Sunnybrook
HEALTH SCIENCES CENTRE

Séminaire
Winter Arrhythmia
School
Annual Cardiac Arrhythmia Meeting
Division of Cardiology, University of Toronto

Amaurosis Fugax and Retinal Arteriolar Occlusive Disorders

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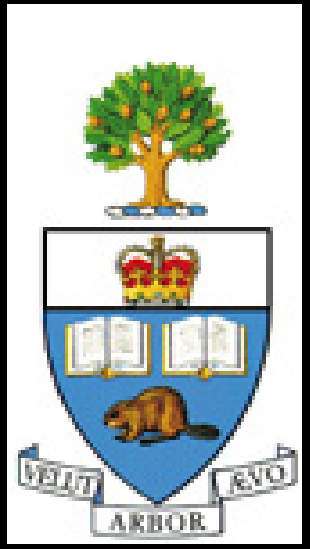


Disclosure

- NO RELEVANT COMMERCIAL INTERESTS
- NO CONFLICT OF INTEREST(S)

Retinal Arteriolar Occlusions

CLASSIFICATION

1. Amaurosis Fugax
2. Central retinal artery occlusion (CRAO)
3. Branch retinal artery occlusion (BRAO)
4. Cotton wool spot

Amaurosis Fugax - Overview

- Amaurosis in Greek means ‘Dark’ and Fugax in Latin refers to ‘Fleeting”
- 1% Risk for permanent visual loss
- Estimated annual risk for stroke is 2% (Poole at al.) when compared to hemispheric TIAs where the annual risk is higher at 5% - 8%
- Transient monocular visual impairment can be also caused by other conditions that may mimic retinal TIAs

Amaurosis Fugax

Task of the physician is to differentiate between Retinal TIAs and other benign causes

Amaurosis Fugax – Clinical Features

- Sudden onset, painless, monocular visual loss
- Altitudinal, central, peripheral, segmental or complete
- Visual loss fairly dense – usually reported as ‘darkening or fogging’ of visual field (and not just blurring)
- In 25% cases there is ‘curtain’ like progression. This is highly suggestive of an embolic cause
- Duration: Usually 1 – 5 minutes; typically less than 10 minutes

Red Flags on the History

1. Transient blurred vision with neck flexion: Ipsilateral high-grade carotid stenosis

2. Elderly patient with new onset headache: ? Temporal arteritis

3. Amaurosis Fugax with contralateral motor/ sensory symptoms and/ or aphasia: Embolism though Ipsilateral carotid artery

4. Head injury or contact sports: Carotid dissection

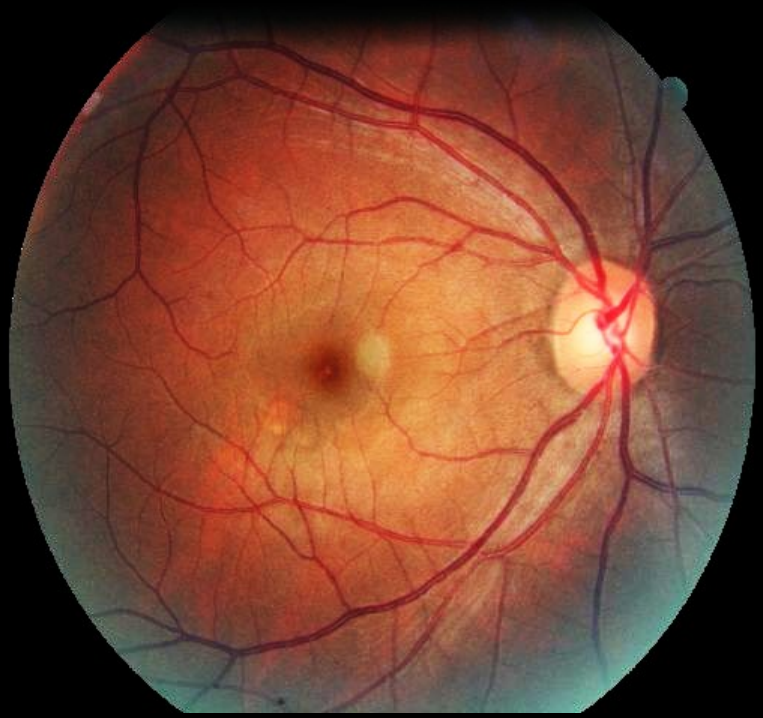
5. Retinal claudication: Temporal arteritis, Severe carotid stenosis. Mechanism: Photoreceptor ischemia

Red Flags on History

6. Postprandial Amaurosis: High-grade carotid stenosis with vascular steal phenomenon

7. Nasal visual defect: Retinal emboli

Temporal



Nasal

Right eye

Transient Monocular Visual Loss

Other causes

- Dry eyes/ Blepharitis
- Transient elevation in intraocular pressure eg. Uveitis
- Intermittent angle-closure glaucoma: Pain, Redness, Halos
- Retinal vasospasm/ Retina Migraine
- Floaters
- Fluctuations in blood sugar

Amaurosis Fugax - Pathophysiology

Mechanism: Temporary interruption of blood flow to the retina (Embolism > Thrombosis)

