True Disc Edema

- **Papilledema**
  - Defines disc edema secondary to intracranial hypertension
  - Increased intracranial pressure must be present in order to diagnose papilledema
  - Bilateral
  - May present with transient visual obscuration, intermittent diplopia, headache, nausea, vomiting, tinnitus
  - Optic nerve is hyperemic; juxtapapillary retina is edematous; vessels are engorged, distended, and tortuous; peripapillary hemorrhages are common
  - Visual fields show enlarged blind spot (early) and arcuate defects with constriction (late)
  - Associated with intracranial abnormalities:
    - Increased brain volume (intracranial mass lesion)
    - Increased intracranial blood volume
    - Increased cerebrospinal fluid volume
  - Management involves stat neuro-imaging, lumbar puncture, and neuro consult

**Anterior Ischemic Optic Neuropathy (AION)**

- Results from local infarction at the level of the optic nerve
- Unilateral presentation but high incidence of subsequent contralateral involvement
- May be arteritic (AAION) or non-arteritic (NAAION)
  - AAION results from giant cell arteritis (GCA) and constitutes a medical emergency
  - NAAION secondary to other systemic disorders, most notably arteriolosclerosis, hypertension, and diabetes
- Presents with sudden devastating vision loss; associated scalp tenderness, weight loss, headache and jaw claudication when associated with GCA
- Optic nerve is pale (more so with AAION) with extensive nerve fiber layer edema; arteriolar constriction, peripapillary hemorrhages evident
- Visual fields variable. Patient is often blind
- Management involves stat erythrocyte sedimentation rate (ESR) and temporal artery biopsy if GCA suspected

Optic Atrophy
Primary optic atrophy
- Uniform nerve fiber degeneration, resulting in glial replacement but no architectural alteration of the optic nerve head.
- Disc appears chalky white but the margins remain distinct and retinal vessels appear normal.
  - Trauma and compression (e.g. tumor) causes
Secondary optic atrophy
- Results from pathological chronic disc edema
  - malignant hypertension, papilledema, or infiltrative diseases like leukemia or sarcoidosis.
Consecutive optic atrophy
- Degenerative retinal conditions
  - Retinitis pigmentosa, pathological myopia and central retinal artery occlusion.
  - Pale, waxy disc, normal margins and marked attenuation of the arterioles.
Temporal disc pallor
- Toxic/ nutritional or demyelinating optic neuropathy (optic neuritis)
Numerous potential etiologies
- Infarction, infection, infiltration, inflammation, trauma, toxicity, metabolic dysfunction or direct compression of the nerve or chiasm
Evaluation:
- MRI studies should be obtained of the orbits, the optic chiasm and the brain with and without contrast, fat suppression for orbits, in a high field scanning unit.
  - Contrast dye (gadolinium) is beneficial in discerning malignant lesions, demyelinating plaques indicative of multiple sclerosis.
Systemic causes of optic atrophy
- sarcoïdosis, tuberculosis, Behçet’s disease, lymphoma, leukemia, systemic lupus erythematosus, nutritional or metabolic disorder (e.g. pernicious anemia, folate deficiency), syphilis, Lyme disease, and antiphospholipid antibody syndrome.
  - Complete blood count (CBC) with white cell differential, erythrocyte sedimentation rate (ESR), angiotensin-converting enzyme (ACE), antinuclear antibody (ANA), serum cardiolipin, serum homocysteine, serum B12 and folate levels, and rapid plasma regain (RPR) for syphilis. Additionally, chest x-rays could prove helpful in suspected cases of TB or sarcoidosis.

Compressive Optic Neuropathy
- Results from compression of the optic nerve at the orbital apex, secondary to:
  - Space occupying orbital lesions, including tumor masses
  - Infiltrated extraocular muscles (Graves’ ophthalmopathy) in thyroid disease (most common)
- Unilateral with orbital masses, bilateral in Graves’ disease
- Presents with slowly progressive, variable vision loss; variable proptosis and motility restriction
- Optic nerve is typically hyperemic with retinal edema, tortuous vessels, and associated hemorrhages; with prolonged compression, may see pallor and optic disc collateral vessels
- Visual fields consistent with papilledema in early stages, ischemic optic neuropathy in later stages
- Management involves orbital imaging and serum thyroid profile if Graves’ suspected

