CMV Retinitis

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Medical Action Myanmar

GreenShoots
FOUNDATION

“Support needing populations through medical assistance and the transfer of knowledge to local medical practitioners.”

Our vision for the

Medical Assistance & Medical Education (MAME) Programs

GreenShoots FOUNDATION

CMV Retinitis

CMV epidemiology

- There is >90% sero-positivity for CMV in the developing world.
- It is the most common opportunistic infection of the eye and accounts for over 90% of HIV-related blindness.
- In resource-limited settings, CMV retinitis is the only clinical manifestation of CMV disease that we can diagnose.
- In the USA, pre-ART, there was a 2%/month (24%/year) incidence of CMV retinitis in patients with CD4<50 cells (*NEJM 1996 June 6;334(23):1491-7.)*

CMV retinitis epidemiology

- CMV retinitis is arguably the most neglected disease of the AIDS pandemic (5). It remains largely undiagnosed and untreated in most resource-limited settings, and therefore determining the true prevalence is difficult.
- Cambodia, Myanmar, Thailand [2007];
  - 25% of patients with CD4<50 had CMV retinitis (5).
  - 33-44% was asymptomatic
- A recent review found that the prevalence of CMV retinitis in resource-limited settings, notably Asian countries, remains high (6).

CMV

- Many late presenting HIV positive patients die of CMV or are left permanently blind, many at young age, from undiagnosed or inadequately treated cytomegalovirus retinitis.

CMV retinitis in high income countries

- Diagnosis with indirect ophthalmoscope
- Treatment with
  - systemic anti-CMV treatment (oral valganciclovir),
  - +/- intraocular ganciclcovir.

CMV retinitis in resource limited settings

- Diagnosis; Indirect ophthalmoscopy rarely performed.
- Usually no diagnosis ….. and no treatment

- In Thailand (National protocol) and some projects in Cambodia, China and Myanmar,
  - Oral valganciclovir too expensive
  - Ganciclovir eye injection to prevent blindness.
  - When patients get ART, it is hoped that the immune system will recover soon enough to prevent mortality from extra-ocular CMV disease.

A CMV retinitis project in Myanmar

and Cambodia, China, South Africa, Thailand and Uganda

- David Heiden (Ophthalmologist) trained since 2006 yearly 6 HIV clinicians (for 1 week) in indirect ophthalmoscopy and intraocular injections
- Evaluation of training by a variety of methods documented high clinical competence.
- Systematic screening of all high-risk patients (CD4 <100 cells/mm3) was carried out in 10 separate AIDS clinics throughout Myanmar.

Diagnosis

- The clinical “gold standard” is examination of the entire retina with an indirect ophthalmoscope through a dilated pupil by a skilled examiner.
- Diagnosis is based on pattern recognition