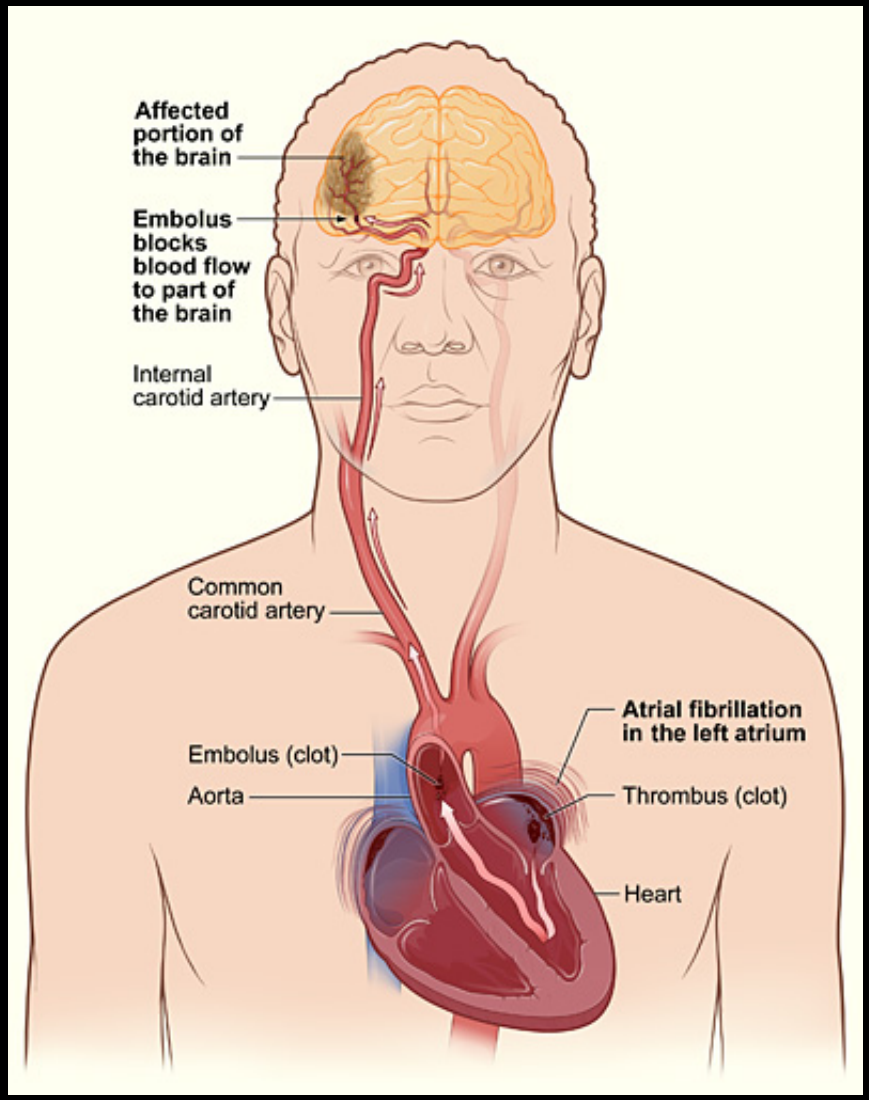
Causes

1. Atherosclerosis of Carotid artery or Aortic arch; Carotid dissection

2. Cardioembolism

3. Vasculitis

4. Hypercoagulable disorders



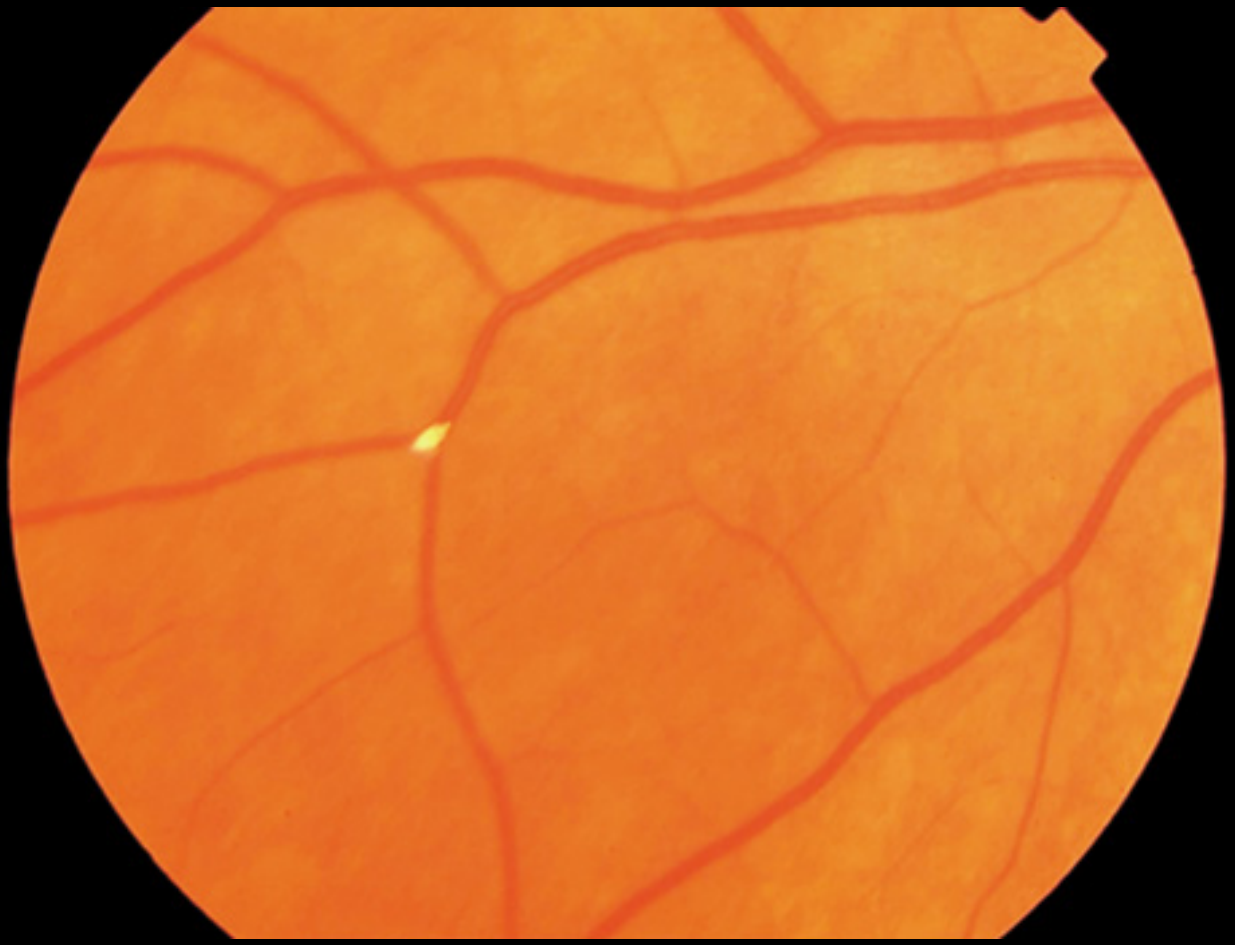
Types of Retinal Emboli

- Hollenhorst plaque (Cholesterol)
- Platelet-fibrin
- Calcific emboli
- Atrial Myxoma
- Bacterial vegetations
- Amniotic fluid, Talc, Air, Fat

- Platelet-fibrin and Hollenhorst emboli predict a high risk for stroke

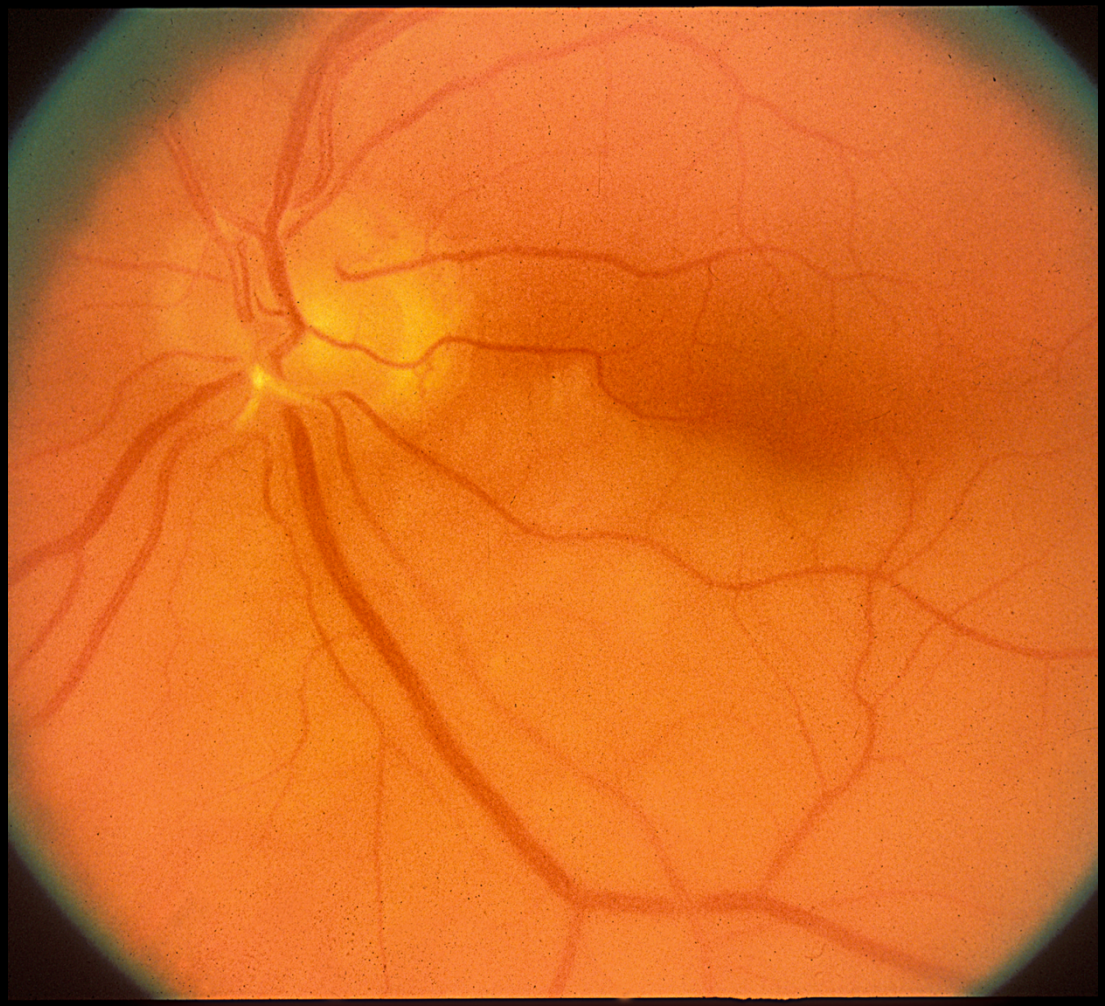
- Annual stroke risk in retinal emboli is 8.5% (Bruno et al. 1995). ALL PATIENTS MUST HAVE DILATED EYE EXAM

