CONVERSATIONS IN RETINAL VASCULAR DISEASE

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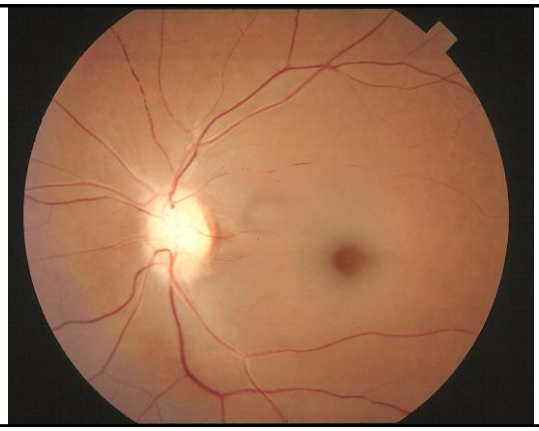
CASE: I (DON'T) FEEL GOOD!

- **66 year old Black male**
- **CC: sudden, painless blurring OS x 3 days**
- **No previous eye or medical care**
- **Wants glasses to clear vision**
- **BVA OD 20/30, OS HM**
- **Pupils: ERRL (+) RAPD OS**
- **Good appetite, poor diet**

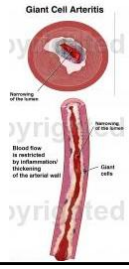


CENTRAL RETINAL ARTERY OCCLUSION (CRAO)

- **Painless, sudden loss of vision**
  - < 20/400 in most cases
- **Retinal edema and white fundus – hypoperfusion**
  - Cherry red spot
- **60's and above**
- **Early and late appearances**
  - Initially normal fundus
  - Optic atrophy with attenuated vessels

CRAO: ETIOLOGY

- **Emboli from heart or carotid lodging at lamina**
- **Intraluminal thrombosis**
- **Dissecting aneurysm**
- **Vasospasm**
- **Arteriolar necrosis**
- **GIANT CELL ARTERITIS!**



CRAO: TREATMENT ?

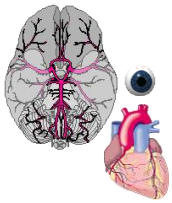
- Paracentesis
- Carbogen
- Digital massage
- Hyperventilation
- Urokinase/streptokinase
- 1-24 hr window of opportunity
- Does anything work?

CRAO: SYSTEMIC CONSIDERATIONS

Atherosclerosis	Hypertension
Carotid artery disease	Diabetes
GCA	Cardiac valve disease
Antiphospholipids ABS	Cardiovascular disease
Infectious endocarditis	Hyperlipidemia
Vasospastic disease	Disc drusen
Cardiac arrhythmia	Mural thrombosis
Clotting factor abnormalities	Hyperviscosity syndromes

CRAO: COMPLICATIONS

- CVA
- MI
  - Main cause of death
  - 9 yr mortality 56%
- NVG
- OIS
- Fellow eye involvement if GCA cause



CRAO: MANAGEMENT

- STAT ESR and CRP for GCA
- Cardiology/ internal medicine referral
- Monitor in 3-6 mos for neovascularization
  - How common is neo?

JAMES' OUTCOME

- Referred for medical care
- Diagnosed with hypertension, NIDDM, hypercholesterolemia
- Returns for ocular follow up 3 months later

  "I'm scared"
- Several toes amputated from diabetes
- Passed away from MI within year

BRAO; CILIORETINAL AO

- BRAO nearly always embolic
- Greater risk of cardiac mortality
- Cilioretinal AO- branch of PCA- high risk of GCA

Guidelines

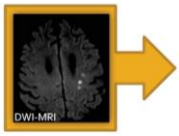
- Any patient with suspected TIA or those with acute retinal ischemia should be evaluated urgently in order to identify those at high risk of immediate cerebral infarction and cardiac ischemia

Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the american heart association/american stroke association. Stroke 2011; 42: 227-276

Adapted from Drs. Nancy Newman and Biousse; 2015

All Patients with Acute Retinal Arterial Ischemia

- MUST have immediate brain imaging
  - Brain MRI with DWI >>> Head CT
- Including patients with transient visual loss (presumed of vascular origin)

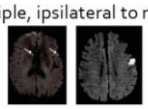


Presence of cerebral ischemia portends higher risk of stroke

Adapted from Drs. Nancy Newman and Biousse; 2015

Concurrent Acute Brain Infarcts in Patients with Monocular Visual Loss

- ¼ with acute retinal ischemia had acute brain infarction (anywhere) on brain DWI-MRI
  - Infarctions often small, multiple, ipsilateral to retinal ischemia, asymptomatic



  - DWI-MRI abnormal in:
    - 33% with CRAO/BRAO vs 18% with TVL
    - 28 % with embolic vs 8% non-embolic retinal ischemia

Adapted from Drs. Nancy Newman and Biousse; 2015

Study #2

Co-occurrence of Acute Retinal Artery Occlusion and Acute Ischemic Stroke: Diffusion-Weighted Magnetic Resonance Imaging Study

JUNWON LEE*, SEUNG WOO KIM*, SUNG CHUL LEE, OH WOONG KWON, YOUNG DAE KIM, AND SUK HO BYEON

Am J Ophthalmol 2014; 157: 1231-1238

Adapted from Drs. Nancy Newman and Biousse; 2015

Co-occurrence of acute retinal artery occlusion and acute ischemic stroke: Diffusion-weighted magnetic resonance imaging study

- 33 patients with CRAO (18) and BRAO (15)
- Evaluated similarly to acute stroke patients (DWI)
- ¼ with acute retinal ischemia had acute brain infarction (anywhere) on brain DWI-MRI
  - 5/18 CRAO; 3/15 BRAO
  - Infarctions often small, multiple, ipsilateral to retinal ischemia, may be asymptomatic
  - Abnormal DWI-MRI strongly correlated with major cause of stroke (even when neurologically asymptomatic)

Adapted from Drs. Nancy Newman and Biousse; 2015

DWI in Acute Retinal TIA/Ischemia

- DWI-MRI identifies subgroup of patients at very high risk of major stroke
- DWI-MRI needs to be performed within 24/48 hours of visual loss to allow for effective prevention of recurrent stroke

Adapted from Drs. Nancy Newman and Biousse; 2015

Tell the patient:

- "Go to the Emergency Department"
- "Tell them you had a retinal stroke"
- Do not send these patients to their PCP, cardiologist, neurologist, neuro-ophthalmologist
- Do not try to obtain the workup yourself

Adapted from Drs. Nancy Newman and Biousse; 2015

ODE TO AN ARTERY OCCLUSION

When the vision is poor and the fundus is pale,
A branch or laminar emboli has caused the fail.
Heroic measures are rarely helpful,
And vision return is doubtful.
In an Oldie, always remember giant cell it may be.
Hurry and get an ESR and CRP.
The retina is infarcted and dead,
So neo you should not dread.
But here is where you must not choke,
Send them to the ER because they are having a stroke

Joseph Sowka, OD

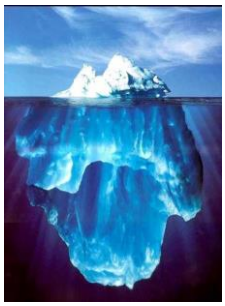
THE CASE OF THE COLORED FLASHING LIGHTS

- **45 YOHF presented with colored "map-like" phosphenes and small black flashing spots OD x two weeks**
- **Noted that she had to "look between the lights" to see out of her right eye.**
  - 20/20 OD, OS
- **Medical history was unremarkable except for treated migraines**
- **Lost 1 pregnancy**

CASE CONTINUED

- **She returned four days later complaining of decreased vision in the right eye, which had reduced to counting fingers at ten feet.**
  - Macular edema, more extensive hemorrhaging, cotton wool spots, disc edema and dilated vessels
- **Underwent IV Kenalog injections and showed improved vision of 20/70 OD during follow up examinations.**
  - Released by retinal specialist
  - No medical evaluation

Now What?



