MAYO CLINIC

Center for Tuberculosis

Ocular TB: Recognizing the Vision-Related Clues

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Accreditation Statement
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Disclosure:

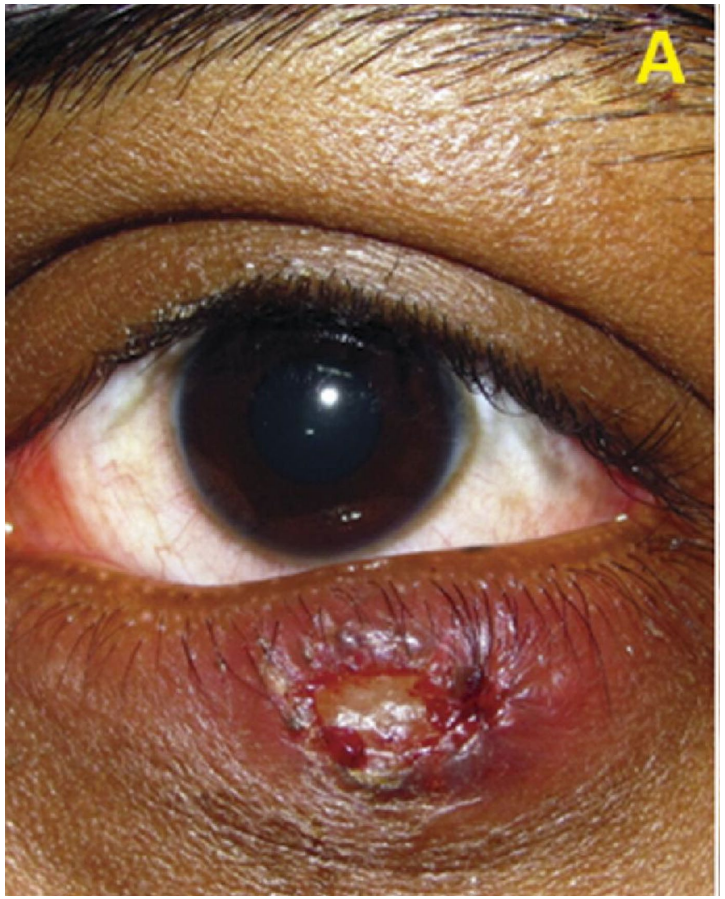
No relevant financial disclosures to report and no mention of off-label use of any medications or products

Learning Objectives

- List ocular symptoms of TB
- Describe diagnostic steps for ocular TB
- Explain referral needs for vision issues

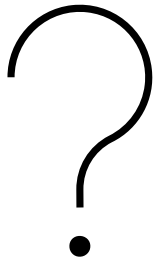
What is Ocular Tuberculosis?

- Infection due to *Mycobacterium tuberculosis* complex involving the eye
  - Can affect any part of the eye
  - Most commonly is associated with hematogenous spread of TB from pulmonary or extrapulmonary site, rarely could also occur from direct inoculation from exogenous source (typically involving lids, conjunctiva)
    - Uveal tract most frequently involved, highly vascular
- Paucibacillary disease, making diagnosis difficult



Mittal et al, *Opthalmology,* 2013

Polling Question



How common is ocular TB within the United States?

A. 10% of extrapulmonary cases, 5% of total cases

B. 5% of extrapulmonary cases, 2% of total cases

C. 2% of extrapulmonary cases, 1% of total cases

D. <1% of extrapulmonary cases

How Common is Ocular TB?

- Reports of ocular involvement in TB cases in high-TB incidence countries varies widely between studies
- Estimated 10.7 million TB cases worldwide in 2024
  - WHO Global Tuberculosis Report 2025
- Among uveitis cases - ~7% in high-incidence countries, 1-3% in low incidence countries
  - Alli et al, *Survey of Ophthal,* 2022

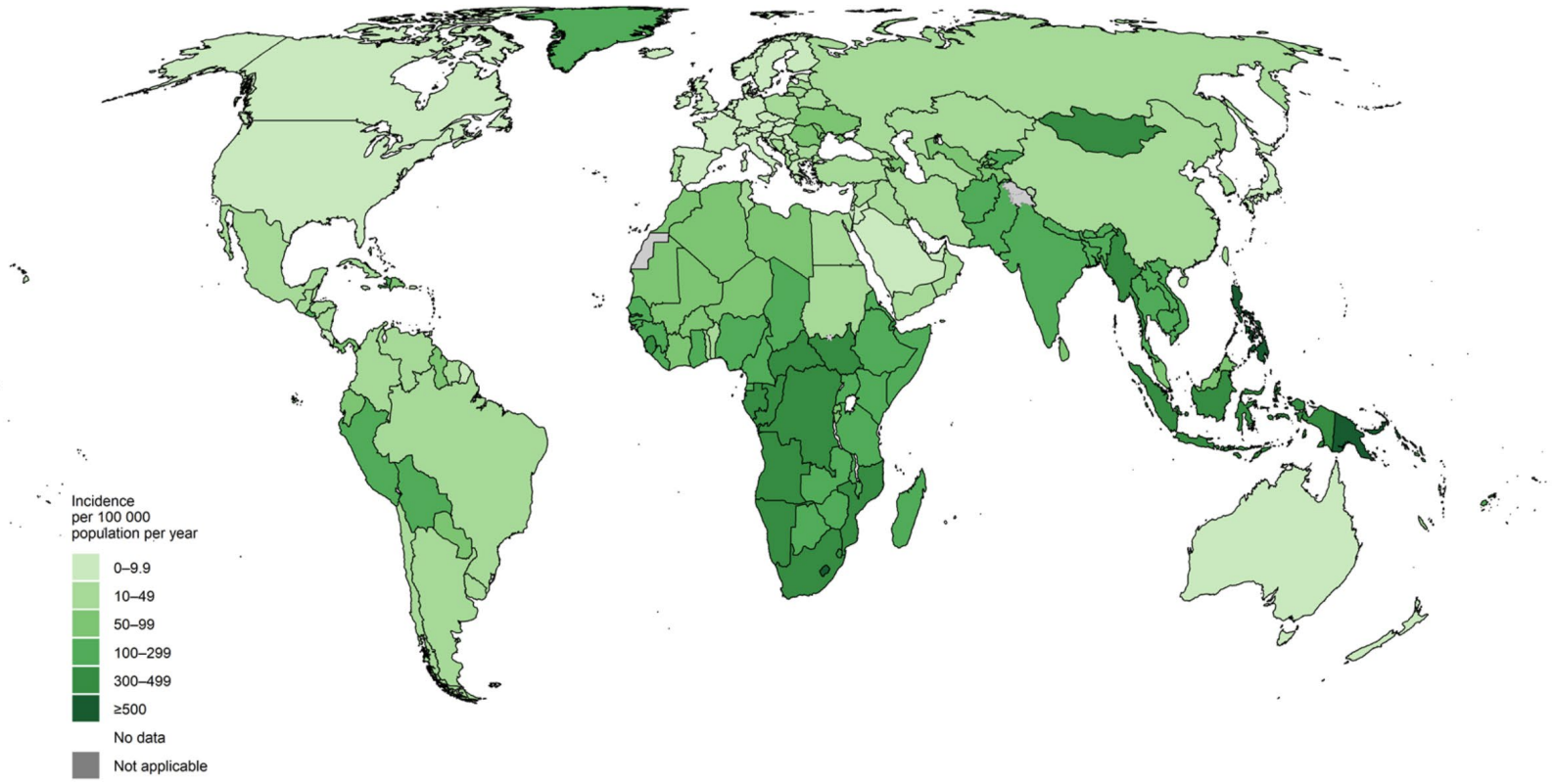
		Percent of TB Patients With Ocular TB	
Year	Author	Number	Percentage
1964	Massaro et al[29]	4/7	57.14
1967	Donahue[32]	154/10,524	1.46
1996	Biswas and Badrinath[12]	14/1005	1.39
1997	Bouza et al[37]	18/100	18.00
2002	Beare et al[38]	3/109	2.02
2004	Mehta[28]	6/24	2.92
2005	Mehta and Gilada[39]	4/17	23.50
Total		203/11,784 = 1.72%	
Total without Donahue*		49/1262 = 3.88%	

Please note that the definition of tuberculosis and ocular tuberculosis varied between these studies.
*We were interested in the average without data from the Donahue study because of the large number of patients in that study.

Bramante et al. *Int Opthalmol Clin,* 2007

How Common is Ocular TB?

Fig. 1.1.4 **Estimated TB incidence rates, 2024**



How Common is Ocular TB?

- Recent studies from higher incidence settings also variable
  - Colombia 2015-2020: 28 total cases over period, incidence of ~55 ocular TB cases/100K TB cases (0.05%)
    - Cifuentes-Gonzalez et al, *Ophthalmic Epi,* 2023
  - Bangladesh: 12% of pts with pulmonary TB found to have ocular involvement, 10% of pts with ocular TB found to have pulmonary disease
    - Rahman, *Mymensigh Med Journal,* 2022
  - India: among 85 TB-HIV co-infected patients, 13% found to have ocular involvement
    - Jain et al, *Ocular Immunology and Inflammation,* 2018

How Common is Ocular TB?

Year	Total pulmonary only cases[1]		Total pulmonary and extrapulmonary cases[2]		Total extrapulmonary only cases[3]		Total extrapulmonary sites[4]	Extrapulmonary site of disease																	
								Pleural		Lymphatic[5]		Bone or joint		Genitourinary		Meningeal		Peritoneal		Laryngeal		Other	
	No.	(%)	No.	(%)	No.	(%)		No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
2024	7,362	(70.9)	1,226	(11.8)	1,747	(16.8)	3,375	812	(24.1)	950	(28.1)	252	(7.5)	115	(3.4)	163	(4.8)	187	(5.5)	28	(0.8)	868	(25.7)
2023	6,732	(69.9)	1,135	(11.8)	1,728	(18.0)	3,223	743	(23.1)	861	(26.7)	282	(8.7)	132	(4.1)	182	(5.6)	184	(5.7)	17	(0.5)	822	(25.5)
2022	5,832	(70.0)	909	(10.9)	1,591	(19.1)	2,822	617	(21.9)	736	(26.1)	267	(9.5)	114	(4.0)	167	(5.9)	174	(6.2)	33	(1.2)	714	(25.3)
2021	5,190	(66.0)	994	(12.6)	1,682	(21.4)	3,002	586	(19.5)	818	(27.2)	368	(12.3)	120	(4.0)	157	(5.2)	210	(7.0)	25	(0.8)	718	(23.9)
2020	4,779	(66.7)	878	(12.2)	1,513	(21.1)	2,640	559	(21.2)	814	(30.8)	215	(8.1)	107	(4.1)	132	(5.0)	196	(7.4)	15	(0.6)	602	(22.8)
2019	6,073	(68.3)	1,006	(11.3)	1,813	(20.4)	3,126	675	(21.6)	1,008	(32.2)	269	(8.6)	115	(3.7)	164	(5.2)	187	(6.0)	27	(0.9)	681	(21.8)
2018	6,155	(68.4)	1,039	(11.5)	1,801	(20.0)	3,116	673	(21.6)	1,015	(32.6)	281	(9.0)	145	(4.7)	148	(4.7)	167	(5.4)	23	(0.7)	664	(21.3)
2017	6,214	(68.5)	966	(10.7)	1,883	(20.8)	3,138	635	(20.2)	1,054	(33.6)	279	(8.9)	137	(4.4)	150	(4.8)	183	(5.8)	21	(0.7)	679	(21.6)
2016	6,425	(69.5)	939	(10.2)	1,867	(20.2)	3,067	593	(19.3)	958	(31.2)	270	(8.8)	161	(5.2)	160	(5.2)	194	(6.3)	25	(0.8)	706	(23.0)
2015	6,624	(69.4)	1,007	(10.6)	1,904	(20.0)	3,167	697	(22.0)	994	(31.4)	302	(9.5)	142	(4.5)	168	(5.3)	191	(6.0)	16	(0.5)	657	(20.7)
2014	6,459	(68.8)	1,001	(10.7)	1,922	(20.5)	3,193	692	(21.7)	1,077	(33.7)	310	(9.7)	152	(4.8)	176	(5.5)	179	(5.6)	18	(0.6)	589	(18.4)
2013	6,657	(69.7)	926	(9.7)	1,972	(20.6)	3,125	648	(20.7)	1,032	(33.0)	325	(10.4)	156	(5.0)	181	(5.8)	171	(5.5)	19	(0.6)	593	(19.0)
2012	6,803	(68.5)	1,043	(10.5)	2,082	(21.0)	3,377	698	(20.7)	1,141	(33.8)	343	(10.2)	169	(5.0)	181	(5.4)	189	(5.6)	29	(0.9)	627	(18.6)
2011	7,272	(69.3)	1,052	(10.0)	2,169	(20.7)	3,476	758	(21.8)	1,134	(32.6)	355	(10.2)	178	(5.1)	226	(6.5)	186	(5.4)	26	(0.7)	613	(17.6)
2010	7,750	(69.5)	972	(8.7)	2,425	(21.8)	3,611	701	(19.4)	1,317	(36.5)	353	(9.8)	186	(5.2)	207	(5.7)	192	(5.3)	20	(0.6)	635	(17.6)

CDC reports cases of TB disease by site of disease in the United States from 2010 to 2024.

Tuberculosis in the United States, 2024 - CDC

How Common is Ocular TB?

Open Forum Infectious Diseases

MAJOR ARTICLE

Epidemiology and Clinical Characteristics of Ocular Tuberculosis in the United States, 1993–2019

Thomas D. Filardo,[1,2] Aryn Andrzejewski,[3] Michael Croix,[3] Julie L. Self,[1] Henry S. Fraimow,[4] and Sonal S. Munsiff[3]

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- Analyzed verified cases submitted to CDC National TB Surveillance System from 1993-2019
  - Ocular TB – if site of disease reported as “eye or ear appendage” or if positive smear, NAAT, or culture from this site

How Common is Ocular TB?

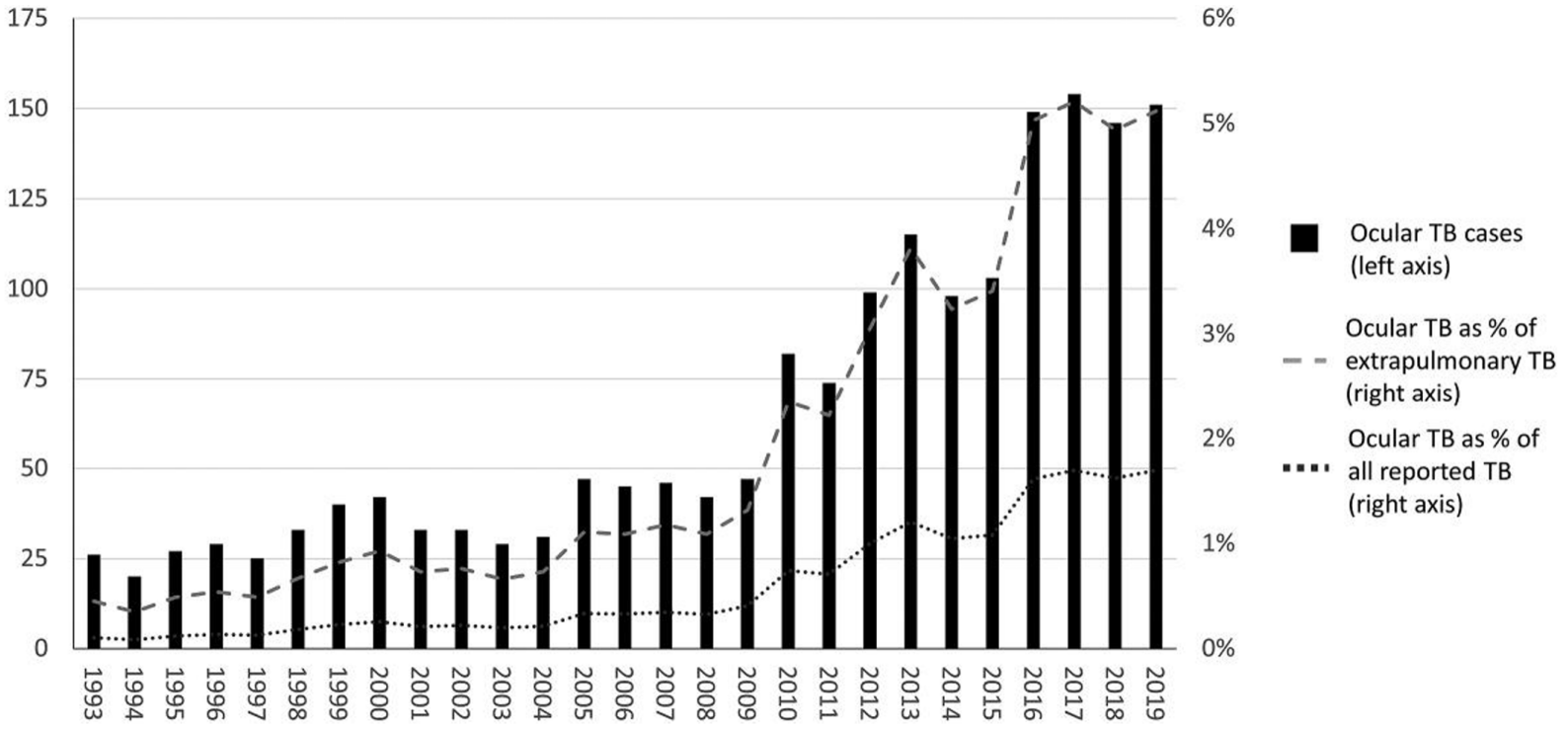


Figure 1. Reported cases of ocular TB in the United States and percentage of reported TB represented by ocular TB, 1993–2019. Abbreviation: TB, tuberculosis.

