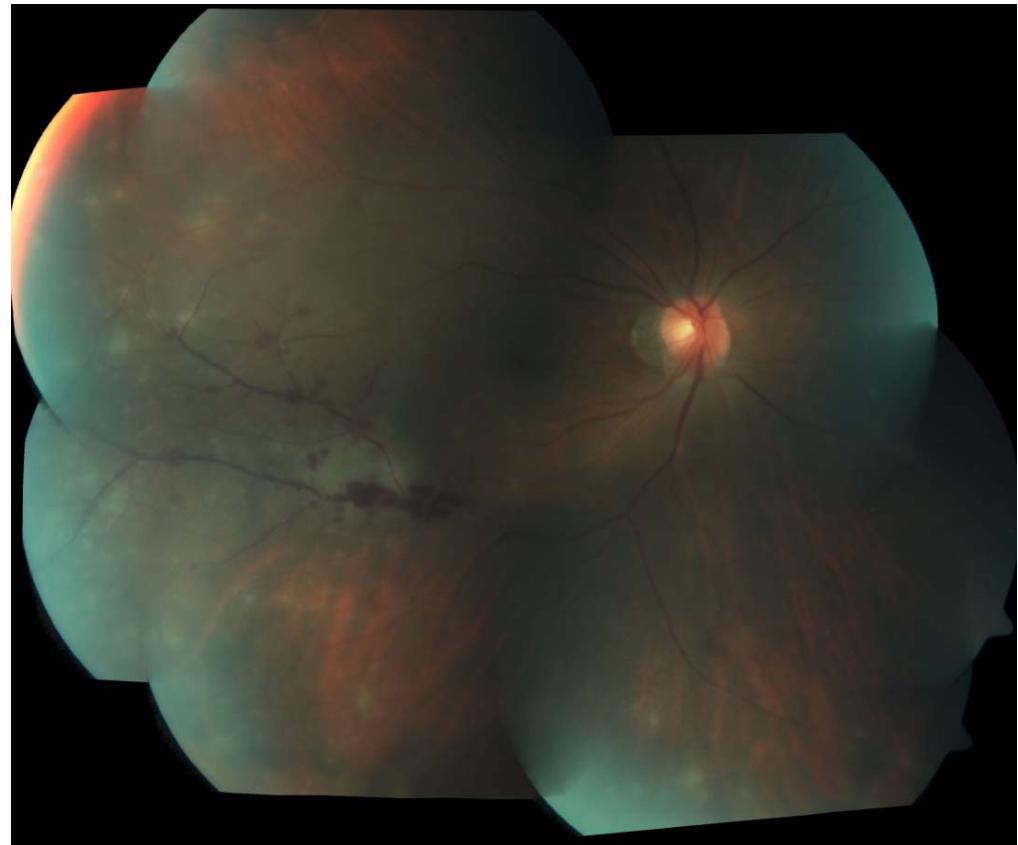
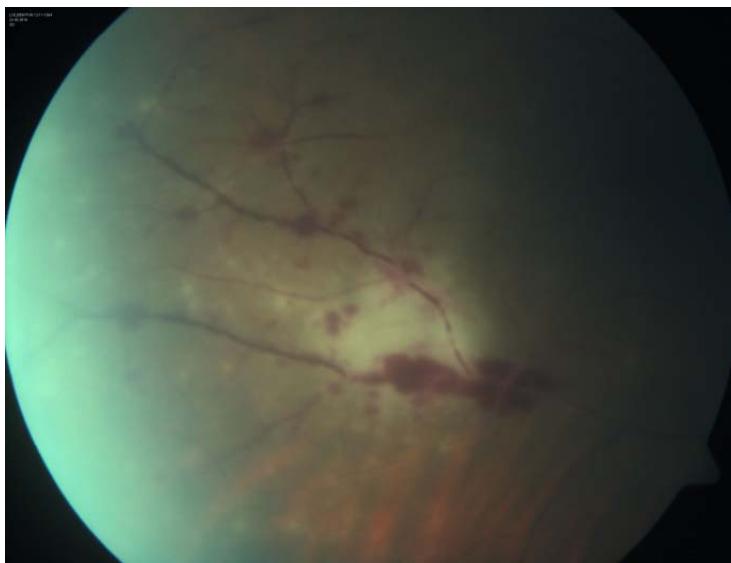
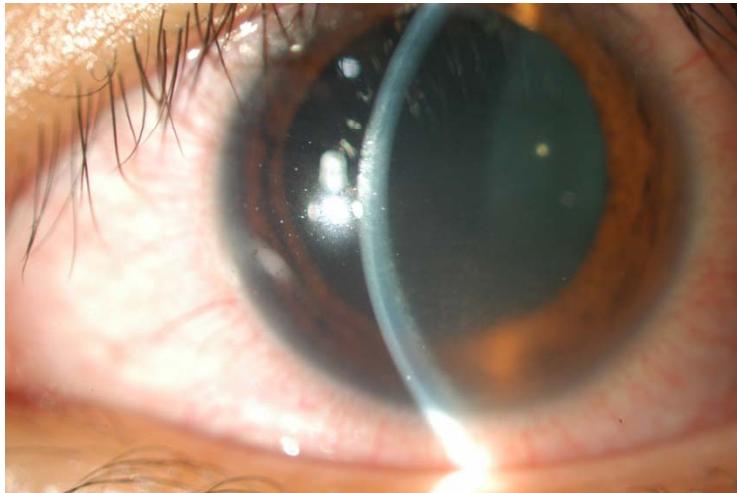
Ophthalmology Volume 108, Number 5, May 2001