Are there any tests that you would like to order?

CRVO: SYSTEMIC CONSIDERATIONS

Hypertension
Hyperviscosity
CV disease
Sickle
Polycythemia
Hyperlipidemia
Autoimmune factors
Homocysteine

Diabetes
Syphilis
Cardiovascular disease
Leukemia
Carotid artery disease
Sarcoid
Clotting abnormalities

TREATMENT & MANAGEMENT

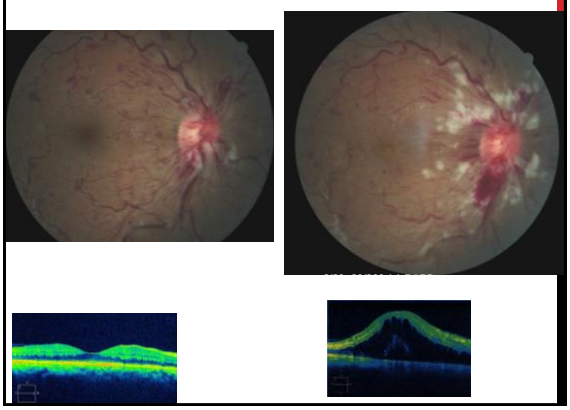
- **Referred blood work through PCP**
  - DM, HTN, hypercoag, ANA, antiphophospholipid antibodies, anticardiolipin, PT, PTT, ESR, CBC with diff
- **Elevated erythrocyte sedimentation rate**
- **Mildly elevated cholesterol level.**
- **Elevated anti-cardiolipin IgM antibodies**
  - Suggestive of antiphospholipid antibody syndrome
  - She was recommended for long term anti-coagulant therapy to prevent future thrombotic events, but patient never followed through.

CASE CONTINUED

- **Seven months later the patient returned with the same signs and symptoms in her right eye.**
- **At this time, the vision was markedly more decreased with more evidence of ischemia**
  - CF @ 6'
- **She was referred to a hematologist**
- **Now on anti-coagulation therapy**

CENTRAL RETINAL VEIN OCCLUSION

- **Thrombotic/atherosclerotic phenomenon**
- **Properties of blood and vein act in concert**
- **Vascular flow and vessel wall abnormalities**
- **Problem at lamina**
  - Turbulent flow
  - Decreased luminal pressure
  - Thrombus
- **Perfused; non-perfused; indeterminant**
- **Evolving condition**



MANAGEMENT-CRVO

- **Standard Care vs. Corticosteroid for Retinal Vein Occlusion (SCORE)**
  - 1-mg of IV triamcinolone should be considered for one to two years to improve vision loss secondary to macular edema following a CRVO.
- **CRUISE Results**
  - Demonstrated efficacy for Lucentis treatment

PRIMARY ANTIPHOSPHOLIPID ANTIBODY SYNDROME

- **Thrombotic disorder**
- **Secondary antiphospholipid syndrome**
  - Associated several autoimmune diseases but most often systemic lupus erythematosus
- **Primary antiphospholipid syndrome is not associated with further systemic disease**
- **Recurrent vascular thrombosis, pregnancy loss and positive anticardiolipin or lupus anticoagulant are all characteristics of this disorder**

PRIMARY ANTIPHOSPHOLIPID ANTIBODY SYNDROME

- **The clinical criteria**
  - One or more vascular thrombotic episodes of venous, arterial or small vessel thrombosis in any organ or tissue or spontaneous abortion.
- **Laboratory testing must show persistently elevated anticardiolipin antibodies, IgG and/or IgM or lupus anticoagulant (inhibits the conversion of prothrombin to thrombin) at least six weeks apart**