Table 1. Demographics, Clinical Characteristics, and Outcomes of Reported Ocular TB Compared With Cases of Extrapulmonary and Isolated Pulmonary TB, 2010–2019

	Ocular TB[a]	Other EPTB[b]	*P* Value (Ocular vs Other EPTB)[c]	Isolated Pulmonary TB[d]	*P* Value (Ocular vs Pulmonary)[c]
Total	1171	29 781		65 158	
Age, median (IQR), y	48 (35–60)	44 (30–61)	<.01	49 (31–64)	.33
Sex					
Male	615 (53)	16 404 (55)	.08	41 534 (64)	<.01
Female	556 (47)	13 374 (45)		23 620 (36)	
Unknown	0	3 (<1)	-	4 (<1)	-
Race/ethnicity[e]					
AIAN	12 (1)	291 (1)	<.01	891 (1)	<.01
Asian	293 (25)	10 764 (36)		20 628 (32)	
Black or African American	327 (28)	7177 (24)		13 318 (20)	
Hispanic or Latino	342 (29)	7950 (27)		19 313 (30)	
NHPI	5 (<1)	364 (1)		530 (1)	
White	187 (16)	2982 (10)		9959 (15)	
Multiple race	1 (<1)	189 (1)		365 (1)	
Unknown/missing	4 (<1)	82 (<1)	-	154 (<1)	-
Birth origin[f]					
US-born	414 (35)	8439 (28)	<.01	23 229 (36)	.84
Non-US-born	756 (65)	21 323 (72)		41 894 (64)	
Unknown	1 (<1)	18 (<1)	-	36 (<1)	-
Concomitant pulmonary disease					
Yes, microbiologically confirmed[g]	39 (3)	10 273 (34)	<.01[h]	N/A	-
Yes, clinically confirmed[i]	39 (3)	1468 (5)		N/A	-
No[j]	1093 (93)	18 040 (61)		N/A	-
Epidemiologic risk factors[k]					
No identified risk factors	614 (52)	15 587 (52)	.95	30 436 (47)	<.01
Known prior untreated LTBI	58 (5)	862 (3)	<.01	1636 (3)	<.01
Homelessness	22 (2)	938 (3)	.01	3979 (6)	<.01
Long-term facility resident	8 (1)	573 (2)	<.01	1288 (2)	<.01
Correctional facility resident	9 (1)	499 (2)	.02	3035 (5)	<.01
Contact of TB case within 2 y	31 (3)	1525 (5)	<.01	6064 (9)	<.01
Occupation[l]					
Health care worker	58 (5)	1288 (4)	-	2057 (3)	-
Corrections	2 (<1)	35 (<1)	-	70 (<1)	-
Migrant/seasonal	8 (1)	301 (1)	-	944 (1)	-
Medical risk factors					
HIV infection					
Positive	11 (1)	2356 (8)	<.01	2785 (4)	<.01
Negative	1015 (87)	23 008 (77)		53 130 (82)	
Not offered testing	49 (4)	2034 (7)	-	4348 (7)	-
Other[m] or missing	96 (8)	2383 (8)	-	4895 (8)	-
Diabetes	195 (17)	3960 (13)	<.01	12 890 (20)	.01
End-stage renal disease	6 (1)	1279 (4)	<.01	1161 (2)	<.01
Non-HIV immunocompromising condition[n]	65 (6)	2277 (8)	.01	3337 (5)	.51

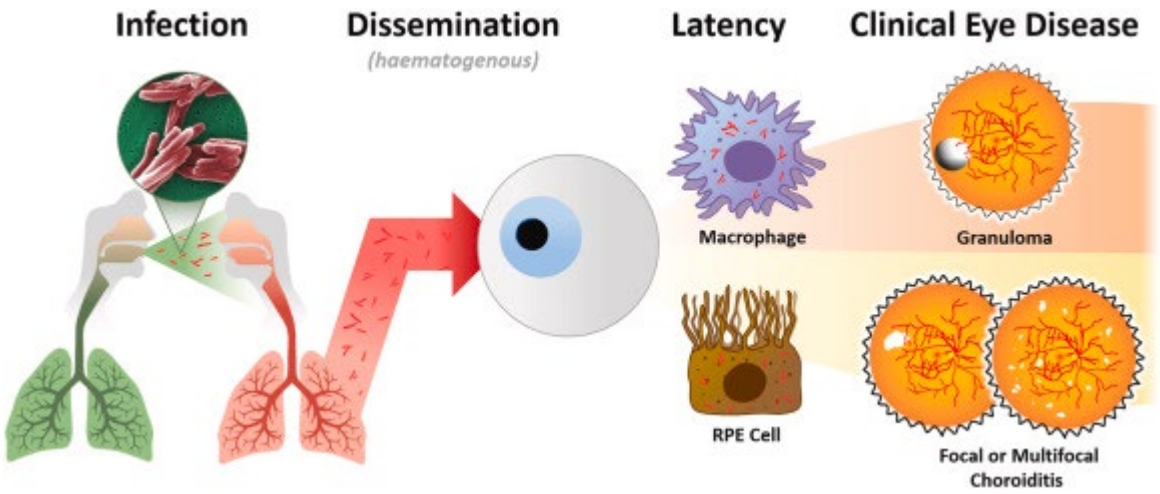
- Only 6% had evidence of pulmonary TB (compared to 39% with other extra-pulmonary TB disease
- >50% with no identified epidemiologic risk factors for TB, ~35% US born
- Diabetes mellitus was most common medical comorbidity (17%), HIV in only 1%, other immunosuppression in 6%

Table 2. Tuberculosis Testing for Reported Ocular TB Compared With Extrapulmonary and Isolated Pulmonary TB, 2010–2019

	Ocular TB[a]	Other EPTB[b]	*P* Value (Ocular vs Other EPTB)[c]	Isolated Pulmonary TB[d]	*P* Value (Ocular vs Pulmonary)[c]
Total	1171	29 781		65 158	
TB infection and chest imaging					
TB skin test performed[e]	349 (30)	10 093 (34)	<.01	26 177 (40)	<.01
TB skin test positive[f]	325 (93)	7841 (78)	<.01	20 879 (80)	<.01
IGRA test performed[e]	987 (84)	16 477 (55)	<.01	31 430 (48)	<.01
IGRA positive[f]	945 (96)	13 100 (84)	<.01	25 415 (85)	<.01
Chest x-ray performed	1111 (95)	27 903 (94)	.10	62 645 (96)	.03
Any chest imaging performed	1147 (98)	29 217 (98)	.70	64 720 (99)	<.01
Microbiology					
NAAT testing performed[e]	242 (21)	12 915 (43)	<.01	39 838 (61)	<.01
NAAT test positive[f]	33 (14)	7326 (61)	-	32 221 (81)	-
Culture positive	55 (5)	21 791 (73)	<.01	52 698 (81)	<.01
Any drug resistance present to first-line TB therapy[g]	8 (15)	3001 (14)	-	6440 (12)	-
MDR[g]	2 (4)	205 (1)	-	817 (2)	-
Any microbiologic confirmation (culture, NAAT, smear)	63 (5)	22 742 (76)	<.01	53 798 (83)	<.01
Ocular-specific testing					
Ocular smear test performed[e]	45 (4)	3 (<1)	-	0	-
Ocular smear positive[f]	16 (36)	0	-	0	-
Ocular NAAT test performed[e]	17 (1)	2 (<1)	-	0	-
NAAT test positive[f]	4 (24)	0	-	0	-
Ocular culture performed[e]	31 (3)	3 (<1)	-	0	-
Culture positive[f]	10 (32)	0	-	0	-
Ocular disease microbiologically confirmed[h]	24 (2)	N/A	-	N/A	-

- Only 24/1171 (2%) of ocular TB cases were microbiologically confirmed

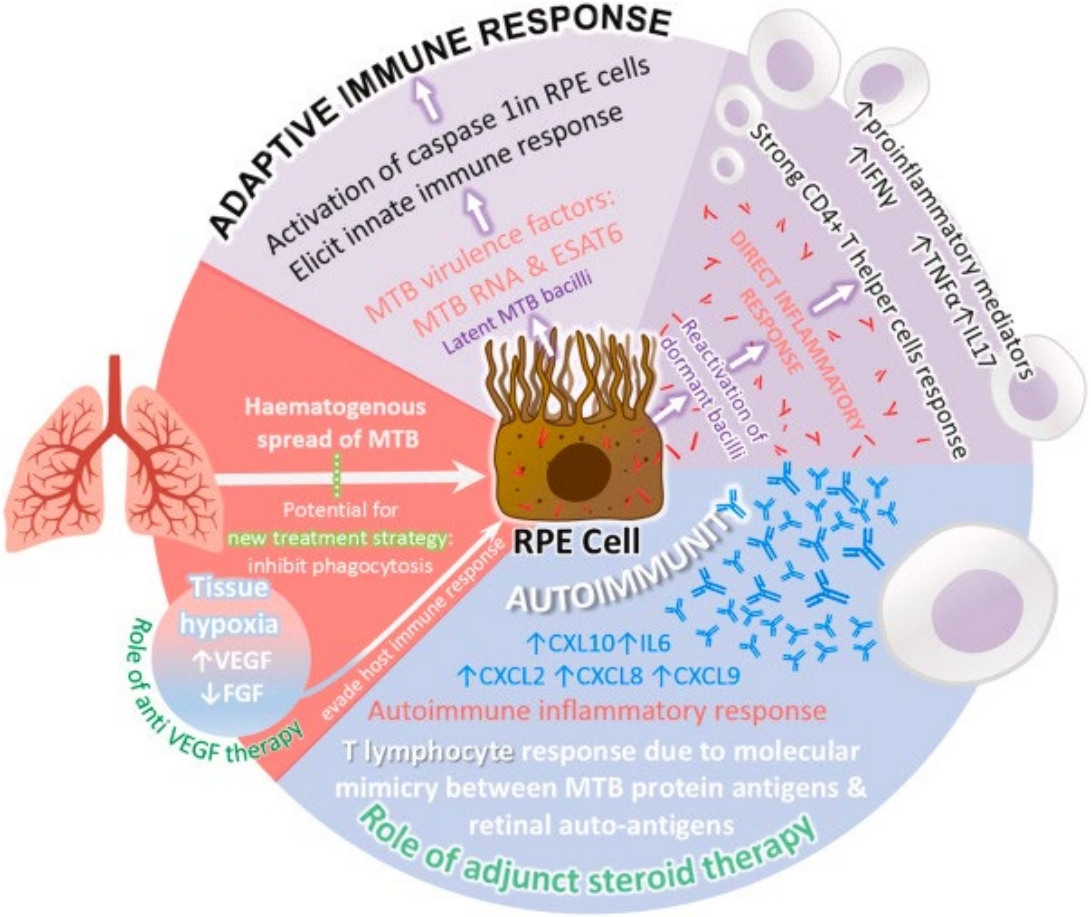
How Does Ocular TB Occur?



Agrawal et al, *Tuberculosis*, 2021

- RPE = retinal pigment epithelium cells
  - Known role phagocytosis of pathogens, in-vitro study shows similar rate of phagocytosis of MTB to macrophages but have higher cell survival rate
    - Suspected that reactivation ocular disease may occur due to reactivation/replication of MTB sequestered within RPE cells

How Does Ocular TB Occur?



Agrawal et al, *Tuberculosis*, 2021

- Ocular TB is associated with significant inflammatory response in eye
  - Direct response against MTB in eye w/ release of inflammatory cytokines
  - Autoimmune response due to presence of MTB and antigens outside of eye
    - Molecular mimicry between MTB and retinal antigens leading to T-cell autoimmune response w/release of inflammatory cytokines

Risk Factors For Ocular TB

- Not well defined – likely immunocompromised are more at risk for disseminated disease/ocular TB, though prior studies have not shown significant difference in rates of ocular TB between patients living with HIV and those not infected
  - Albert D, Raven M, *Micro Spectrum*, 2016

Ocular TB symptoms and diagnosis by Dr. Smith

Ocular TB: recognizing the vision-related clues

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April 16, 2026

Financial Disclosure

- I have no financial interests or relationships to disclose

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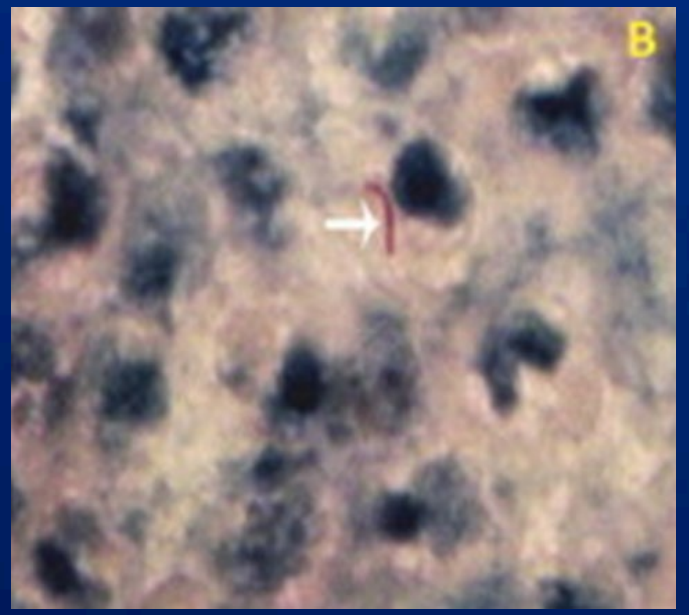
Tuberculosis and the Eye

- Ancient disease: evidence in Egyptian mummies dating back to 2400 BC
- *Mycobacterium tuberculosis* identified as the causative agent by Robert Koch in 1882
- Identified in the eye by Julius von Michael in 1883
  - Ocular disease is rare
  - May affect any ocular tissue



- Direct invasion
- Hematogenous dissemination
- Hypersensitivity reaction to bacillus infection outside the eye

Mittal R et al. Ophthalmology. 2013 May; 120(5): 1103.e1-4

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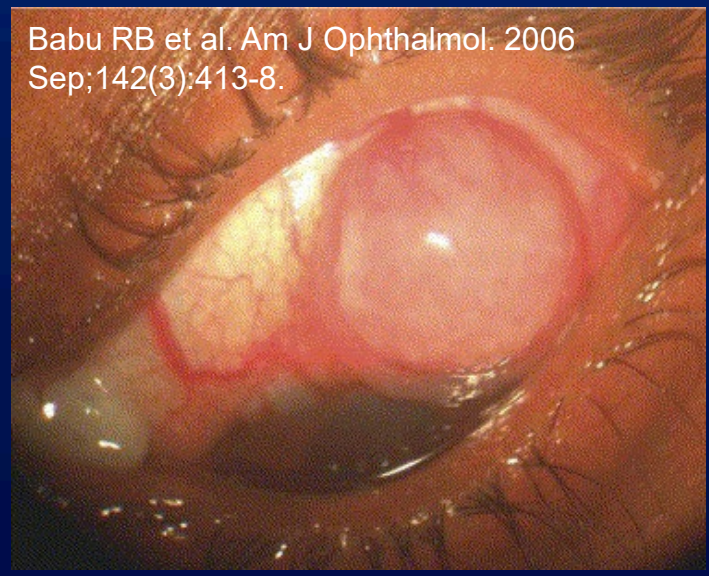
Ocular TB

- Tuberculosis of the conjunctiva and eyelids
- Tuberculous chancre and gumma of eyelids → atypical chalazion
- Mucopurulent conjunctivitis with regional lymphadenopathy
- Chronic blepharitis
- Interstitial keratitis
- Phlyctenular conjunctivitis

Mittal R et al. Ophthalmology. 2013 May; 120(5): 1103.e1-4


Babu RB et al. Am J Ophthalmol. 2006 Sep;142(3):413-8.

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Ocular TB

- Scleritis
  - most commonly anterior necrotizing or non-necrotizing
  - less often posterior
- Orbital or adnexal disease

Madge SN et al. Orbit. 2008;27(4):267-77.

Biswas J et al. Ocul Immunol Inflamm. 2012 Feb;20(1):49-52.

