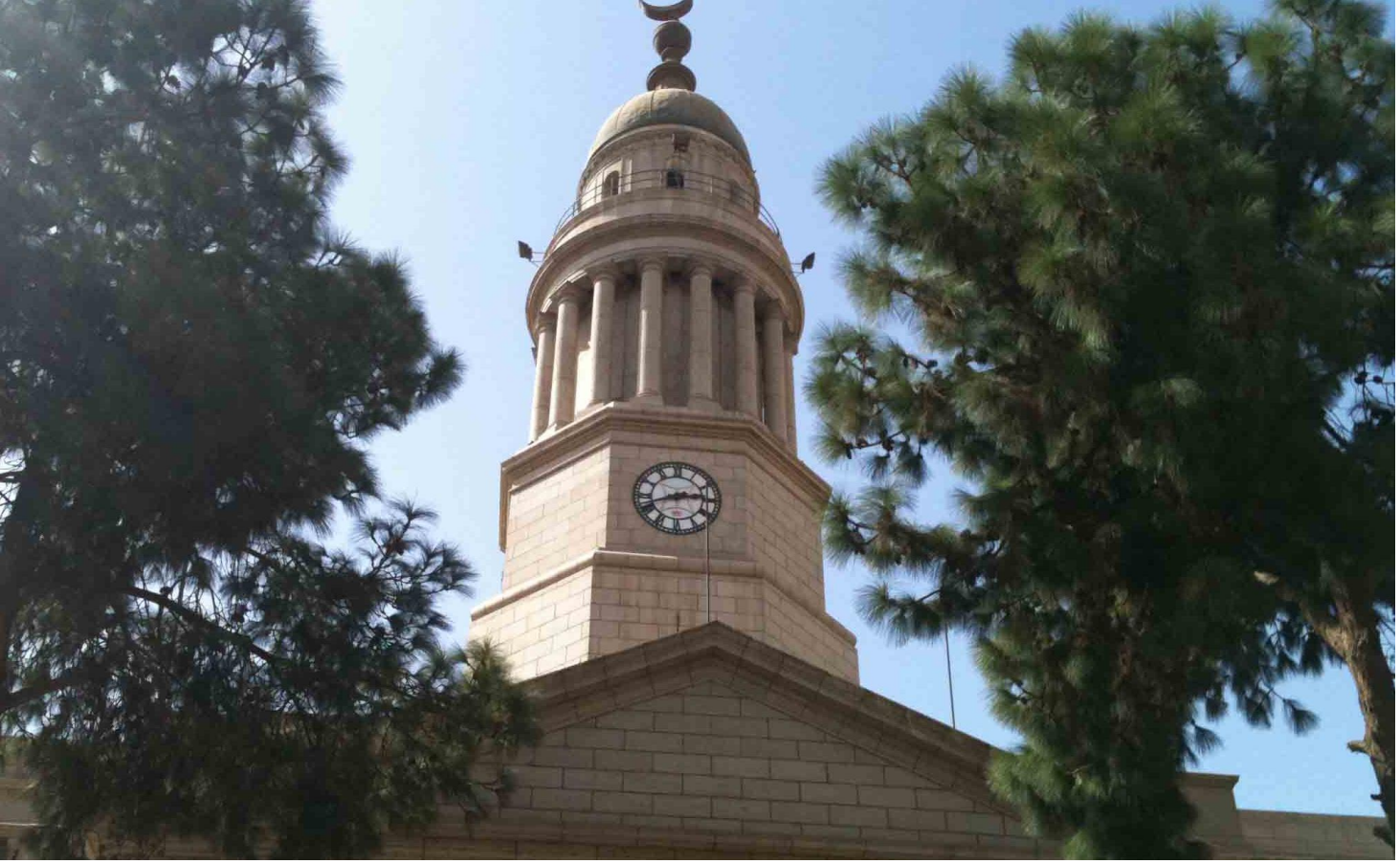


Optic Neuropathy

Amr Hassan, M.D.,FEBN

Associate professor of Neurology

Cairo University

Optic Neuropathy

Clinical diagnosis

Optic Neuritis : History taking

O C D

Distribution: Uni/Bilateral.
Symm/Asymmetrical
Simultaneous/ Sequential

Severity

Painful or not.

Limitation of ocular motility(double vision)

Ptosis

Field defect

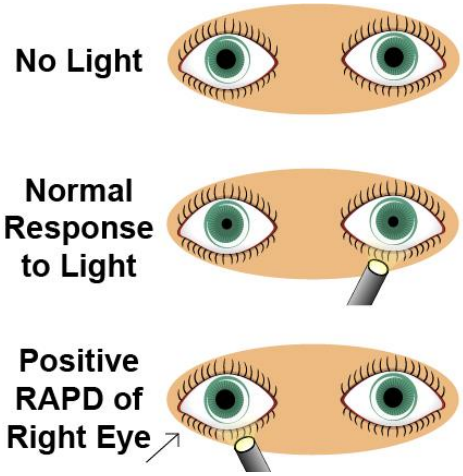
Local eye manifestations: (photophobia, lacrimation, exophthalmos, red eye)

Optic Neuritis : Common presentation

Visual field defect

Dyschromatopsia

Abnormal papillary response



± Diminution/loss of vision

Optic Neuropathy

Clinical diagnosis

Aetiology

Optic Neuropathies : Causes

- Demyelinating
- Inflammatory
- Non-arteritic Ischemic
- Arteritic Ischemic
- Traumatic

Rapid onset

- Infiltrative
- Compressive
- Hereditary
- Radiation
- Paraneoplastic
- Toxic/nutritional

Gradual onset

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- Traumatic

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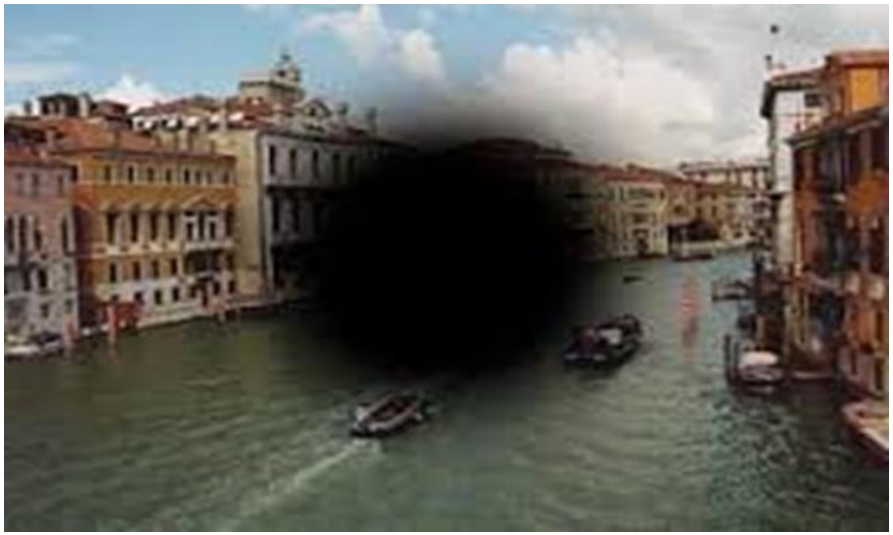
- Compressive
- Hereditary
- Radiation
- Paraneoplastic
- Toxic/nutritional

