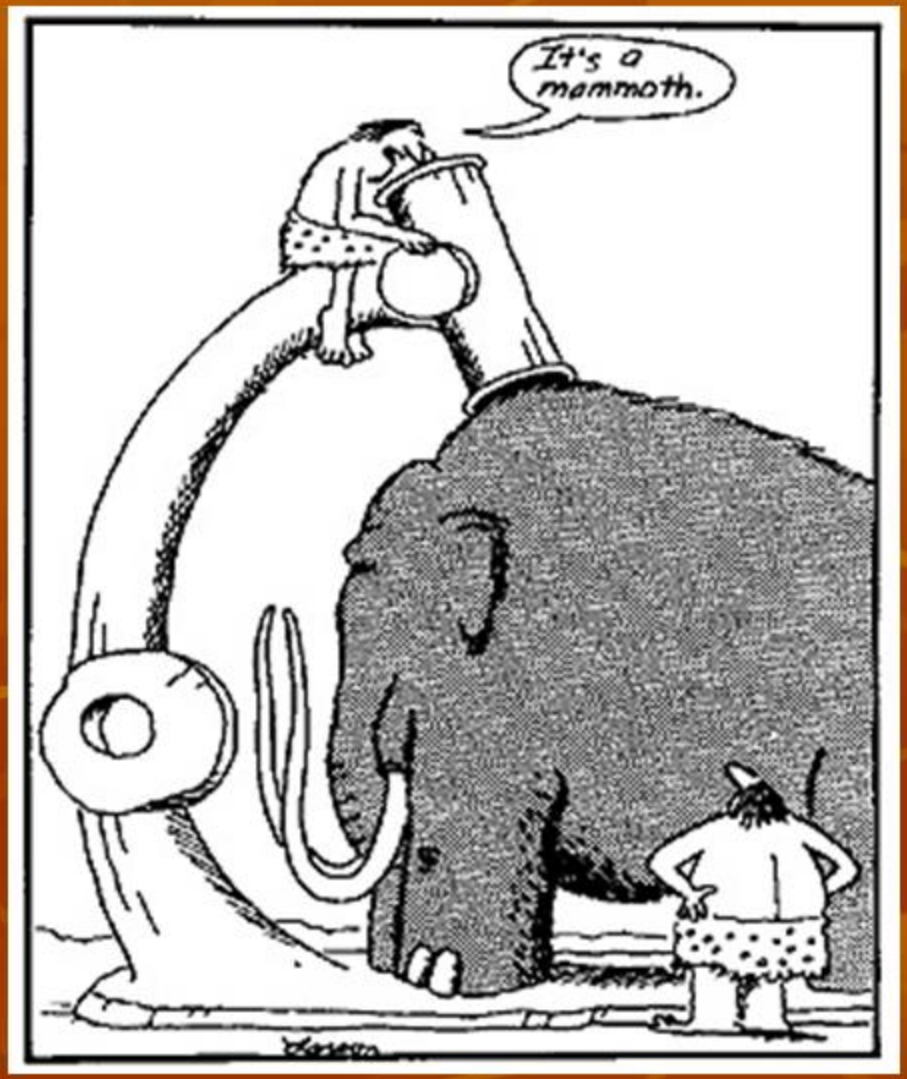
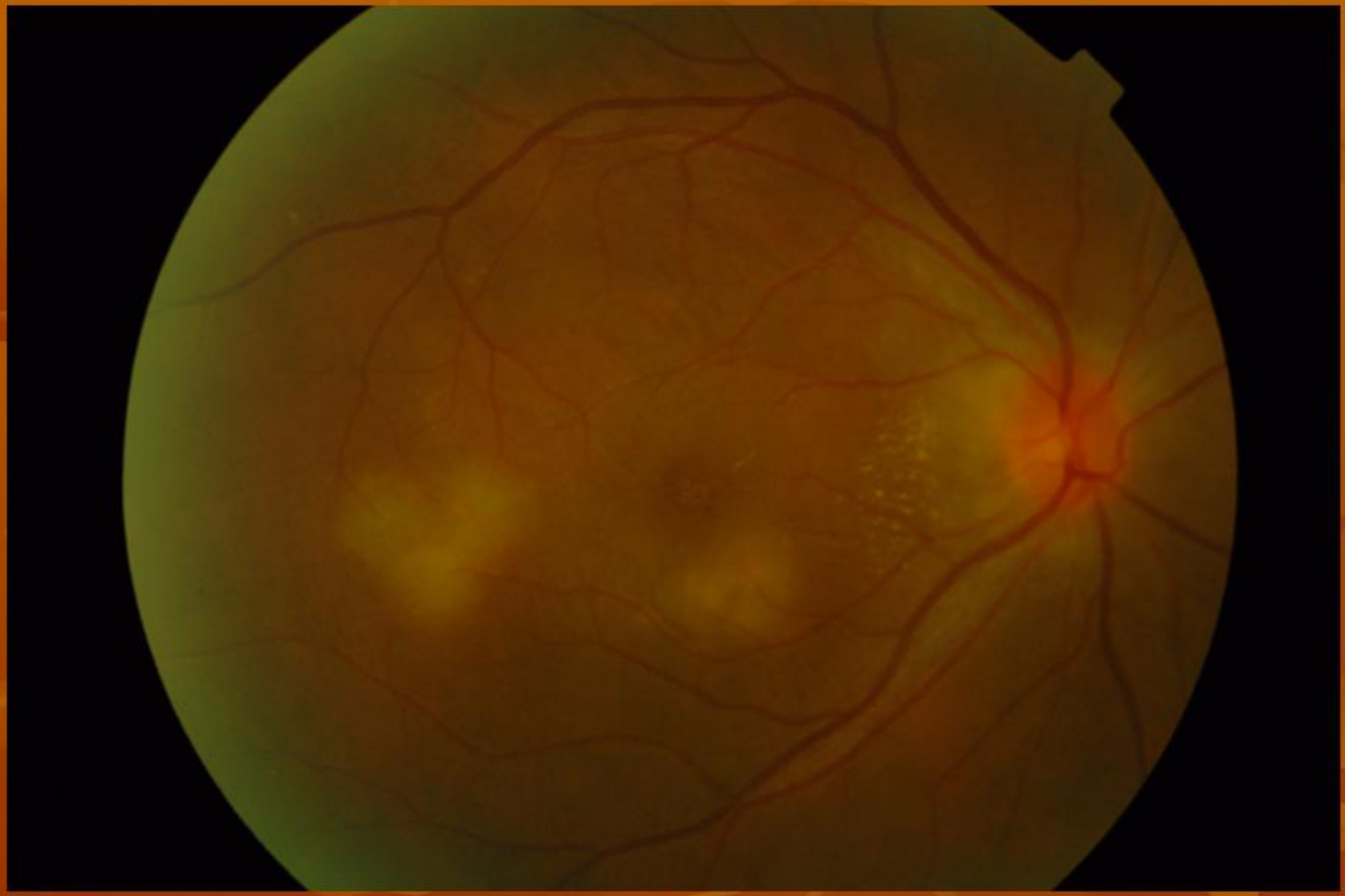
# TB or not TB