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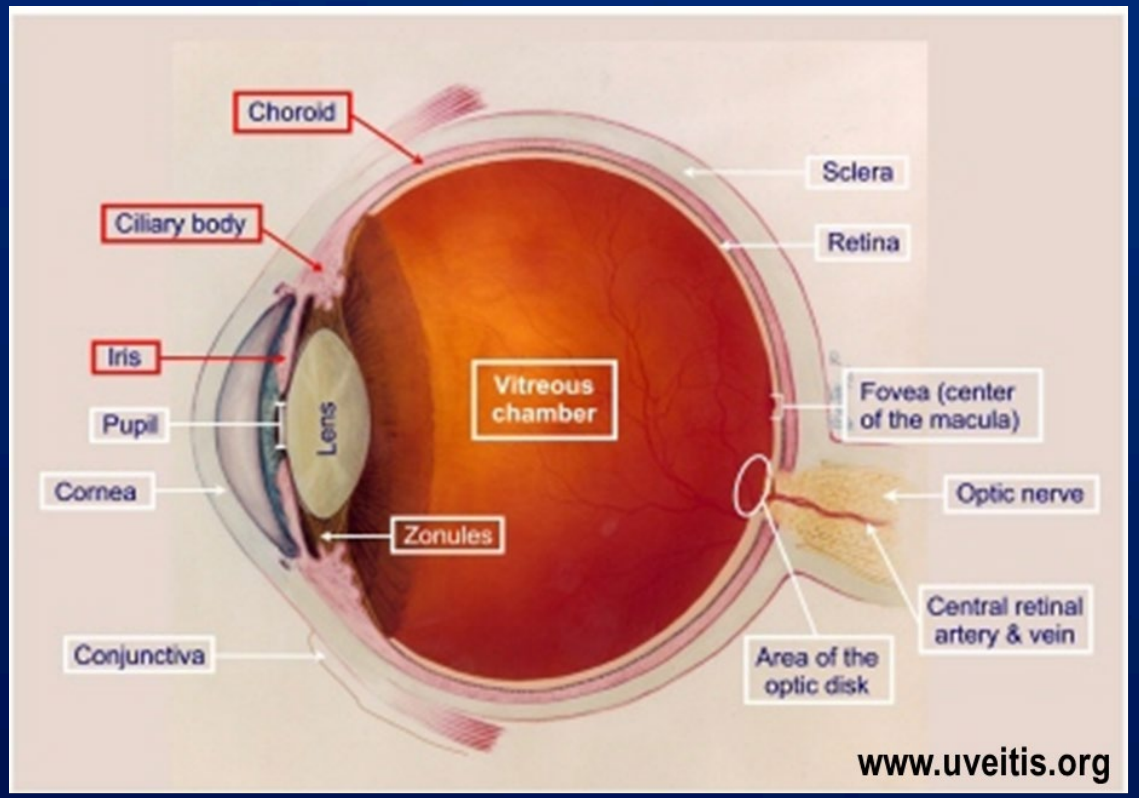
Intraocular TB = Uveitis

- Uveitis = inflammation of the uveal tract (iris, ciliary body, retina/choroid)
- Uveitis attributed to TB:
  - Once the most common cause of uveitis (up to 40% of granulomatous uveitis)
  - Now rare (1-16% of uveitis, depending on region)



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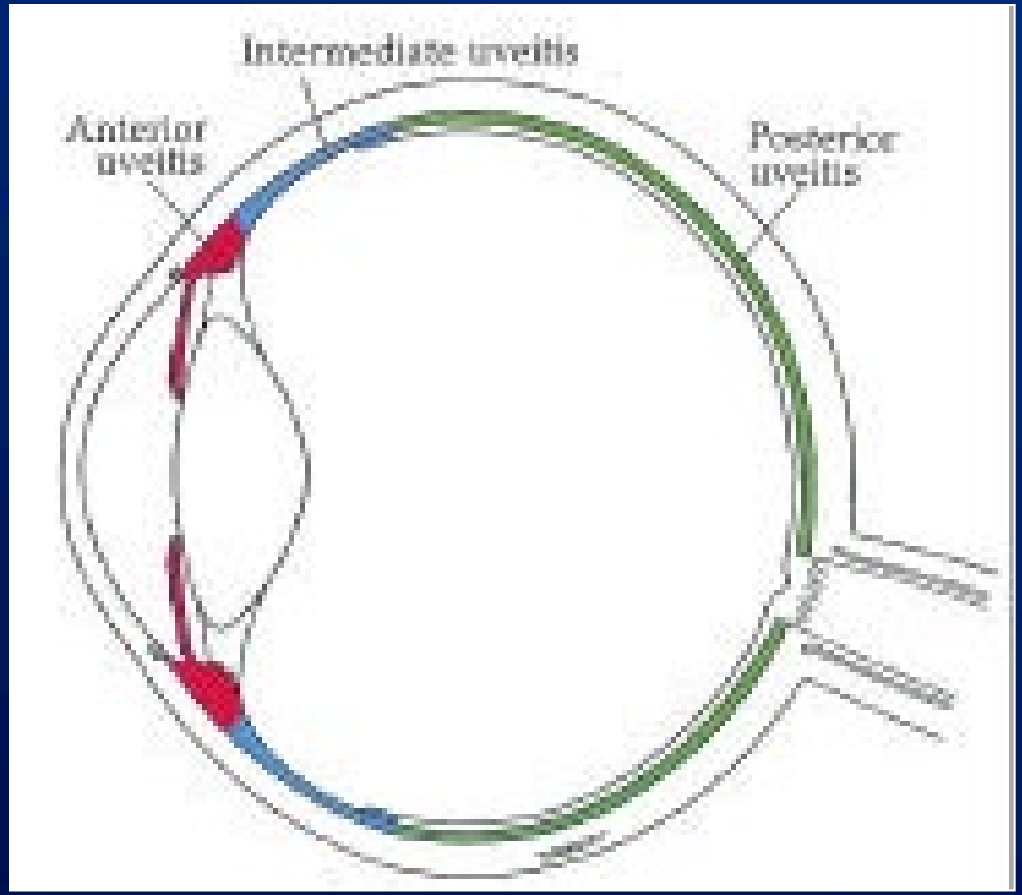
Classification of Uveitis

- Anterior uveitis
  - iris and pars plicata (CB)

"front"

- Intermediate uveitis
  - pars plana and vitreous
- Posterior uveitis
  - retina + choroid
- Panuveitis

"back"



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Signs/Symptoms of ocular inflammation (non-specific)

Front of the eye:

- Conjunctival/scleral injection
- Eye pain
  - Globe itself, around the eye
  - With palpation
  - with eye movement
- Eye irritation, burning, tearing
- Light sensitivity (pain from bright lights)
- Blurred vision, tiny floaters

Back of the eye:

- Floaters
- Blurred vision
- Photopsias (flashing light)
- Blind spots
- Peripheral vision changes

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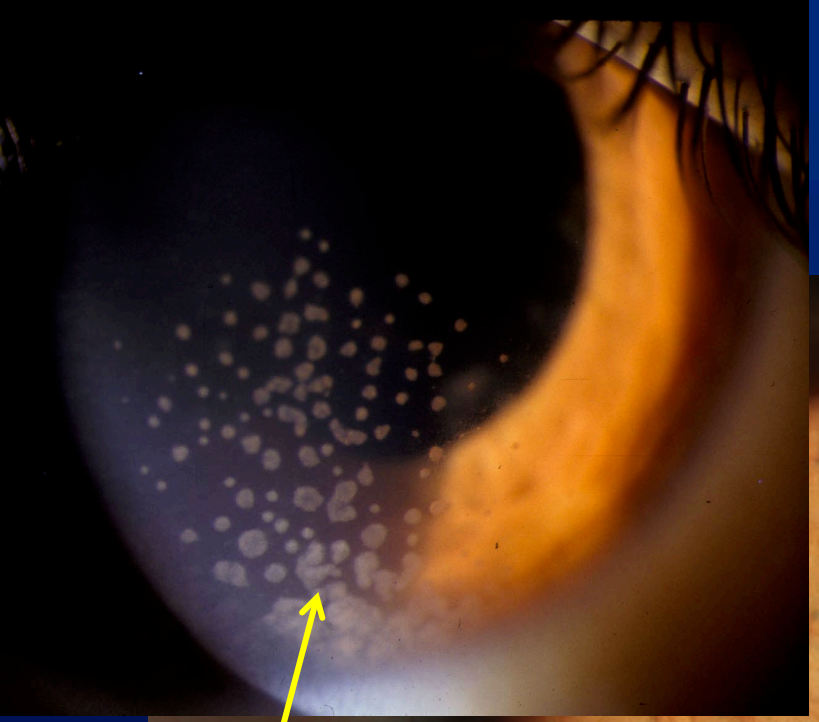
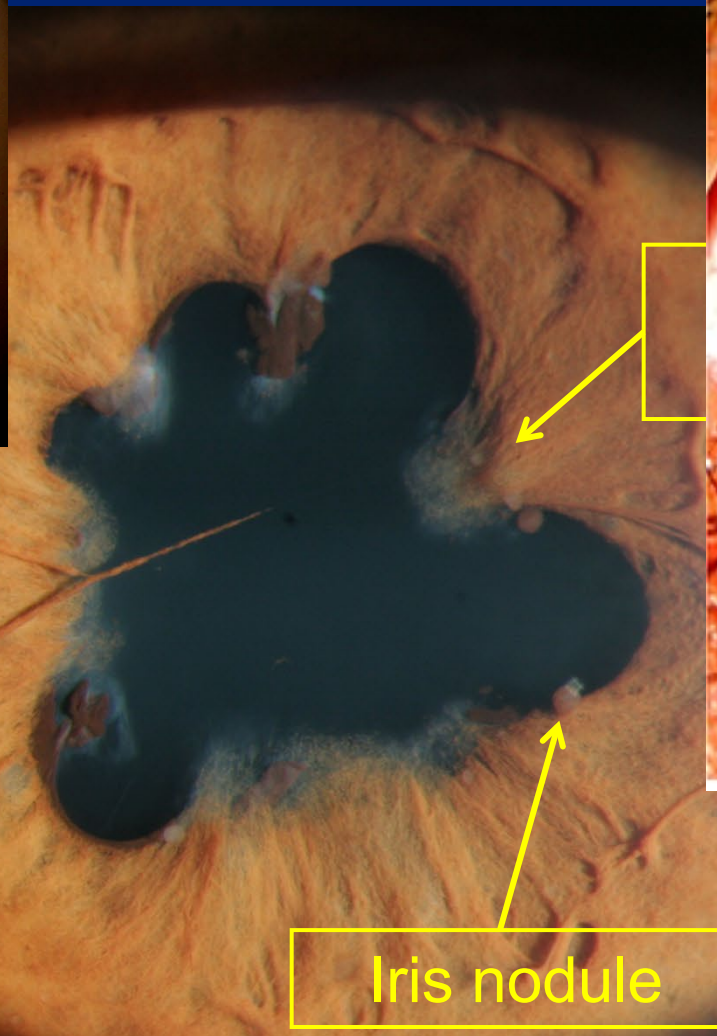
ANTERIOR UVEITIS

Granulomatous or Non-granulomatous



Keratic precipitates



Iris nodule

Rathinam SR, Lalitha P. Eye 2007 May;21(5):667-8.

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Intraocular TB

- Tuberculoma
- Granulomatous uveitis
- Granulomatous choroiditis
- Retinal vasculitis – non-occlusive or occlusive (Eales disease)
- Retinal and/or vitreous hemorrhage
- Papilledema
- Optic neuritis, neuroretinitis

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Most common presentations of ocular TB

- Demirci et al (2004): review of 92 published case reports
  - Choroidal mass +/-inflammatory signs (34%)
  - Choroiditis/chorioretinitis (27%)
  - Vitritis (24%)
  - Iridocyclitis/anterior chamber reaction (13%)
  - Panuveitis (11%)

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Collaborative Ocular Tuberculosis Study (COTS)

- 25 international eye care centers
  - East/Asia, Middle East, Australia, West
  - No centers from sub-Saharan Africa
- January 2004 – December 2014
- Approximately 950 patients with tubercular uveitis
- Retrospective case cohort review
- Consensus recommendations regarding diagnosis, indications for treatment

- Choroidal involvement (45.4%)
- Occlusive retinal vasculitis (41%)
- Retinal vasculitis w/o occlusion (31.5%)
- Disc hyperemia/edema (20.5%)
- Cystoid macular edema (17.6%)
- Snowballs (16.2%)
- Snowbank (6.1%)

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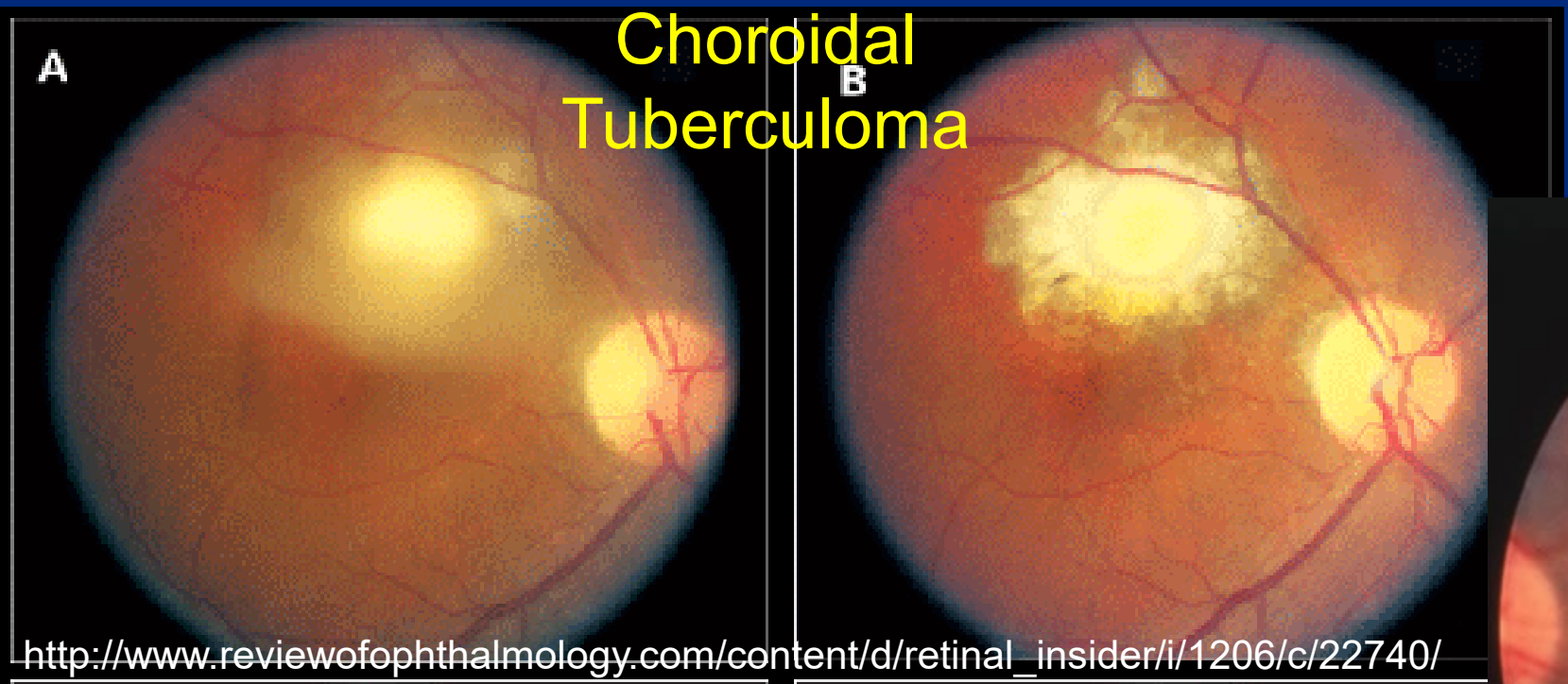
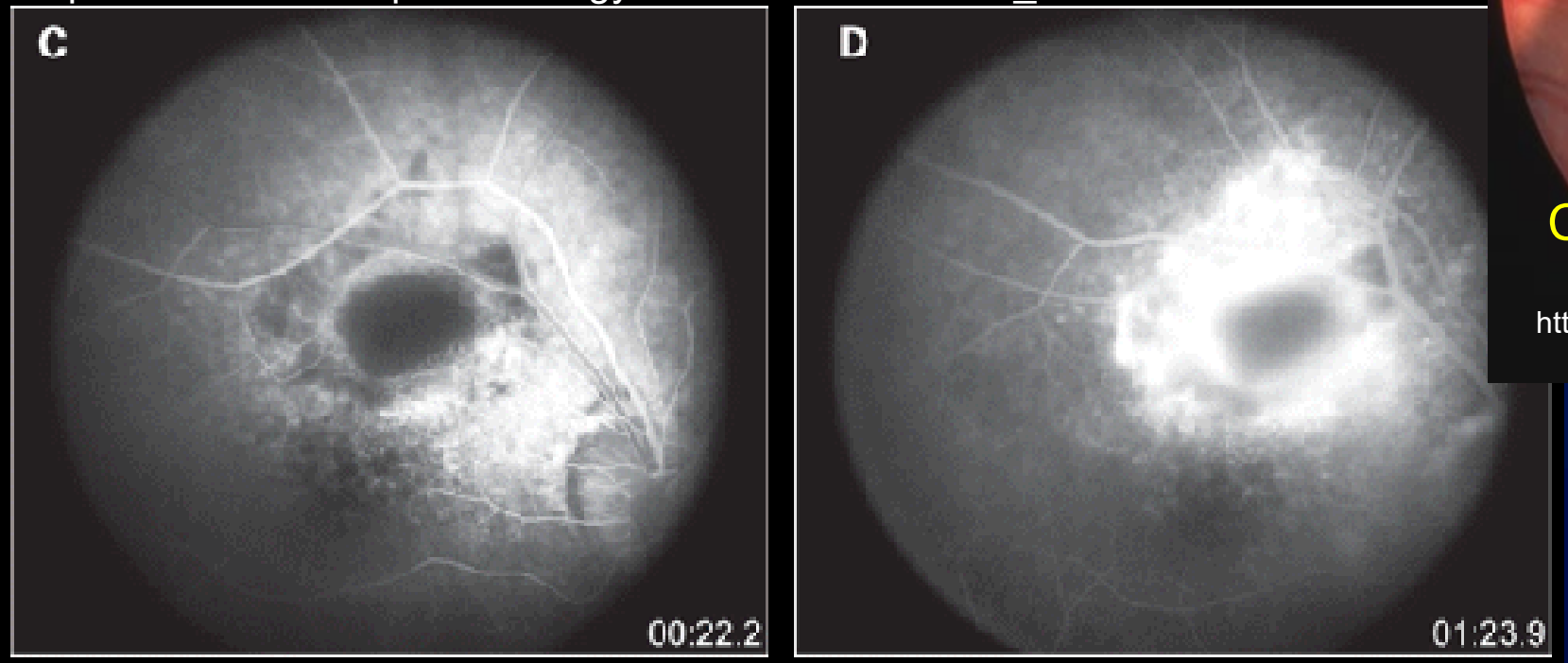
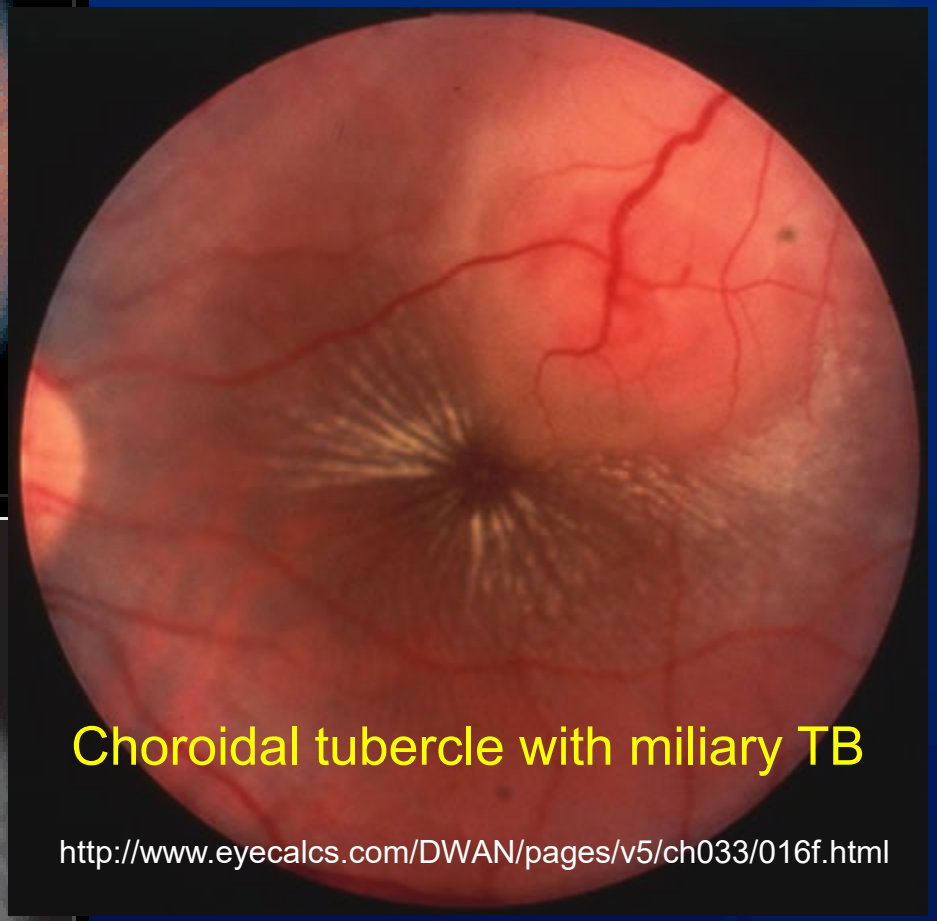
Choroidal Tuberculoma