PRIMARY ANTIPHOSPHOLIPID ANTIBODY SYNDROME

- **Phospholipids are identified by the body as "foreign."**
  - The antiphospholipid antibodies are produced against the "foreign" antigen.
- **The antibodies appear to react with the cell membranes causing irritation or stimulation, thus disrupting the coagulation cascade**
- **This disruption leads to abnormal blood clotting and inhibits normal phospholipid binding.**

PRIMARY ANTIPHOSPHOLIPID ANTIBODY SYNDROME

- **This abnormal or inhibition of proper phospholipid binding leads to a hypercoagulable state thus causing thrombosis.**
- **Propensity of clot formation is within the venous and arterial portions of the vascular tree, especially targeting the retinal vessels and placenta**

MORAL OF THE STORY

Just because you refer somebody out doesn't mean that everything will be addressed

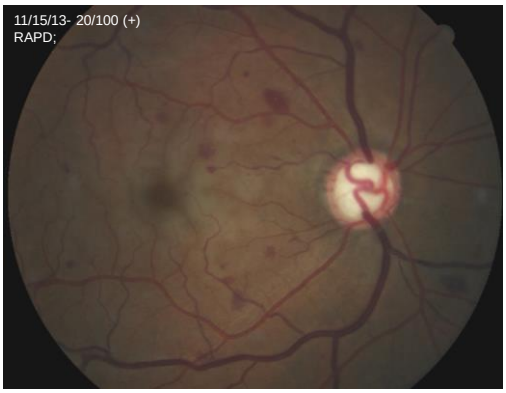
ODE TO A CENTRAL VEIN OCCLUSION

When the veins are tortuous and dilated,
A laminar thrombus has violated.
With hemorrhages in all four quads,
Macular edema reduces vision at odds.
A pupil defect and poor vision,
Mark the division,
Between ischemia and not.
Laser doesn't help edema,
And shouldn't be in the schema.
Steroids and anti-VEGF you can inject,
So vision won't be wrecked.
Remember neo forms front not back
PRP is needed to prevent the eye from seeing black

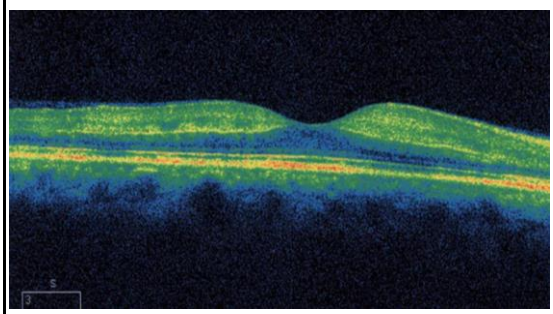
Ok, now that we have warmed up… Let's see if we can figure this one out.

50 YOIF

- **POAG OU x 10 years- medically controlled**
  - PGA, beta blocker
- **Hx CVA at age 17**
  - No cause found
- **N/S x 1 year**
- **Presents with sudden onset vision loss OD (6 hrs)**
  - IOP 22 mm OU; using PGA, not using beta blocker
- **20/100 OD; 20/20 OS; 3+ RAPD OD**
  - Never present before



So, What are your thoughts?



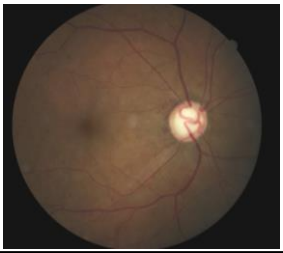
- **Digital massage and combigan given**
  - No improvement
- **Recommend retinal consult for angiogram- pt initially declines**
  - Pt ultimately sees retinal specialist next day
- **Angiogram *normal*.**
  - Normal arterial filling 'somewhat delayed' venous filling. No evidence of edema or ischemia- pt released

- **Pt returns 6 days later**
- **Some visual improvement**
  - 20/60 OD
  - RAPD now grade 2
  - IOP 12 mm OU
  - Ischemia
- **f/u 1 mos**

- **Pt returns 3 weeks later**
- **Vision improved to 20/30**
- **RAPD diminished to grade 1**

So,
What are your thoughts?