Retinal Emboli – Hollenhorst plaque



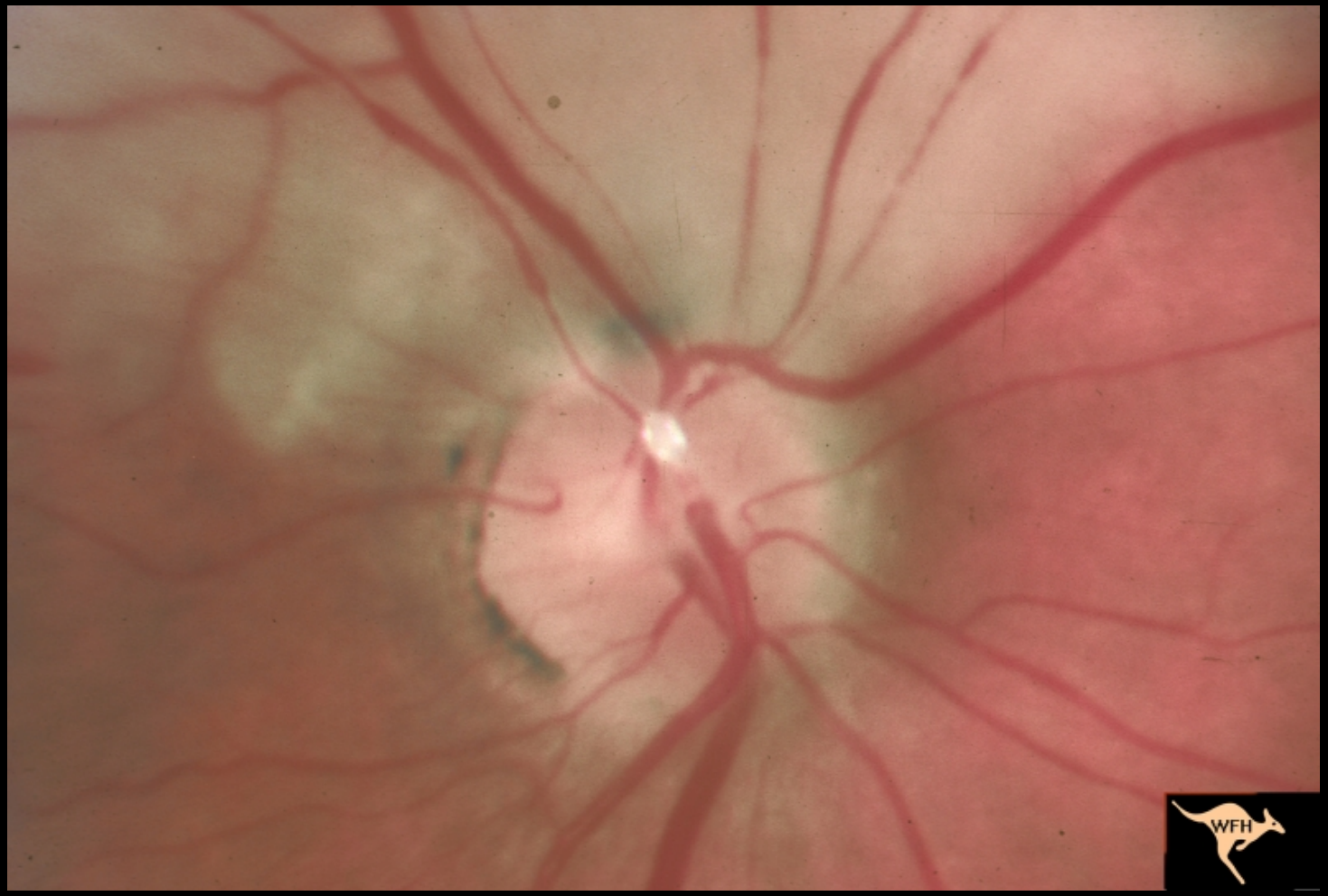
Hollenhorst (Cholesterol) plaque: Copper colored refractile bodies that lodge at bifurcation

Retinal Emboli – Platelet-fibrin



Platelet-fibrin embolus: Yellowish-grey, elongated cast like appearance

Retinal Emboli - Calcific



Calcific embolus: Large, whitish, globoid embolus

Central Retinal Artery Occlusion

- Sudden catastrophic monocular visual loss
- 12% have warning Amaurosis Fugax
- There is no definitive treatment; interventions are often disappointing
- Potential for visual restoration, at least partly, within 4 hours
- Acute management: Anterior chamber paracentesis, Ocular massage, Diamox, Carbogen inhalation (95% oxygen and 5% CO_2) to induce retinal vasodilation

Central Retinal Artery Occlusion

Cherry red spot

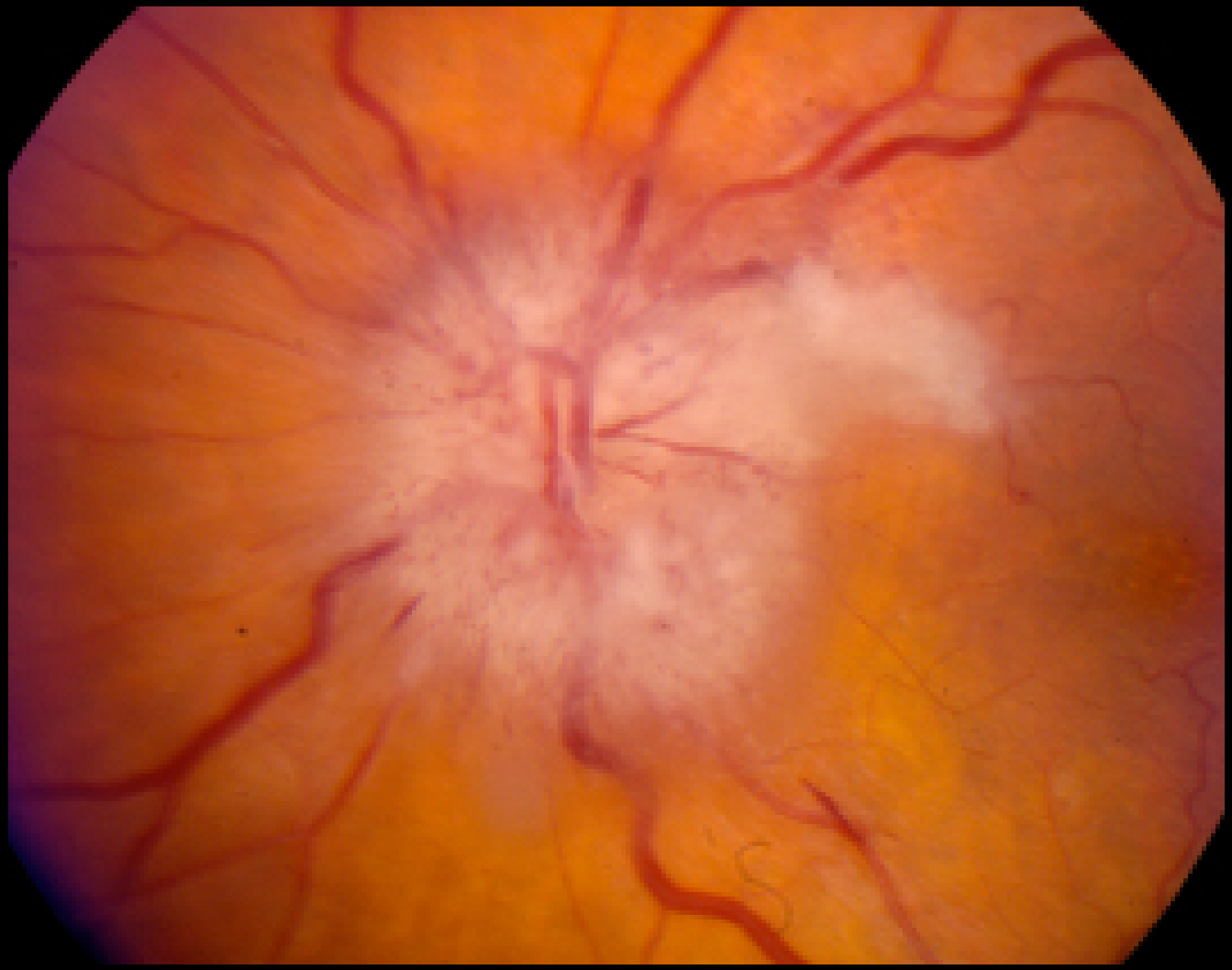
Giant Cell Arteritis

- A true neuro-ophthalmic emergency
- Vasculitis of large and mid-sized arteries containing elastic lamina
- Age: Usually > 70, risk increases over 80
- Acute visual loss due to optic nerve head infarction (Arteritic Anterior Ischemic Optic Neuropathy) or Retinal artery occlusion from vasculitic process
- Simultaneous bilateral involvement in 20 – 60% patients
- Headache, scalp tenderness, jaw claudication, fever, malaise, weight loss and/or polymyalgia rheumatica