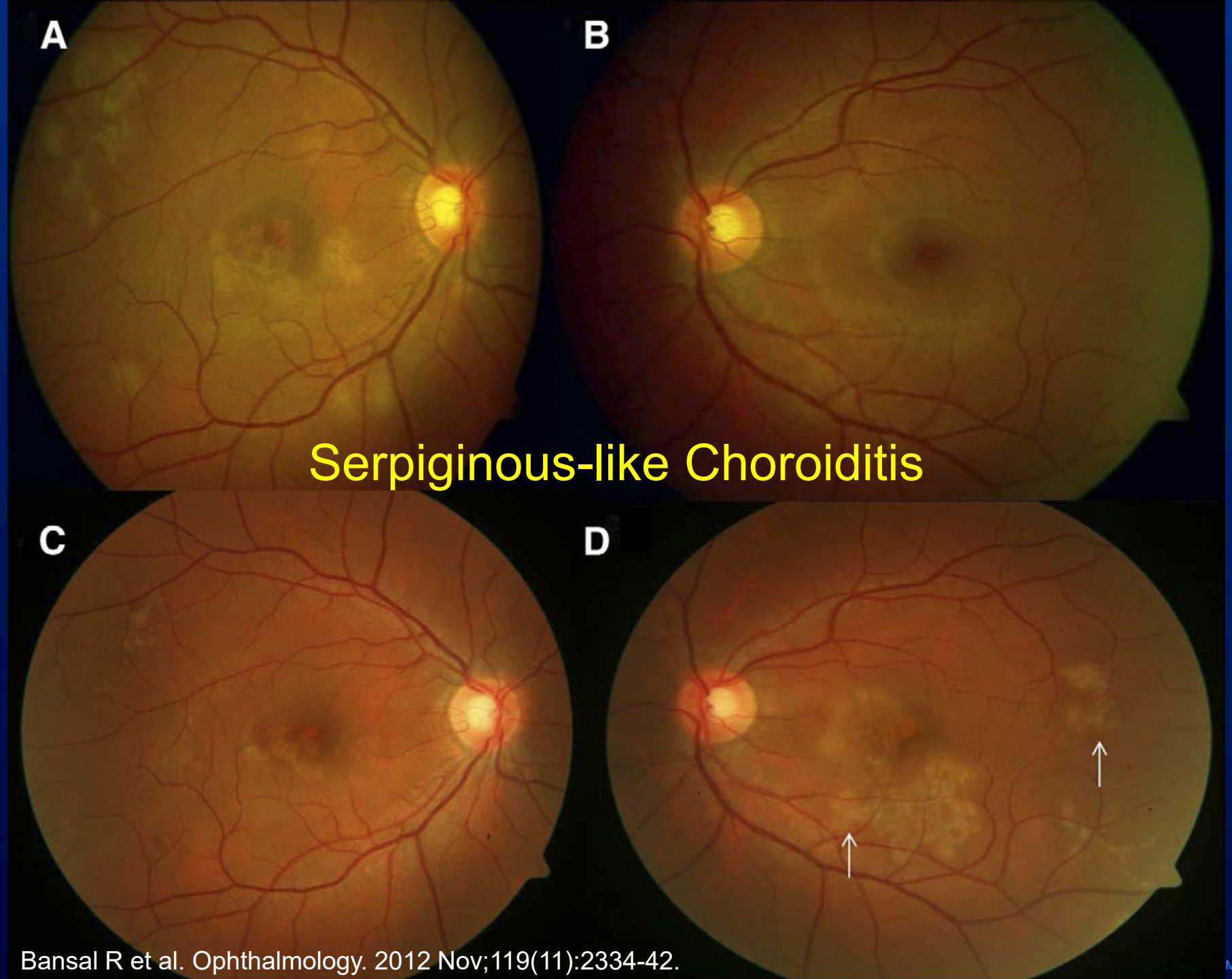
http://www.reviewofophthalmology.com/content/d/retinal_insider/i/1206/c/22740/





Choroidal tubercle with miliary TB

http://www.eyecalcs.com/DWAN/pages/v5/ch033/016f.html



Serpiginous-like Choroiditis

Bansal R et al. Ophthalmology. 2012 Nov;119(11):2334-42.

Case: 45 yo F from Pakistan, U.S. x 11 years

Sudden onset of “wavy lines” in vision

Aunt had tuberculosis, but no direct exposure
Yearly PPD for work (teacher)

Chest x-ray: normal
Quantiferon: indeterminate, but she was on systemic immunosuppression

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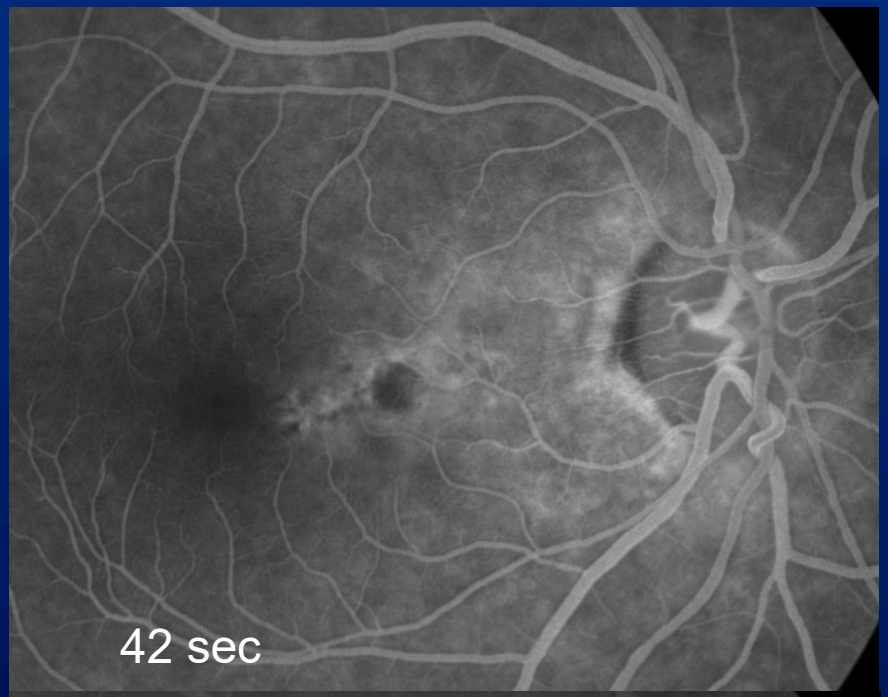
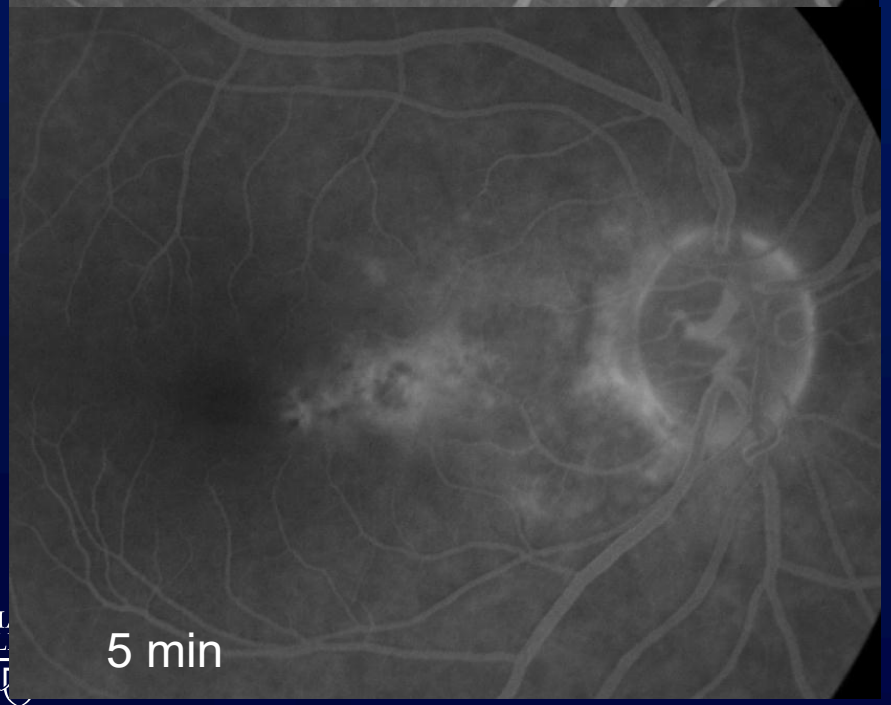
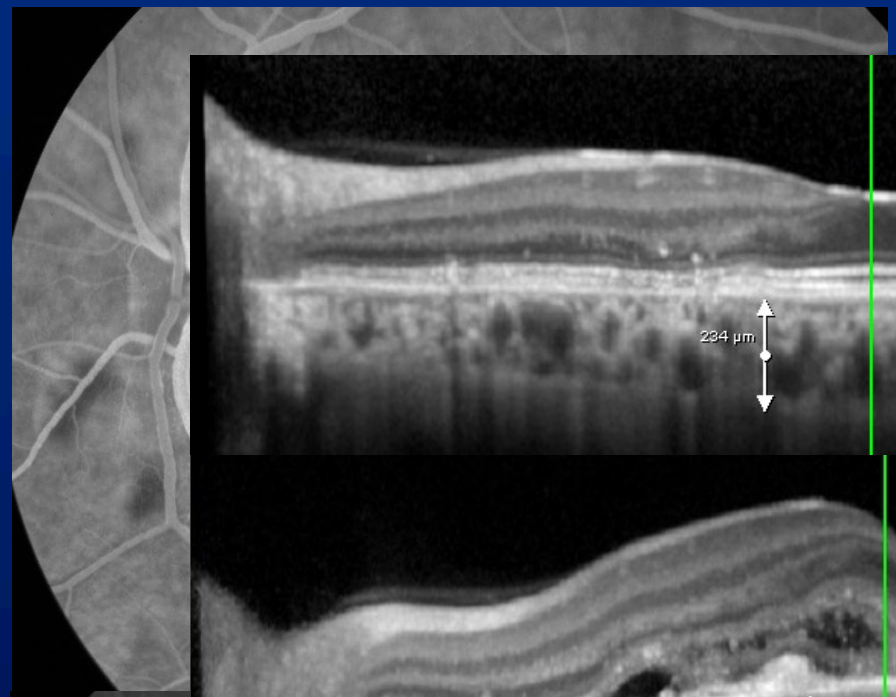
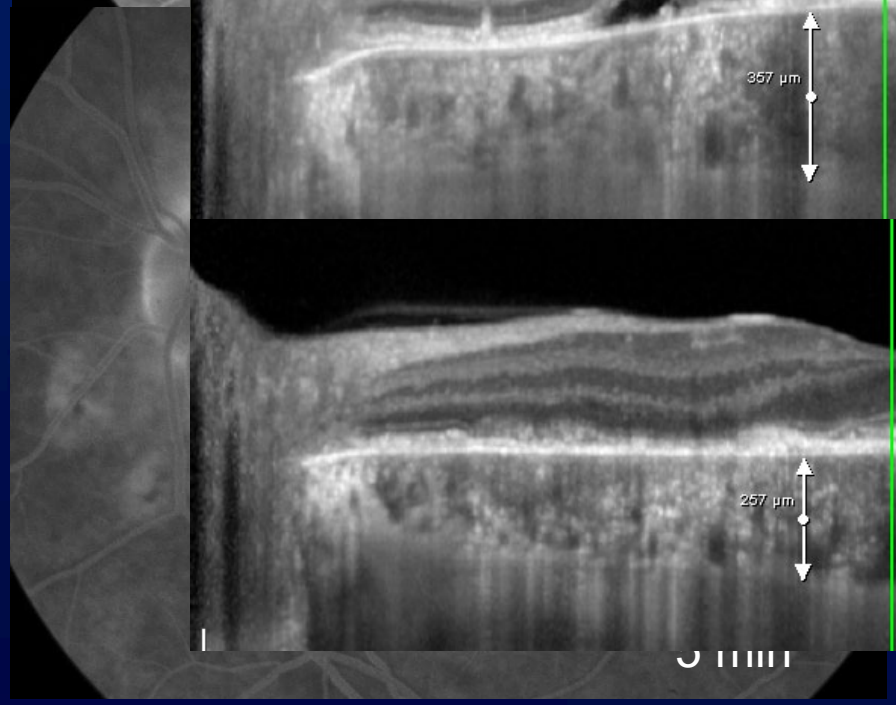
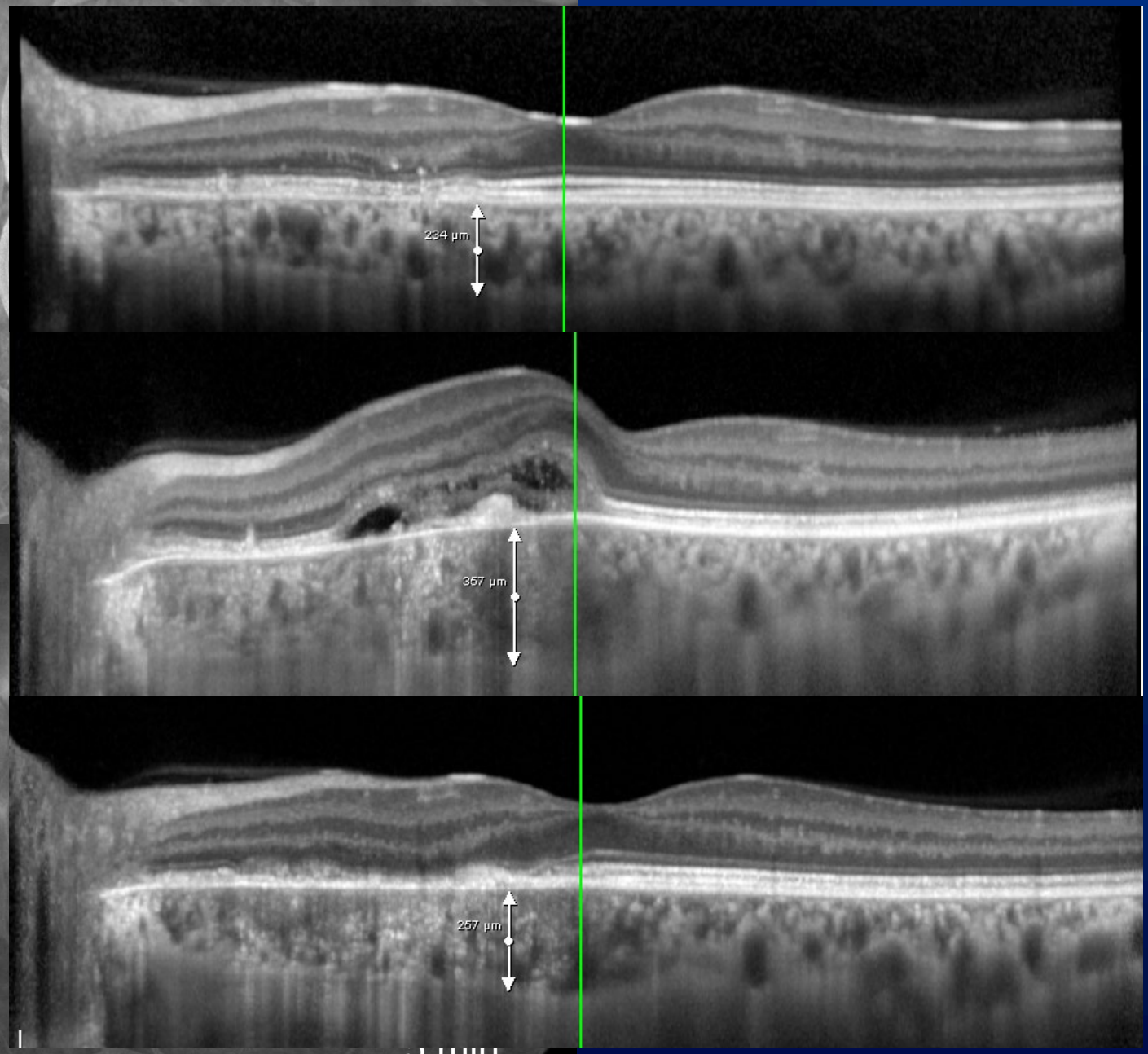