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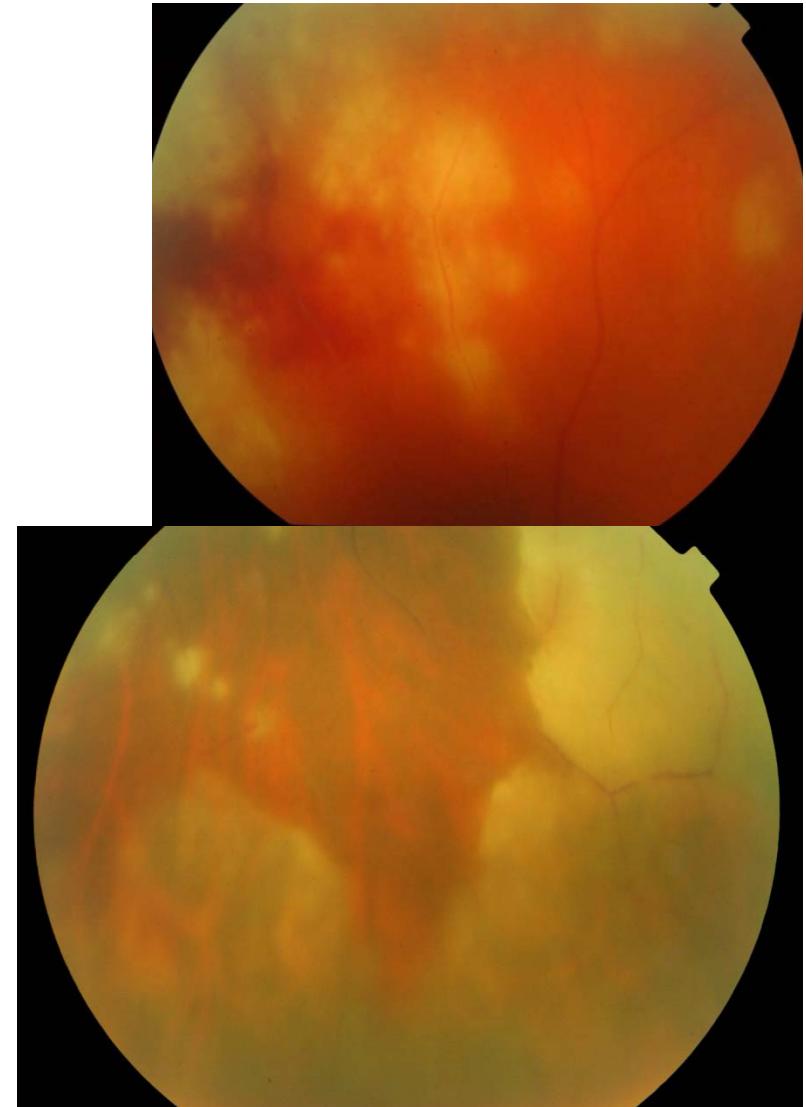
Viral retinitis – Acute Retinal Necrosis





Clinical Features

- **normal or immunosuppressed**
- **variable severity**
- **rapidly progressive**
- **pan-uveitis**
 - **retinitis**
 - **retinal vasculitis**
 - **optic neuropathy**
- **HSV 1, HSV 2, VZV**
- **high risk of ret detachment & 2nd eye involvement**