Giant Cell Arteritis

- 31% patients have preceding Amaurosis Fugax
- ESR and CRP must be checked in all patients over age 50 with Amaurosis Fugax
- Temporal artery biopsy Gold standard
- If untreated, fellow eye is involved in 75%, usually within one week
- No reason to hold treatment while awaiting biopsy
- Non ocular complications: MI, Aortic dissection, Stroke
- Treatment with steroids for 1 – 2 years, sometimes longer

Giant Cell Arteritis



Anterior Ischemic Optic Neuropathy
Chalky white disc edema extending beyond the disc margin

Initial Approach to Amaurosis Fugax

- Vitals
- Visual acuity and Visual fields to confrontation technique
- Pupils: Relative afferent pupillary defect
- Attempt fundoscopic exam
- Carotid bruit; Auscultation of heart; Temporal artery tenderness
- Brief neurological exam
- Advice a Baby Aspirin, if not contraindicated
- CRAO? Send to emergency room

Investigations

ALL PATIENTS MUST HAVE A STROKE WORK UP

- Carotid doppler
- ESR, CRP for all patients over 50 years
- Screen for vascular risk factors, Hypercoagulable screen
- Echo/ Holter monitor: Rule out cardioembolism
- MRI brain: Incidental embolic hits in the cerebral hemisphere
- CT or MR angiogram if carotid dissection is suspected

Treatment

- Antiplatelet therapy
- Add statin, especially in Carotid artery disease and Hollenhorst plaque
- Carotid endarterectomy within 2 weeks after the event, if ipsilateral carotid stenosis of more than 70%
- Anticoagulation if patient had Atrial fibrillation
- Address vascular risk factors
- Corticosteroids for Temporal arteritis

Summary

- Amaurosis Fugax (retinal TIA) causes sudden painless visual loss lasting for less than 10 minutes
- Estimated annual risk for stroke is 2% in Amaurosis Fugax, but this increases to 8.5% if a retinal embolus is detected
- All patients with Amaurosis Fugax should have a stroke work up and dilated fundoscopic examination
- Carotid atherosclerosis is the most common cause of Amaurosis Fugax
- Patients with High-grade symptomatic carotid artery disease benefit from Carotid endarterectomy within 2 weeks

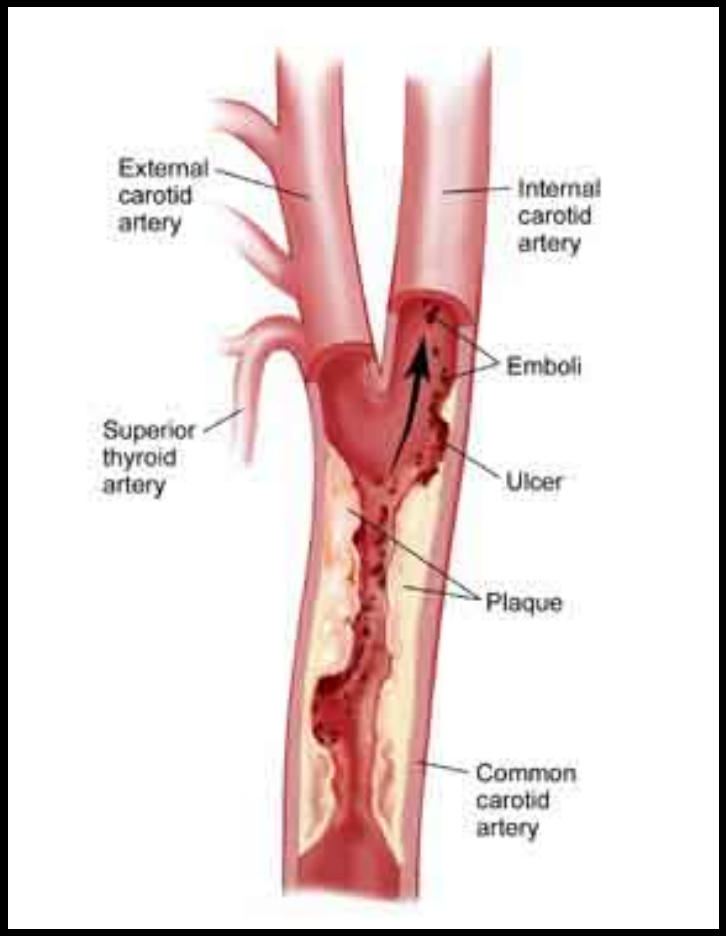
Summary

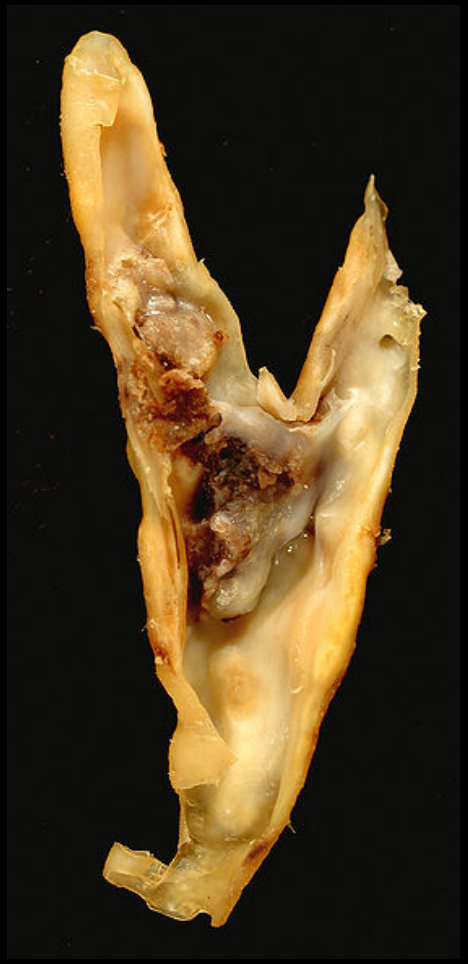
- Central retinal artery occlusion is an ocular emergency with some potential for visual improvement with timely intervention
- 12% of patients with CRAO experience Amaurosis Fugax before the catastrophic visual loss
- Temporal arteritis is a serious systemic vasculitic disorder which can present with Amaurosis Fugax in 31% cases
- Patients with suspected temporal arteritis should be started on Corticosteroids while temporal artery biopsy is pending
- Advise an antiplatelet agent (if not contraindicated) while the patient is under investigations for Amaurosis Fugax

Thank you!

Supplementary Slides

Carotid Stenosis





66% of patients with retinal embolus have carotid stenosis
18% have hemodynamically significant stenosis

Carotid stenosis

- Symptomatic carotid disease: Sudden onset of Retinal or hemispheric TIA resulting in visual or neurological symptoms within 6 months (North American Symptomatic Carotid Endarterectomy Trial 1991; European Carotid Surgery Trial1991)

- These randomized controlled trials have proven that CEA is safe and effecting in reducing stroke risk in patients with symptomatic carotid disease

- CEA is recommended with symptomatic carotid disease between 70%-90% in patient with life expectance over 5 years if:
    1. Lesion surgically accessible
    2. No risk for anesthesia
    3. No prior ipsilateral endarterctomy

North American Symptomatic Carotid Endarterectomy Trial

- Randomized, prospective, multi-center controlled trial that studied 659 patients

- Studied patients with symptomatic carotid stenosis of 70 % - 99%, who had retinal TIA or hemispheric TIA or non-disabling stroke within 120 days

- Study terminated prematurely because of evidence that surgery was highly beneficial in the selected group of patients

North American Symptomatic Carotid Endarterectomy Trial - Conclusions

- A lower risk for any stroke or death (15.8% CEA versus 32.3% Medical therapy)
- Lower risk for ipsilateral stroke (9% CEA versus 23% Medical therapy)
- Lower risk for major or fatal ipsilateral stroke (2.5% versus 13.1%)
- Lower risk of any major stroke or death (8% versus 19.1%)
- Patients older than 75 had more benefits from CEA compared to younger subjects. So CEA need not be withheld in patients over 75 who are fit

North American Symptomatic Carotid Endarterectomy Trial

Moderate stenosis (50 – 69% stenosis)

- Marginal statistical significance favouring surgery
- 5-year rate of any ipsilateral stroke: 15.7% in CEA and 22.2% in Medical therapy

Stenosis of less than 50%

- No benefit from surgery

North American Symptomatic Carotid Endarterectomy Trial

- Risk for perioperative stroke and death was higher at 30 day (5.8% in CEA compared to 3.3% with medical therapy)

Five baseline variables that were predictive of high perioperative risk:

1. Hemispheric (versus retinal TIA) as the qualifying event
2. Left sided procedure
3. Contralateral carotid occlusion
4. Ipsilateral ischemic lesion on CT
5. Irregular or ulcerated plaque

Pooled data of NASCET, ECST, VA Studies

- 70% or more symptomatic stenosis: CEA is beneficial with absolute risk reduction of 16% over 5 years
- Near occlusion: No significant benefit with CEA. ARR over 2 years was 5.6% and -1.7% over 5 years
- 50-69% symptomatic stenosis: CEA was beneficial with ARR 4.6% over 5 years
- CEA not beneficial in patients between 30-49% stenosis
- CEA harmful in patients with symptomatic stenosis less than 30%

Pooled data of NASCET, ECST, VA Studies

- Women did not benefit from CEA for 50-69% stenosis
- Men had more favourable benefit from CEA
- Women had significantly high perioperative stroke and or death compared to men
- Medically treated women had significantly less risk for ipsilateral stroke compared to men

Timing of CEA – NASCET and ECST Pooled data (within 2 weeks after TIA)

- ARR in 70% or more symptomatic stenosis who had CEA:
  - Within 2 weeks = 30.2% ARR
  - 2-4 weeks = 17.6% ARR
  - 4-12 weeks: 8.9% ARR

- In symptomatic stenosis 50 to 60%:
  - Clinically important benefits were noticed only when CEA was performed within 2 weeks of the last event

- In women, the decline of benefit of CEA was more rapid. So surgical benefit in women was confined to those who had the CEA within 2 weeks after the event, irrespective of the degree of stenosis

Timing of CEA – Meta analysis (within 2 days versus 2 weeks after event)

- Meta analysis of 47 studies published between Aug 2008 and Mar 2015

  - CEA within 48 hours: Peri-procedural risk for stroke and death in stroke as index event 8.4 % and with TIA as event 2.8%

  - CEA within 2 weeks: Peri-procedural stroke and death in stroke as index event 4.9% and TIA as event 1.9%

  De Rango et al. 2015

CEA

1. Patient age: Favourable for CEA in older age
2. Sex: Higher perioperative risk in women; medically treated women had significantly less ipsilateral stroke compared to men
3. Degree of senosis: Better ARR in high grade stenosis; not favourable in near complete occlusion
4. Type of event: Retinal TIA as the index event have better prognosis compared to hemispheric TIA
5. Time since last event (2 days versus 2 weeks): Higher perioperative stroke and death in CEA within 2 days
6. Plaque morphology: Ulcerated irregular plaque carry higher perioperative sroke/ death

Carotid artery stenting

- CEA versus CAS show similar long-term outcomes in syptomatic carotid diseae

- CAS has higher periprocedural risk for 30 days compared tp CEA

CAS is preferred over CEA in:

1. A carotid lesion with poor surgical access
2. Restenosis after carotid endarterectomy
3. Radiation-induced stenosis
4. High anesthesia risk from cardiac or pulomonary disease

Carotid artery stenting

- Meta analysis compared CEA and CAS in symptomatic carotid disease (Bonati et al. 2012)

1. CAS has high periprocedural stroke/ death (8.2% CAS versus 5.0% CEA)
2. Patients over 70 have higher periprocedural risk
3. CAS was associated with significantly lower risk for MI
4. Long-term outcome similar in CAS and CEA, past the periprocedural period

CEA versus CAS

- International carotid stenting study investigator (ICSS) 2010. 1700 patients randomized to CEA or CAS
- Stent protected angioplasty versus carotid endarterectomy (SPACE) 2—6: 1183 patients randomized
- Stenting versus endarterectomy for carotid-artery stenosis (CREST) 2502 patients studied 2010

Retinal Emboli

- Carotid stenosis
  - 66% had carotid disease
  - 30% with more than 50% stenosis ipsilaterally
  - 18% had more than 80% stenosis

  PRESENCE OF RETINAL EMBOLUS IS NOT A GOOD PREDICTOR OF HIGH GRADE STENOSIS. Presence of plaques in the carotid artery is of much greater importance than the degree of stenosis

- Abnormal echo suggesting cardiac source of embolism in 62%

- EMBOLUS COULD HAVE COME FROM CAROTID ARTERY OR THE HEART OR BOTH

(Hayreh et al. 2009)

Retinal Emboli

- ECHO as source
  - Mitral valve 26%: Calcified valve 57%, MVP 17%, Other 26%
  - Aortic valve 36%: Calcified valve 8%, 22% others

(Hayreh et al. 2009)

Central Retinal Artery Occlusion

Prognosis

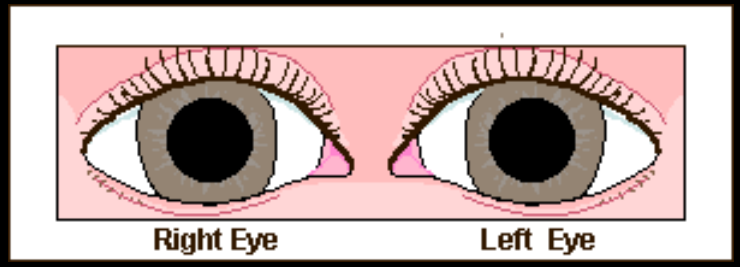
- Patients may show spontaneous visual improvement, primarily within 7 days

- Patients with poor vision (counitng finger or less) improved
  - 87% with transient Non-arteritic CRAO
  - 67% of Non-arteritic CRAO with cilioretinal sparing
  - 22% of Nonarteritic CRAO
  - Little, if at all, in patients with Arteritic CRAO

    (Hayreh et al. 2005)

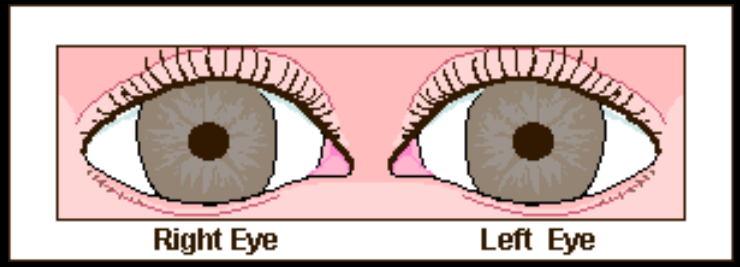
    - Some authors believe that this spontaneous improvement in CRAO may erroneously be attributed to various treatment