Gradual onset

Optic Neuritis : Common Symptoms

- Monocular
  (Central Vision loss)
- Pain
  (eye movement)
- Altered colour vision
- Uhthoff's symptom
- Flashes



Optic neuritis in multiple sclerosis

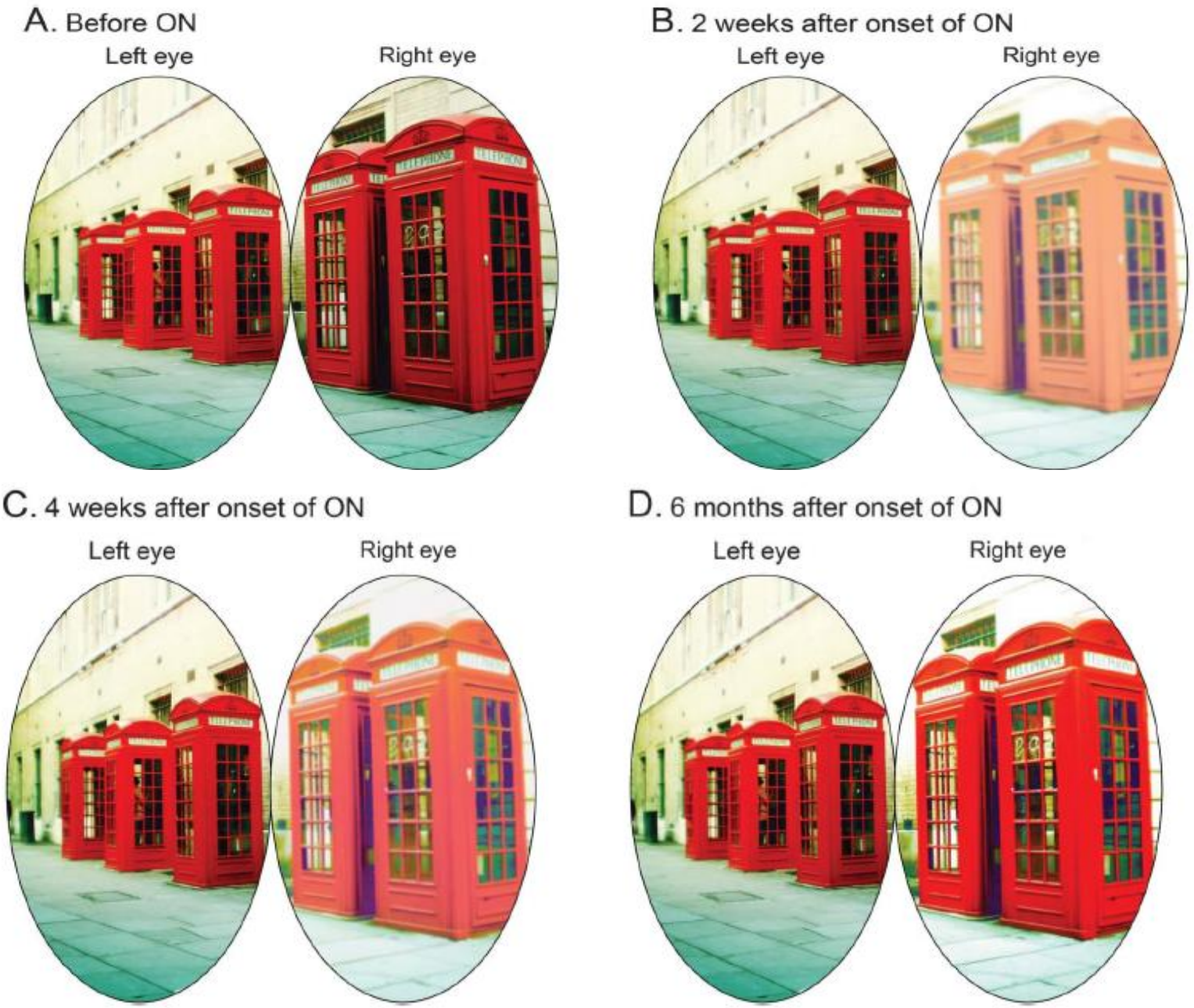
Looking from a patient's eyes

Paolo Preziosa, MD, Giancarlo Comi, MD and Massimo Filippi, MD

+ SHOW AFFILIATIONS | + SHOW FULL DISCLOSURES
Correspondence to Prof. Filippi: filippi.massimo@hsr.it

doi: http://dx.doi.org/10.1212/WNL.0000000000002869
Neurology July 19, 2016 vol. 87 no. 3 338-339

Figure A photograph taken in London by a patient with multiple sclerosis



An Egyptian Patient

Uhthoff's Symptom

- Uhthoff described 3 patients in whom exertion and fatigue caused a desaturation in colour vision
- Patient XVIII had decreased acuity after walking around the room

Flashes

Movement phosphenes in optic neuritis: A new clinical sign
(Davis F, Bergen D, Schauf C, McDonald I, Deutsch W)
Neurology 1976; 26: 1100-1104.