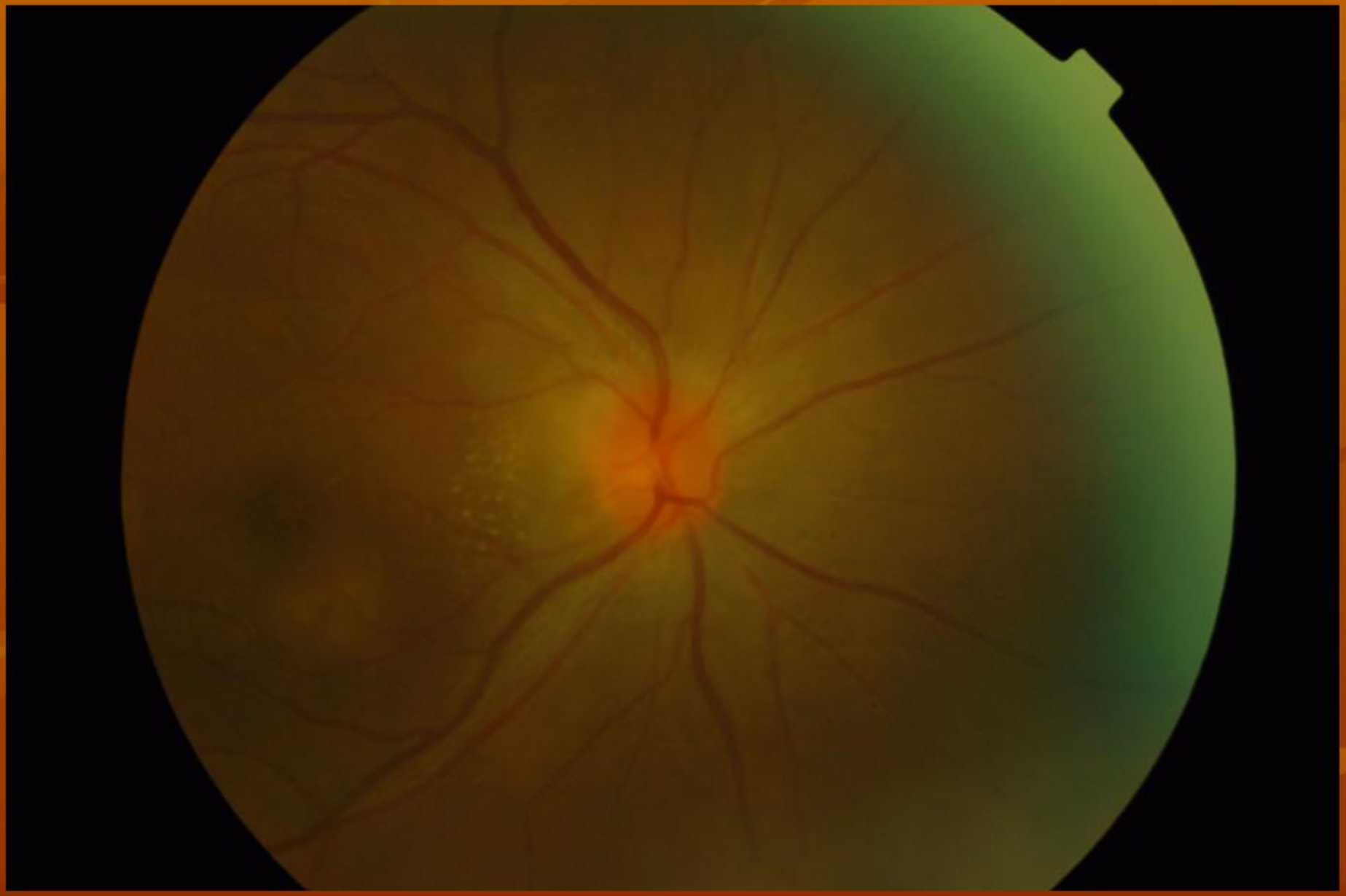
Dr Danny Mitry


It's a mammoth.

- 54 yo Indian woman
- Sept 2013 – 5/7 hx painless blurring of vision RE
- VA RE 6/36 (6/18) LE 6/9
- Seen in India 6/12 previously with similar complaint – HIV neg, MRI, VEPs – NAD
- Given IV steroids – no diagnosis made