Clinical Features

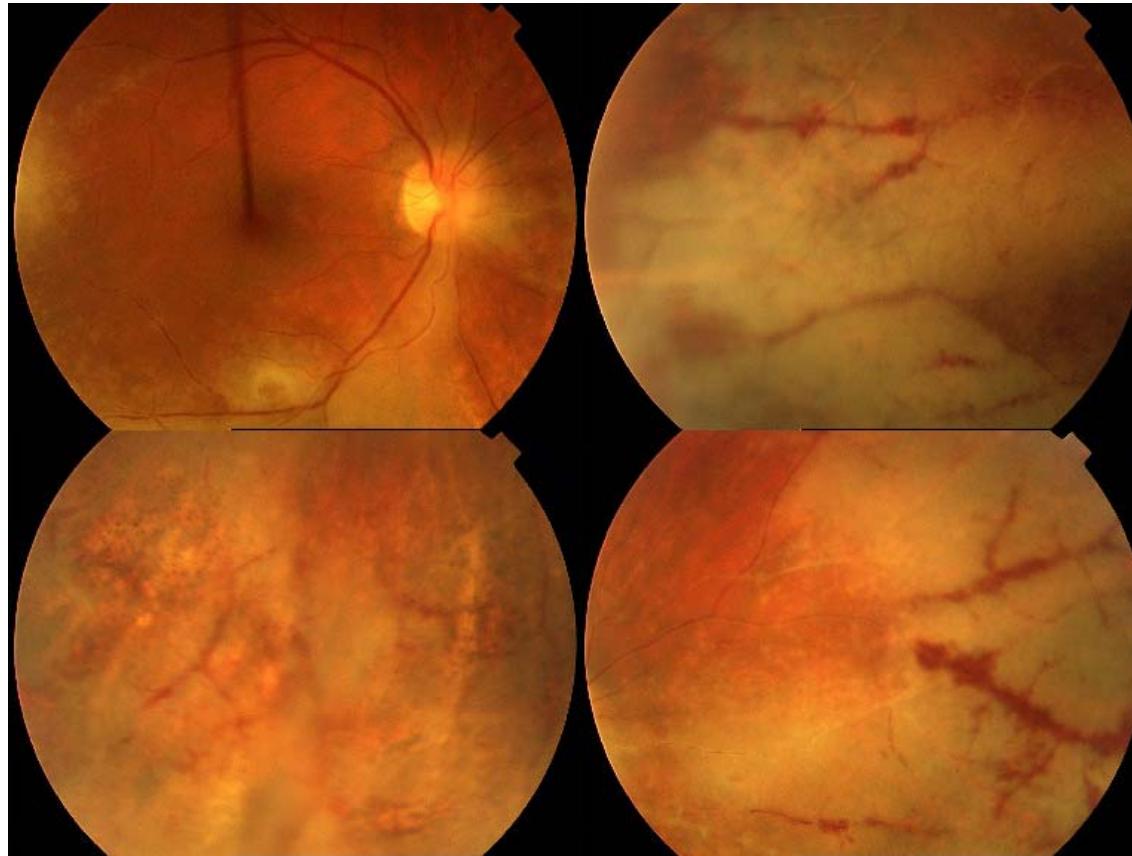
- immunosuppressed
- hyperacute ARN
- VZV infection
- widespread retinitis
 - outer retina
 - posterior pole
 - retinal vasculitis
 - optic neuropathy
- bilateral
- retina rapidly destroyed
- retinal detachment