- Bright flashes in dark
- Eye movement
- Differentiate from Lightning Streaks of Moore
- Eye equivalent of L’hermittes symptom

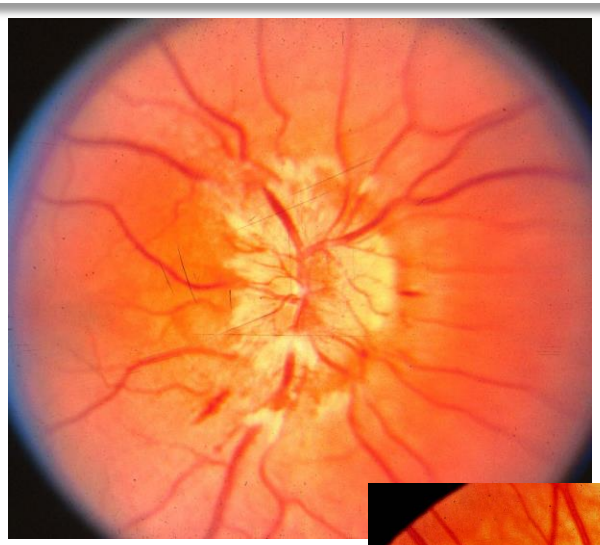
Optic Neuritis: Physical signs

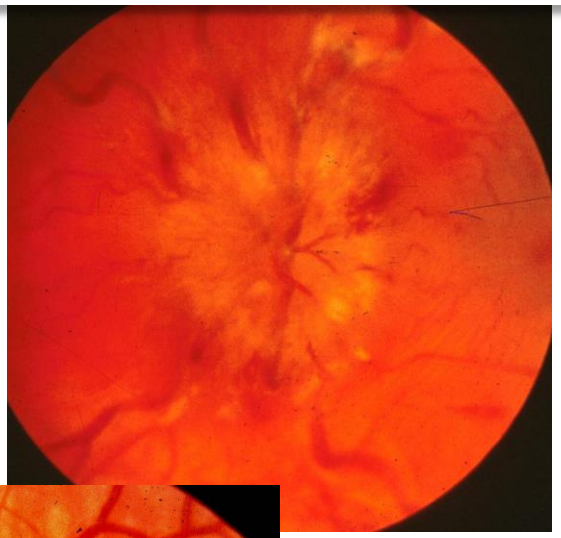
- Decreased visual acuity
- VF defect

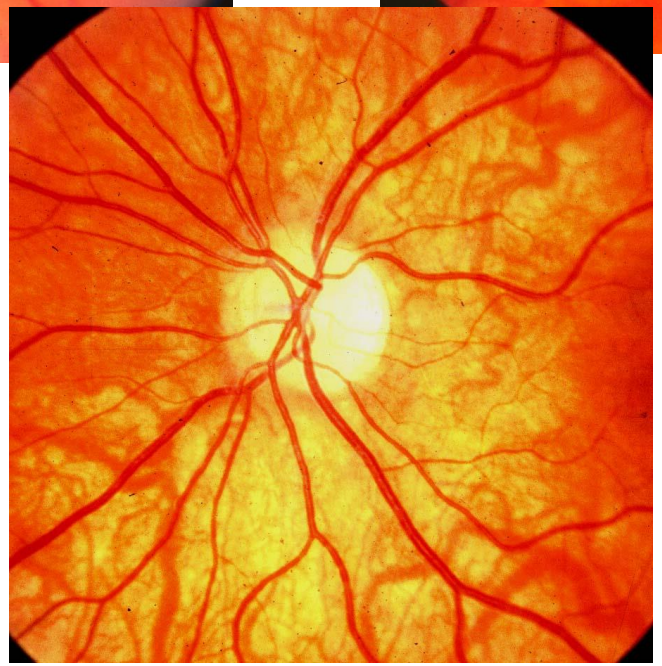
(Central/Altitudinal 29%)

- Dyschromatopsia
- Afferent Pupil Defect (RAPD)
- Optic disc swelling 35%
- Optic disc pallor
- Abnormal Contrast Sensitivity
- Abnormal VEP
- Altered Flicker Perception
- Altered depth perception