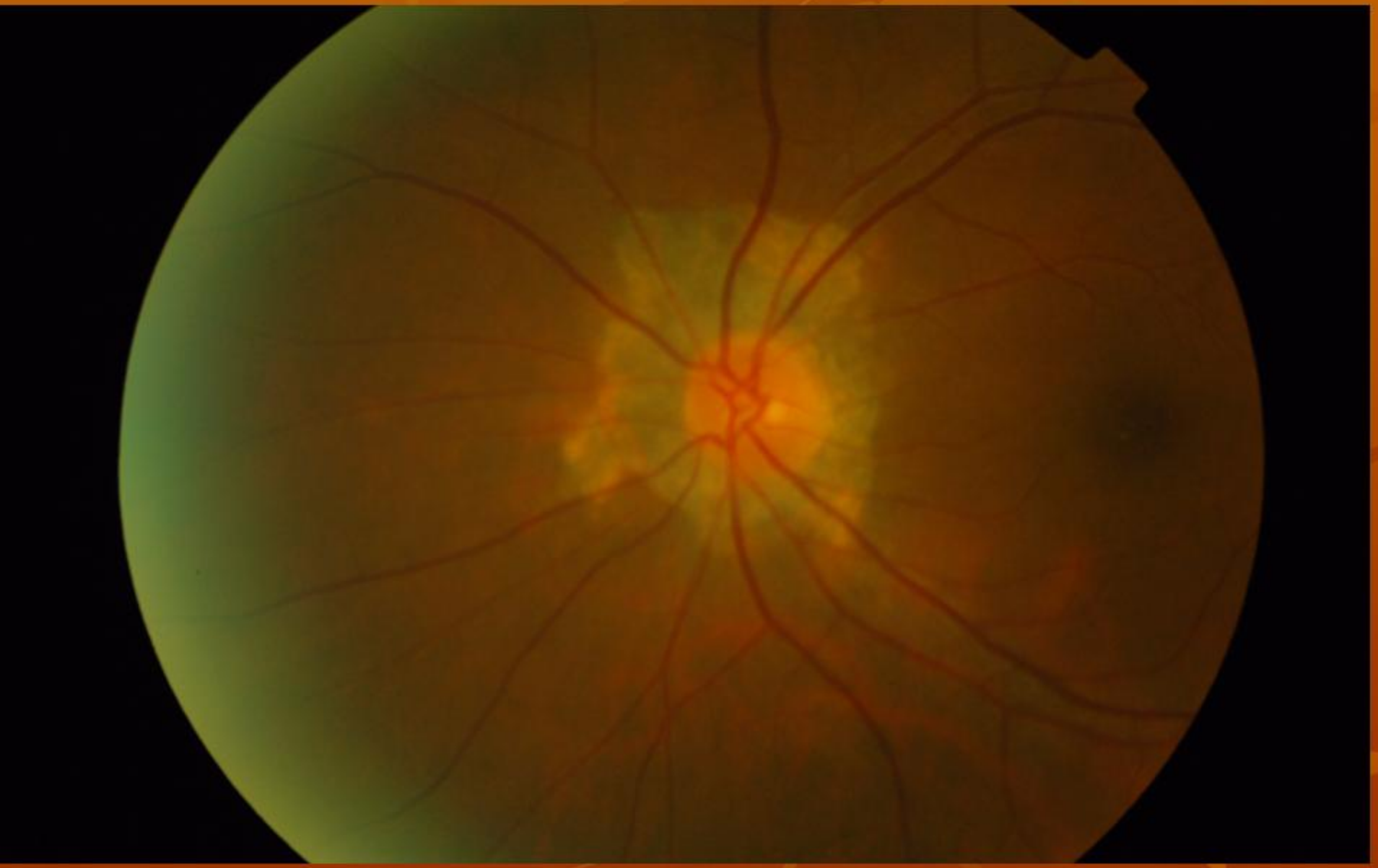
- IOP 15|16
- A/C - quiet
- Vitreous – quiet





- Anything else on history?

- Anything else on examination?



# Thoughts?

- I would have to be on call today…

- Quick find Moloy

# DDx

– Focal/diffuse choroidal and retinal inflammation

- Non-infectious
- Infectious
- Masquerade

- **Non-infectious**
  - WDS (APMPEE, Serpiginous, MEWDS, Birdshot, MCP, PIC AZOOR)
  - Bechets
  - Lupus
  - Sarcoid
  - VKH
  - Sympathetic

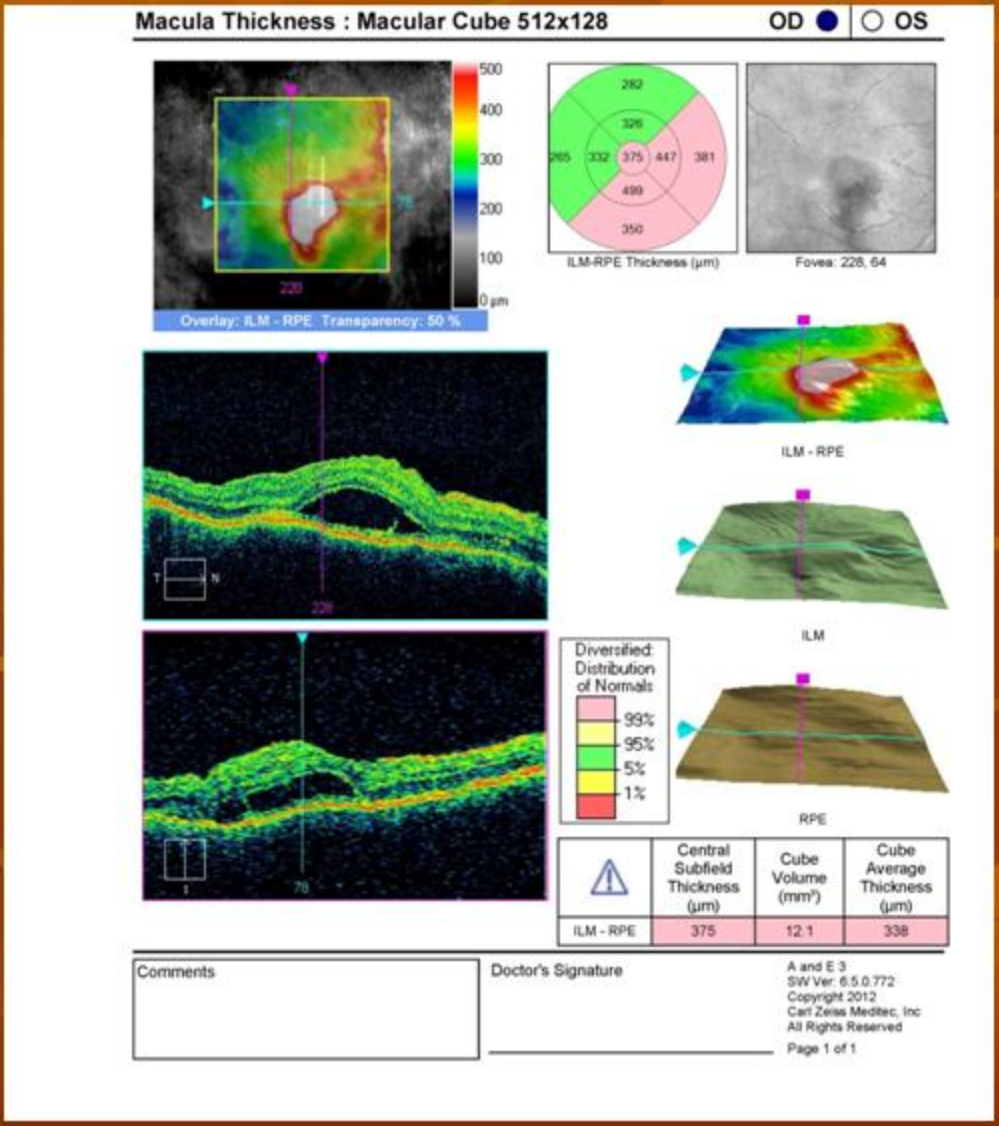
- **Infectious**
  - TB
  - CMV
  - ARN
  - Endogenous endophthalmitis
  - Syphilis
  - Cat-scratch
  - Toxo
  - Lyme
  - DUSN