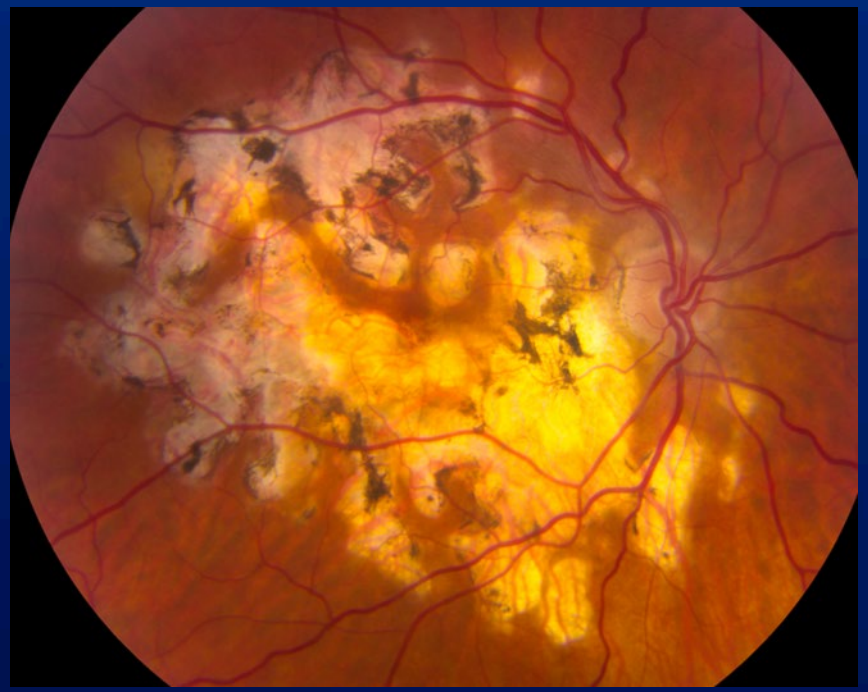






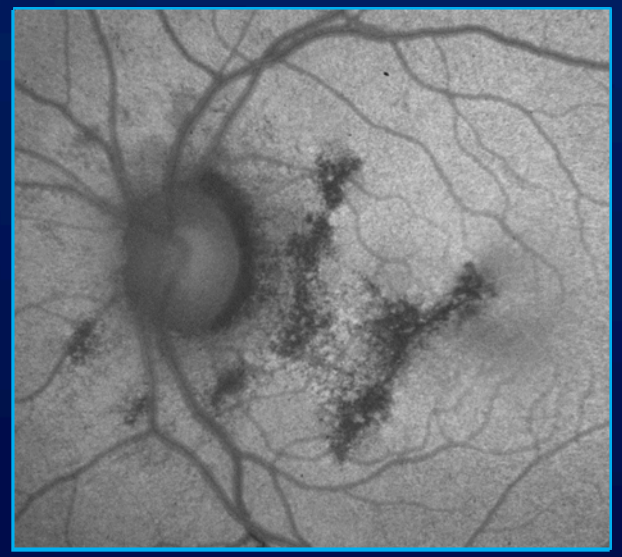


Serpiginous vs Serpiginous-like Choroiditis



Differences from Classic Serpiginous:

- From TB endemic region
- More likely unilateral
- Multifocal lesions involve posterior pole, mid-periphery, periphery and spare juxtapapillary region (unlike classic serpiginous)
- Inflammation in anterior chamber & vitreous
- Inflammation stops in response to anti-TB meds



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Eales Disease

Idiopathic peripheral perivasculitis → proliferative vascular retinopathy, recurrent vitreous hemorrhages, and tractional retinal detachment

Young, otherwise healthy men, 20-40 yrs India, PPD+

TB identified by PCR on aqueous, vitreous, epiretinal membrane

Case: 28 yo M from Kenya, in the US x 8 years

- 2 months earlier: clouding in peripheral vision
- Then, black spot in vision, not a floater
- A week earlier: awoke with red, painful eye
- In college, PPD rxn left scar on his arm
- 2009: PPD 25mm
- 2013: nml CXR

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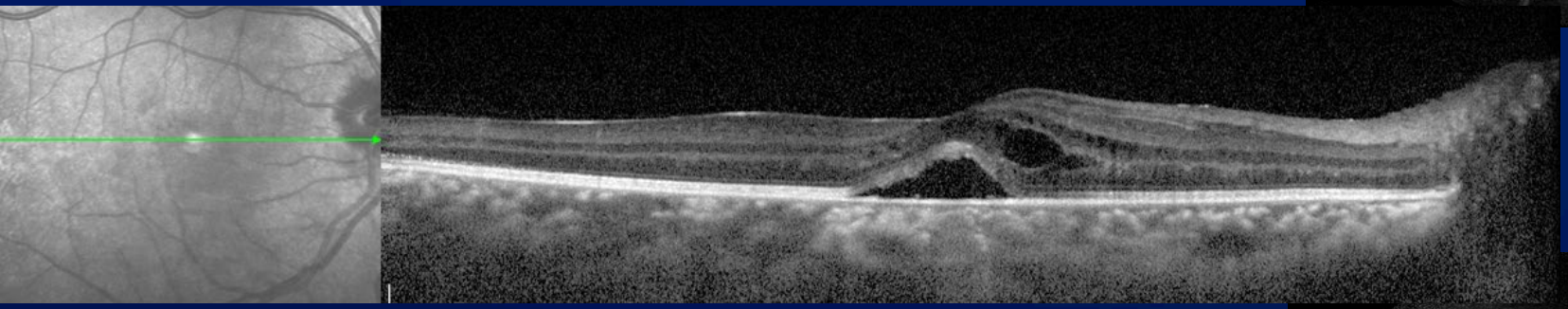
28 yo M from Kenya

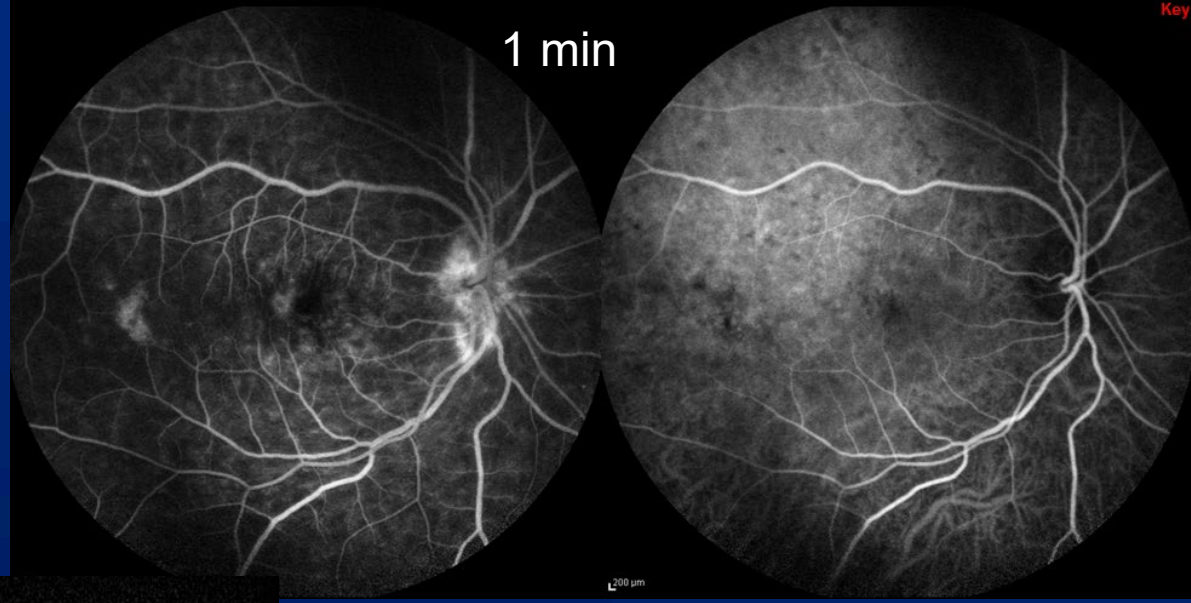
Visual acuities (with correction): 20/50 OU
Intraocular pressures: 10 and 9

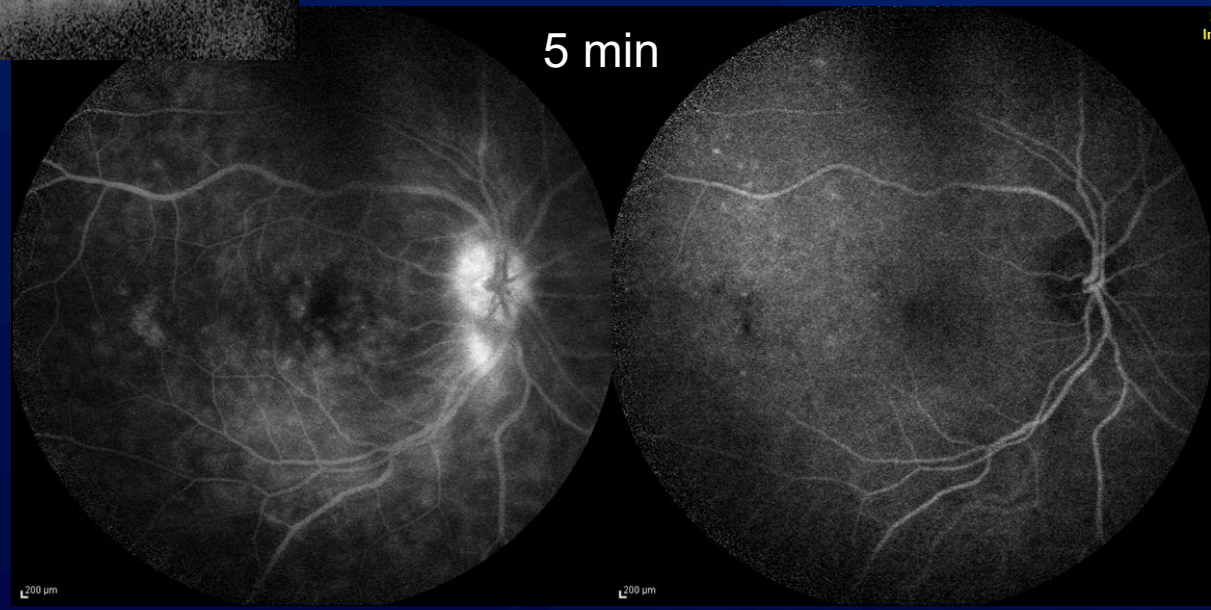
Cornea, both eyes: inferior subepithelial opacification, neovascularization, pigmented KPs, endothelial debris



Anterior chambers, both eyes: 3+ cell, 1+ flare

Vitreous, both eyes: 2+ cell, 1+ haze, veils





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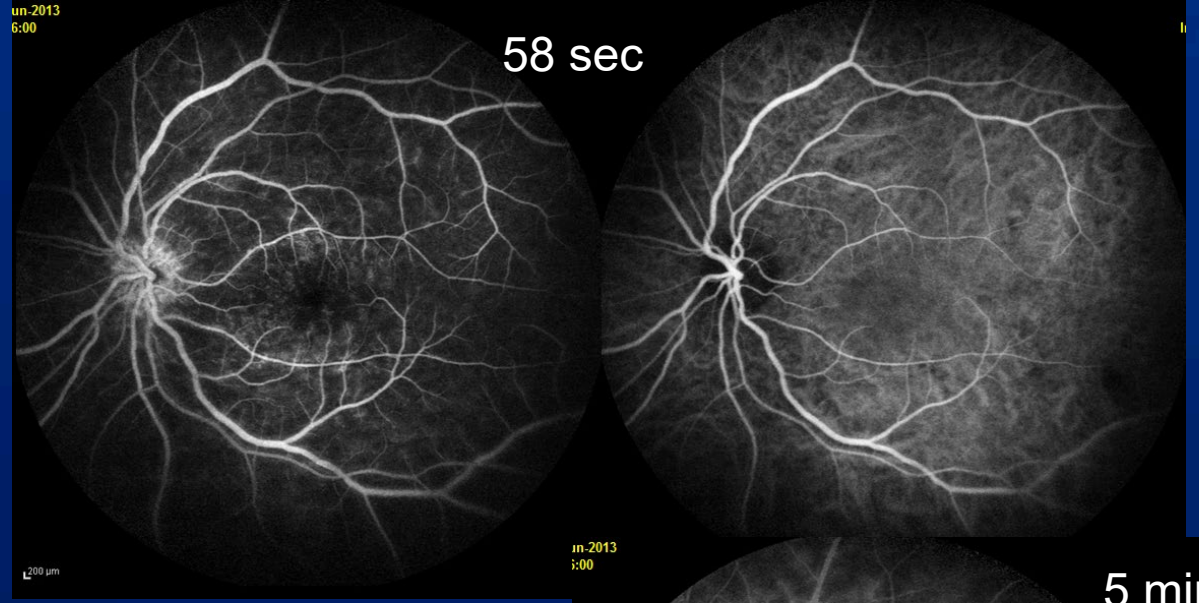
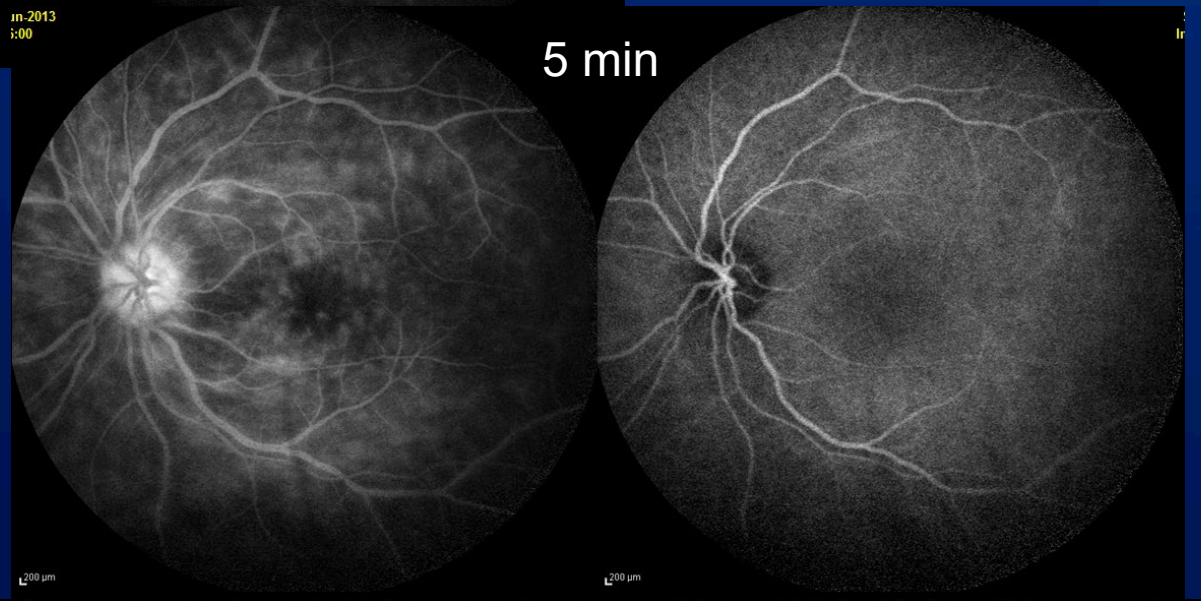
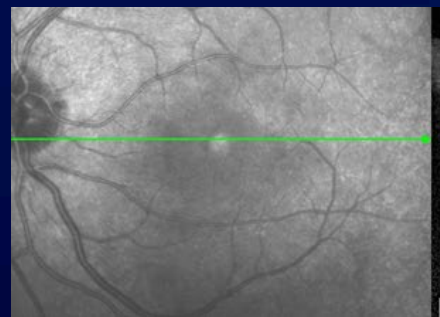
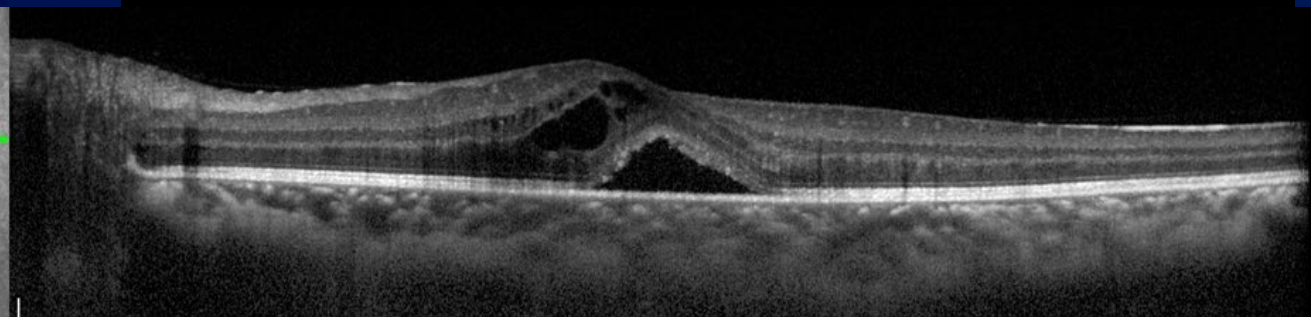
28 yo M from Kenya