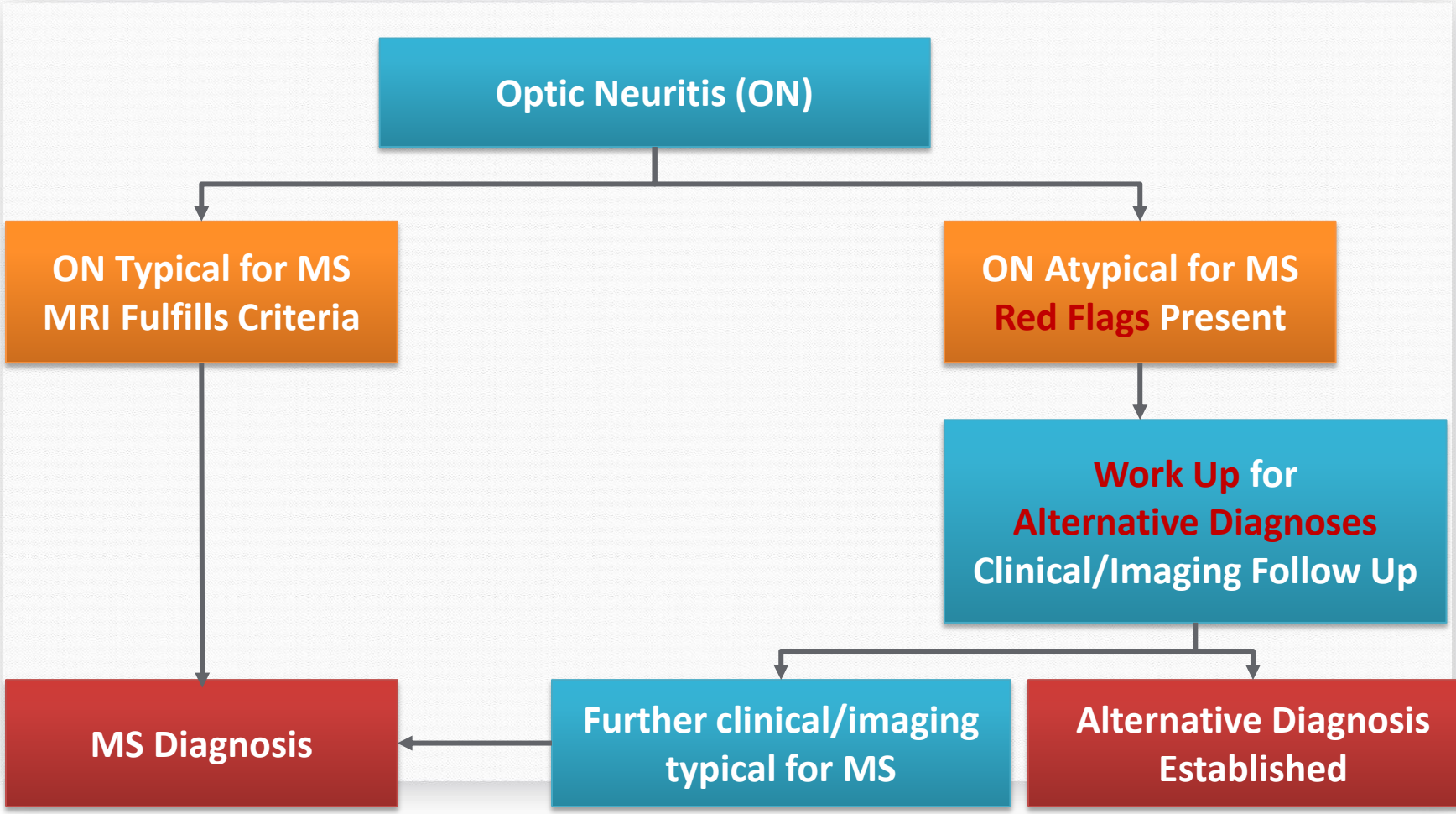
Optic Neuritis: Optic Disc







Mental map for diagnosis of ON



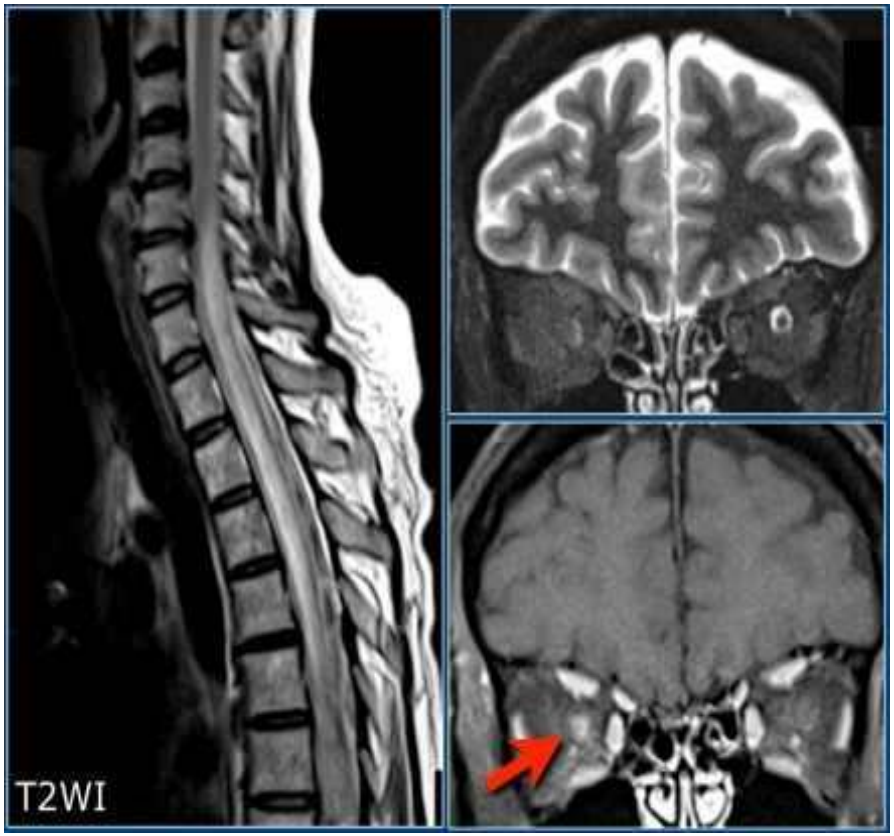
Optic Neuritis : Red Flags

Typical	Atypical
• Acute or subacute attack	• Progressive disease
• Mostly young adults (age 20-55 y)	• Age group < 12 and > 50 y
• Unilateral visual acuity loss	• Bilateral visual loss
• Improvement with/without treatment	• No spontaneous visual improvement
• Continued improvement after corticosteroid withdrawn	• Deterioration after corticosteroid are discontinued
• Mild pain that worsens with eye movement	• Following loss of vision, painless to severe pain
• The optic disc appears normal or mildly swollen	• Severe swelling and hemorrhage in optic disc
• Variable visual field defects may occur	• Variable signs and symptoms, depending on etiology
• Altered perception of motion (the pulfrich phenomenon)	
• Vision blurs when body temperature rises (Uhthoff's phenomenon)	
• Bright, fleeting flashes of light (phosphenes)	

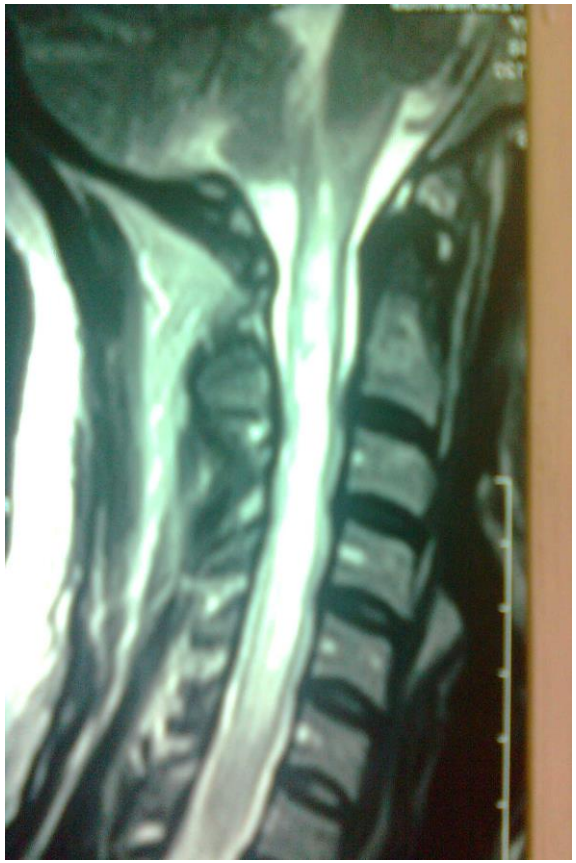
Demyelinating Optic Neuritis: D.D.