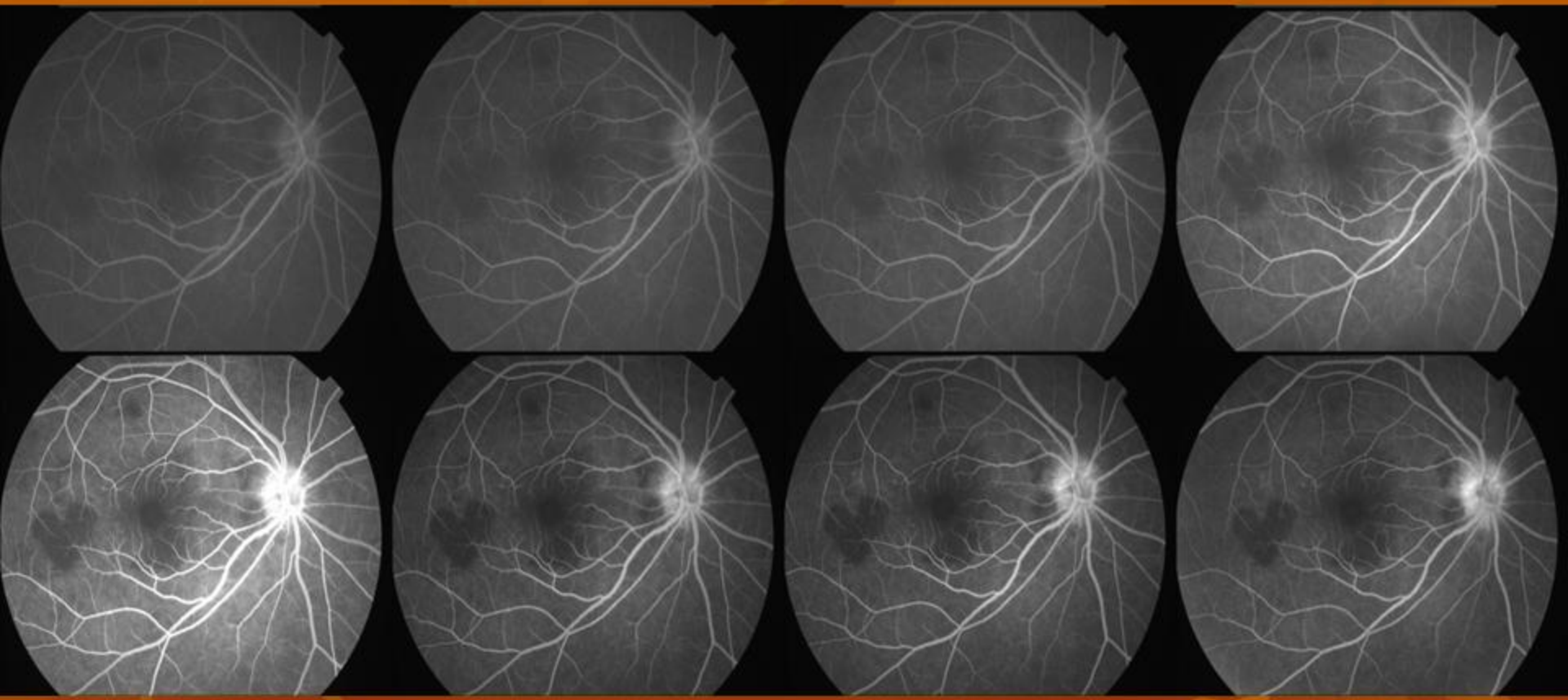
- **Masquerade**
- Lymphoma

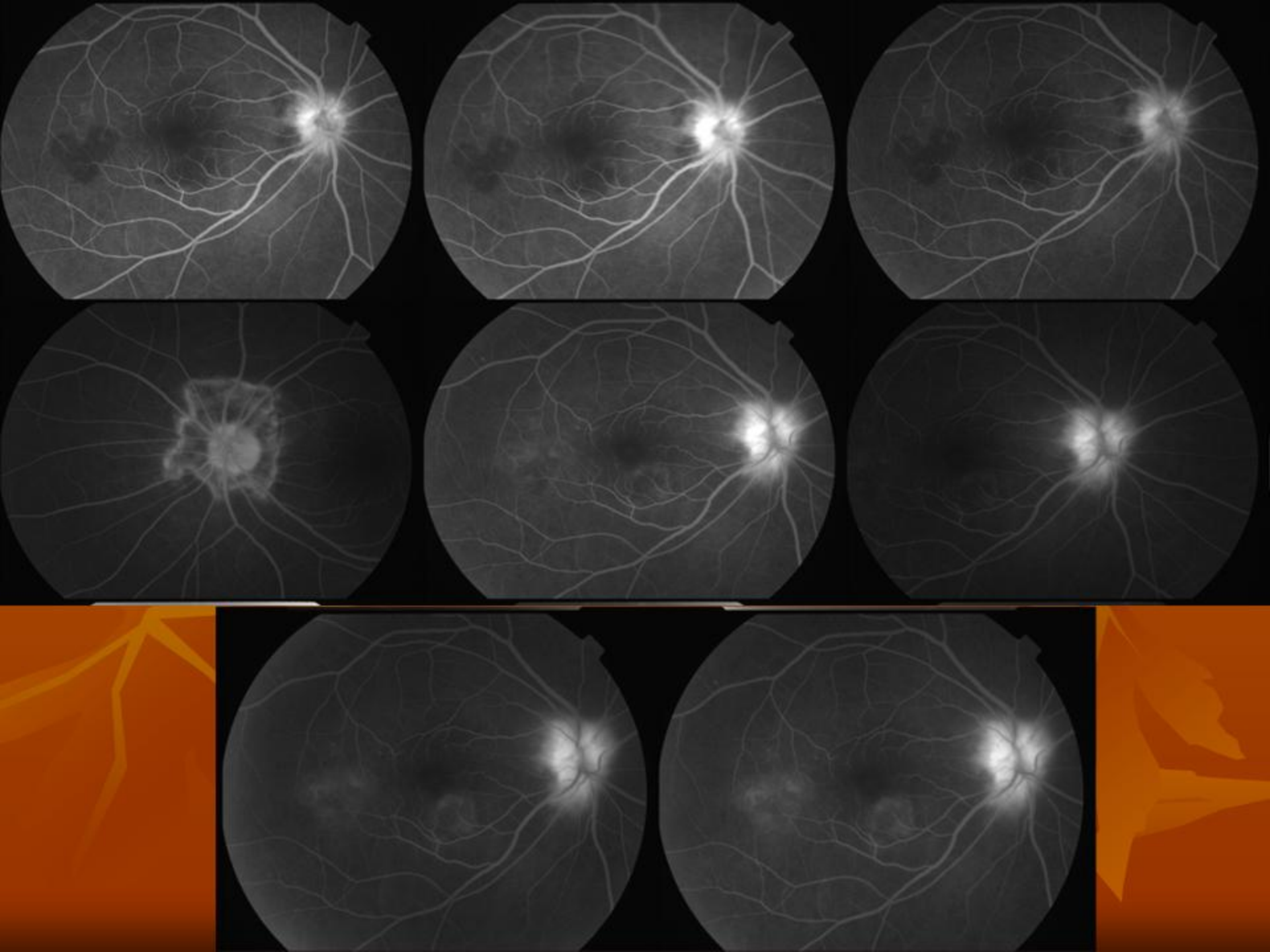
# Tests

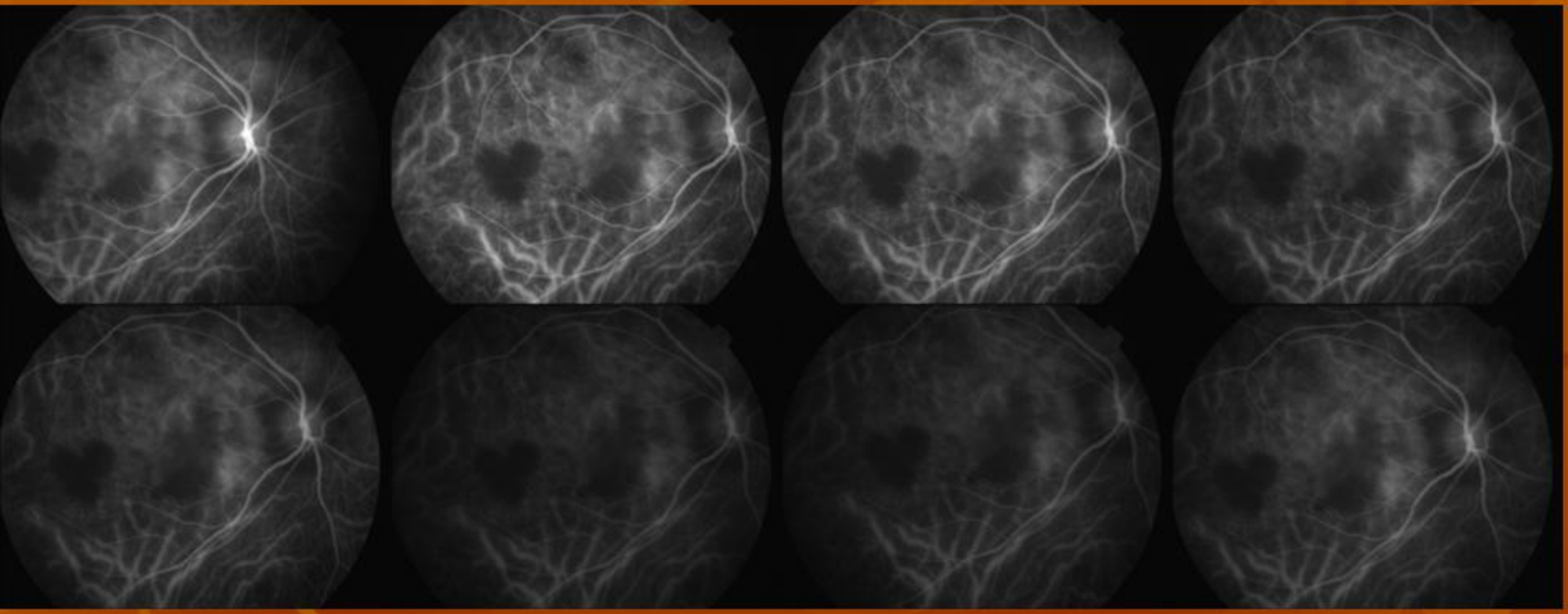
- Mantoux – 20mm
- CXR – NAD
  CT Head – NAD
- FBC, U+E – NAD
- VDRL/Lyme/Borrelia titres - Neg
- ESR and CRP – mildly raised
- Serum ACE – Normal
- ANA – Not done