- Bilateral panuveitis
  - Keratitis
  - Anterior uveitis
  - Vitritis
  - Posterior uveitis/choroiditis
- CRP 14.5
- Quantiferon: positive
- ANA low positive 1:1
- wnl/neg: CBC (except low MCV), diff, Cr, UA, ESR, ACE, lysozyme, dsDNA, RF, CCP, toxoplasma IgG/M, Lyme abs, HepB/C, Syphilis IgG, HIV









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Chest CT

- Calcified granuloma in the superior segment of the left lower lobe
- Scattered tiny indeterminant pulmonary nodules with an upper lung predominance
- These may all represent old granulomas, and are consistent with the diagnosis of prior TB lung infection, but can be seen with other granulomatous processes

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- ID consult:
  - requested aqueous humor testing → negative acid fast smear and culture
- Quadruple drug tx (ethambutol, isoniazid, pyrazinamide, rifampin) for 6 months
- Oral prednisone taper
- One month after finishing prednisone and anti-TB meds, no active uveitis

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Diagnosis of Ocular TB

Clinical context + clinical findings

- Immigration from or travel to TB endemic region
- Exposure to active TB
- Healthcare worker
- Worker or resident of nursing home or prison
- Immunocompromised (HIV+, iatrogenic, chronic disease, elderly)
- Homeless (unhoused)

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Diagnostic Testing

- Assessments for other infectious and non-infectious causes of uveitis
- Chest imaging (x-ray, CT, PET/CT)
- TST/PPD
  - False negative in 20-30% active TB
  - Low positive predictive value in non-endemic areas
- Interferon-gamma release assay
  - In vitro test using M tb antigens to stimulate release of interferon gamma from peripheral blood cells
- Biopsy: Smear, Culture, PCR

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Challenges in Ocular TB Diagnosis

- Limited specimen
  - aqueous humor – 150-200 uL
- Morbidity of obtaining specimen
  - Vitrectomy
  - Chorioretinal biopsy

Van der Lelij A, Rothova A. Br J Ophthalmol. 1997 Nov;81(11):976-9.

- Presence of DNA not necessarily indicative of active disease
- Low organism load in aqueous and vitreous
- Inflammation might be response to extraocular infection (no organism in the eye)

MAYO CLINIC

COTS – PCR in tubercular uveitis

- 59/962 (6.13%) had PCR of intraocular fluids (14 of 25 participating centers)
- PCR positive: 33/59 (56%)
  - 6/33 (18%) had systemic TB
  - 1 anterior uveitis, 1 intermediate uveitis, 20 posterior uveitis, 11 panuveitis
  - 22/30 positive TST
  - 4/10 positive quantiferon
- PCR negative:
  - 8/26 (31%) had systemic TB
  - 2 anterior uveitis, 1 intermediate uveitis, 13 posterior uveitis, 10 panuveitis
  - 10/14 positive TST
  - 3/6 positive quantiferon
- Significant heterogeneity in the testing between centers
- Majority of uveitis specialists use clinical findings (consistent with TB uveitis), imaging findings, systemic immunologic testing

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Case: 37 yo F originally from Somalia

- Lived in a refugee camp in Uganda x 5 years
- Came to the U.S. (Minnesota) 2 years earlier
- Blurred vision x 5-6 years, worsened ~2 yrs ago.
- Eye pain, left > right, headaches, vertigo
- History of positive PPD upon arrival to the U.S. → treatment for latent TB was recommended
- Neck swelling, abdominal pain associated with eating (despite recent cholecystectomy)
- No fevers, night sweats, weight loss, cough

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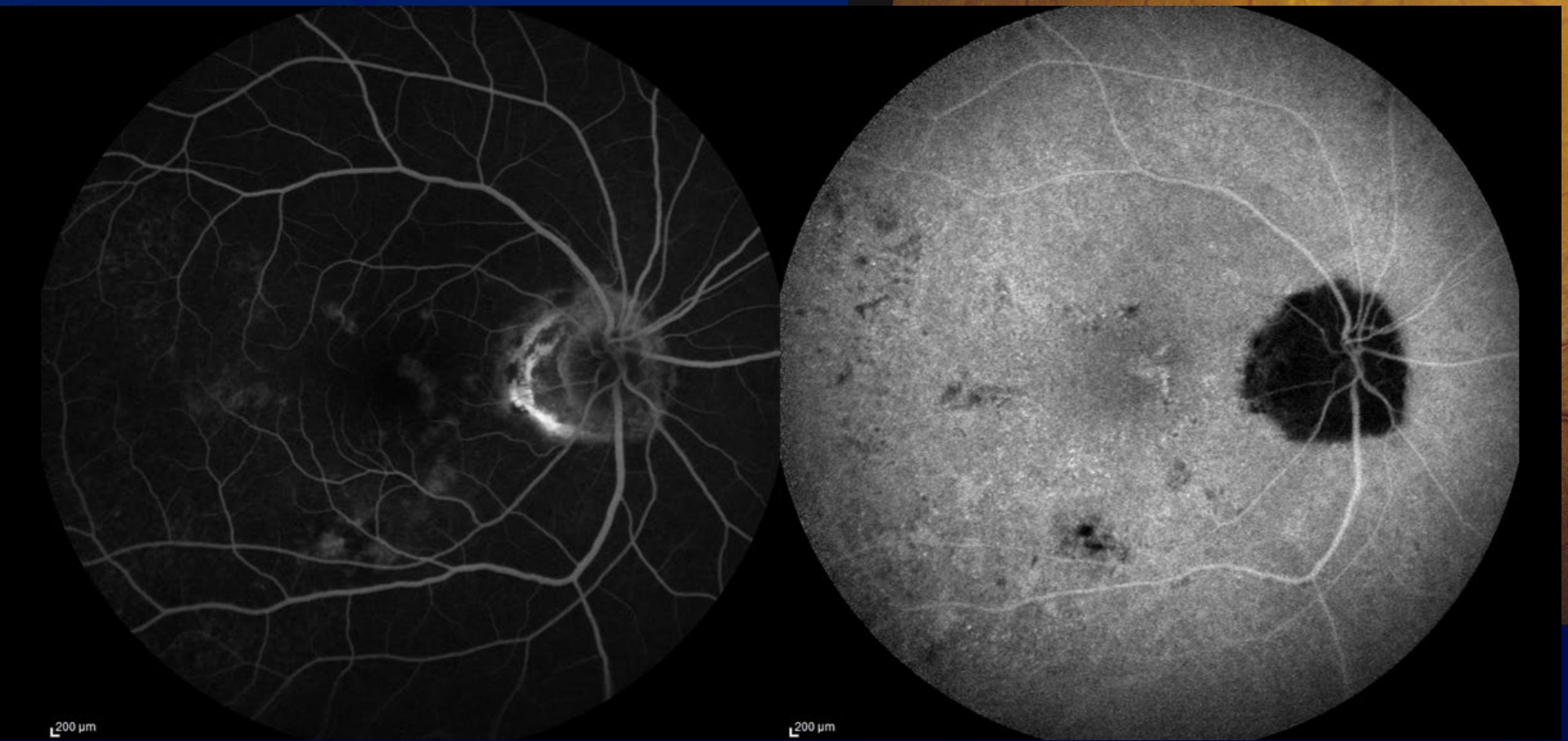
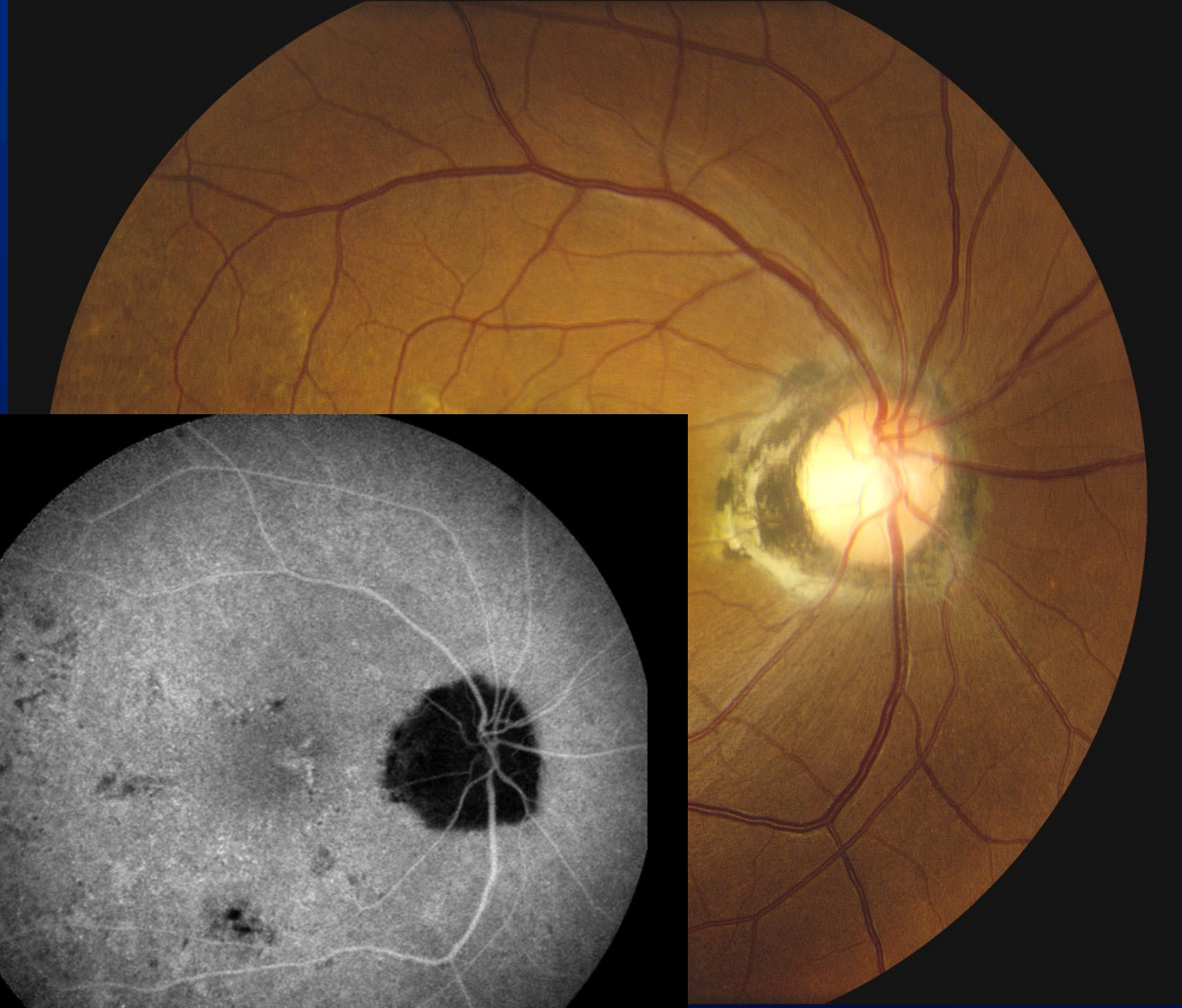
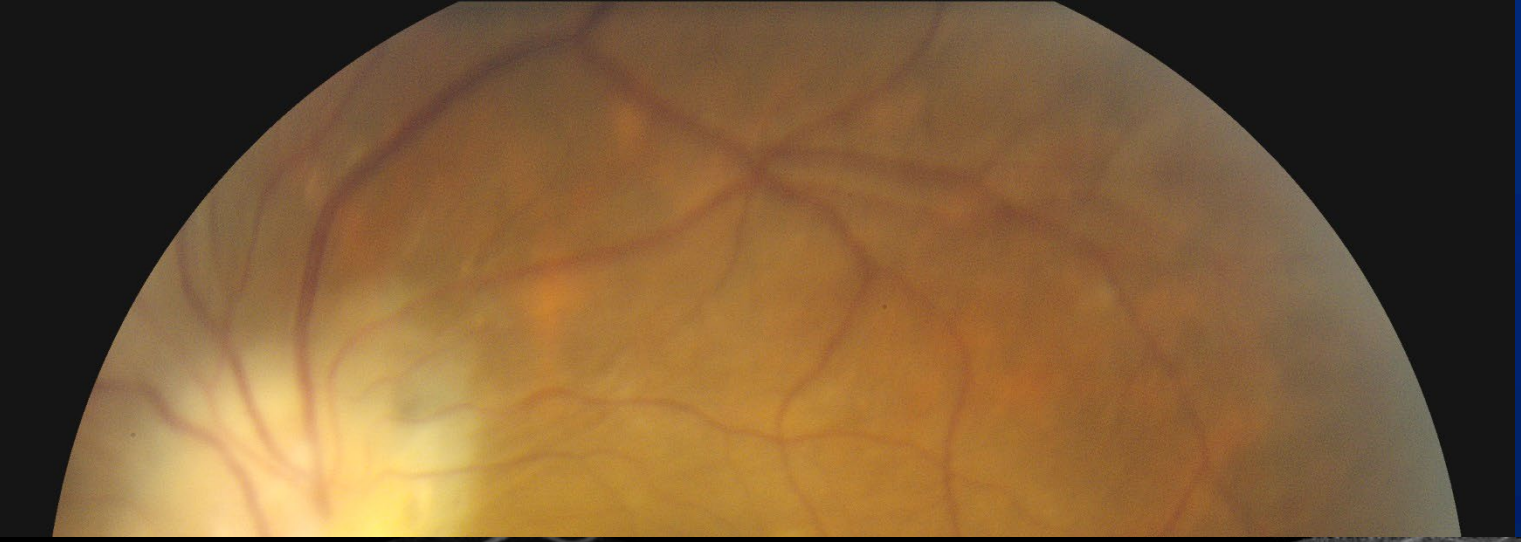
Visual Acuities, both eyes: 20/70 (without correction)