- NMO
- CRION
- ADEM
- anti-Myelin oligodendrocyte glycoprotein–associated (MOG) optic neuritis

NMO



NMO



NMO diagnostic criteria 2015

Diagnostic criteria for NMOSD with AQP4-IgG

1. At least 1 core clinical characteristic
2. Positive test for AQP4-IgG using best available detection method (cell-based assay strongly recommended)
3. Exclusion of alternative diagnoses[a]

Diagnostic criteria for NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status

1. At least 2 core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements:
   a. At least 1 core clinical characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome
   b. Dissemination in space (2 or more different core clinical characteristics)
   c. Fulfillment of additional MRI requirements, as applicable
2. Negative tests for AQP4-IgG using best available detection method, or testing unavailable
3. Exclusion of alternative diagnoses[a]

Core clinical characteristics

1. Optic neuritis
2. Acute myelitis
3. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
4. Acute brainstem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions (figure 3)
6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions (figure 3)

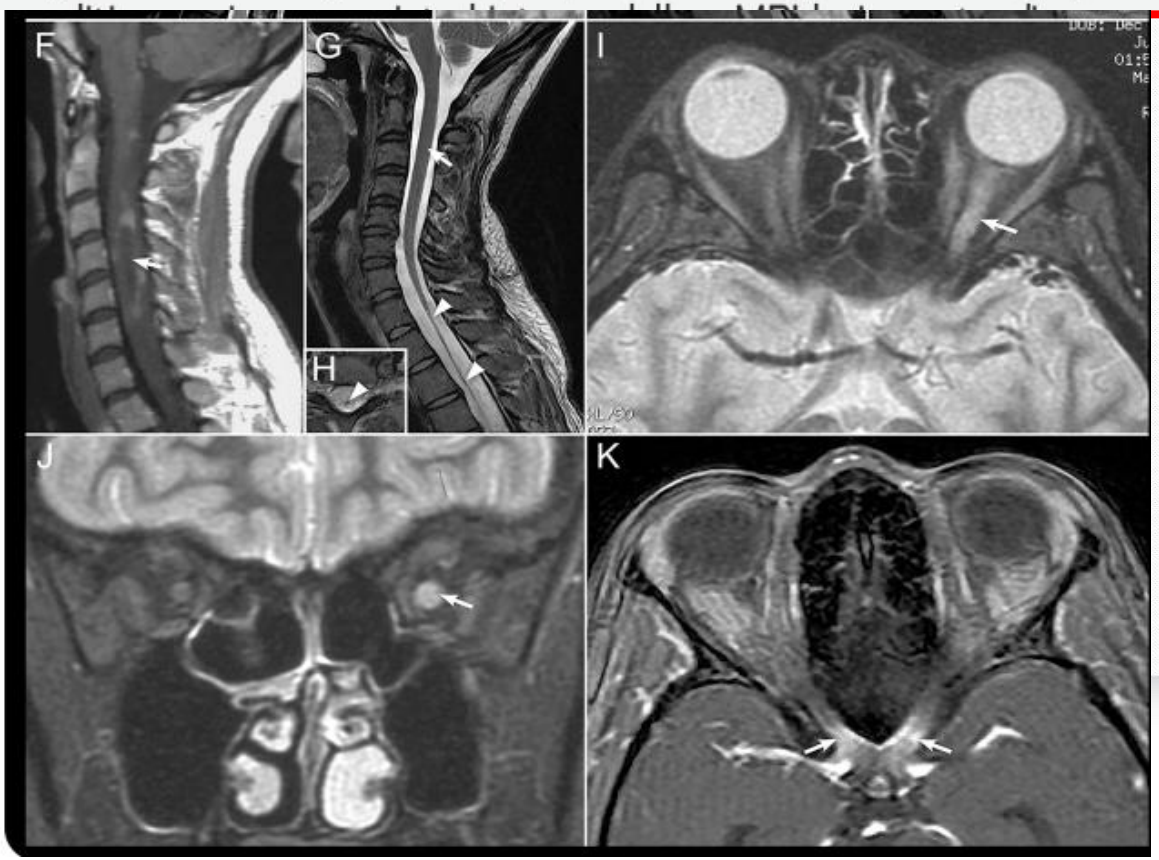
Additional MRI requirements for NMOSD without AQP4-IgG and NMOSD with unknown AQP4-IgG status

1. Acute optic neuritis: requires brain MRI showing (a) normal findings or only nonspecific white matter lesions, OR (b) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium-enhancing lesion extending over >1/2 optic nerve length or involving optic chiasm (figure 1)
2. Acute myelitis: requires associated intramedullary MRI lesion extending over ≥3 contiguous segments (LETM) OR ≥3 contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis (figure 1)
3. Area postrema syndrome: requires associated dorsal medulla/area postrema lesions (figure 2)
4. Acute brainstem syndrome: requires associated periependymal brainstem lesions (figure 2)