**Infectious/infiltrative optic neuropathy**

**Infectious**
- Syphilis
  - Retrobulbar, papillopathy, neuroretinitis, perineuritis
  - Retrolubar, bulbar: severe vision reduction
  - Perineuritis has normal vision, normal CSF pressure, normal MRI
- Lyme
  - Mimic syphilitic optic neuropathy
- Toxoplasmosis, HIV/AIDS, CMV
  - Destructive to vision
- Neuroretinitis
  - Good visual function
  - Typically benign lymphoreticulosis (cat scratch disease)
  - Gram-negative bacillus

**Infiltrative**
- Sarcoidosis
- Systemic lupus erythematosus
- Leukemia
- Lymphoma
- Carcinoma

**Tilted Disc Syndrome**
- Appears rotated about axis- long axis may be horizontal rather than vertical
- No actual rotation occurs. Inferior tissue is missing while superior tissue is crowded together. Overall appearance is of rotation.
- Abnormal morphology of choriocapillaris canal gives this appearance
- Optic nerve and fundus typical coloboma due to incomplete closure of fetal fissure at 6 weeks gestation.
- Findings include:
  - Inferior conus –inferior and inferior nasal
    - Can extend to involve the optic nerve as well and mimic glaucomatous notching
    - Corresponding field defect
  - Ectasia
  - Staphyloma
  - Hypopigmentation of inferior fundus (retina, choroid, and RPE)
    - Colobomatous disruption of RPE can lead to choroidal neovascularization
  - Situs inversus
  - Myopic astigmatism of oblique axis
    - Due to inferior staphyloma
• Unchanging with possible stationary field defect- temporal defect
• Field defect is superior temporal corresponding to inferior nasal conus

**Buried Drusen of the Optic Disc**
• Pseudo disc edema and disc elevation
  • Often confused with papilledema
• Retained hyaline bodies in anterior optic nerve head
• 1% incidence; 70% bilaterality
• Primarily in Caucasians
• Autosomal dominant with incomplete penetrance
• Asymptomatic
  • Mild acuity decrease and field loss may be present
• Small or non-existent cup
• Anomalous branching pattern arising from central vessel core
• SVP present
• May have associated sub-retinal hemorrhage
• Field defect: nasal step, arcuate scotomas
• Hyaline bodies in anterior optic nerve head can compress fibers and vascular supply
  • Leads to optic atrophy and visual loss in rare cases
• High reflectivity on b scan ultrasonography (except in children)
  • B scan is definitive diagnosis in most cases

**Optic Nerve Head Hypoplasia**
• Congenitally small nerves with pronounced scleral crescent (double ring sign)
• Dysplasia of retinal ganglion cells with loss of NFL
• ONH underdevelopment and sclera “fills in”
• Associated brain disorders and gestational diseases
• Maldeveloped growth
• Associated disorders include:
  • Gestational diabetes
  • Maternal infection (CMV, syphilis, rubella)
  • Fetal alcohol syndrome
  • Maternal drug abuse
• Septo-optic dysplasia
  • Short stature
  • Congenital nystagmus
  • Hypoplastic disc
• Unchanging, but may have drastically reduced acuity and field
• Normal acuity to NLP
• Strabismus, typically esotropia, frequently present (50%)
  • Must distinguish from amblyopia
  • Amblyopia, refractive error, binocular anomalies are secondary to hypoplasia
Upon discovery, patient (if child) should be referred for full neurologic and endocrinologic evaluation, esp. if associated neurological signs are present or child is abnormally small for age.

**Optic Pits**
- A type of optic nerve coloboma (atypical) resulting from incomplete closure of the fetal fissure
- Confused with notching of neuroretinal rim in glaucoma
- Will have field/vision loss corresponding to axon absence
- Serous detachment of the posterior pole
- Atypical because not always found in inferior disc

**Morning Glory Syndrome**
- Specific type of coloboma
  - Associated retinal vascular anomalies, glial proliferation, and perivascular pigmentation
  - Funnel-like ectasia of disc and posterior fundus
  - Optic disc is displaced posteriorly into a funnel shaped staphyloma
- Vision highly variable
  - Typically less than 20/100 (to hand motion) in complete form
  - Vision may be good in forme fruste
  - Complete form is typically unilateral (though with other fellow eye colobomas) and forme fruste is typically bilateral
- Typically unilateral, but fellow eye often has other congenital defects
- Associated with non-rhegmatogenous retinal detachment of the posterior pole