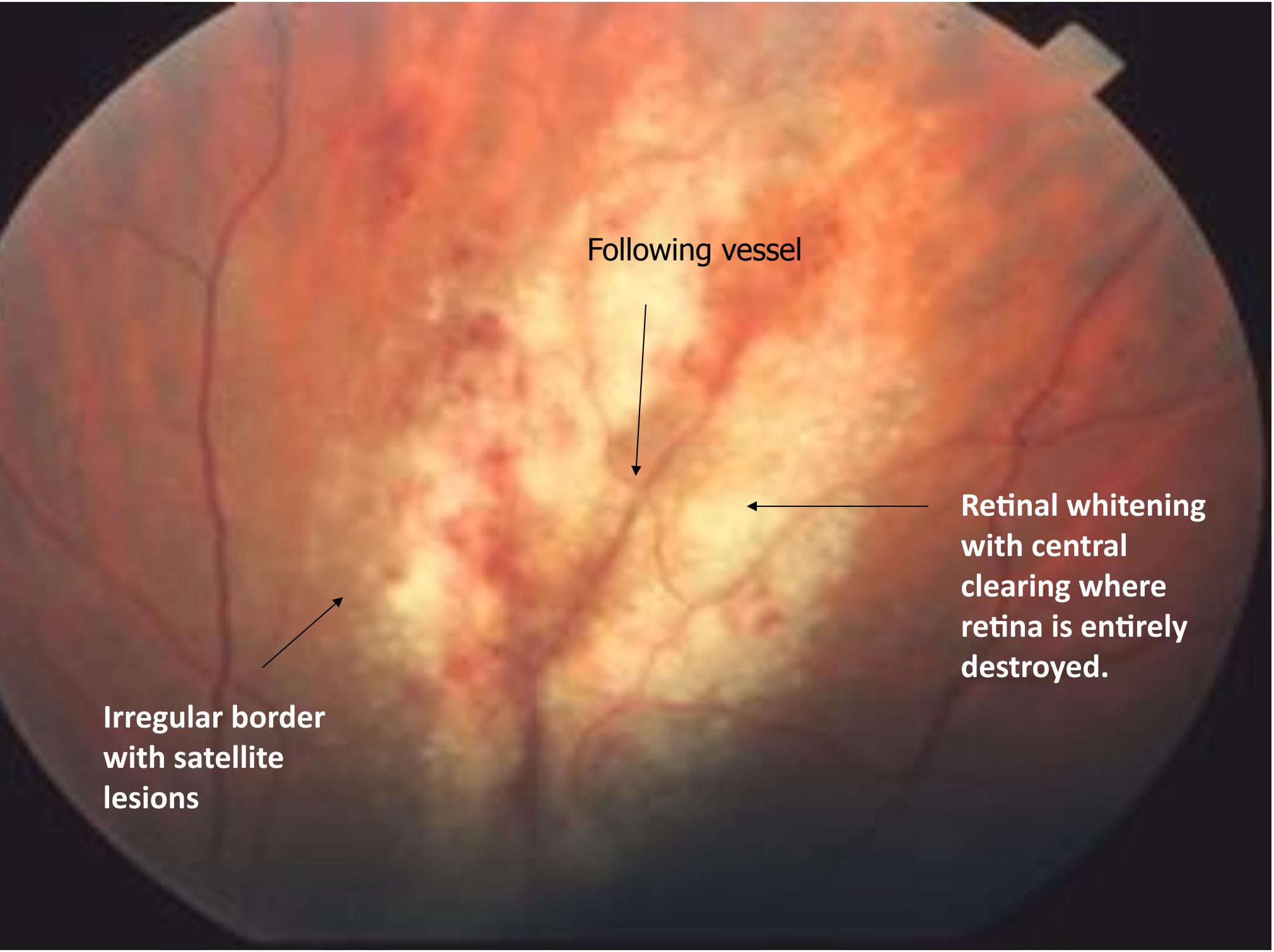
Pattern Recognition

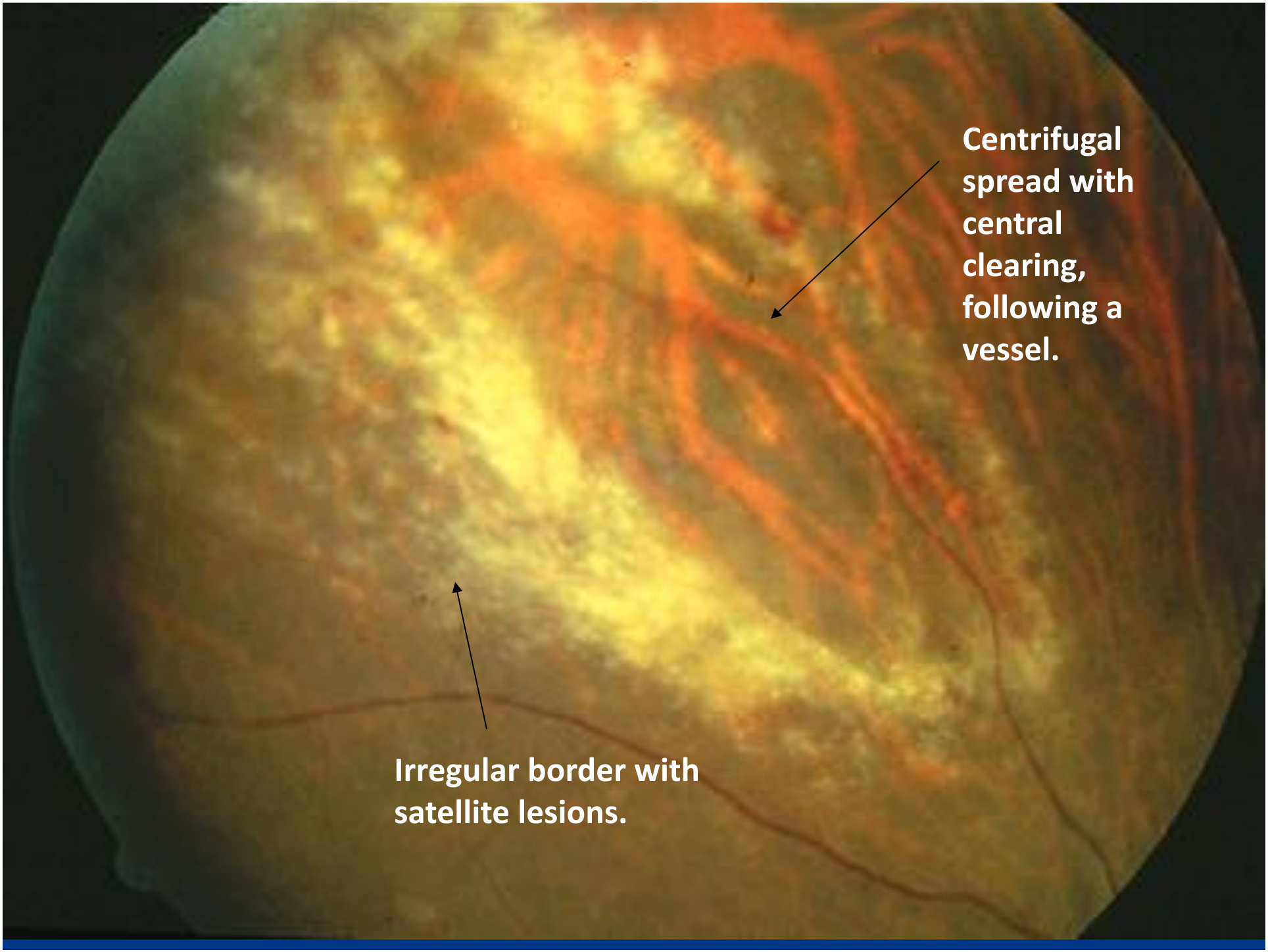
1. Dense opaque retinal whitening
2. Irregular border with small white satellite lesions
3. Centrifugal spread with Central clearing
4. Tends to follow vessels
5. Hemorrhage, but this is highly variable