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Viral retinitis – PORN

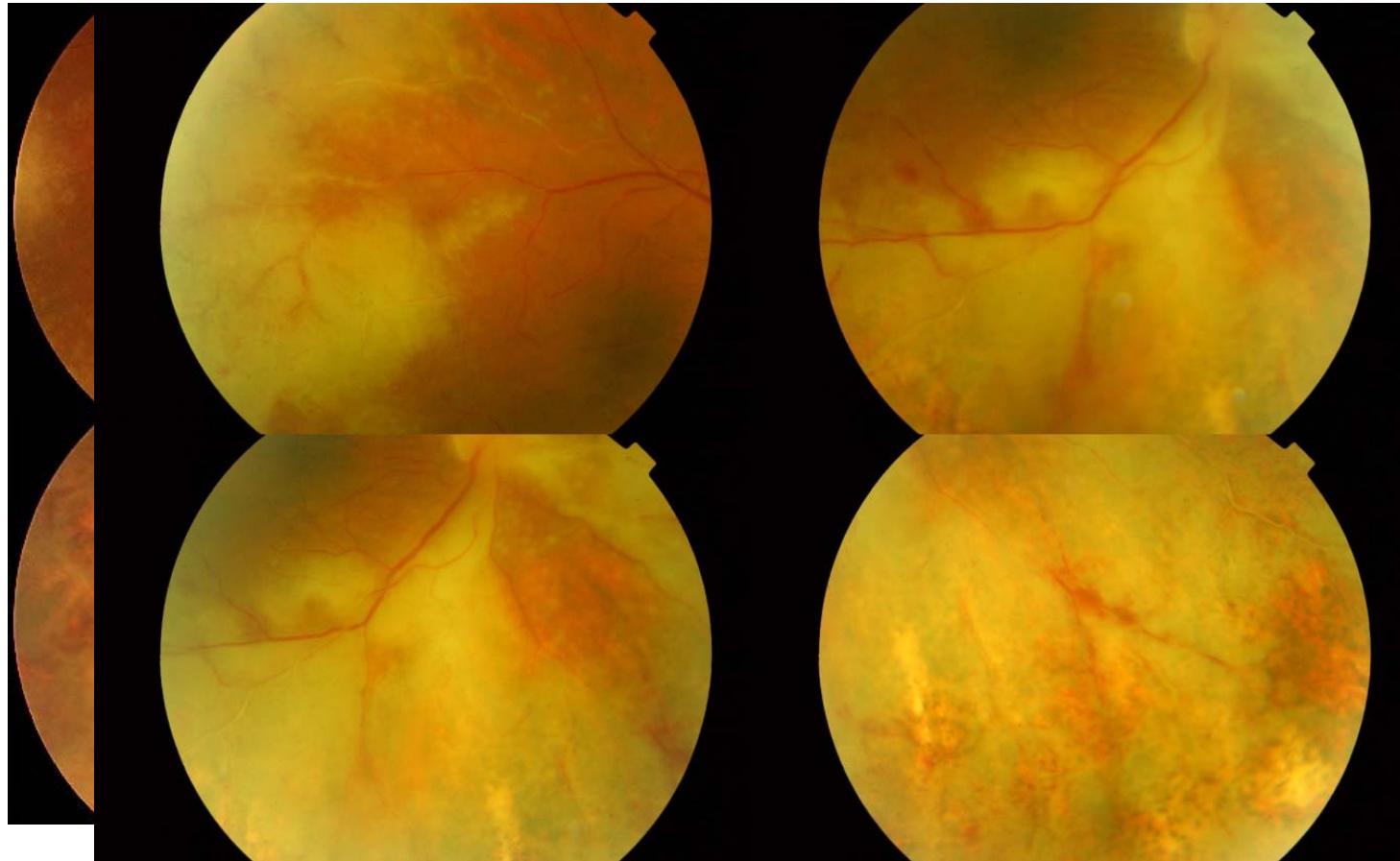


2 March 2007



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Viral retinitis – PORN



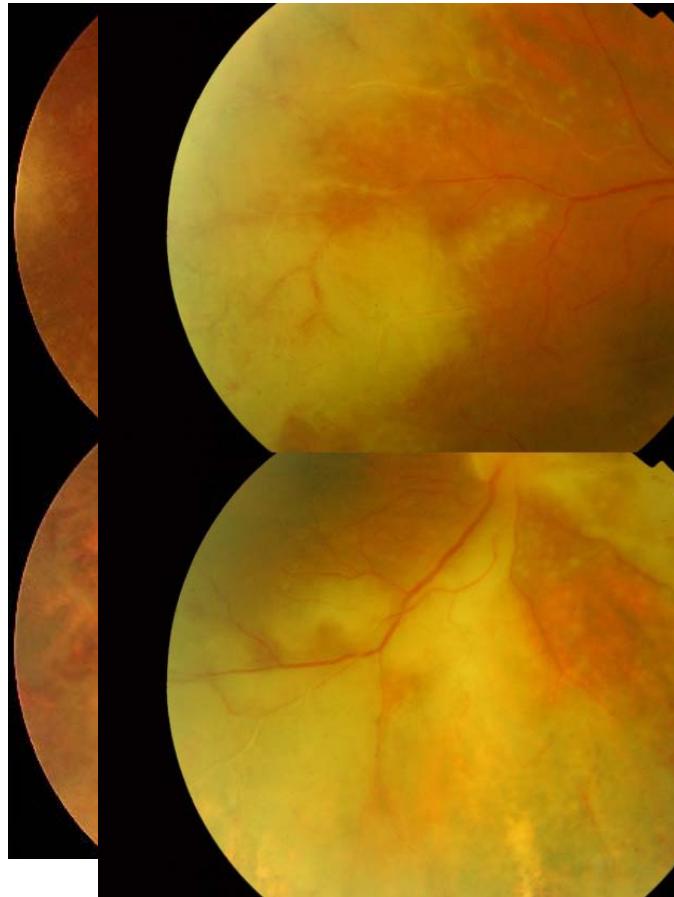
2 March 2007

7 March 2007



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Viral retinitis – PORN



2 March 2007



7 March 2007

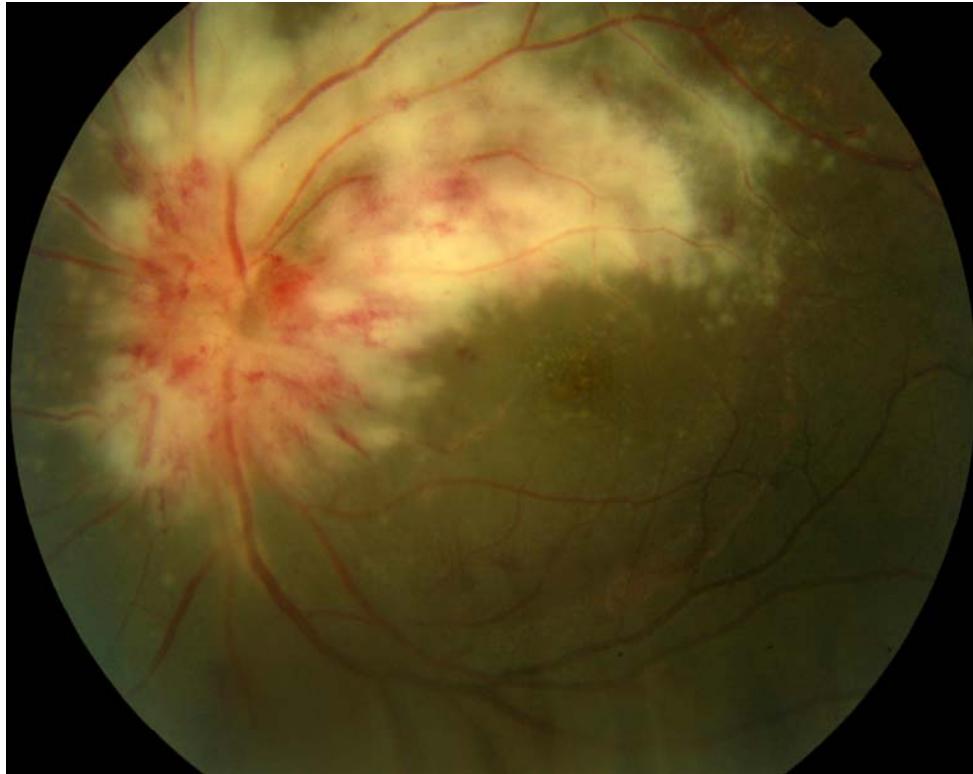