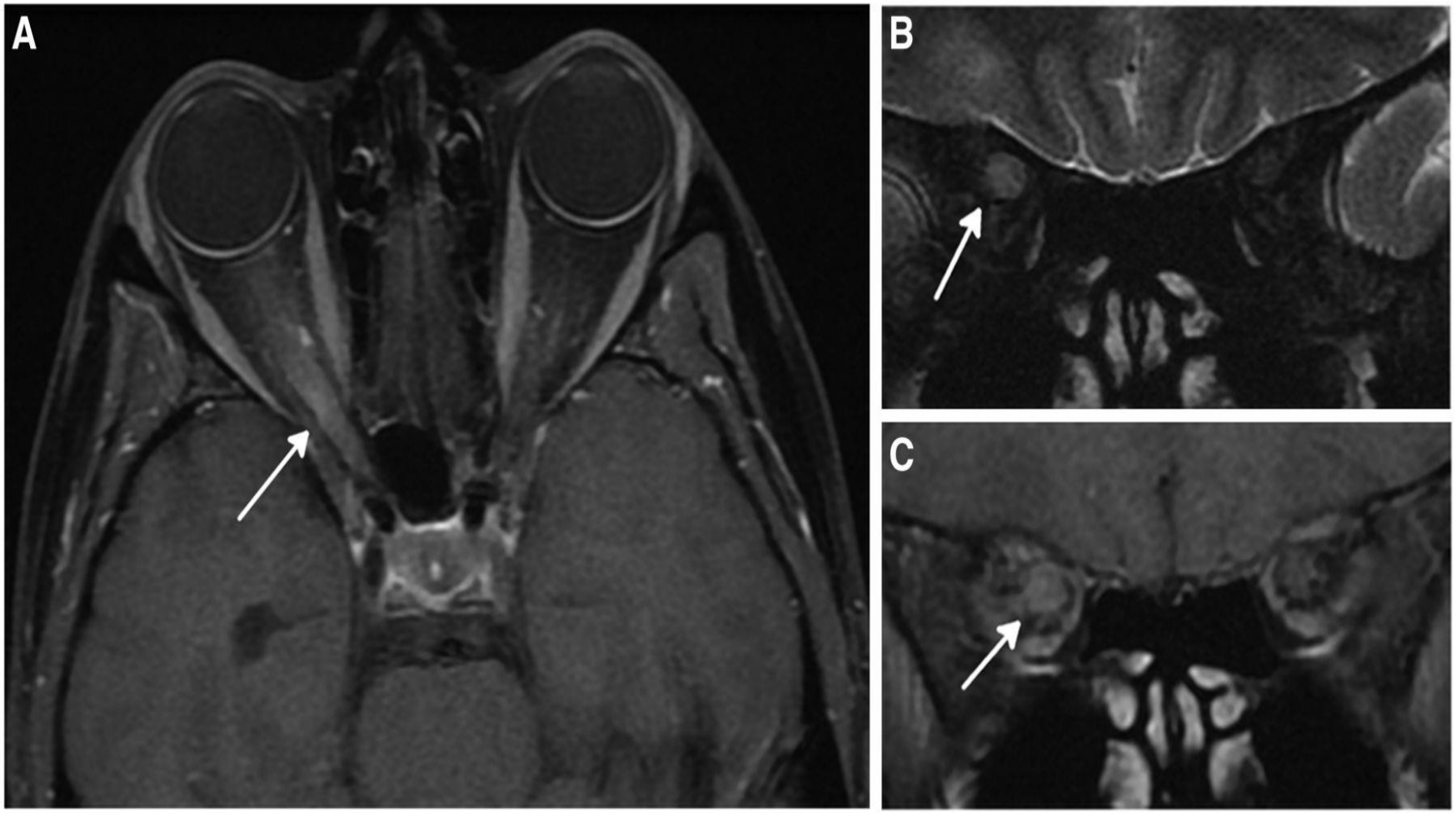
NMO diagnostic criteria

Additional MRI requirements for NMOSD without AQP4-IgG and NMOSD with unknown AQP4-IgG status

1. Acute optic neuritis: requires brain MRI showing (a) normal findings or only nonspecific white matter lesions, OR (b) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium-enhancing lesion extending over >1/2 optic nerve length or involving optic chiasm (figure 1)



NMO diagnostic criteria



New 2016 MAGNIMS MRI criteria

Dissemination in space

DIS is established by detecting involvement of at least two of the five following areas of the CNS:

- Periventricular: ≥3 lesions
- Cortical-juxtacortical: ≥1 lesions
- Infratentorial: ≥1 lesions
- Spinal cord: ≥1 lesions
- **Optic nerve: ≥1 lesions**

Optic Neuritis: D.D.

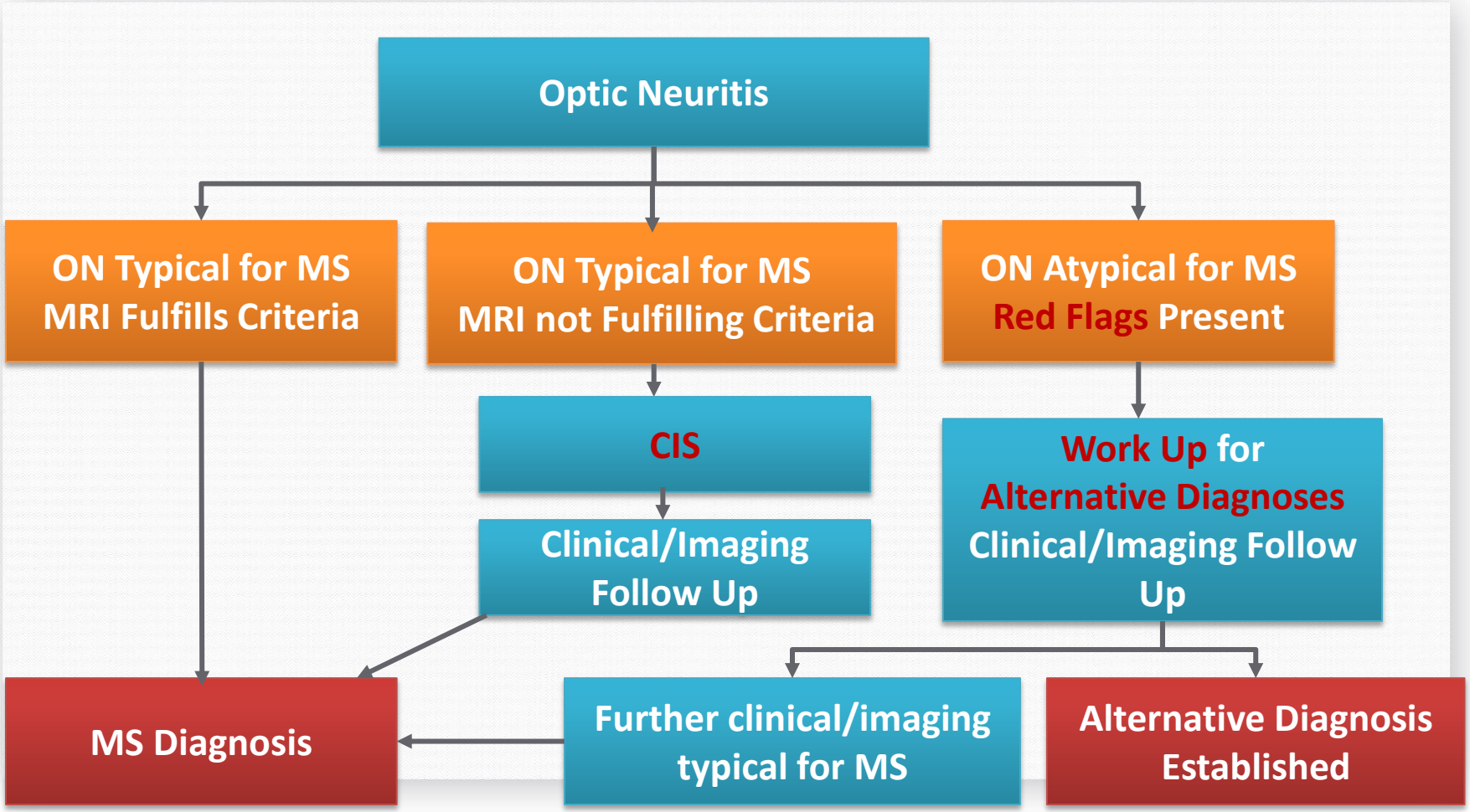
Nosology	Definition	NMO-IgG	MRI	Treatment
Isolated optic neuritis (ION*)	A single and isolated episode of optic neuritis	Negative	MRI of the optic nerve abnormal but brain and spinal cord are normal	IV steroids
Relapsing isolated optic neuritis (RION)	A spontaneously relapsing and isolated episode of optic neuritis	Negative	MRI findings as for ION	IV steroids followed by Immunosuppressants
Chronic relapsing inflammatory optic neuropathy (CRION)	Relapses of isolated episodes of optic neuritis on steroid withdrawal	Negative	MRI findings as for ION	IV steroids followed by Immunosuppressants
Neuromyelitis optica-optic neuritis (NMO-ON)	Spontaneously relapsing episodes of optic neuritis	Positive	MRI findings not typical for multiple sclerosis	IV steroids followed by Immunosuppressants
Multiple sclerosis-associated optic neuritis (MSON)	An episode of optic neuritis in association with radiological evidence for dissemination in space and dissemination in time	Negative	MRI findings typical for multiple sclerosis	IV steroids followed by DMD for MS
Reactive OPN	Post infectious/post-vaccinial/ADEM	Negative	Atypical brain lesions possible MRI consistent with ADEM	IV steroids