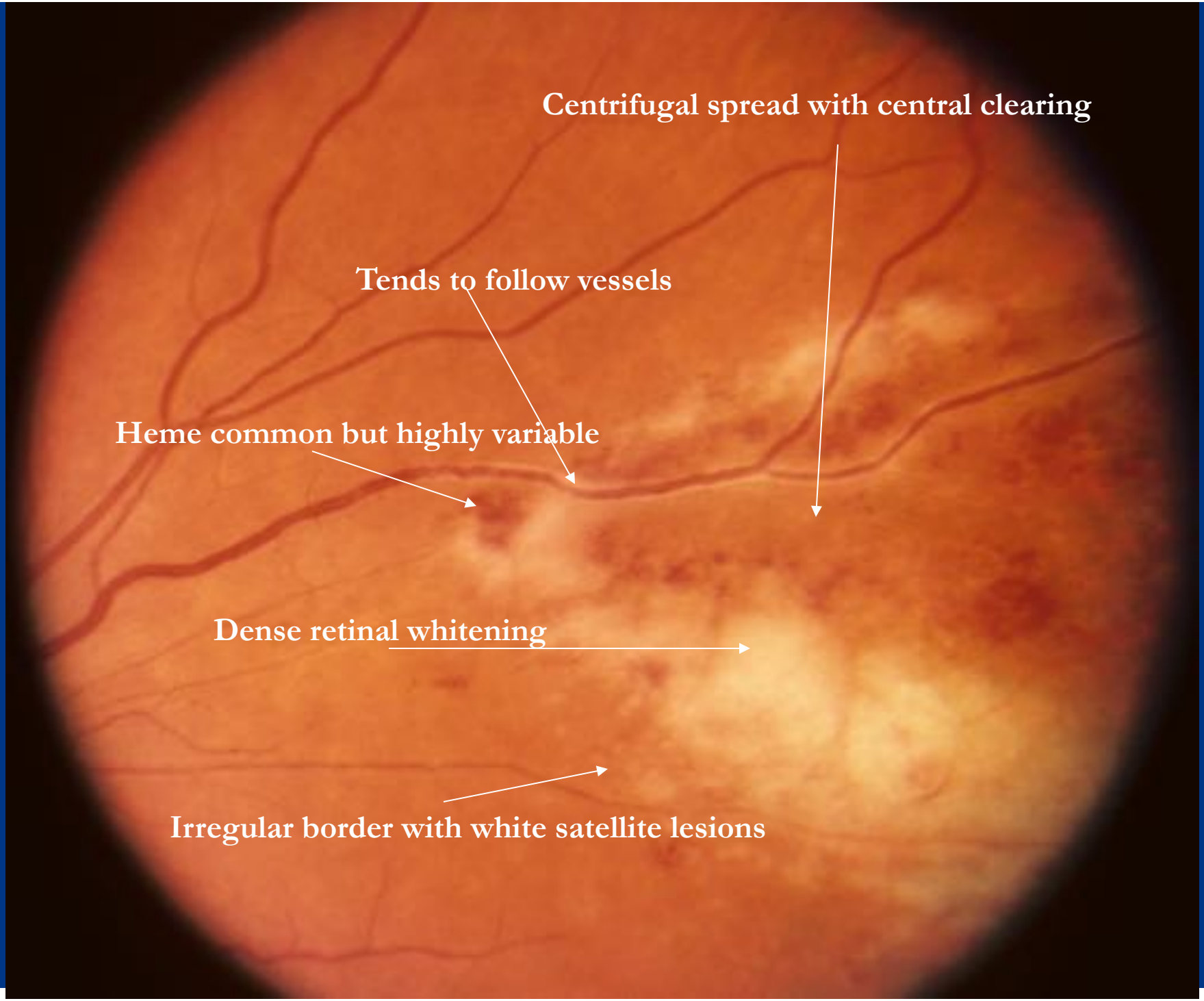
CWS

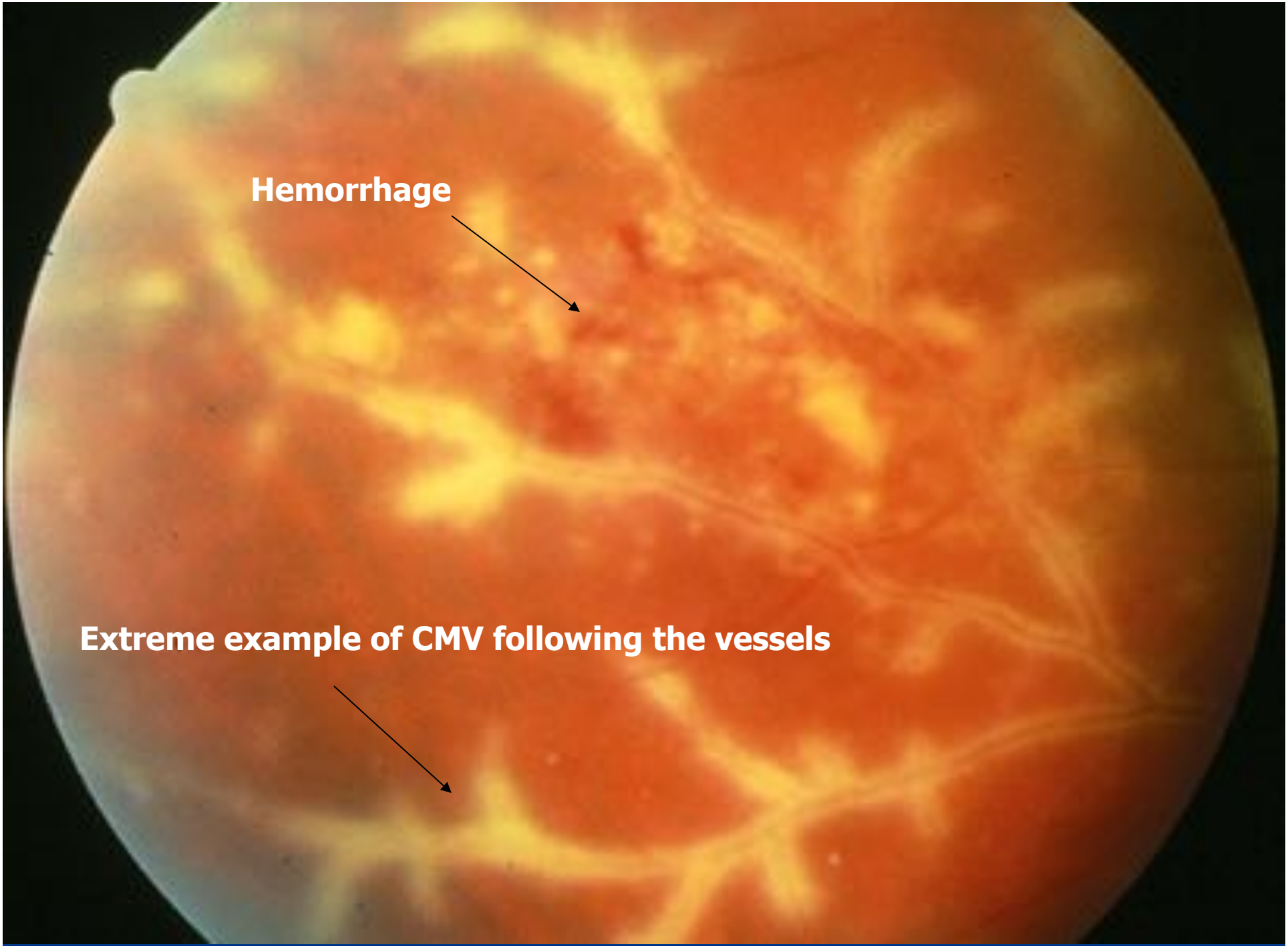
CWS

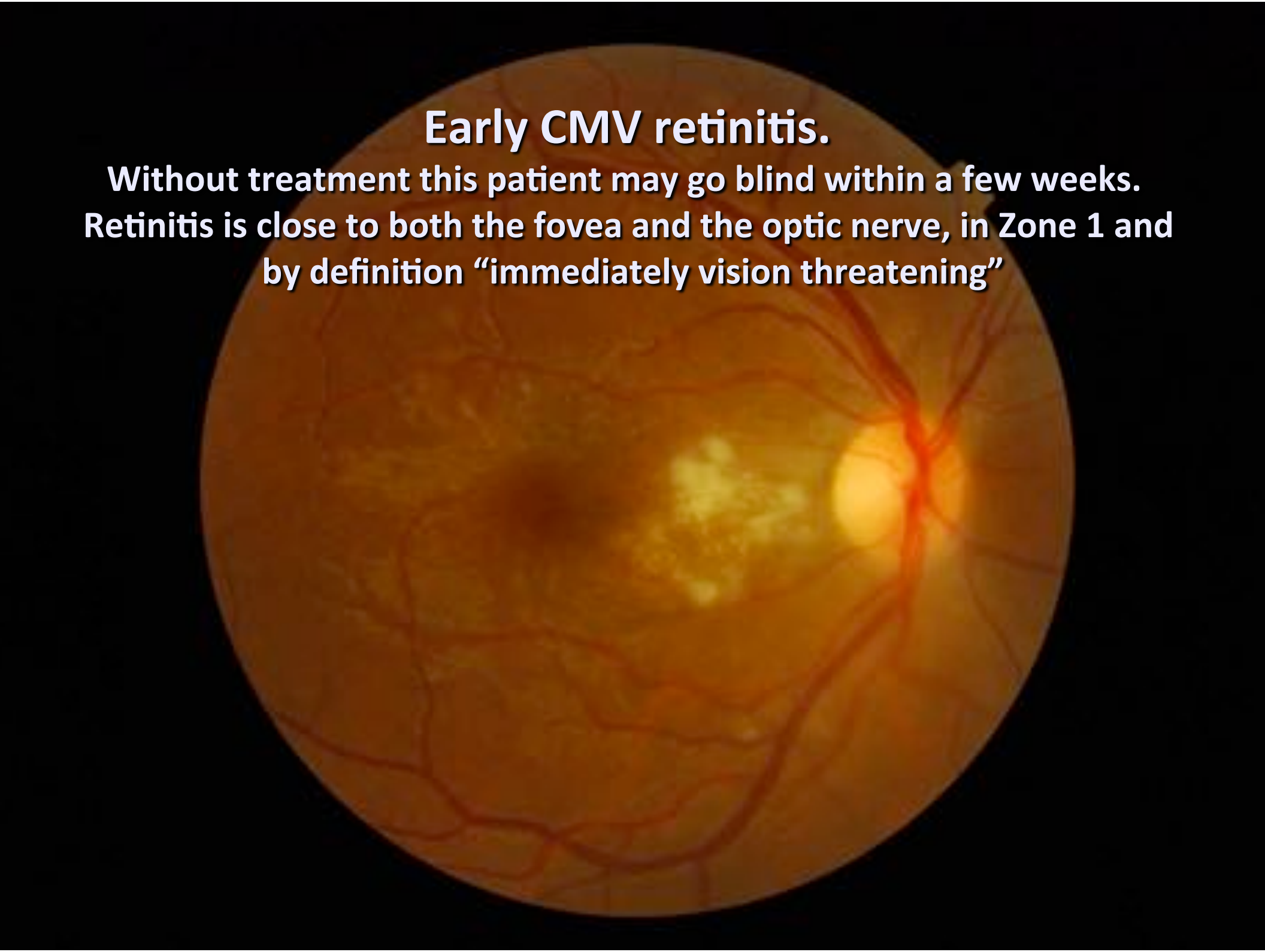
CMV retinitis

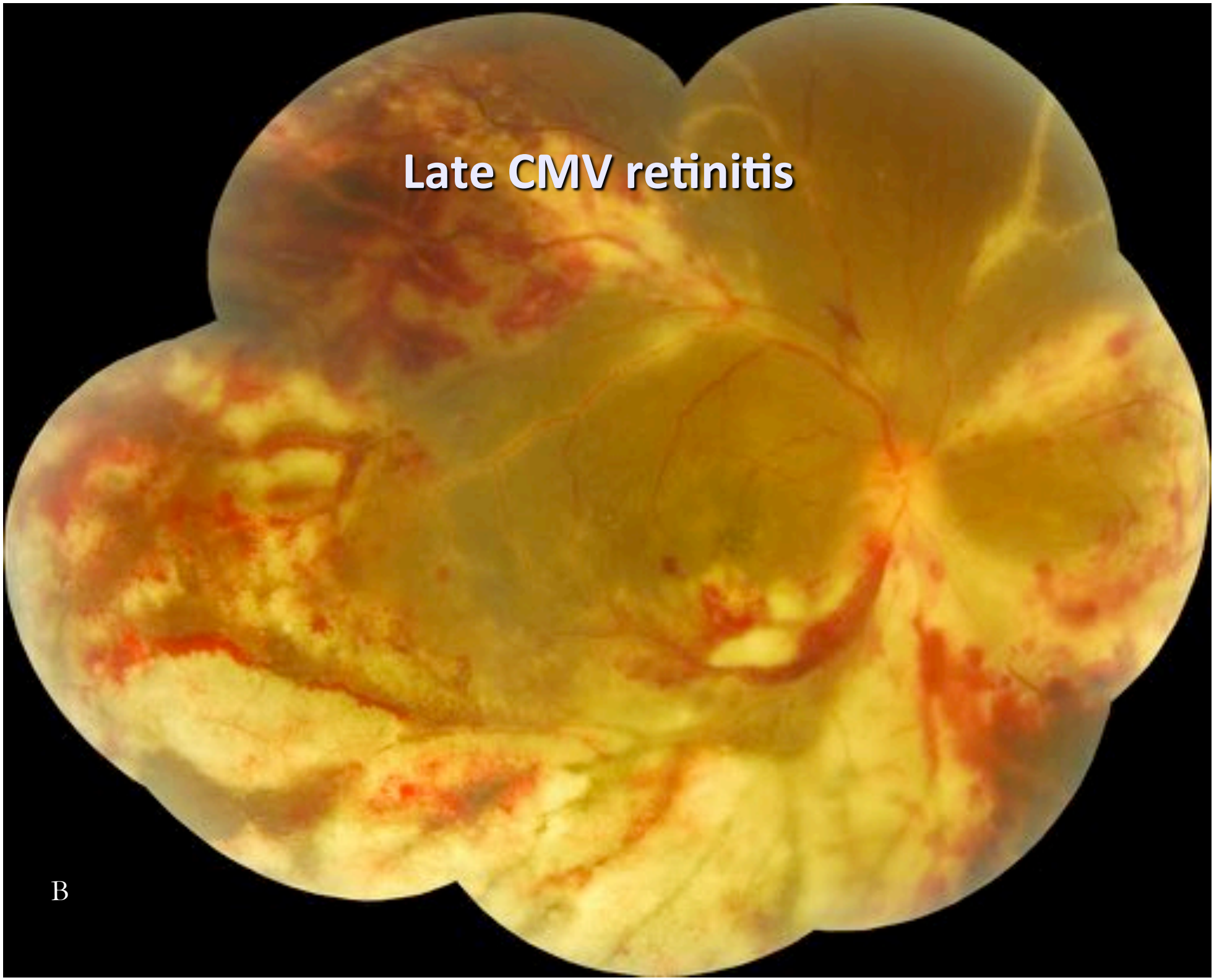

Following vessel
Retinal whitening with central clearing where retina is entirely destroyed.
Irregular border with satellite lesions


Centrifugal spread with central clearing, following a vessel.
Irregular border with satellite lesions.


Centrifugal spread with central clearing
Tends to follow vessels
Heme common but highly variable
Dense retinal whitening