**Oblique Insertion**
- Hyperopia is typically present
- Typically bilateral
- Unchanging with no field defect
- Nasal aspect heaped up while temporal aspect depressed or buried
  - Frequently misdiagnosed as glaucoma and disc edema
- Especially prominent in Asian patients

**Central Retinal Artery Occlusion**
- Clinical Picture:
  - Painless, sudden loss of monocular vision
  - Vision is markedly reduced
  - Retinal edema causing white appearance to fundus
  - Mean age is 60's
  - “Cherry red” macula due to underlying choriocapillaris perfusion
  - Optic atrophy ensues eventually
- Pathophysiology:
  - Emboli is most common cause
- Emboli from carotid artery or heart lodging in central retinal artery at laminar constriction.
  - Cardiac emboli more common than carotid emboli in CRAO
- Other possible etiologies:
  - Intraluminal thrombosis
  - Hemorrhage under atherosclerotic plaque
  - Vasospasm
  - Dissecting aneurysm
  - Hypertensive arteriolar necrosis
  - Circulatory collapse
  - Giant cell arteritis (10% of CRAO caused by GCA) ***

- Complications:
  - CVA
  - Myocardial infarction: main cause of death
    - Low survivorship: 9 year mortality of 56% (compared to 17% in age matched group)
  - Neovascularization rare (17% of cases and occurs within 4 weeks)
  - Ischemic ocular syndrome (a complication of carotid artery disease)

- Management:
  - In patients over 60, CRAO may be caused by giant cell arteritis; MUST get a STAT ESR and C-reactive protein on every patient over the age of 60 years with CRAO!
  - Internal medicine referral most appropriate to reduce mortality
  - Monitor for complications Q 3 months

**Cilioretinal Artery Occlusion:**
- Local infarcted area
- Severe loss of central acuity with preservation of peripheral field
- Systemic causes similar to CRAO
- Higher incidence of GCA, especially if concurrent AION exists

**Branch Retinal Artery Occlusion:**
- Visible retinal emboli lodged in arteriole
  - Cholesterol
  - Calcific
  - Fibrin-platelet
  - Infectious
- Rarely caused by GCA
- Acuity 20/20 to hand motion depending upon the degree of involvement (macula)
  - Patients commonly report sudden onset of field loss
  - Whitened retina in distribution of arteriole
  - With resolution, retina becomes more normal in appearance (but not function)
  - Neovascularization is rare
  - Systemic associations same as CRAO, but lower survivorship
  - Internal medicine/ Cardiology referral
Central Retinal Vein Occlusion

- Thrombotic phenomenon: Properties of the blood and central retinal vein act in concert to cause thrombotic occlusion. Causes partial or complete blockage of venous return
  - Vein inflammation
  - Vascular flow and/or vessel wall abnormalities stimulate vein thrombosis
  - Hypercoagulability states, elevated viscosity, and systemic states of decreased thrombolysis promote thrombus formation. (i.e., changes in blood constituents)
  - Turbulent blood flow causing thrombus formation at lamina
  - Laminar constriction site is the nidus for occlusion. Intraluminal pressure of the vein decreases, rendering it susceptible to collapse. Compression by an arteriolosclerotic CRA further affects flow and thrombus formation. CRV and CRA share common sheath passing through lamina cribrosa.
  - External factors such as increased IOP in POAG and papilledema (causing increased pressure in the optic nerve sheath) may cause further compression and contribute to occlusion.
  - Other factors that result in compression include: orbital tumor and abscesses, cavernous sinus thrombosis, and retrobulbar intraneur sheath injection.
  - Systemic diseases influence thrombus formation through:
    1. External compression
    2. Primary thrombus formation (Antiphospholipid antibodies)
    3. Degenerative or inflammatory disorders of the vein itself