- **CRVO? CRAO? Variant?**
- **Reappointed for 1 month**
- **Pt returns as scheduled- vision improved**
  - 20/25+
  - RAPD disappeared

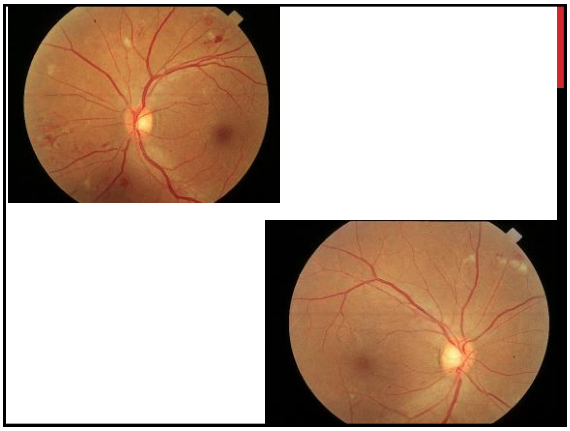


QUESTIONS

- **Artery or vein occlusion?**
- **Why OCT and FANG normal?**
- **How does RAPD form and disappear over 2 months?**

THE MEDICINE MAKES ME SICK

- **52 YOWF**
- **Medical history: hypertension x 10 years; NIDDM x 2 yrs**
  - Medicines unknown
  - Poorly controlled
  - Pt non-compliant
  - "God will take care of me"
- **BP: 157/109 RAS**

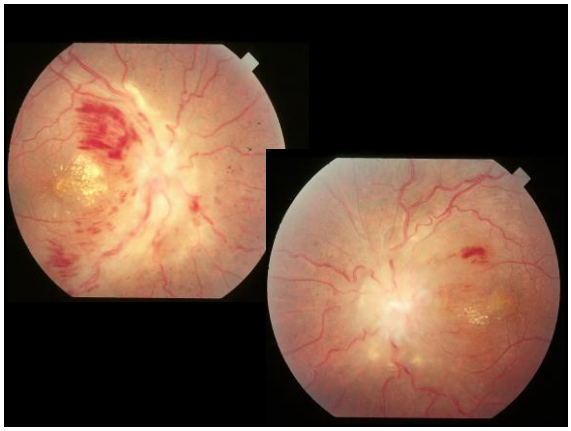


HYPERTENSIVE RETINOPATHY

- **Arteriolosclerotic vessel changes**
  - Some classification schemes include vessel changes in hypertensive retinopathy and others don't
- **Elschnig's spots – subtle choroidal infarcts**
- **CWS**
- **Flame shaped hemorrhages**
- **Macular edema (rare)**
- **Macular star/ ring of exudates**
- **Disc edema**

NOW A TWIST

- **47 YOBM**
- **Obese**
  - 400 lbs (and that's being kind!)
- **Headaches x 3 months**
- **Vision reduction x 2 months**
  - 20/50 OU
- **BP: 212/155 RAS**



BLOOD PRESSURE

- **"Normal" blood pressure: 120/80 (systolic / diastolic) JNC 7, 2003**
- **Hypertension is defined as <u>any elevation of blood pressure above the norm</u>, as measured by sphygmomanometry <u>on two separate occasions</u>**

Prehypertension: 120-139 (S) and/or 80-89 (D)
Stage 1 hypertension: 140-159 and/or 90-99
Stage 2 hypertension (severe): ≥160 and/or ≥100