Irregular border with white satellite lesions


Hemorrhage
Extreme example of CMV following the vessels


Early CMV retinitis.
Without treatment this patient may go blind within a few weeks.
Retinitis is close to both the fovea and the optic nerve, in Zone 1 and
by definition “immediately vision threatening”


Late CMV retinitis
B


The classic descriptions: “cottage cheese and catchup” or
“pizza pie”

Do not rely on Symptoms

- CMV retinitis does not cause redness or pain.
- Characteristic symptoms include floaters, scotoma (holes in vision), photopsia (flashing lights) and blurred vision.
- Although some studies report high prevalence of symptoms, they are often discounted or ignored, leading to late presentation of disease
- A study by MSF/B in Cambodia reported 44% of patients with CMV retinitis had no symptoms.

CMV screening criteria

- CD4 <100 cells/ul
- CMV related eye complaints. (floaters, scotoma ….)
- Features of systematic CMV infection.
- Patients with CWS are re-examined q 3 weeks until resolved
- Patients with normal retinas re-screened 3 monthly as long as the CD4 count remains <100

A CMV retinitis project in Myanmar

- Data from 2007-2009 in 2 clinics in Yangon (7);
  - Screening was done for 891 patients
  - CMV retinitis was diagnosed in 24% (211/891).
  - Bilateral disease was present in 36% of CMV patients.
  - A total of 1296 injections were administered.
  - There was a single case of infectious endophthalmitis.
- Since 2007 till 2014 thousands of patients have been screened in 10 clinics through this project.
- Approx. 1,000 patients with CMV retinitis have been treated with intraocular injections.