Vascular occlusions and antiphospholipid antibody syndrome

- Patients with antiphospholipid antibody syndrome (APAS) are typically female and tend to be young
- Approximately 50% of patients with antiphospholipid antibodies also have systemic lupus erythematosus (SLE) or other autoimmune diseases.
- However, in many cases, there exists APAS without associated autoimmune disease.
- The most common conditions that result from APAS which affect the eye and visual system are arterial or venous thrombosis with resultant ischemia. This manifests as central retinal vein or artery occlusion (CRVO or CRAO), papillophlebitis, anterior ischemic optic neuropathy (AION), migraine, ophthalmoparesis and diplopia, amaurosis fugax, isolated retinal hemorrhages and cotton wool spots, and retinal neovascularization.
- While these conditions typically occur in elderly patients, the patient with APAS experiences them at a younger age.
- Younger (under age 50) patients with retinal vascular occlusions should be investigated for antiphospholipid antibody syndrome
- In addition to ocular manifestations, there are often thrombi in other systems. Venous thromboses of the arm and leg, pulmonary embolism, sagital, pelvic, mesenteric, portal, and axillary have all been encountered in APAS. Transient ischemic attack (TIA) and cerebrovascular accidents are the most common occurrences from thrombosis in the arterial system. Another systemic finding that is thrombocytopenia (reduced platelet count).
A common, and in many cases defining, event in APAS is recurrent pregnancy loss that can occur in any trimester. Preeclampsia and intrauterine growth retardation have also been found in association with APAS.

Antiphospholipid antibodies are a group of circulating antibodies that include anticardiolipin antibody, lupus anticoagulant, and the Biologic False Positive Test for Syphilis (BFP-TS). These antibodies are directed against phospholipid binding proteins, which prolong phospholipid-dependent coagulation assays. In this condition, phospholipids, present in cell membranes, are erroneously identified by the body as being foreign and, consequently, the body produces antibodies to the phospholipids. These antibodies appear to have an affinity for the cell membranes found in platelets, vessel endothelial cells, and clotting factors.

Antiphospholipid antibody syndrome is an autoimmune disorder with two forms: Primary Antiphospholipid Antibody Syndrome and Secondary Antiphospholipid Antibody Syndrome. Antiphospholipid antibodies (anticardiolipin antibodies and lupus anticoagulant) are all known to commonly occur in patients with SLE.

When these antibodies occur in the presence of SLE, it is considered a secondary syndrome. It wasn’t until 1985 that Hughes identified these antibodies in seemingly normal patients experiencing thrombotic events and pregnancy loss in the absence of SLE. This primary form exists in the absence of clinically or serologically proven autoimmune disease and has been termed Primary Antiphospholipid Antibody Syndrome and occasionally referred to as Hughes’ Syndrome.

Antiphospholipid antibody syndrome is diagnosed by arterial and venous thrombosis, pregnancy loss and/or thrombocytopenia in the presence of lupus anticoagulant and anticardiolipin antibodies. The method of promoting thrombosis by the antiphospholipid antibodies is unclear. Thrombosis appears to be the cause of pregnancy loss.

**Signs and symptoms of impending stroke**
- Transient ischemic attack (TIA)
  - Amaurosis fugax (AF) - amaurosis = blindness; fugax = fleeting
    - Transient monocular blindness
  - Visible retinal emboli

Clinical Pearl: TIA and AF are straws that tell which way the intracranial wind is blowing.

**Transient Ischemic Attack**
- The definition of transient ischemic attack has changed from a focal, neurologic event that lasts less than 24 hours to one that typically lasts less than 1 hour and is not associated with changes on neuroimaging. A brief episode of neurologic dysfunction caused by focal brain or retinal ischemia, with clinical symptoms typically lasting less than one hour, and without evidence of acute infarction.
  - Most transient ischemic attack symptoms last less than 1 hour and typically less than 30 minutes
- Symptoms consistent with transient ischemic attack include hemiparesis, hemisensory loss, hemifacial weakness of upper motor neuron distribution, *amaurosis fugax*, and aphasia
  - Weakness and/or numbness of parts or all of the contralateral side with loss of motor
and/or sensory system. Typically arm (most common), leg, face & arm, arm & leg. Numbness in the hand, foot, face, ½ of tongue

- Aphasia/ dysphasia
  - Inability to understand spoken words or unable to speak, depending upon which part of the brain is ischemic
- The anterior circulation consists of the internal carotid arteries, the middle cerebral arteries, the anterior cerebral arteries, and their tributaries. It receives 80% of the cerebral blood flow and accounts for 80% of transient ischemic attacks and strokes. Amaurosis fugax indicates an abnormality in the ophthalmic branch of the internal carotid artery distal to the bifurcation.
- Painless
- Diplopia may occur from TIA involving posterior circulation (vertebrobasilar vascular distribution)
  - Dizziness is a common finding
  - TIA may have no ocular involvement whatsoever