# More familiar tests





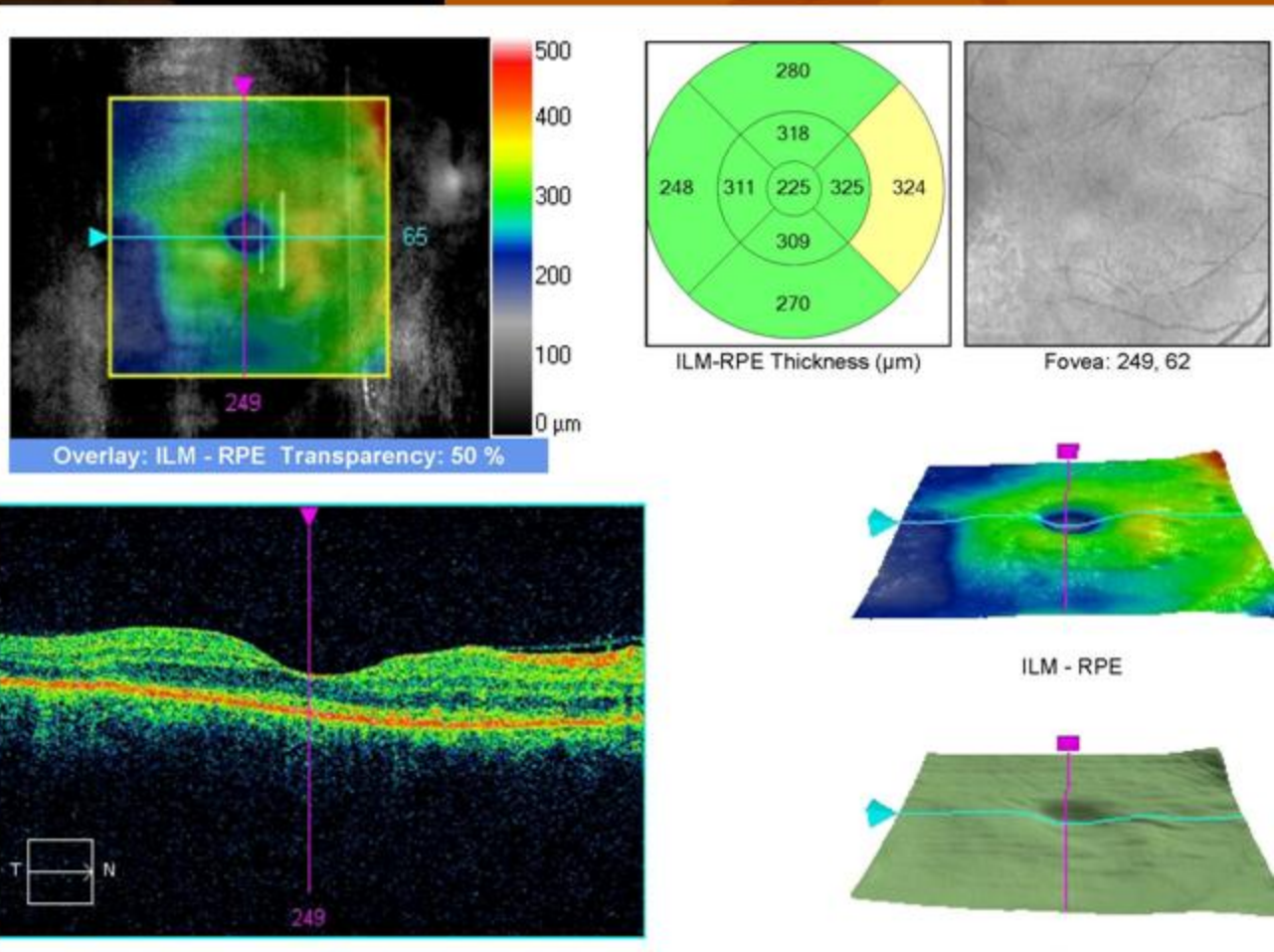




# What happened?

- She saw Prof Stanford and 6 months later

6/6 unaided



# VOGT-KOYANAGI-HARADA DISEASE

# Vogt-Koyanagi-Harada disease

- Inflammatory condition of autoimmune nature in which cytotoxic T cell target melanocytes (eyes, inner ears, skin)
- Described by Persian Physician (Ali-ibn-Isa 940-1010 AD) –Poliosis + eye inflammation
- 1932- Combined disorders described by Vogt, Koyanagi and Harada manifestations were under the same disease process

New insights into Vogt-Koyanagi-Harada disease. Arq Bras Oftalmol. 2009;72(3):413-20

# Epidemiology

- Predilection for more darkly pigmented races: Asians, Hispanics, American Indians
- 6.8-9.2% of all Uveitis referrals in Japan

# Vogt-Koyanagi-Harada disease
## Classification

- International Nomenclature Committee Revised Diagnostic Criteria
- Classification:
  - Complete VKH disease
  - Incomplete VKH disease
  - Probable VKH disease

New insights into Vogt-Koyanagi-Harada disease. Arq Bras Oftalmol. 2009;72(3):413-20

Complete Vogt-Koyanagi-Harada disease (criteria 1 to 5 must be present)
1. No history of penetrating ocular trauma or surgery preceding the initial onset of uveitis.
2. No clinical or laboratory evidence suggestive of other ocular disease entities.
3. Bilateral ocular involvement (a or b must be met, depending on the stage of disease when the patient is examined).
a. Early manifestations of disease. (1) There must be evidence of a diffuse choroiditis (with or without anterior uveitis, vitreous inflammatory reaction, or optic disk hyperemia), which may manifest as one of the following:
(a) Focal areas of subretinal fluid, or
(b) Bullous serous retinal detachments.
(2) With equivocal fundus findings; both of the following must be present as well: (a) Focal areas of delay in choroidal perfusion, multifocal areas of pinpoint leakage, large placoid areas of hyperfluorescence, pooling within subretinal fluid, and optic nerve staining (listed in order of sequential appearance) by fluorescein angiography, and (b). Diffuse choroidal thickening, without evidence of posterior scleritis by ultrasonography.
b. Late manifestations of disease. (1) History suggestive of prior presence of findings from 3a, and either both (2) and (3) below, or multiple signs from (3): (2) Ocular depigmentation (either of the following manifestations is sufficient): (a) Sunset glow fundus, or (b) Sugiura sign.
(3) Other ocular signs: (a) Nummular chorioretinal depigmented scars, or (b) Retinal pigment epithelium clumping and/or migration, or (c) Recurrent or chronic anterior uveitis.
4. Neurological/auditory findings (may have resolved by time of examination).
a. Meningismus (malaise, fever, headache, nausea, abdominal pain, stiffness of the neck and back, or a combination of these factors; headache alone is not sufficient to meet definition of meningismus, however), or
b. Tinnitus, or
c. Cerebrospinal fluid pleocytosis.
5. Integumentary finding (not proceding onset of central nervous system or ocular disease).
a. Alopecia, or
b. Poliosis, or
c. Vitiligo,
Incomplete Vogt-Koyanagi-Harada disease (criteria 1 to 3 and either 4 or 5 must be present)
1. No history of penetrating ocular trauma or surgery preceding the initial onset of uveitis, and
2. No clinical or laboratory evidence suggestive of other ocular disease entities, and
3. Bilateral ocular involvement.
4. Neurologic/auditory findings; as defined for complete Vogt-Koyanagi-Harada disease above, or
5. Integumentary findings; as defined for complete Vogt-Koyanagi-Harada disease above.