Anti-CMV Treatment

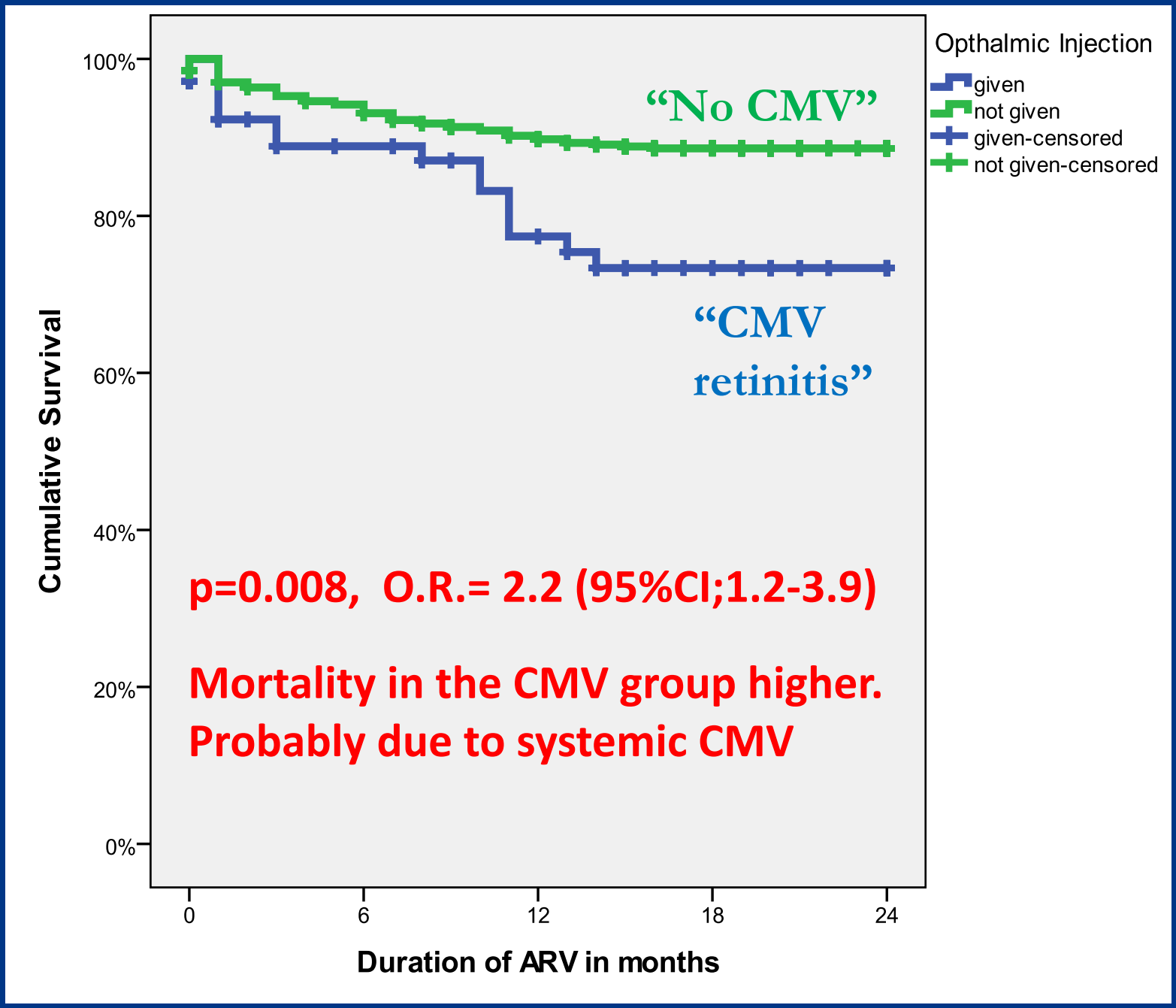
Ganciclovir administered systemically (daily intravenous infusion), or locally (intraocular injection).

Valganciclovir, a well-absorbed oral prodrug of ganciclovir, can achieve equivalent blood levels and is equally effective.

Local Anti-CMV treatment

Intraocular ganciclovir injection

2.5mg in 0.05ml, every week


Opthalmic Injection
given
not given
given-censored
not given-censored
"No CMV"
"CMV retinitis"
Cumulative Survival
100%
80%
60%
40%
20%
0%
0
6
12
18
24
Duration of ARV in months
p=0.008, O.R.= 2.2 (95%CI;1.2-3.9)
Mortality in the CMV group higher.
Probably due to systemic CMV

- Blindness has been prevented
- But mortality remains high.

How can we decrease CMV blindness and mortality in Myanmar?

- Systematic screening of patients CD4<100
- Management of CMV retinitis at the primary care level is feasible in resource-poor settings.
- With appropriate training and support, CMV retinitis can be diagnosed and treated by AIDS clinicians (non-ophthalmologists), just like other major opportunistic infections.
- Oral valganciclovir should be made available for the treatment of CMV retinitis to prevent blindness **and** reduce mortality.

November 2006

November 2007

A woman with AIDS, totally blind in right eye and raging infection in left eye. Complete blindness expected soon.

One year follow up. Ganciclovir into the left eye (5x) and vision saved

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Thank you

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