Swinging flash light test – Normal



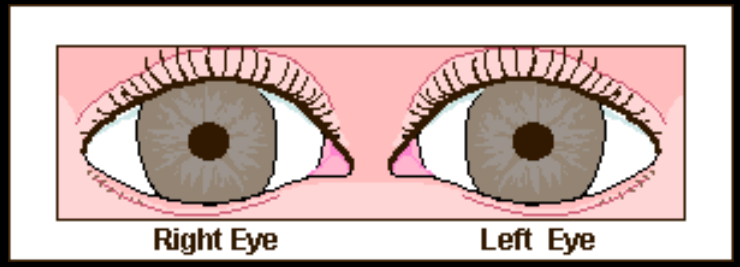
Resting pupil size

Swinging flash light test – Normal



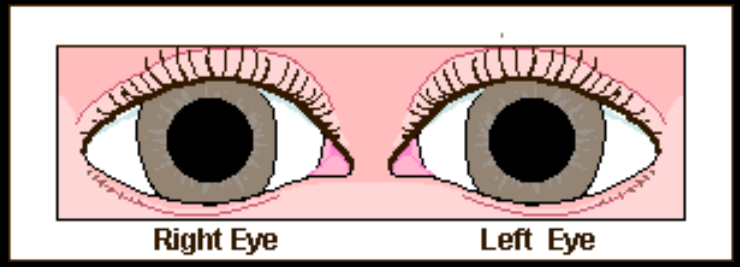
Light in right eye

Swinging flash light test – Normal



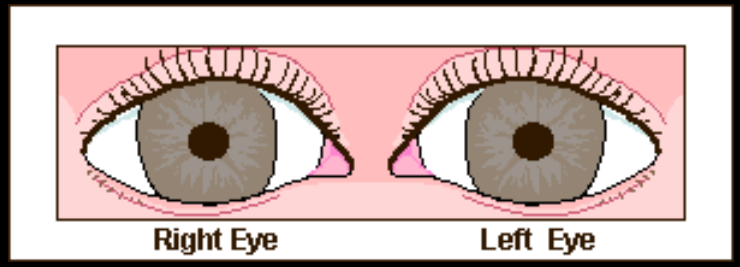
Light in left eye

Swinging flash light test – Left RAPD



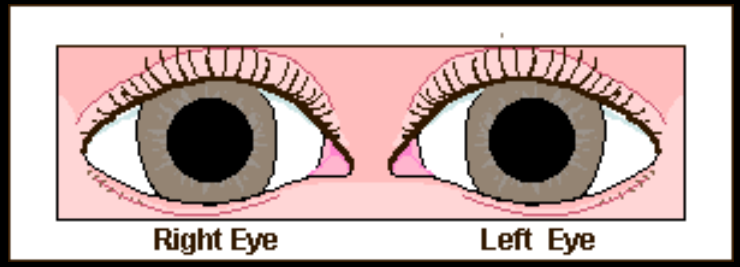
Left Optic neuropathy

Swinging flash light test – Left RAPD



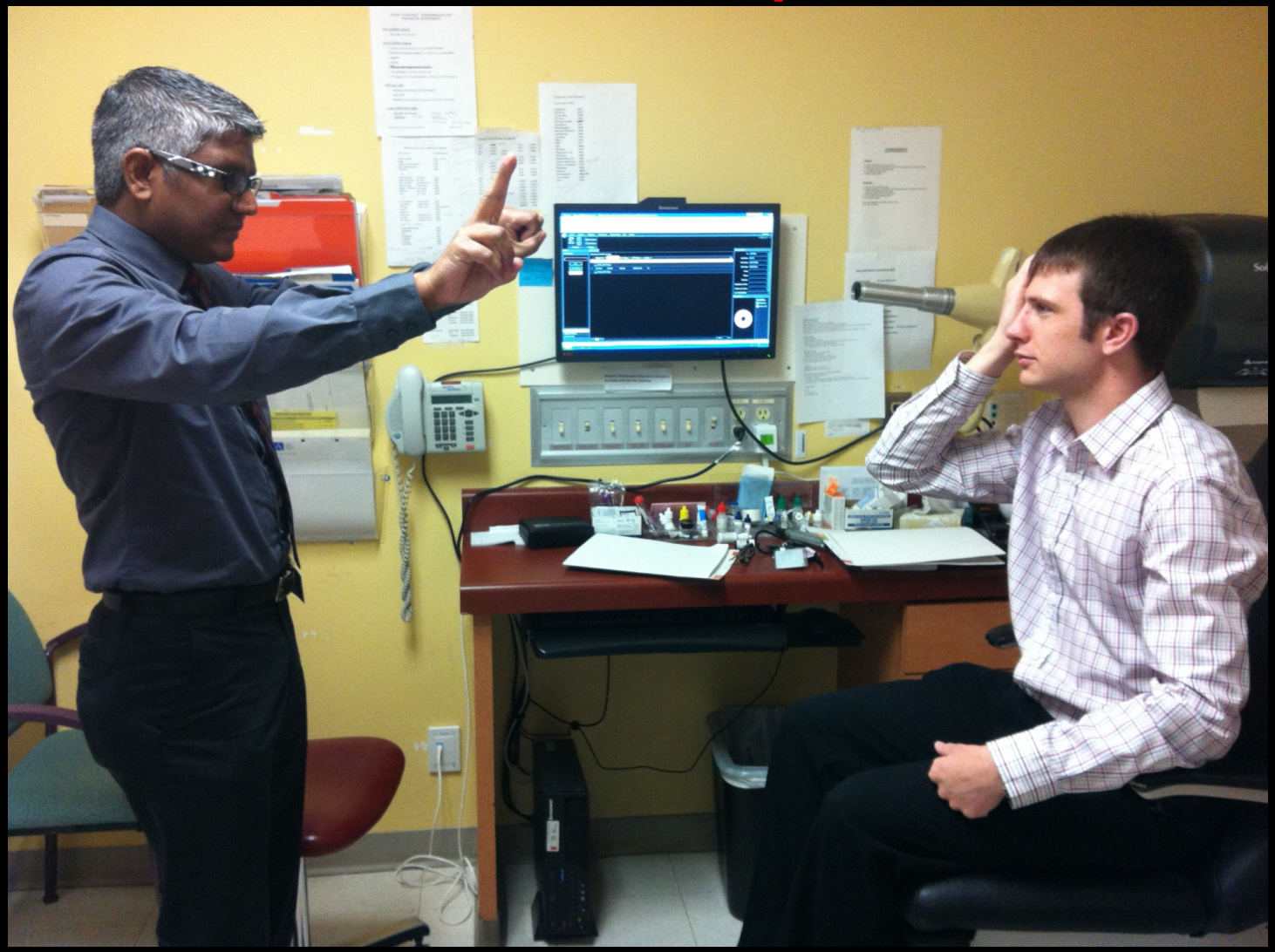
Light in right eye

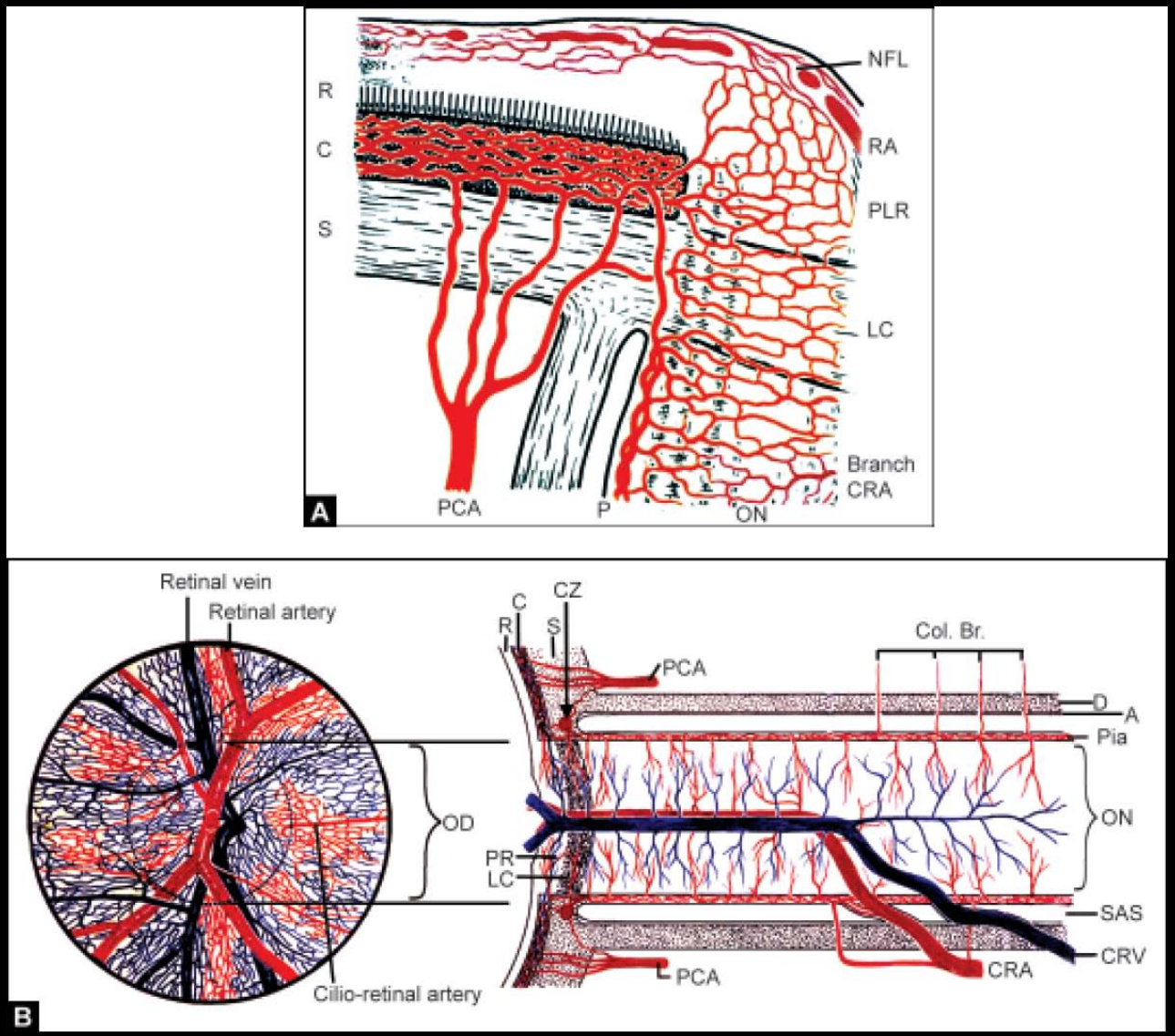
Swinging flash light test – Left RAPD



Light in left eye

Testing visual fields by confrontation technique





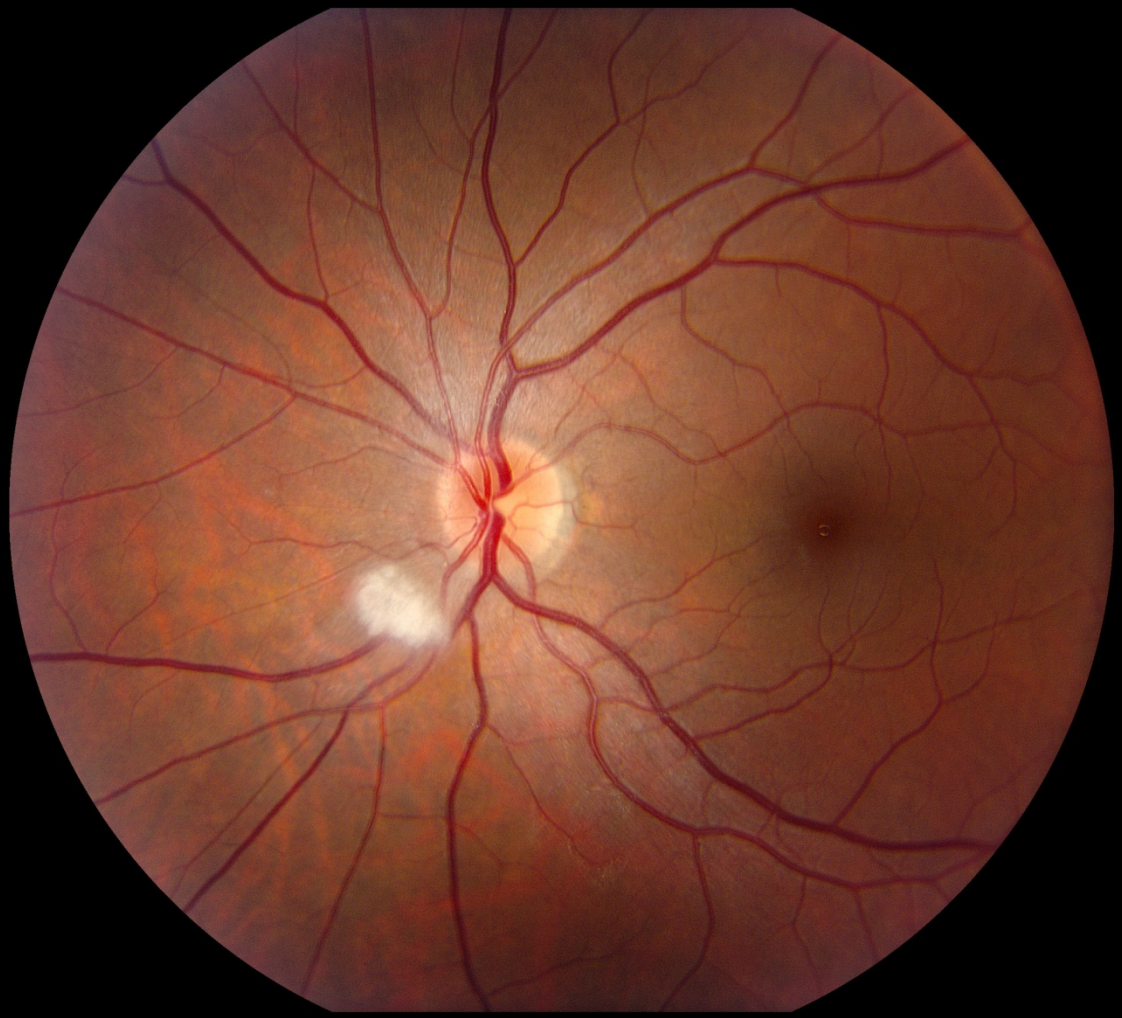
Posterior ciliary artery, branch of ophthalmic artery supplies the choroid, and forms a circle around the optic nerve head (Circle of Zinn-Haller)