HYPERTENSIVE CRISES

Hypertensive EMERGENCIES

&

Hypertensive URGENCIES

BP Category	Systolic BP		Diastolic BP	Treatment
Normal	<120 mmHg	**and**	<80 mmHg	Healthy lifestyle
Elevated	120-129 mmHg	**and**	<80 mmHg	Healthy lifestyle
Hypertension Stage 1	130-139 mmHg	**or**	80-89 mmHg	• ASCVD <10%: Healthy lifestyle • ASCVD >10%: Healthy lifestyle and 1 BP lowering medication
Hypertension Stage 2	≥140 mmHg	**or**	≥90 mmHg	Healthy Lifestyle and 2 BP lowering medications

Hypertensive Crises	Systolic BP		Diastolic BP	Treatment
Hypertensive urgency	>180 mmHg	**and/or**	>120 mmHg	Check medication adherence; no organ damage
Hypertensive emergency	>180 mmHg	**and/or**	>120 mmHg + target organ damage	Evidence for organ damage Admit for continuous BP monitoring and IV lowering medication

- **Pharmacologic dilation can help to identify target end-organ damage, particularly hypertensive encephalopathy (Stage 4 hypertensive retinopathy) and intracerebral hemorrhage (Terson's syndrome). Therefore, in patients with significantly elevated BP, dilated funduscopy is of PARAMOUNT importance, but…**

IS THERE A SUBSTANTIAL RISK TO THE PATIENT??

INDUCTION OF ADVERSE EVENTS SECONDARY TO TOPICAL PHENYLEPHRINE

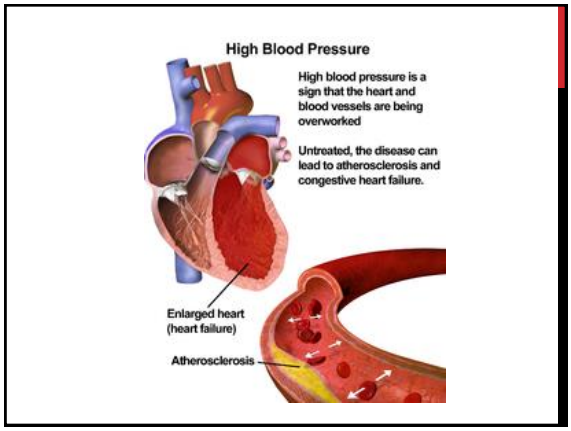
- **Regarding 2.5% phenylephrine (PE), numerous reports suggest there is little concern over adverse responses:**
  - ***Jennings et al (1986)*** – 252 patients (3 – 92 years); no significant changes in systolic or diastolic BP in patients dilated with 2.5% PE.
  - ***Malhotra et al (1998)*** – 54 consecutive patients undergoing cataract extraction; no sustained changes in BP or heart rate after 2.5% PE.
  - ***Lam et al (2003)*** – 217 consecutive patients undergoing phacoemulsification; no untoward cardiovascular effects with 2.5% PE.