4 April 2007



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Viral retinitis – CMV





Clinical Features

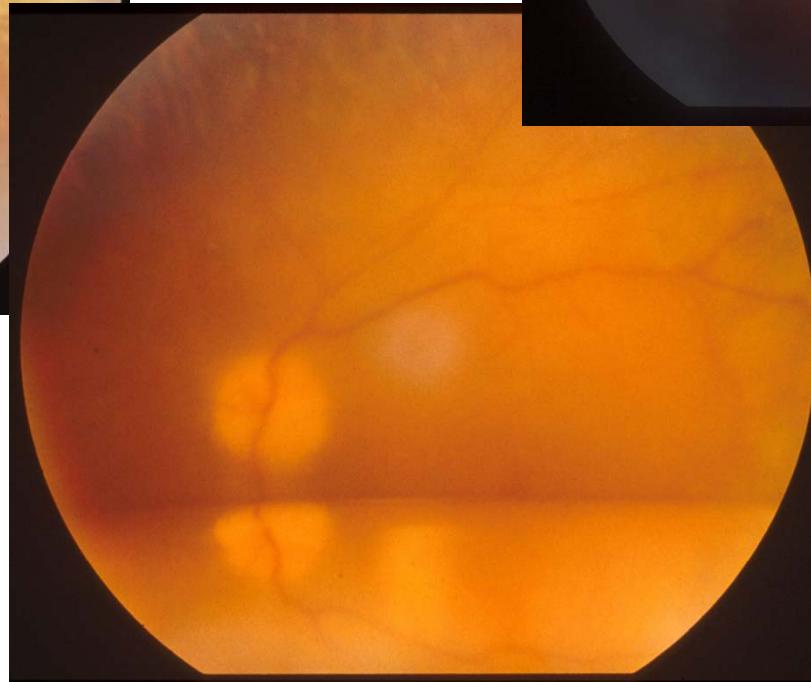
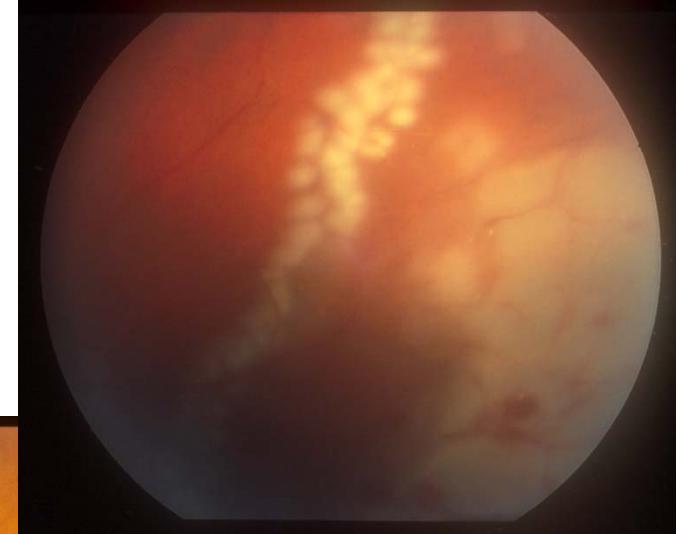
- always immunosuppressed
- slowly progressive
- often asymptomatic
- clear media
- haemorrhagic retinitis
- retinal vasculitis
- active edge and atrophic scars
- high risk of ret detachment & 2nd eye involvement