No anterior uveitis or vitreous inflammation





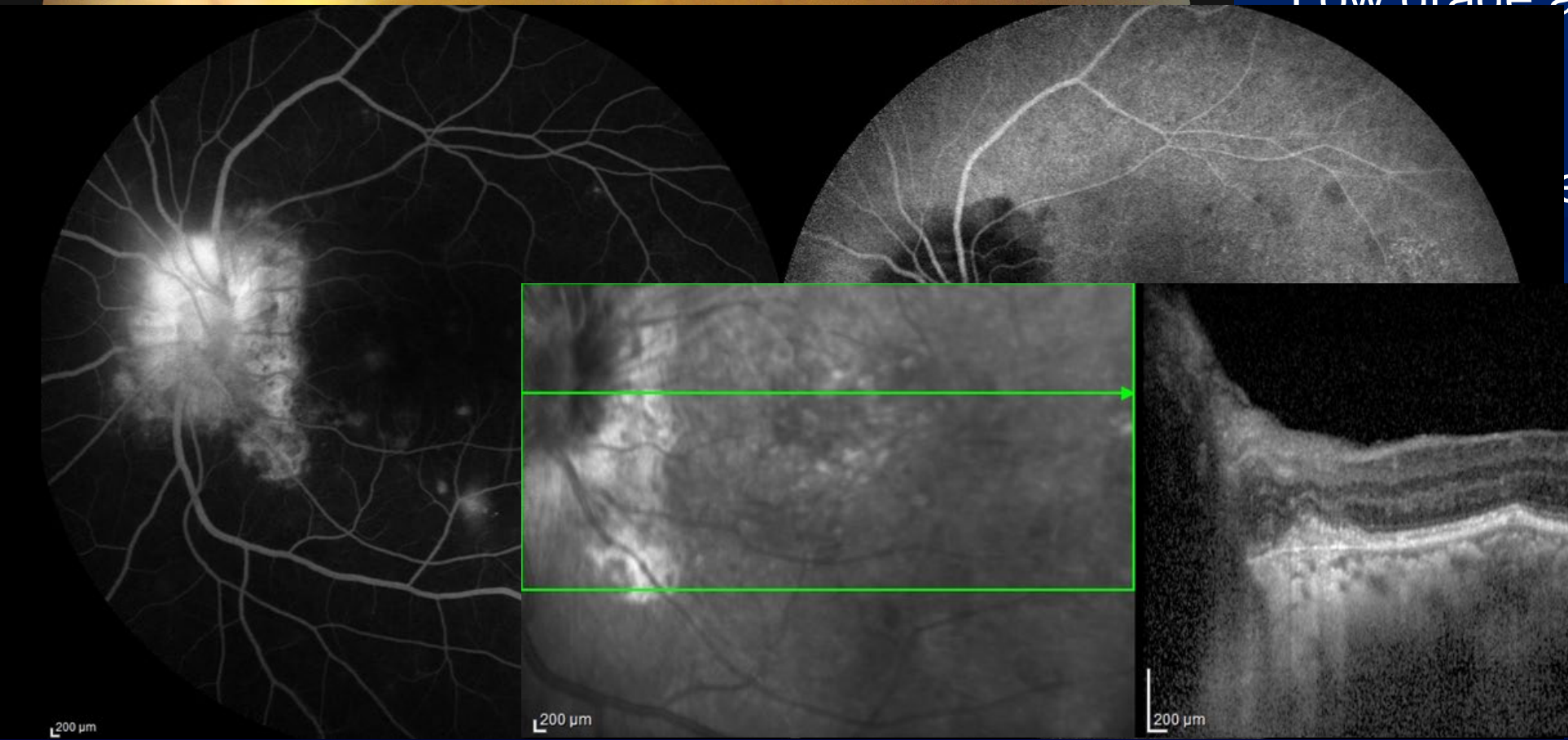


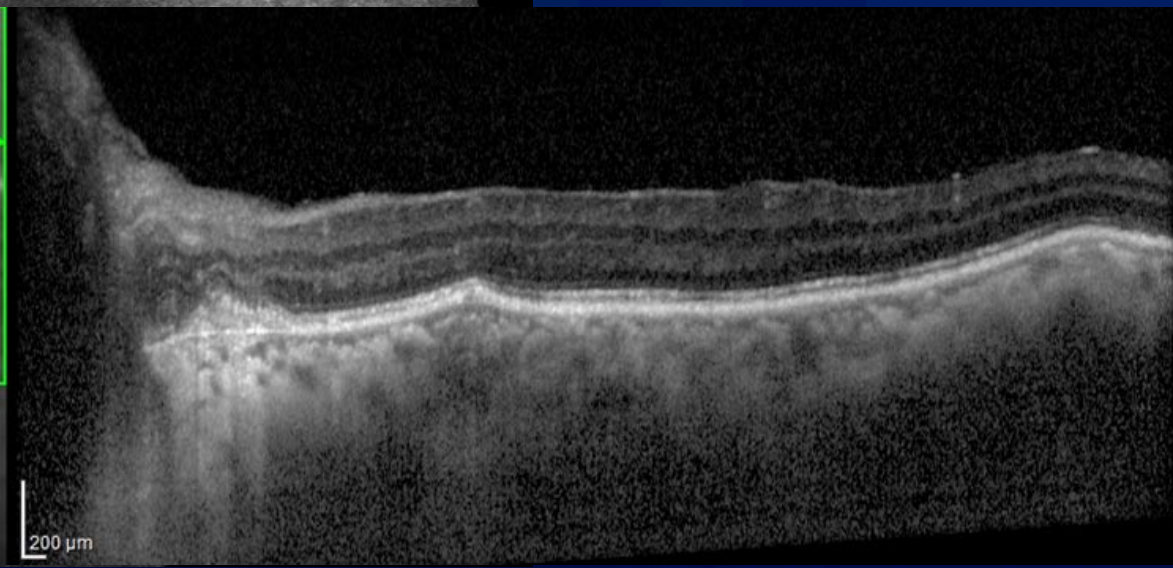
VA 20/80 (without correction)

Treated with periocular triamcinolone injection three months earlier

Low grade anterior uveitis

eous cell





Lab work up

- Positive
  - Quantiferon (9.42 antigen value)
  - CRP 15.3 mg/dL (<8.0)
  - Hepatitis A total ab, Hep Bs Ab (neg HBs Ag)
  - Toxoplasma IgG
  - Lyme ELISA equivocal (negative Western blot)
- Negative/Within normal limits
  - Syphilis IgG, Hepatitis C, HIV, ANA, TSH, Free T4, Creatinine, AST, lysozyme, ESR, CBC

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Case continued

- Neck CT: multiple, prominent, mildly enlarged lymph nodes in the right neck.
  - Differential: tuberculosis, inflammatory disease, neoplastic entities
  - Biopsy recommended
- Chest CT: previous granulomatous infection with associated non-calcified nodules (likely reflective of previous active TB). right middle lobe bronchiostenosis with partial collapse of the right middle lobe

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Case continued

- She did not show up for cervical lymph node biopsy
- Case reviewed by ID. Due to concern for disseminated tuberculosis (lymphadenopathy) with ocular involvement, contacted her county tuberculosis clinic with recommendations to establish follow up and start quadruple drug treatment for at least two months
- She stopped medication after one month and said that she did not believe that she had TB

MAYO CLINIC

Ocular TB – when to treat?
COTS: consensus statements (Delphi technique)

- Exclusion of other diagnoses mimicking TBU
- Ocular phenotype suggestive of TBU
  - Granulomatous anterior uveitis
  - Intermediate uveitis with snowballs, diffuse retinal vasculitis
  - Retinal vasculitis with occlusive disease, perivascular choroiditis patches
  - Serpiginous-like choroiditis, choroidal tuberculoma, multifocal or unifocal choroiditis

Strong consensus to treat:

- Recurrent anterior uveitis, intermediate uveitis, panuveitis
  - TB endemic or non-endemic
  - 2 positive immunologic tests
  - Positive radiologic tests
- Active retinal vasculitis
  - TB endemic
  - 2 positive immunologic tests
  - Positive radiologic tests

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COTS Online calculator

- Online clinical scoring system for initiating antitubercular therapy in patients with ocular TB
- https://www.ocularTB.net/cots-calc
- Derived from COTS Consensus (COTS CON) data
- Using a two-step Delphi method, 81 experts evaluated 486 clinical scenario-based questions, ranking their likelihood of initiating ATT in each specific scenario.
- The median scores and interquartile ranges (IQR) of each scenario were tabulated, representing the expert consensus on whether to initiate ATT in that scenario. The consensus table was encoded to develop the COTS Calculator.

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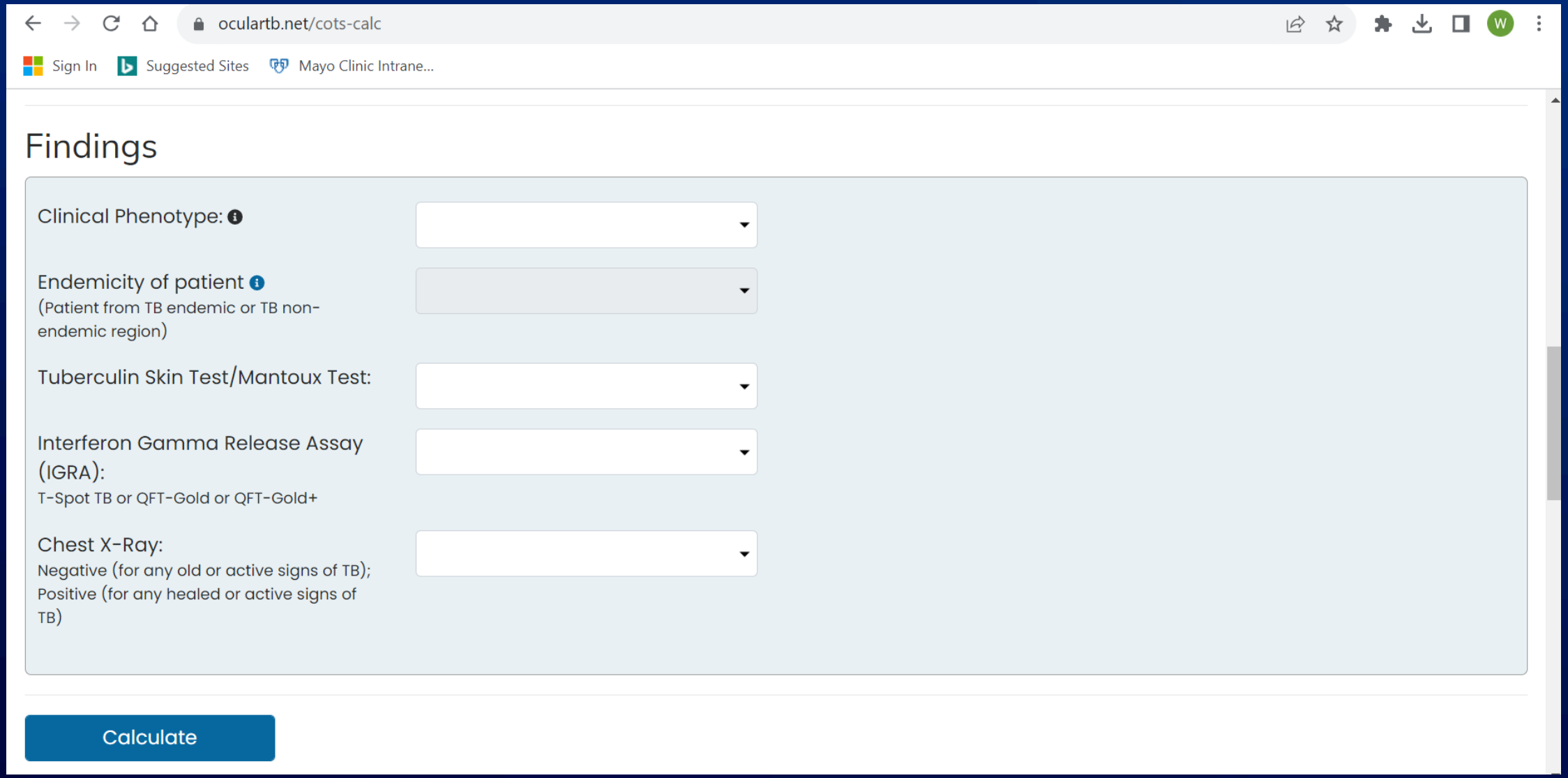
COTS online calculator
https://www.ocularTB.net/cots-calc

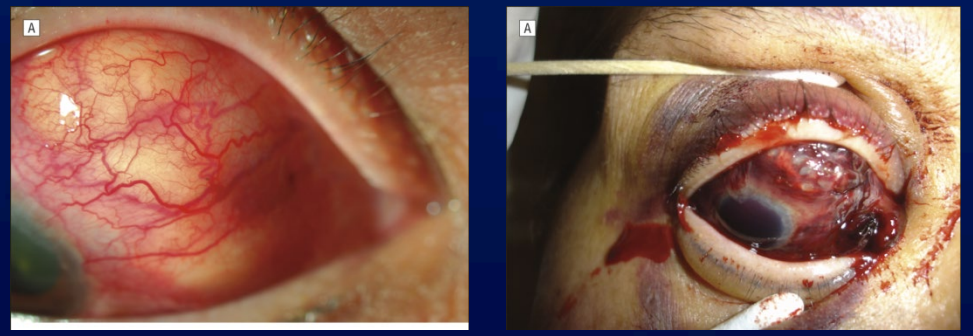


Delayed diagnosis/treatment: Sight- and/or life-threatening consequences

Patel et al. JAMA Ophth 2013:

- Midwestern U.S. cohort of 14 patients
- Average delay from ocular disease onset to uveitis referral: 755.3 days
  - Non-Hispanic white race, posterior uveitis
- Vision loss associated with diagnosis after 500 days, age >50 yrs

Corneoscleral perforation
Choroiditis affecting macula, optic nerve
Choroidal neovascular membrane
Endophthalmitis



Kesen MR. Arch Ophthalmol. 2009 Aug;127(8):1079-80.

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Summary – ocular TB

- Direct or hematogenous spread vs immune response to extraocular TB
- Ocular TB: any ocular structure may be involved
- Orbital involvement/scleritis: risk of loss of the eye
- Tubercular uveitis: risk of vision loss
- Features suggestive of tubercular uveitis: granulomatous inflammation (iris nodules, snowballs, choroidal granulomas), occlusive retinal vasculitis
- Positive testing on ocular fluids NOT required to treat
- Clinical context, ocular features, supportive extraocular testing (immunologic, radiographic)

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Pre-test Question

Which test is most likely to indicate that ATT should be initiated for tubercular uveitis?

A. MTB PCR of ocular fluid

B. Ophthalmic photography

C. Interferon gamma release assay

D. B and C

MAYO CLINIC

Pre-test Question

Which test is most likely to help guide the decision to initiate ATT for tubercular uveitis?

A. MTB PCR of ocular fluid

B. Ophthalmic photography

C. Interferon gamma release assay

D. B and C

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References

1. Agarwal A et al. The Collaborative Ocular Tuberculosis Study (COTS)-1 Report 3: Polymerase Chain Reaction in the Diagnosis and Management of Tubercular Uveitis: Global Trends. Ocul Immunol Inflamm. 2019;27(3):465-473.
2. Agrawal R et al. Collaborative Ocular Tuberculosis Study Consensus Group. Collaborative Ocular Tuberculosis Study Consensus Guidelines on the Management of Tubercular Uveitis-Report 2: Guidelines for Initiating Antitubercular Therapy in Anterior Uveitis, Intermediate Uveitis, Panuveitis, and Retinal Vasculitis. Ophthalmology. 2021 Feb;128(2):277-287.
3. Agrawal R et al. The Collaborative Ocular Tuberculosis Study (COTS) calculator-a consensus-based decision tool for initiating antitubercular therapy in ocular tuberculosis. Eye (Lond). 2023 May;37(7):1416-1423.
4. Alvarez GG, Roth VR, Hodge W. Ocular tuberculosis: diagnostic and treatment challenges. Int J Infect Dis. 2009 Jul;13(4):432-5.
5. Babu RB, Sudharshan S, Kumarasamy N, Therese L, Biswas J. Ocular tuberculosis in acquired immunodeficiency syndrome. Am J Ophthalmol. 2006 Sep;142(3):413-8.
6. Bansal R, Gupta A, Gupta V, Dogra MR, Sharma A, Bambery P. Tubercular serpiginous-like choroiditis presenting as multifocal serpiginoid choroiditis. Ophthalmology. 2012 Nov;119(11):2334-42.
7. Biswas J, Aparna AC, Annamalai R, Vaijayanthi K, Bagyalakshmi R. Tuberculous scleritis in a patient with rheumatoid arthritis. Ocul Immunol Inflamm. 2012 Feb;20(1):49-52.
8. Bodaghi B, LeHoang P. Ocular tuberculosis. Curr Opin Ophthalmol. 2000 Dec;11(6):443-8.
9. Cutrufello NJ, Karakousis PC, Fishler J, Albini TA. Intraocular tuberculosis. Ocul Immunol Inflamm. 2010 Aug;18(4):281-91.
10. Demirci H, Shields CL, Shields JA, Eagle RC Jr. Ocular tuberculosis masquerading as ocular tumors. Surv Ophthalmol. 2004 Jan-Feb;49(1):78-89.
11. Gupta A, Bansal R, Gupta V, Sharma A, Bambery P. Ocular signs predictive of tubercular uveitis. Am J Ophthalmol. 2010 Apr;149(4):562-70.
12. Ishaq M, Feroze AH, Shahid M, Baig MA, Ameen SS, Feroze SH, Chishti RA. Intravitreal steroids may facilitate treatment of Eales' disease (idiopathic retinal vasculitis): an interventional case series. Eye (Lond). 2007 Nov;21(11):1403-5.
13. Kesen MR, Edward DP, Rao NA, Sugar J, Tessler HH, Goldstein DA. Atypical infectious nodular scleritis. Arch Ophthalmol. 2009 Aug;127(8):1079-80.
14. Madge SN, Prabhakaran VC, Shome D, Kim U, Honavar S, Selva D. Orbital tuberculosis: a review of the literature. Orbit. 2008;27(4):267-77.
15. Mittal R, Tripathy D, Sharma S, Balne PK. Tuberculosis of eyelid presenting as a chalazion. Ophthalmology. 2013 May;120(5):1103.e1-4.
16. Nazari Khanamiri H, Rao NA. Serpiginous choroiditis and infectious multifocal serpiginoid choroiditis. Surv Ophthalmol. 2013 May-Jun;58(3):203-32.
17. Patel SS, Saraiya NV, Tessler HH, Goldstein DA. Mycobacterial ocular inflammation: delay in diagnosis and other factors impacting morbidity. JAMA Ophthalmol. 2013 Jun;131(6):752-8.
18. Rathinam SR, Lalitha P. Paradoxical worsening of ocular tuberculosis in HIV patients after antiretroviral therapy. Eye (Lond). 2007 May;21(5):667-8.
19. Sheu SJ, Shyu JS, Chen LM, Chen YY, Chirn SC, Wang JS. Ocular manifestations of tuberculosis. Ophthalmology. 2001 Sep;108(9):1580-5.
20. Testi I et al. Tubercular Uveitis: Nuggets from Collaborative Ocular Tuberculosis Study (COTS)-1. Ocul Immunol Inflamm. 2020 Sep 30;28(sup1):8-16.
21. Van der Lelij A, Rothova A. Diagnostic anterior chamber paracentesis in uveitis: a safe procedure? Br J Ophthalmol. 1997 Nov;81(11):976-9.