ADEM - Acute disseminated encephalomyelitis, IV steroids - Intravenous steroids (Methylprednisolone 1g daily for 5 days), DMD - Disease-modifying drugs, MS - Multiple sclerosis, MRI - Magnetic resonance imaging

Optic Neuritis: lab workup

- Complete blood count (CBC)
- Serum vitamin B-12 and folate levels (eg, bilateral central scotoma)
- Lyme titers (eg, endemic area, tick exposure, rash of erythema chronica migrans)
- Tuberculin skin testing, chest radiography, or QuantiFERON-TB testing (eg, tuberculosis [TB] exposure, endemic area)
- Fluorescent treponemal antibody (FTA) testing (eg, syphilis serology) or nontreponemal testing (eg, Venereal Disease Research Laboratories [VDRL] testing or rapid plasma reagin [RPR] testing)
- Antinuclear antibody (eg, systemic lupus erythematosus)
- HIV testing (eg, high-risk patients)
- Angiotensin-converting enzyme (ACE) level, chest radiography, lysozyme (eg, sarcoidosis)
- Erythrocyte sedimentation rate (eg, inflammatory disorders)
- Serum NMO antibody IgG (anti–aquaporin-4 [AQP4] antibody) testing

Mental map for diagnosis of ON



PLEASE

ORAL STEROIDS

PLEASE

The ONTT was a prospective, randomized, multicenter placebo-controlled clinical trial designed to compare the benefits of treatment with

(1) intravenous methylprednisolone (IVMP) (250 mg administered every 6 h for 3 days followed by oral prednisone [1 mg/kg/day] for 11 days);

(2) oral prednisone (1 mg/kg/day); or

(3) oral placebo in 457 patients with acute optic neuritis.

Beck RW, Cleary PA, Anderson MM Jr, Keltner JL, Shults WT, Kaufman DI. A randomized, controlled trial of corticosteroids in the treatment of acute optic neuritis. The Optic Neuritis Study Group. *N Engl J Med*. 1992 Feb 27. 326(9):581-8.

PLEASE

- The ONTT showed that treatment with standard-dose oral prednisone was associated with an increased rate of new attacks of optic neuritis.

- After 5 years, the recurrence rate was found to be higher in the oral prednisone (1 mg/kg) group (41%) than in those who received IVMP or oral placebo (25%).

1. Costello F, Burton JM. An approach to optic neuritis: the initial presentation. *Expert Rev Ophthalmol*. 2013. 8(6):539–551.
2. Shams PN, Plant GT. Optic neuritis: a review. *Int MS J*. 2009 Sep. 16(3):82-9.

Optic Neuropathies : Causes

- **Demyelinating**
- Inflammatory
- Non-arteritic Ischemic
- Arteritic Ischemic
- Traumatic

Rapid onset

- Infiltrative
- Compressive
- Hereditary
- Radiation
- Paraneoplastic
- Toxic/nutritional

Gradual onset

Optic Neuropathies : Causes

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Gradual onset

Optic Neuritis: Inflammatory causes

- Some of the features that should raise the suspicion of an inflammatory optic neuritis:

✓ Lack of spontaneous improvement of visual function after 30 days

✓ Exquisite steroid-responsiveness

✓ Steroid-dependency.

Optic Neuritis: Inflammatory causes

- Sarcoidosis
- SLE
- Behcet's disease
- Inflammatory bowel disease
- Sjogren's syndrome
- Wegener's granulomatosis

Non Infectious

- Syphilis
- Lyme disease
- Cat-scratch disease

Infectious

Optic Neuritis: Inflammatory causes

- Optic disc swelling frequently occurs with posterior uveitis and retinitis.
- Optic neuropathy can also occur in the context orbital inflammatory disease (orbital pseudotumor).
- MRI of the orbit will show inflammation of the optic nerve sheath (optic perineuritis)

Optic Neuritis: CRION

- Chronic relapsing inflammatory optic neuropathy is another entity characterized by:

✓ Recurrences and steroid-responsiveness.

✓ Can behave as granulomatous optic neuropathy

✓ May require long-term immunosuppressive therapy (kidd et al 2003).