Courtesy Dr. Hayrey

Cotton Wool Spot

- Caused due to occlusion of terminal retinal arterioles resulting in focal infarction of the retinal nerve fibre layer
- White fluffy areas in the retina with irregular shapes and feathery margins
- Also called as ‘soft exudates’ by some
- Causes: Diabetes, HTN, GCA, SLE, Wegner’s granulomatosis, SArcoidosis, HIV, CMV, Bartonella, Radiation therapy

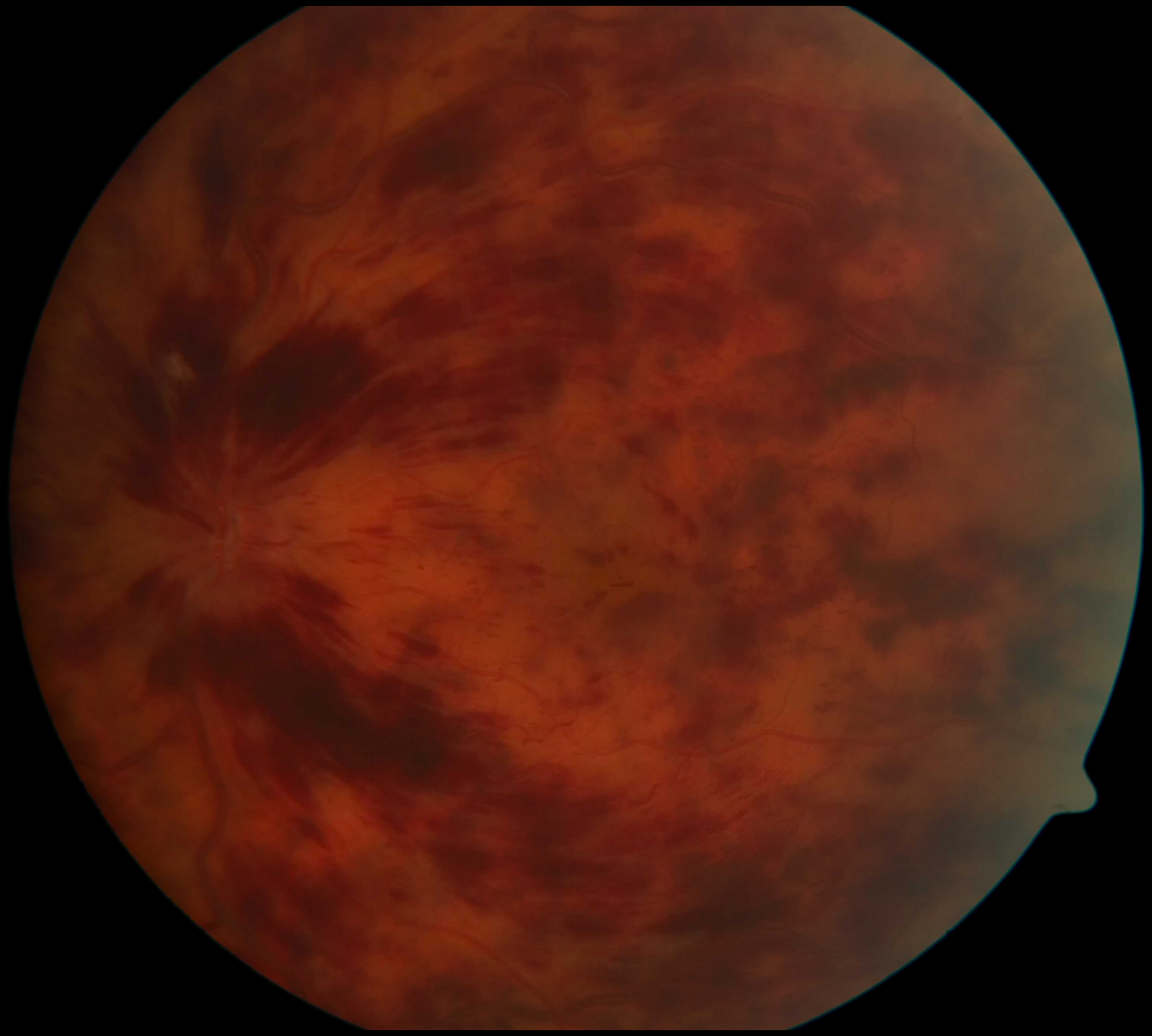
Isolated Cotton Wool Spot



Central Retinal Vein Occlusion

- Subacute monocular visual loss
- Incidence 5 per 1000
- Mechanism: Thrombosis of CRV; Not carotid artery disease. Exact cause not known
- Commonly seen in HTN, DM, CAD and Collagen vascular disease
- Types: Ischemic (poor prognosis), Non-ischemic
- Fundus: Optic disc swelling, dilation of retinal veins, retinal edema, intraretinal hemorrhages and cotton wool spots