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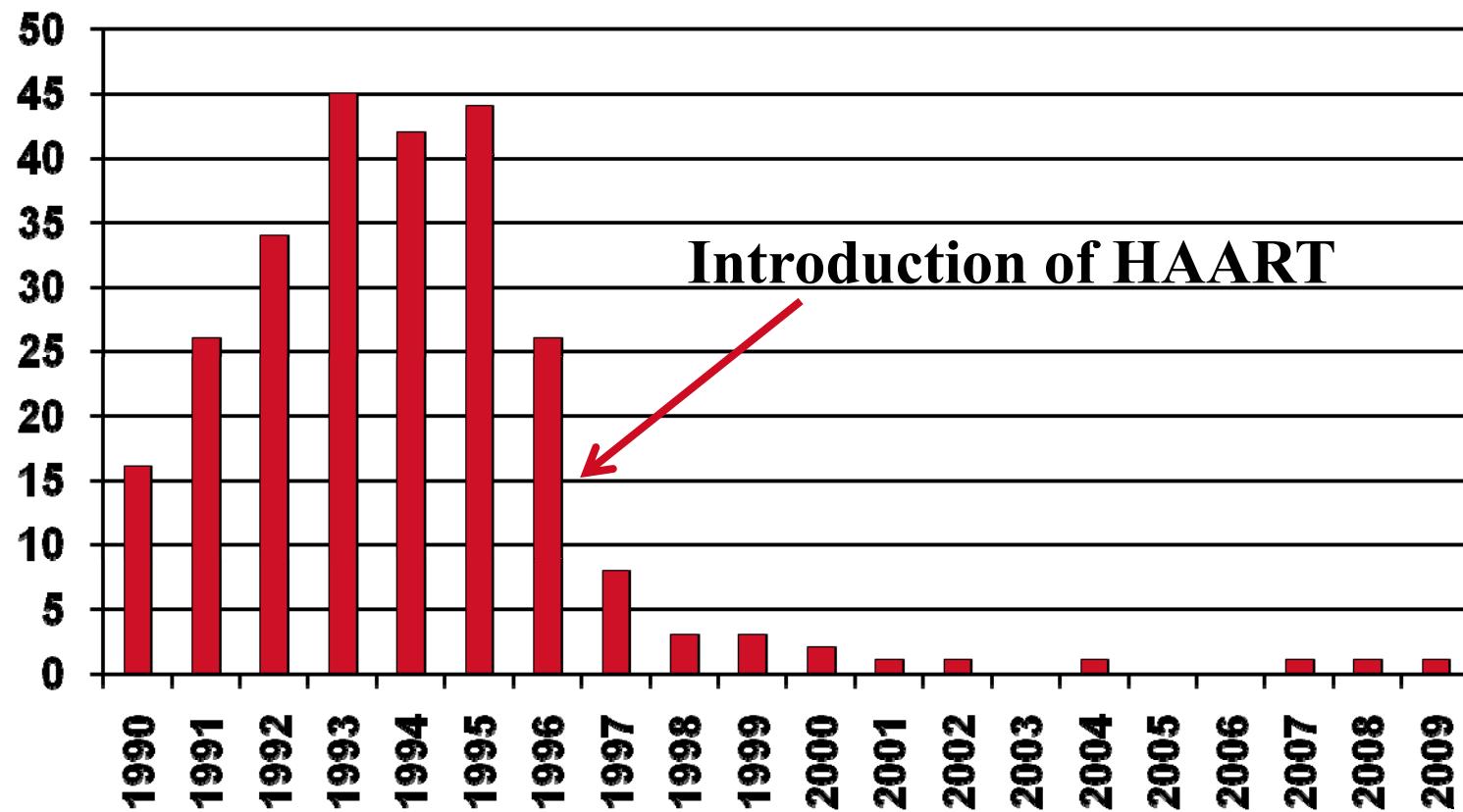
Viral retinitis – Retinal Detachment





Incidence of CMV Retinopathy

Sydney Experience





HAART and CMV retinitis

- **immune reconstitution uveitis**
 - **anterior chamber and vitreous inflammation**
 - **cystoid macular oedema**
- **regression of CMV lesions without therapy**
- **prolonged regression of CMV lesions**
- **able to discontinue CMV therapy in HAART responders**