Probable Vogt-Koyanagi-Harada disease (isolated ocular disease; criteria 1 to 3 must be present)
1. No history of penetrating ocular trauma or surgery preceding the initial onset of uveitis.
2. No clinical or laboratory evidence suggestive of other ocular disease entities.
3. Bilateral ocular involvement as defined for complete Vogt-Koyanagi-Harada disease above.

Applicability of the 2001 revised diagnostic criteria in Brazilian Vogt-Koyanagi-Harada disease patients
Arq Bras Oftalmol. 2008;71(1):67-70

# Vogt-Koyanagi-Harada disease
## Stages

- Prodromal stage
- Acute uveitic stage
- Convalescent stage
- Chronic recurrent stage

# Stages

| Prodromal | Acute Uveitic Stage (2-6 wks) | Convalsecent stage | Chronic Recurrent stage |
|---|---|---|---|
| Mimics viral Infection | Bilateral blurring of vision<br><br>Ocular pain secondary to Ciliary spasm | Vitiligo<br>Alopecia<br>Poliosis | 43% in 1st three months<br>52% in 1st six months |
| Fever<br><br>Neurological Symptoms (headache, tinnitus, meningism, high freq snesorineural loss) | Multifocal Choroidtis<br>Multifocal detachment of the sensory retina<br>Exudative retinal detachment<br><br>(B-scan useful – choroidal thickening) | Uveal depigmentation<br>Sunset glow<br><br>Foci of hyperpigmentation of RPE | Glaucoma<br>Cataract<br>Subretinal Fibrosis |

# PATHOPHYSIOLOGY

## Vogt-Koyonagi-Harada Disease

# Vogt-Koyanagi-Harada disease
## Autoimmunity Against Melanocytes

- **Clinical features** of choroidal and skin depigmentation
- **Transmission electron microscopy** (early stage): close contact between melanocytes and lymphocytes in the uvea
- **Histopathology** (end stage): disappearance of choroidal melanocytes, and
- **Immunohistochemistry** (end stage): T and B lymphocytes in the choroid (DF nodules)



New insights into Vogt-Koyanagi-Harada disease. Arq Bras Oftalmol. 2009;72(3):413-20

# Vogt-Koyanagi-Harada disease
## Autoimmunity Against Melanocytes

- ***Immunogenetics***
  - HLA-DR4/DR53
  - secondary association with HLA-DR1 involving a shared sequence linked to susceptibility to rheumatoid arthritis.
  - HLA-DRB1*0405



New insights into Vogt-Koyanagi-Harada disease. Arq Bras Oftalmol. 2009;72(3):413-20

# Clinical findings in acute phase of VKH

**Figure 1 - A & B: Fundus pictures of both eyes show disc hyperemia, white-yellowish choroidal lesions, and localized exudative retinal detachments; C & D: Fluorescein angiographies of both eyes show pin-point hyperfluorescence and dye pooling corresponding to areas of retinal detachments; E & F: Indocyanine green angiographies show areas of diffuse hyperfluorescence, dark spot, and "hot-spots"**