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Thank you!

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Recognizing the Vision-Related Clues by Dr. Kubat

Management of Ocular TB

AMERICAN ACADEMY OF OPHTHALMOLOGY®

Collaborative Ocular Tuberculosis Study Consensus Guidelines on the Management of Tubercular Uveitis—Report 1

Guidelines for Initiating Antitubercular Therapy in Tubercular Choroiditis

Rupesh Agrawal, MD,[1,2,3,4] Ilaria Testi, MD,[2] Sarakshi Mahajan, MBBS,[5] Yew Sen Yuen, FRCS,[6] Aniruddha Agarwal, MD,[7] Onn Min Kon, MD,[8] Talin Barisani-Asenbauer, MD,[9] John H. Kempen, PhD,[10,11] Amod Gupta, MD,[7] Douglas A. Jabs, MD,[12,13] Justine R. Smith, MD,[14] Quan Dong Nguyen, MD,[15] Carlos Pavesio, FRCOphth,[2] Vishali Gupta, MD,[7] for Collaborative Ocular Tuberculosis Study Consensus Group*

AMERICAN ACADEMY OF OPHTHALMOLOGY®

Collaborative Ocular Tuberculosis Study Consensus Guidelines on the Management of Tubercular Uveitis—Report 2

Guidelines for Initiating Antitubercular Therapy in Anterior Uveitis, Intermediate Uveitis, Panuveitis, and Retinal Vasculitis

Rupesh Agrawal, MD,[1,2,3] Ilaria Testi, MS,[2] Baharam Bodaghi, MD,[4] Talin Barisani-Asenbauer, PhD,[5] Peter McCluskey, MD,[6] Aniruddha Agarwal, MD,[7] John H. Kempen, PhD,[8,9] Amod Gupta, MD,[7] Justine R. Smith, PhD,[10] Marc D. de Smet, PhD,[11] Yew Sen Yuen, FRCOphth,[12] Sarakshi Mahajan, MD,[13] Onn Min Kon, MD,[14] Quan Dong Nguyen, MD,[15] Carlos Pavesio, FRCOphth,[2] Vishali Gupta, MD,[7] for Collaborative Ocular Tuberculosis Study Consensus Group

Tuberculosis

BMJ Open Respiratory Research

BTS clinical statement for the diagnosis and management of ocular tuberculosis

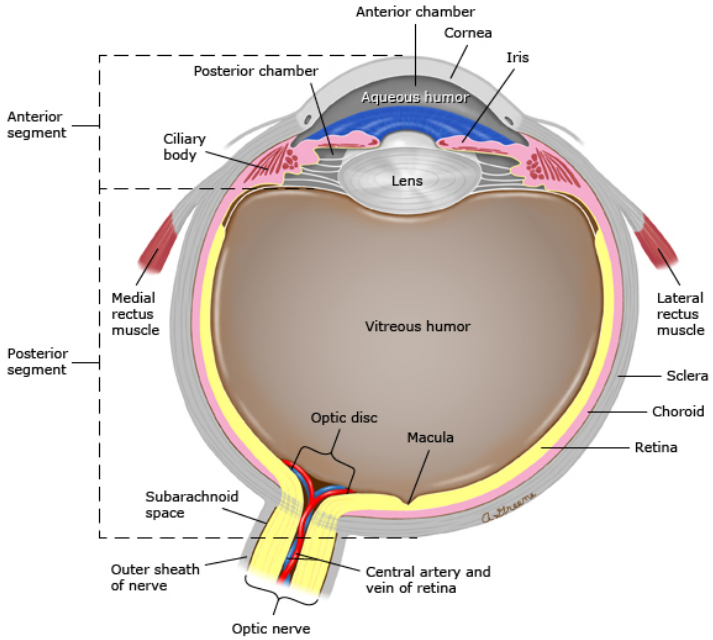
Onn Min Kon ,[1,2] Nicholas Beare ,[3,4] David Connell,[5] Erika Damato,[6] Thomas Gorsuch,[7] Guy Hagan,[8] Felicity Perrin,[9] Harry Petrushkin,[10] Jessica Potter,[11] Charanjit Sethi,[12] Miles Stanford[13]

Management of Ocular TB

- General recommendations:
  - **Pts with suspected ocular TB should be jointly managed by ophthalmologists + TB centers**
  - Consider ocular TB as cause of ocular symptoms when pts have TB risk factors
  - Be aware of increased risk for disseminated TB including ocular TB in immunosuppressed individuals with TB
  - Consider ocular TB even in absence of evidence of pulmonary TB, particularly in immunosuppressed population

Management of Ocular TB

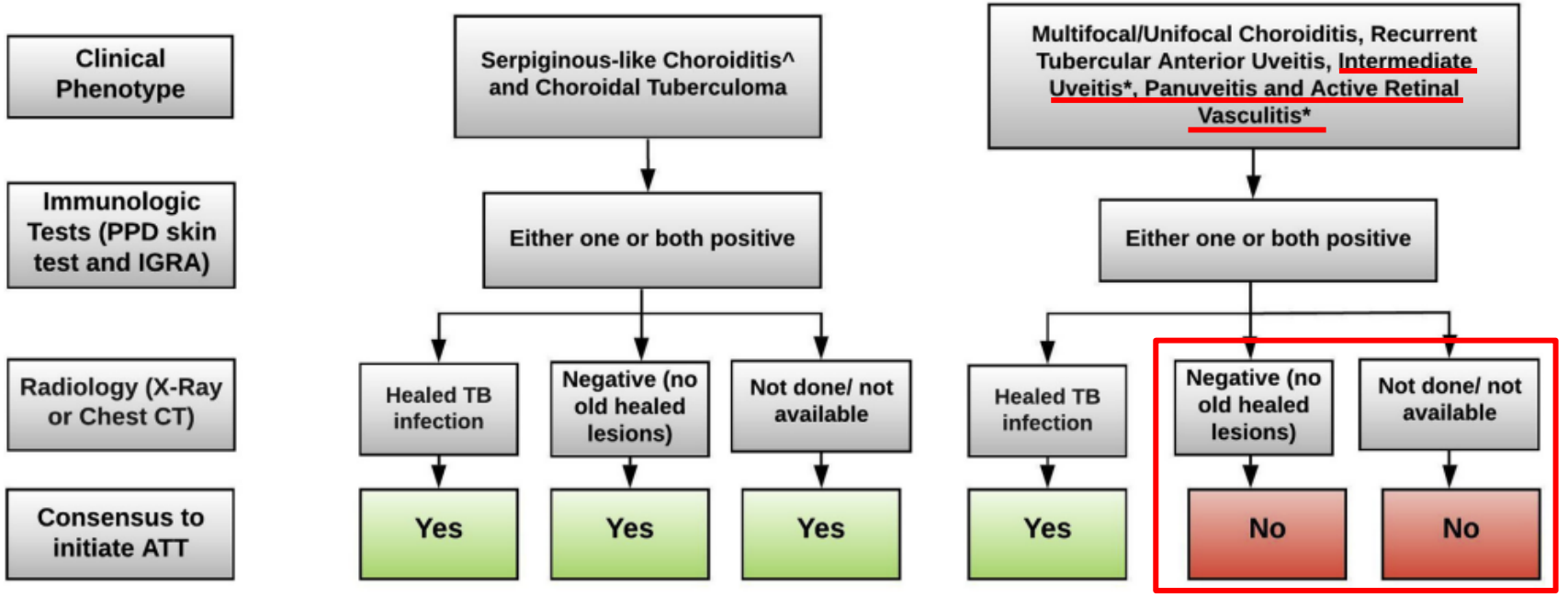
- Ophthalmology evaluation:
  - All pts with uveitis and positive IGRA should have CBC, CMP, syphilis and HIV screens, HBV and HCV screens
    - Consider HLA-B27, ACE level, ESR/CRP, ANA, ANCA, Toxoplasma and Lyme serology
  - Recommend color fundoscopic images for documentation and monitoring, macular ocular coherence tomography (OCT) for evaluation of macular lesions and macular edema, wide field fluorescein angiography (WFFA) if suspected retinal vasculitis or to further characterize chorioretinitis
  - Consider ocular fluid sampling if positive IGRA, pt at high risk for TB, but uveitis appearance less typical for TB
    - MTB PCR on ocular fluids is specific but low sensitivity (33-67%)
    - Aqueous fluid has similar yield to vitreous fluid, easier to obtain



Management of Ocular TB

- Other recommended testing for uveitis with positive IGRA/suspicion for ocular TB
  - Urgent CXR
  - Obtain AFB sputa if radiographic or clinical concern for pulmonary TB
  - Could consider more advanced imaging (CT, PET) when available to evaluate for nidus of pulmonary or extrapulmonary infection and guide sampling
  - As with all forms of TB, negative IGRA **DOES NOT** completely rule out active TB disease
    - Can consider use of both IGRA and TST for improved sensitivity

Management of Ocular TB

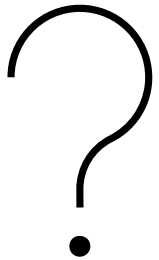


Immunologic tests: PPD (Purified Protein Derivative) skin test- positive with induration of >10mm; **IGRA** (Interferon Gamma Release Assays) - QuantiFERON-TB Gold, Qiagen, Germantown, MD; or T-Spot TB; Oxford Diagnostic laboratories, Memphis, TN; **ATT** - Antitubercular Therapy; **TB** - Tuberculosis
* For endemic regions only

The algorithm illustrates the consensus to initiate ATT in patients from both TB endemic and non-endemic regions. In addition, consensus to initiate ATT was obtained for:- **First episode of anterior uveitis** - if both immunologic tests positive and evidence of healed TB infection on radiology. **Intermediate uveitis** patients from TB non-endemic region with positive PPD, IGRA not done/not available with evidence of healed TB infection on radiology and for patients with negative PPD, one of the two IGRA test positive with evidence of healed TB infection on radiology. ^**Serpiginous-like choroiditis** patients from TB endemic region with positive PPD, negative IGRA, radiological test negative or not done/not available or in patients from TB non-endemic region with negative PPD, positive IGRA, radiological test negative or not done/not available. **Tuberculoma**– for patients from TB-endemic region with only evidence of healed TB infection on radiology even with the absence of any positive immunologic test. Agrawal et al, *Ophthalmology,* 2021

- Note: these were criteria for which consensus to start therapy was achieved within the guideline group – not exhaustive, assess individual risk/suspicion for ocular TB to guide decision to start therapy

Polling Question



What special considerations are a part of management of ocular TB?

A. Treatment duration may need to be extended, particularly if severe disease or slow response to therapy

B. Steroids (local or systemic) may be needed as part of therapy

C. Fluoroquinolones can be considered in place of ethambutol

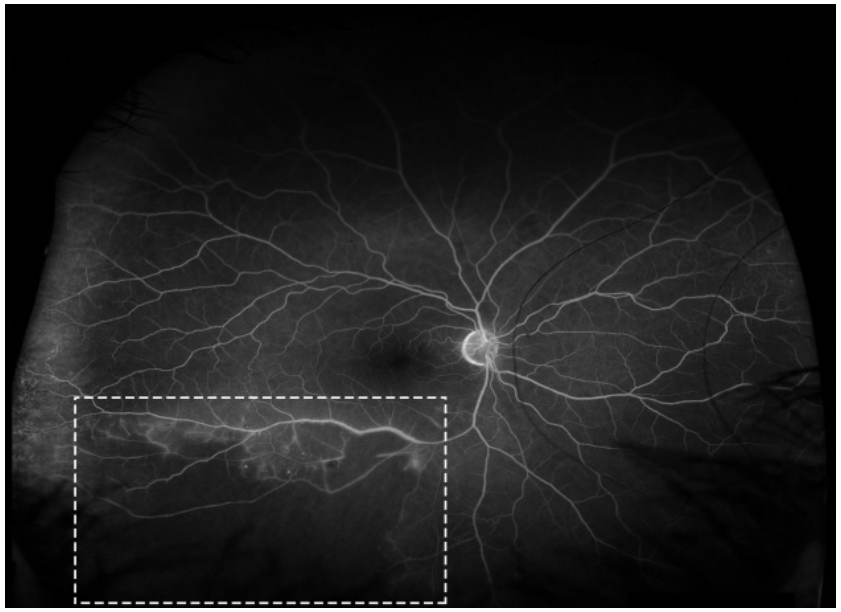
D. All of the above

Management of Ocular TB

- Anti-tuberculous therapy:
  - Standard TB therapy with RIF + INH + PZA + EMB x2 months, followed by 4 months of RIF + INH recommended
    - Consider long continuation phase (9-12 months total) particularly if slow improvement or initial severe disease
      - Retrospective cohort study (UK) – 175 pts, >9 months of TB treatment associated with reduced risk of recurrent inflammation (Agrawal et al, *Ocular Imm and Inflamm,* 2015)
      - Retrospective cohort study (Philippines) – 182 pts, 64 received 6 months or more TB therapy - >9 months TB therapy had lower rate of recurrent eye disease compared to no treatment (OR 0.09), <9 months of therapy did not reach statistical significance
    - Can consider substitution of levofloxacin or moxifloxacin for ethambutol
      - 43 pts given MFX in place of EMB, no sig difference in treatment failure (Potter et al, *Ocular Imm and Inflamm,* 2016)

Management of Ocular TB

- Adjunctive therapy:
  - Use of local (topical or intravitreal) and systemic steroids or other immunosuppressive agents should be guided by the extent of disease, evidence of structural damage, and response to TB therapy
    - Specifically recommend high-dose systemic steroids in setting of occlusive retinal vasculitis and choroidal lesions typical of ocular TB
    - Can sometimes see paradoxical worsening of inflammation with initiation of TB treatment, may need increased steroids
  - Laser retinal photocoagulation should be considered for occlusive retinal vasculitis if signs of neovascularization
  - Pars plana vitrectomy can be considered in some cases



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Monitoring on Therapy

- Monitor for Improvement
  - Visual acuity measurements
  - Reduction in inflammatory changes on fundoscopic exam
  - Reduction in steroid dosing
- Monitor for Toxicity
  - Standard lab monitoring for toxicities with TB therapy
  - Ethambutol – regular evaluation for ethambutol toxicity at ophthalmology visits, close monitoring for new visual symptoms (in particular change in color vision or reduced central vision)

Outcomes of Ocular TB

- Goal of Treatment – improvement in vision/visual functioning or prevention of further deterioration in vision due to progression/spread of disease
- COTS-1 Study (Agrawal, *JAMA Ophthal*, 2017) - 801 pts with ocular tuberculosis
  - Treatment failure in 12.7% - higher in group receiving steroids (21%), mostly driven by those receiving steroids prior to initiation of TB therapy - ?confounding by severity of disease
    - Persistence or recurrence of inflammation w/in 6 months of completing TB treatment, inability to taper oral steroids to <10 mg/day or topical steroids to <2 drops daily, or persistent inflammation requiring steroid-sparing agent
- Meta-analysis showed that 69% of patients receiving therapy showed improvement in visual acuity, 92% showed improvement in inflammation
  - Kee et al, *Surv Ophthal,* 2016

Take Home Points

- Ocular TB should be considered for patient's even in absence of evidence of pulmonary TB/TB at other sites
- Ocular TB is a difficult diagnosis, usually clinical based on ophthalmic exam findings + IGRA – ocular fluid sampling limited by poor sensitivity
- Ocular TB treatment should be carefully co-managed by ophthalmologist + TB physician

Questions and Answers

Thank you