Central Retinal Vein Occlusion



Central Retinal Vein Occlusion

- Glaucoma is a risk factor for CRVO
  - Raised IOP produces venous stasis
  - Glaucomatous optic cups may predispose CRVO due tp mechanical effect

TREATMENT

- Available evidence indicate that Aspirin or anticoagulation can worsen retinal hemorrhage
- Oral or intravitreal steroids to reduce macular edema
- Intravitreal antiVEGF has no significant benefit
- Acetazolamide can temporarily reduce macular edema
- Panretinal photocoagulation: Almost universally considered treatment of choice to prevent ocular neovascularization and Neovascular glaucoma

Retinal Migraine

- Least common, most difficult to differentiate from Amaurosis
- Duration 5 – 60 minutes
- Tunnel vision, altitudinal or quadrantic defect
- Permanent blindness from CRAO, BRAO (Lewis et al. ‘89)
- Non invasive inv: TTE, Carotid duplex, Hypercoagulable
- Retinal vasospasm may be seen during episodes (Burger, Selhorst et al. 1991 – NEJM)
- Treatment: Ca channel blockers (Winterkorn et al. 1993)

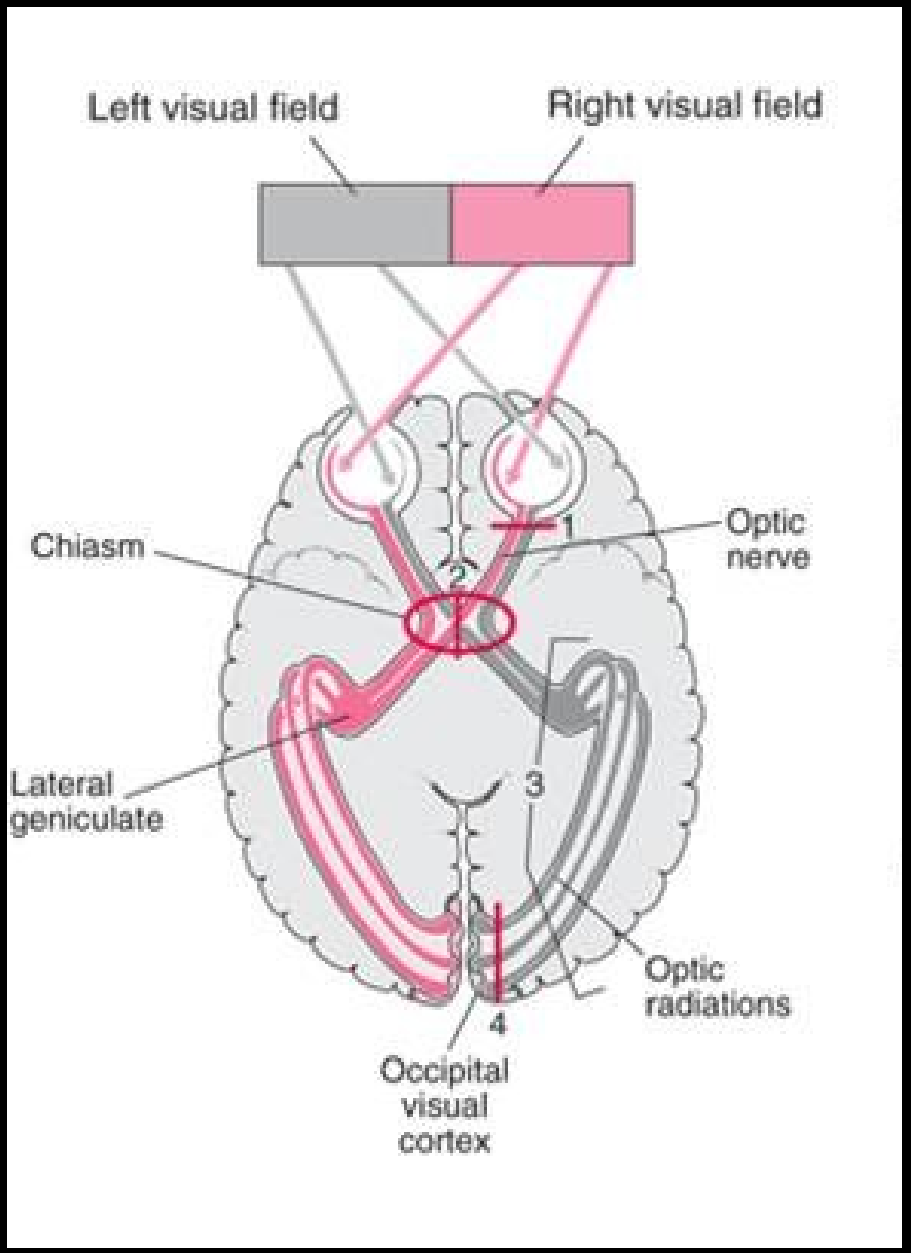
Giant Cell Arteritis

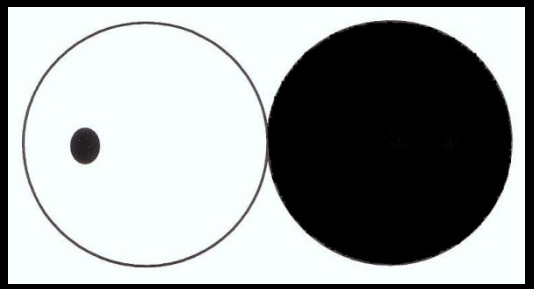
- Histology: Early – Lymphocytic infiltration in the internal and/ or elastic lamina or adventitia, with destruction of those layers. More marked involvement is typified by necrosis and granulomas containing multinucleated foreign-body giant cells, histiocytes and lymphocytes

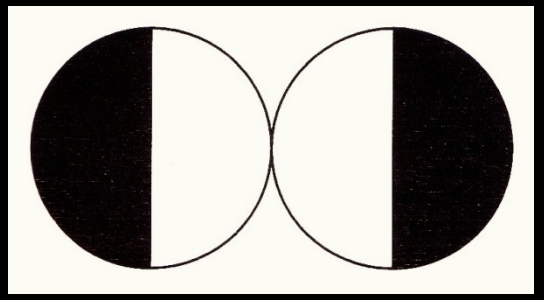
- Inflammation and narrowing of the lumen result in thrombosis and occlusion

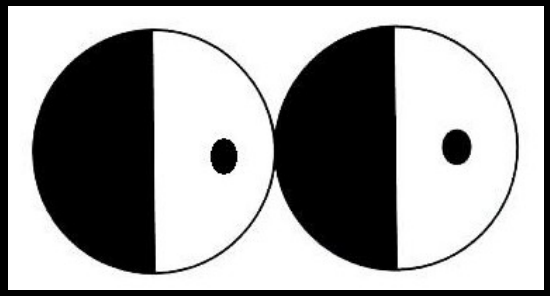
- Greater incidence in patients with HLA antigens DR3, DR4, DR5, DRB1 and Cw3 suggest a genetic predisposition

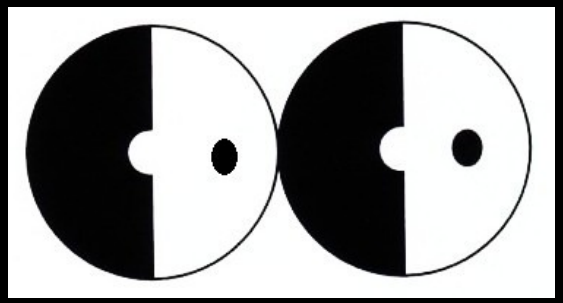
Visual Loss - Localization











Cherry red spot

1. CRAO
2. Tay-Sachs disease
3. Neiman Pick disease
4. Metachromatic leukodystrophy
5. Infantile GM2 gangliosidosis
6. Farber disease
7. Sialidosis

- Lysosomal storage diseases are inherited disorders caused due to deficiency of enzymes required for normal metabolism of lysosomal macromolecules

- Accumulation of lysosomal materials in the ganglion cells, resulting in optic atrophy

- Lysosomal material accumulation give a pale color to the retinal nerve fibre layer. Macula lacks RNFL and appears bright due to choroidal vasculature