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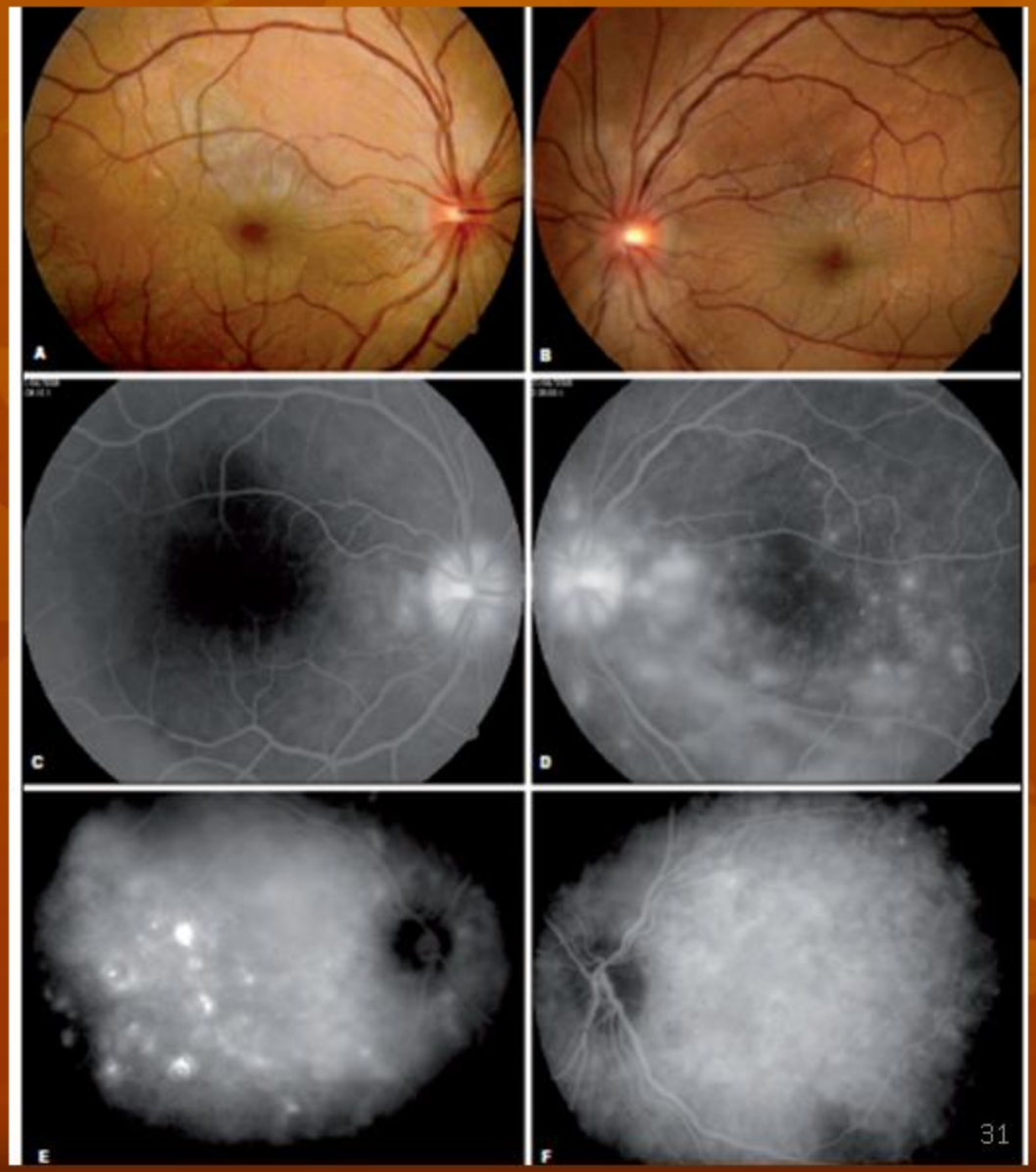
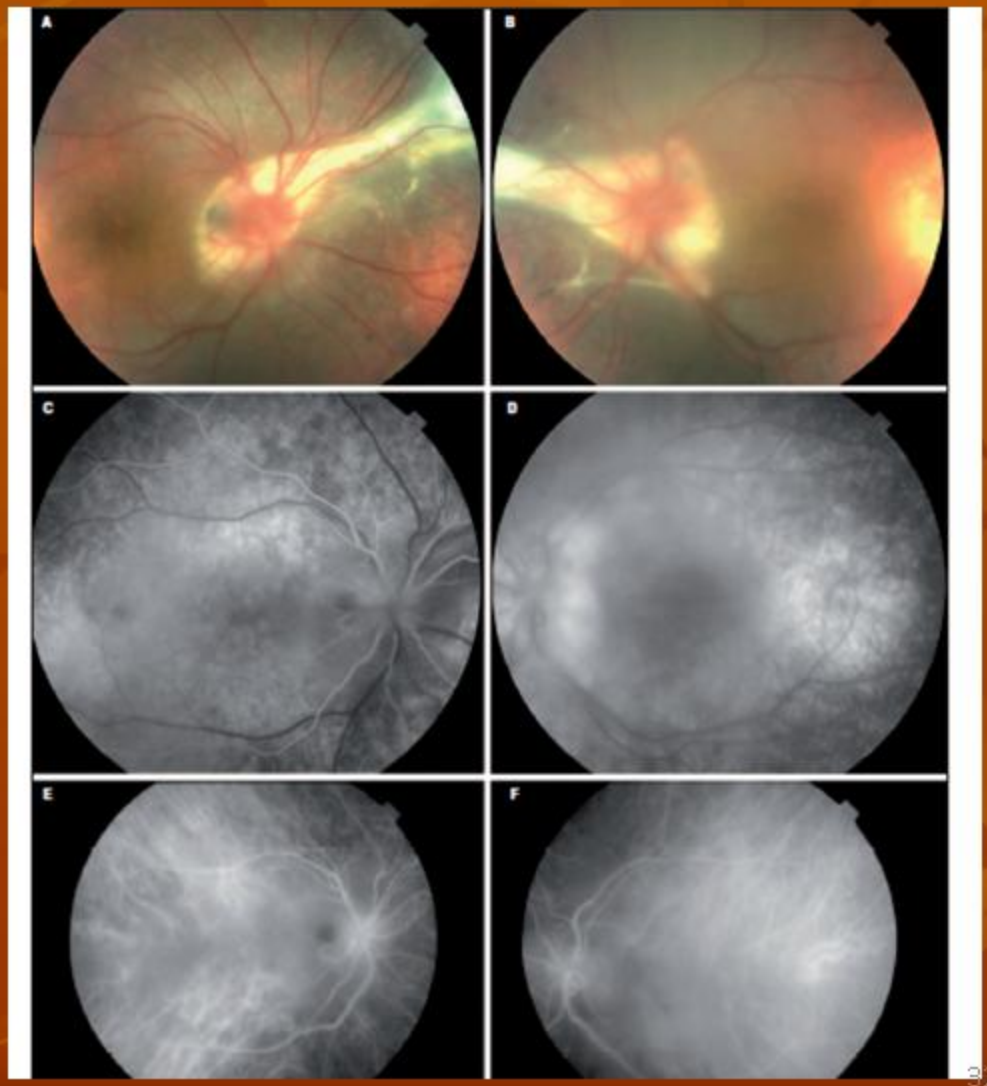


# Clinical findings in chronic phase of VKH

**Figure 2 – A & B: Fundus pictures of both eyes show diffuse retinal depigmentation and peripapillary fibrosis;**

**C & D: Fluorescein angiographies of both eyes show diffuse window retinal pigment epithelium defects; E & F: Indocyanine green angiographies**

**show dark spots and diffuse late hyperfluorescence suggestive of disease activity**

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# Treatment- Corticosteroids

For most patients with bilateral serous detachments and severe visual loss, begin therapy with systemic prednisone

**Severe Cases**

- use intravenous methylprednisolone (up to 1 g/d) for several days before beginning oral prednisone (1 mg/kg/d)

# Treatment- Systemic Corticosteroids

Prednisone

- Decrease inflammation
  - reversing increased capillary permeability and suppressing PMN activity
- DOSE
  - 1-1.5 mg/kg/d PO initially
  - length of treatment and tapering individualized for each patient
    - not be less than 3 mo to avoid recurrence

# Treatment- Immunosuppressives

For those patients who fail to respond to high-dose systemic corticosteroids or develop intolerable adverse effects, immunodulatory therapy

- Cyclosporine
- Mycophenolate mofetil
- Azathioprine
- Tacrolimus
- Cyclophosphamide