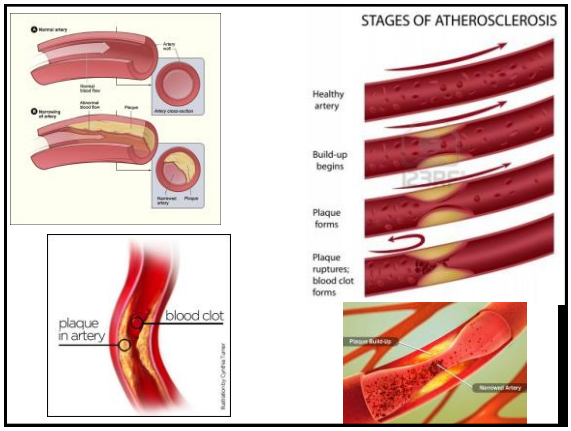
INDUCTION OF ADVERSE EVENTS SECONDARY TO TOPICAL PHENYLEPHRINE

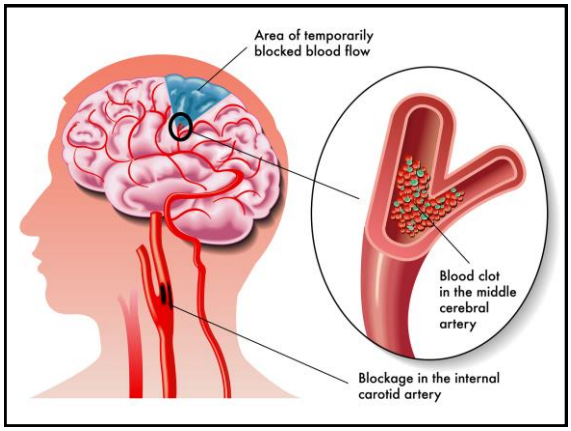
- **Approximately 41 cases involving adverse systemic reactions to 10% phenylephrine have been reported...**
  - 15 patients suffered myocardial infarction after instillation of 10% PE, of which 11 resulted in fatality; these individuals had an average age of 71 years, and nine had a known history of cardiac disease.

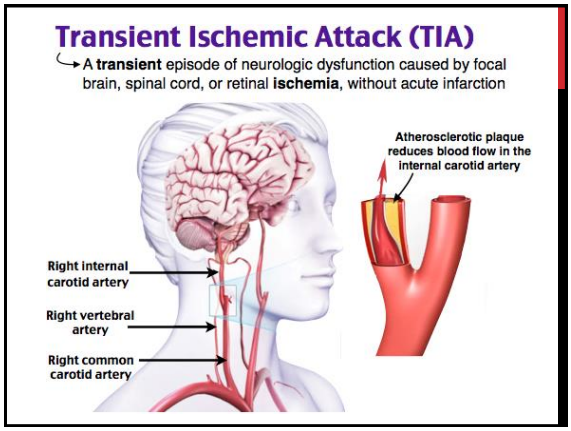
CONCLUSIONS & RECOMMENDATIONS

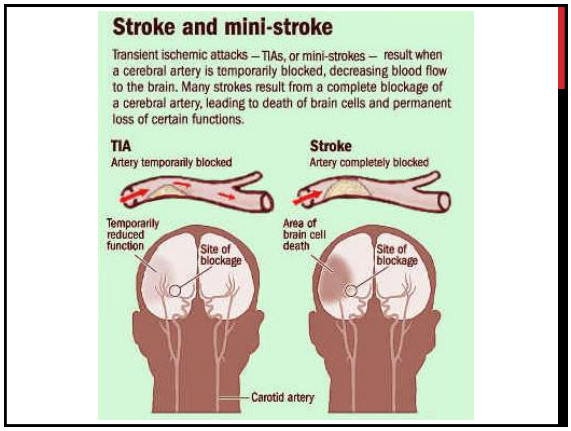
- **Based on data submitted to the National Registry of Drug-Induced Ocular Side Effects:**
  - 2.5% PE is recommended for routine pharmacologic dilation.
  - 10% PE should be avoided in the elderly, infants, and patients with cardiac disease, idiopathic orthostatic hypotension, hypertension, aneurysms, Type 2 diabetes, and advanced arteriosclerosis.
  - 10% PE should also be avoided in patients using MAO inhibitors, tricyclic antidepressants, reserpine, guanethidine, or methyldopa.