HAART and CMV retinitis

CMV Retinitis and HAART

- new CMV infections still occur
- may be clinically impossible to determine whether CMV, VZV or HSV
- HAART failure will lead to relapse of CMV retinitis
- CMV in patients failing HAART will have similar natural history to pre - HAART CMV retinitis



Ocular Infection & Organ Transplantation

- an important cause of morbidity
- fungal endophthalmitis:
 - early – first 12 months
 - related to high grade immunosuppression
 - usually systemic fungal infection
- viral retinitis:
 - late – 3-5 years post transplant
 - related to duration of immunosuppression
 - VZV, CMV, HSV - PCR Dx
 - otherwise well

*Ng P, McCluskey PJ et al Ocular complications of heart,
lung and liver transplantation.
Brit J Ophthalmol 1998; 82:423-428.*



Viral retinitis

Acute Retinal Necrosis

- normal or I/S patient
- sudden onset
- rapidly progressive severe loss of vision
- “hot” inflamed eye
- triad of signs – peripheral retinitis, vasculitis, optic neuropathy

CMV Retinopathy

- always I/S or HIV infected
- insidious onset or asymptomatic
- slowly progressive
- clear quiet media
- characteristic retinal signs – “pizza fundus”

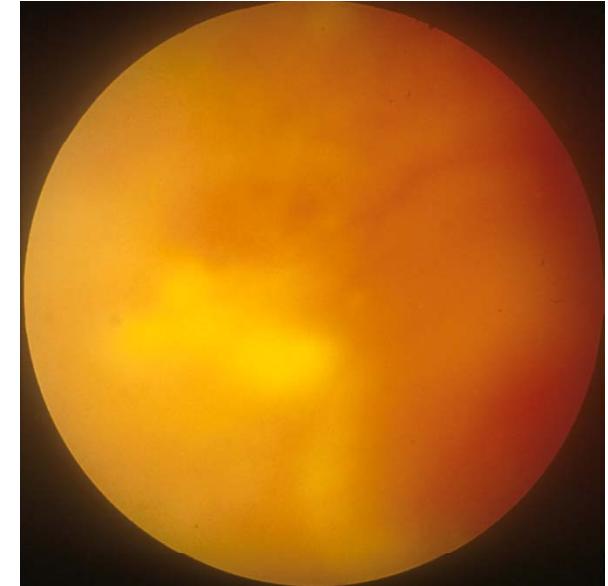
NB. Confounding effects of immunosuppression & HAART



Viral Retinitis

Role of PCR

- **clinical features non specific**
- **PCR for viral DNA in vitreous critical (\pm Toxoplasmosis PCR)**
- **PCR positive \rightarrow**
virus is cause of retinitis
- **intravitreal foscarnet at time of vitreous biopsy**





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Viral Retinitis – Differential Dx

- Toxoplasmosis
- Syphilis
- TB uveitis
- infective (metastatic) endophthalmitis
- Behcet's disease
- VKHD
- intermediate uveitis
- drug induced uveitis



Viral Retinitis

Treatment - “The Friday night special approach”

- must cover acute blinding possibilities
- may need to empirically treat multiple diseases
 - intravitreal antibiotics, antifungals & antivirals
 - systemic valtrex/acyclovir
 - systemic ciproxin, voriconazole
- high dose oral steroids
- empiric anti Toxoplasmosis therapy
- consider empiric penicillin / TB therapy



Immunocompetent

- **intravenous acyclovir 10mg/kg/day for 7 days**
- **then oral valtrex 1 gram tds for 6 weeks**
- **watch second eye**
- **systemic steroids**
- **laser demarcation**
- **?aspirin**

Immunosuppressed

- **liaise closely with physicians**
- **intravenous acyclovir 10mg/kg/day for at least 7 days**
- **then oral valtrex 1 gram tds for at least 6 weeks**
- **watch second eye**
- **local Rx useful**
- **often need ongoing suppressive therapy**