**Amaurosis Fugax**

- Transient monocular blindness/ transient monocular vision loss
- May be a manifestation (criterion) of TIA, though can occur from other causes
- Painless and isolated- Involve vision only
- Total or sectorial
  - Amaurosis fugax can manifest in a variety of ways aside from the classic “curtain-like” visual loss, including clouding, graying, or darkening of vision. A horizontal visual field defect suggests segmental embolization to the superior or inferior branch of the retinal artery
- Disease of the carotid artery (typically)
  - Emboli are reaching the retinal arterial system and causing temporary occlusion
- Isolated or antecedent (long ago) without current symptoms are less dangerous than many current episodes of AF
- No associated neurological baggage and may be the sole finding in a TIA
- Seconds to hours
  - Typically 2-5 minutes
- Resolves completely
- Other types of amaurosis fugax
  - Light-induced amaurosis fugax:
    - Patient may report loss of vision in the ipsilateral eye after exposure to bright light (e.g., looking outside on a sunny day). Indicates significant internal carotid artery stenosis or occlusion
  - Gaze-induced amaurosis fugax- when looking in a certain direction, the patient loses vision
    - Usually indicative of a retro-orbital mass lesion

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**Clinical Pearl:** Amaurosis fugax has historically been considered as an isolated finding. Today, it is considered a manifestation of TIA. Previously, transient monocular vision loss alone was called amaurosis fugax. Now, it is called a TIA.
Clinical Pearl: Things other than emboli can cause amaurosis fugax.

Transient Ischemic Attack: Prognosis
- TIA portends the possibility of a subsequent CVA/ stroke with permanent neurologic deficits.
- TIA also indicated widespread vascular disease putting patients at risk of myocardial infarction and cardiac death.
- Patients with 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 future events for TIA dictated by cause and degree or carotid stenosis.

Clinical Pearl: A patient experiencing amaurosis fugax is considered to have experienced a TIA if the cause of the AF is vascular. Patients can experience TIAs that have no visual involvement as well.

Pathophysiology of TIA and AF:
1. Hypertension leading to atherosclerosis with subsequent thromboembolism formation
   - Cholesterol ➔ fatty streak ➔ atheroma ➔ ulceration ➔ thrombus ➔ plaques ➔ emboli

2. Emboli-forming conditions (other than HTN)
   - Rheumatic heart disease
   - Prosthetic heart valves
   - Bacterial endocarditis
   - Indwelling catheters
   - Rhythm disturbance - Mitral valve prolapse (Barlow’s syndrome).
     - 17% of females
     - Blood regurgitates back into atrium and pools where platelets can aggregate and clots can form

3. Giant Cell Arteritis (GCA)- Thrombus formation due to vessel wall and lumen obliteration from inflammation
   - In patients over the age of 60 years with transient visual loss (TVL), either TIA or AF, you must get an erythrocyte sedimentation rate (ESR) and C-reactive protein to look for GCA. AF in an elderly patient due to transient occlusion of the ophthalmic or central retinal artery is a sign of impending, permanent, severe vision loss (often within several weeks).

4. Vasospastic
   - Non-embolic arterial narrowing
   - Vasospastic substance (Cocaine) use
   - Migraine?

5. Hematological
   - Polycythemia (Too much hemoglobin)
   - Sickle cell (#1 hematological cause of transient vision loss)
   - Anemia (Too little hemoglobin)
• Hypercoagulability states
• Anti-phospholipid antibody syndrome

**Emboli: Just the Facts**
- May be symptomatic (AF or TIA) or asymptomatic
- The main factor associated with retinal emboli is smoking
- Three types of plaques: Fischer, Hollenhorst, calcific
- Fischer- fibrin/platelet aggregate (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

**Clinical Pearl:** The patient most likely to manifest asymptomatic retinal emboli is an older hypertensive man that smokes. Smoking cessation is absolutely essential for these patients.

**Clinical Pearl:** The literature does not support carotid evaluation for patients with asymptomatic retinal emboli because the majority does not have significant carotid stenosis. There is no definitive management of these patients. It’s best to refer them for an atherosclerotic evaluation and let the internist decide what to do.