TIA

- **Anterior circulation**
  - internal carotid, middle cerebral, anterior cerebral arteries, and their tributaries.
  - Receives 80% of the cerebral blood flow and accounts for 80% of transient ischemic attacks and strokes.
  - Amaurosis fugax (retinal TIA) indicates an abnormality in the ophthalmic branch of the internal carotid artery distal to the bifurcation
    - CRA, BRA

TIA

- **Possibility of a subsequent CVA**
- **TIA also indicates widespread vascular disease putting patients at risk of myocardial infarction and cardiac death**
- **Patients with vision loss (amaurosis fugax) as only manifestation of TIA are at lesser risk than pts. with hemispheric TIA**
  - Risk of arterial occlusion (with permanent vision loss), CVA, and MI.
  - Risk of recurrent TIA or stroke after retinal TIA: **up to 24.2% at 3 years**
- **Risk of future events for TIA dictated by cause and degree or carotid stenosis**

Guidelines

- Any patient with suspected TIA or those with acute retinal ischemia should be evaluated urgently in order to identify those at high risk of immediate cerebral infarction and cardiac ischemia

Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the american heart association/american stroke association. Stroke 2011; 42: 227-276

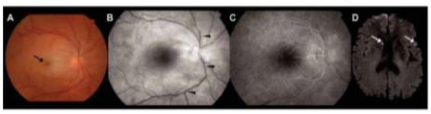
Adapted from Drs. Nancy Newman and Valerie Biousse; 2015

Study #1

Concurrent Acute Brain Infarcts in Patients with Monocular Visual Loss

Johanna Helenius, MD,[1] E. Murat Arsava, MD,[1] Joshua N. Goldstein, MD, PhD,[2] Dean M. Cestari, MD,[3] Ferdinando S. Buonanno, MD,[4] Bruce R. Rosen, MD, PhD,[1] and Hakan Ay, MD[1,4]

ANN NEUROL 2012;72:286–293



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Concurrent Acute Brain Infarcts in Patients with Monocular Visual Loss

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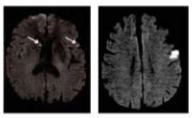
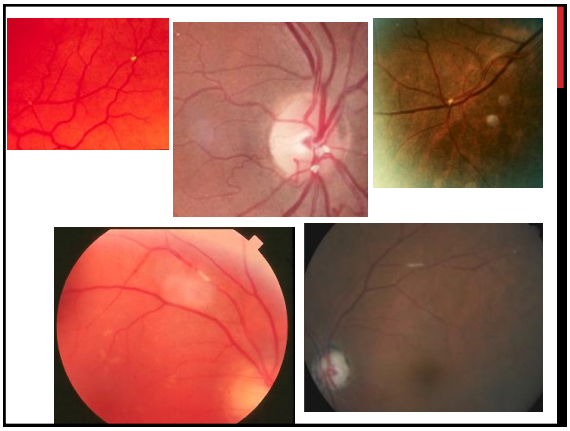
- Evaluated similarly to acute stroke patients (DWI-MRI)
- ¼ with acute retinal ischemia had acute brain infarction (anywhere) on brain DWI-MRI



Adapted from Drs. Nancy Newman and Valerie Biousse; 2015

VISIBLE RETINAL EMBOLI

- **Fibrin/platelet aggregate (Fisher plaque-carotid in origin, also walls of arteries and valves of heart)**
  - Dull gray or white
  - Readily migrate through vascular system producing symptoms (AF)
- **Hollenhorst- cholesterol (carotid in origin)**
  - Refractile, glistening, yellow
  - Most common (87%) of all emboli
  - Typically do not occlude artery
  - Malleable and allows for blood to pass though the artery may appear totally blocked
  - Will readily break up and move distally, so will not be seen typically in patients complaining of AF
  - common cause of AF
- **Calcific (cardiac)**
  - Dull white and non-refractile
  - Usually from valvular calcification
  - Most likely to cause artery occlusion and stroke



MANAGEMENT OF ASYMPTOMATIC EMBOLI

- **Literature does NOT support carotid evaluation**
  - Typically low grade non-surgical
- **Complications of endarterectomy**
- **Internal medicine approach**

THANK YOU FOR YOUR ATTENTION. ALWAYS REMEMBER TO RECYCLE AND PROTECT THE PLANET THAT WE WILL ULTIMATELY LEAVE TO KEITH RICHARDS