Management of CMV Retinopathy

Systemic

- biphasic treatment regimen

intravenous

- ganciclovir
- foscarnet
- combination Rx

oral

- valganciclovir

Local

- biphasic treatment regimen

intravitreal

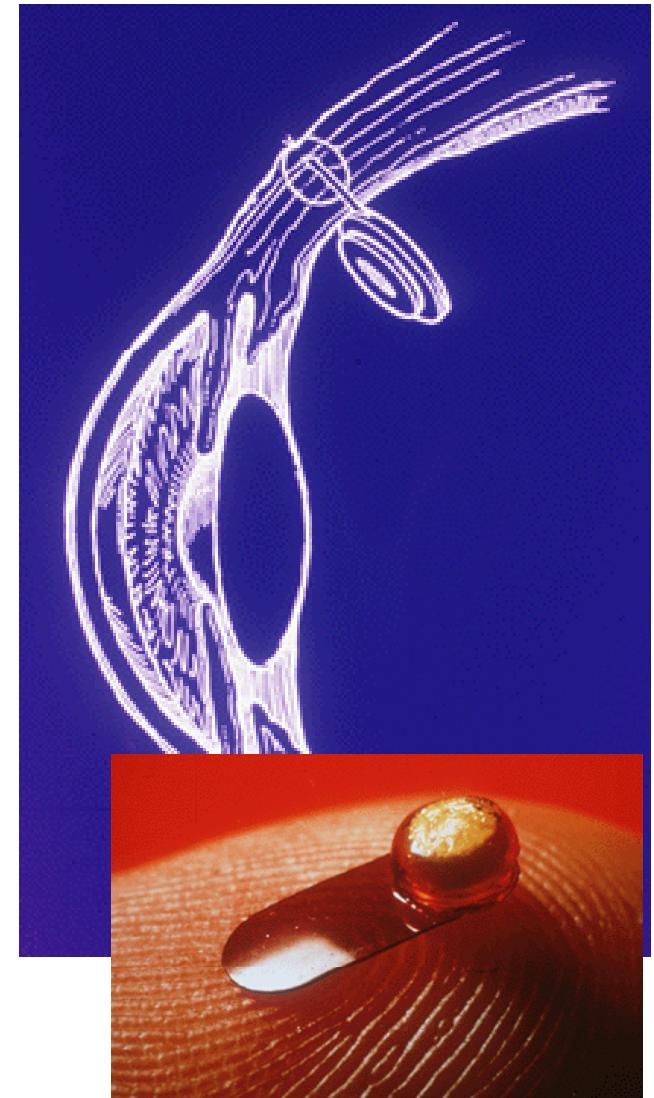
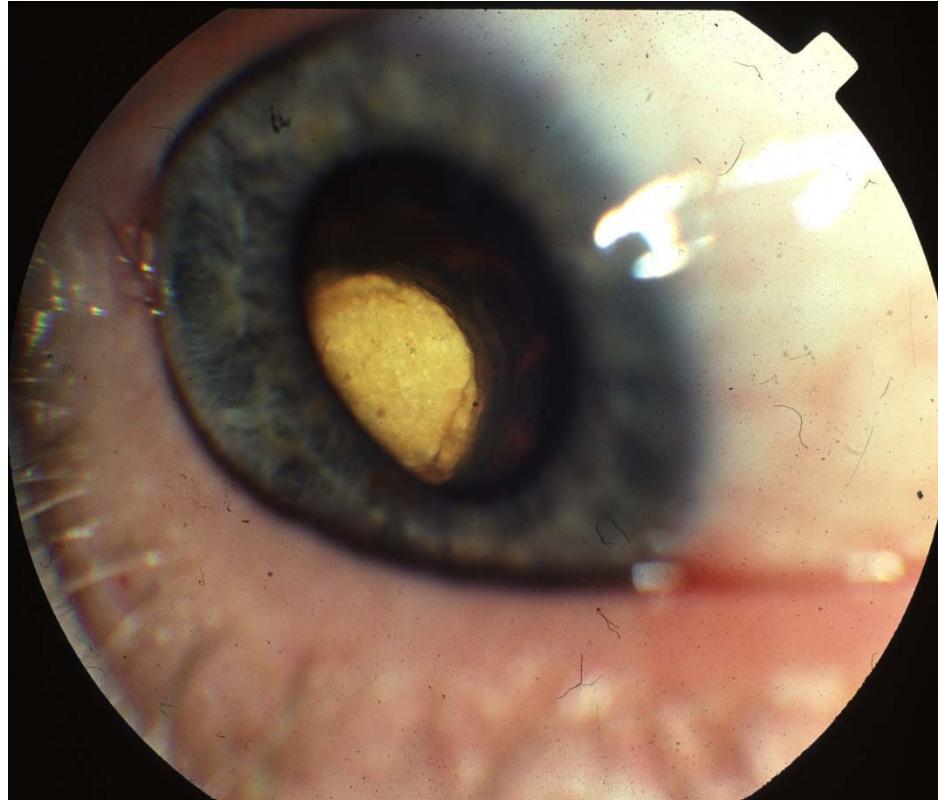
- ganciclovir
- foscarnet

- ganciclovir implant



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Ganciclovir implant





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Ganciclovir implant





Viral Retinitis

Take Home Messages

- rapidly progressive irreversible vision loss common eg herpetic retinitis (ARN)
- acute and chronic vision threatening disorders
- immunosuppression a clinical confounder
- increasing range of systemic and local therapies



- Ophthalmologists are real physicians and can help
- need help managing complex medical disease