Optic Neuropathies : Causes

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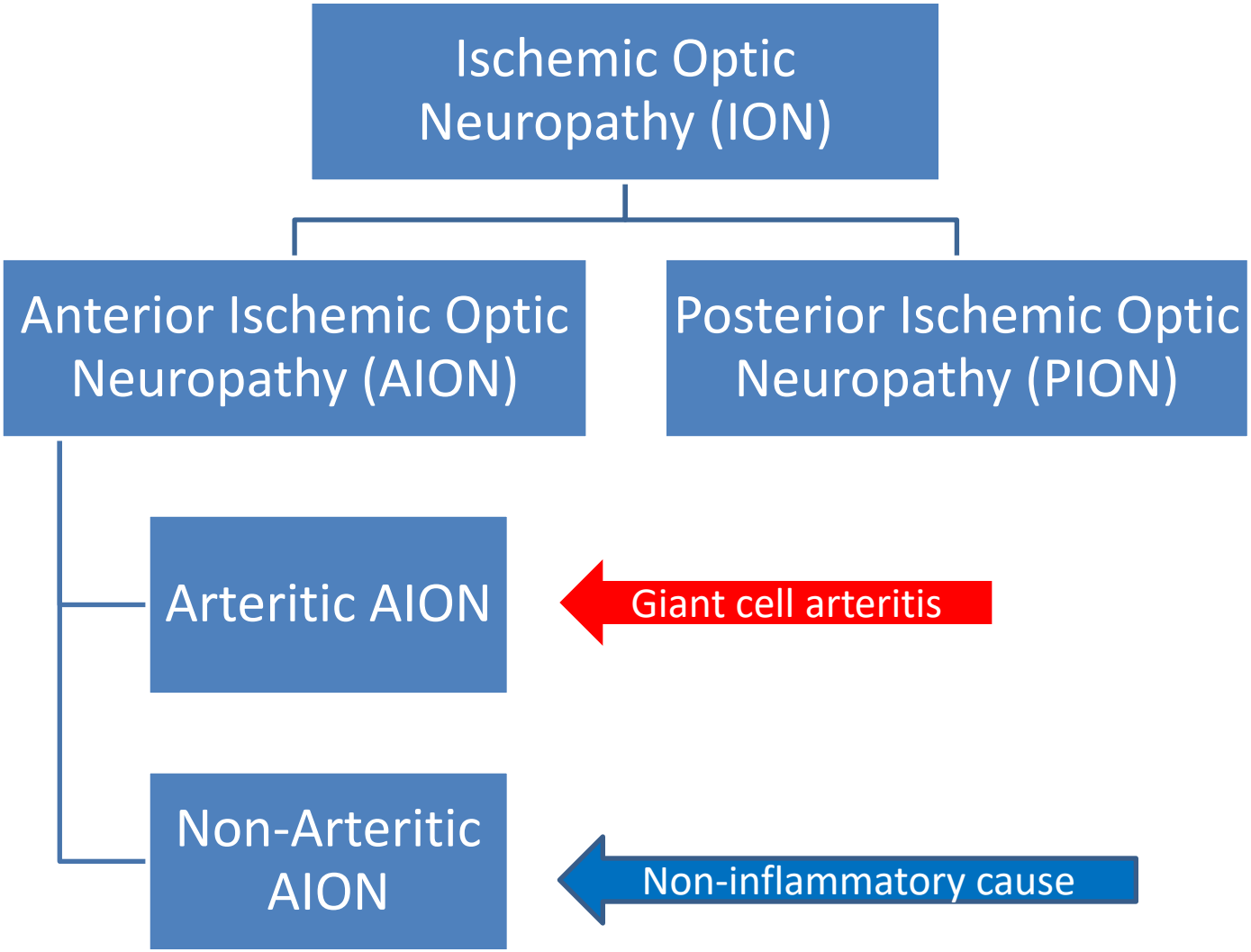
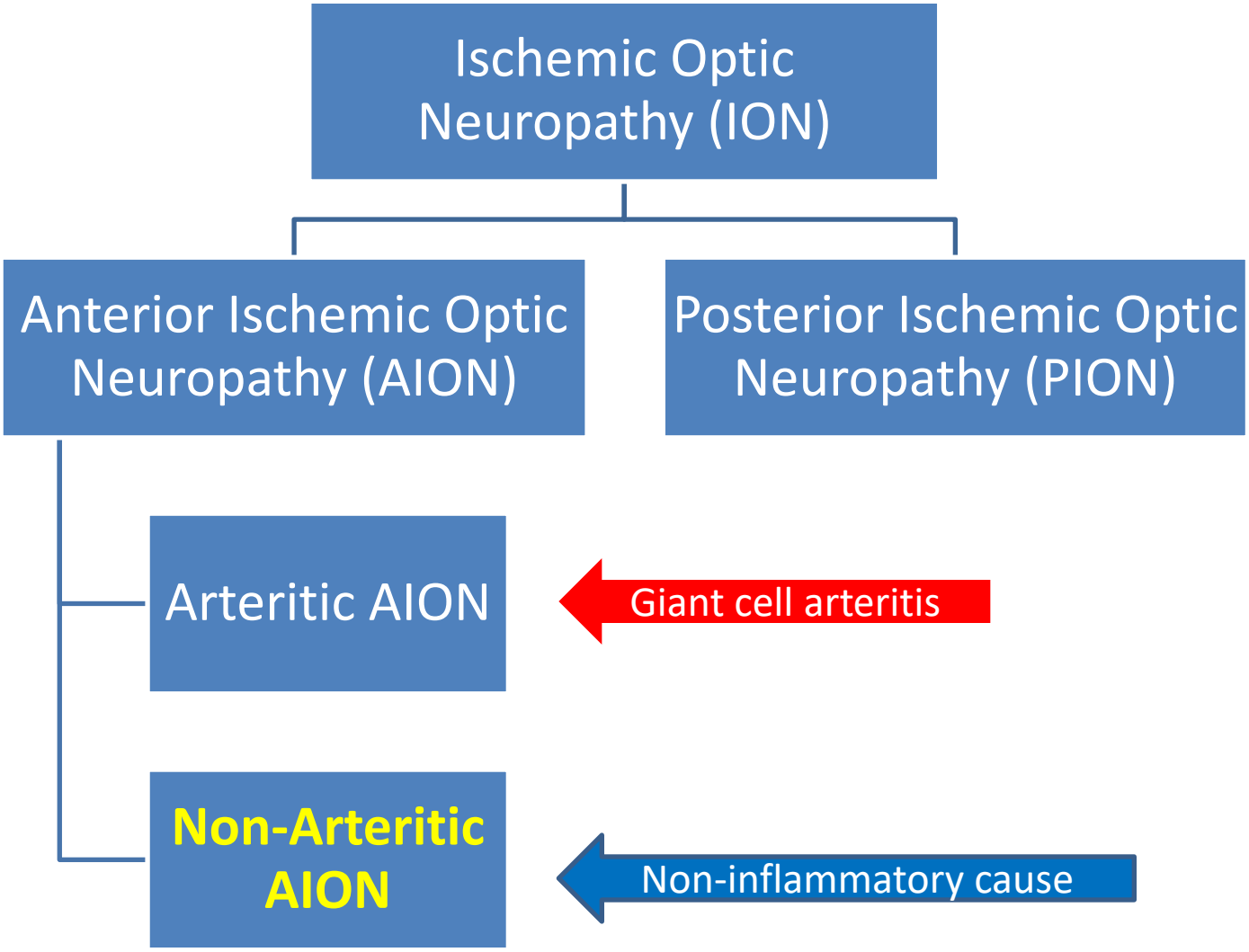
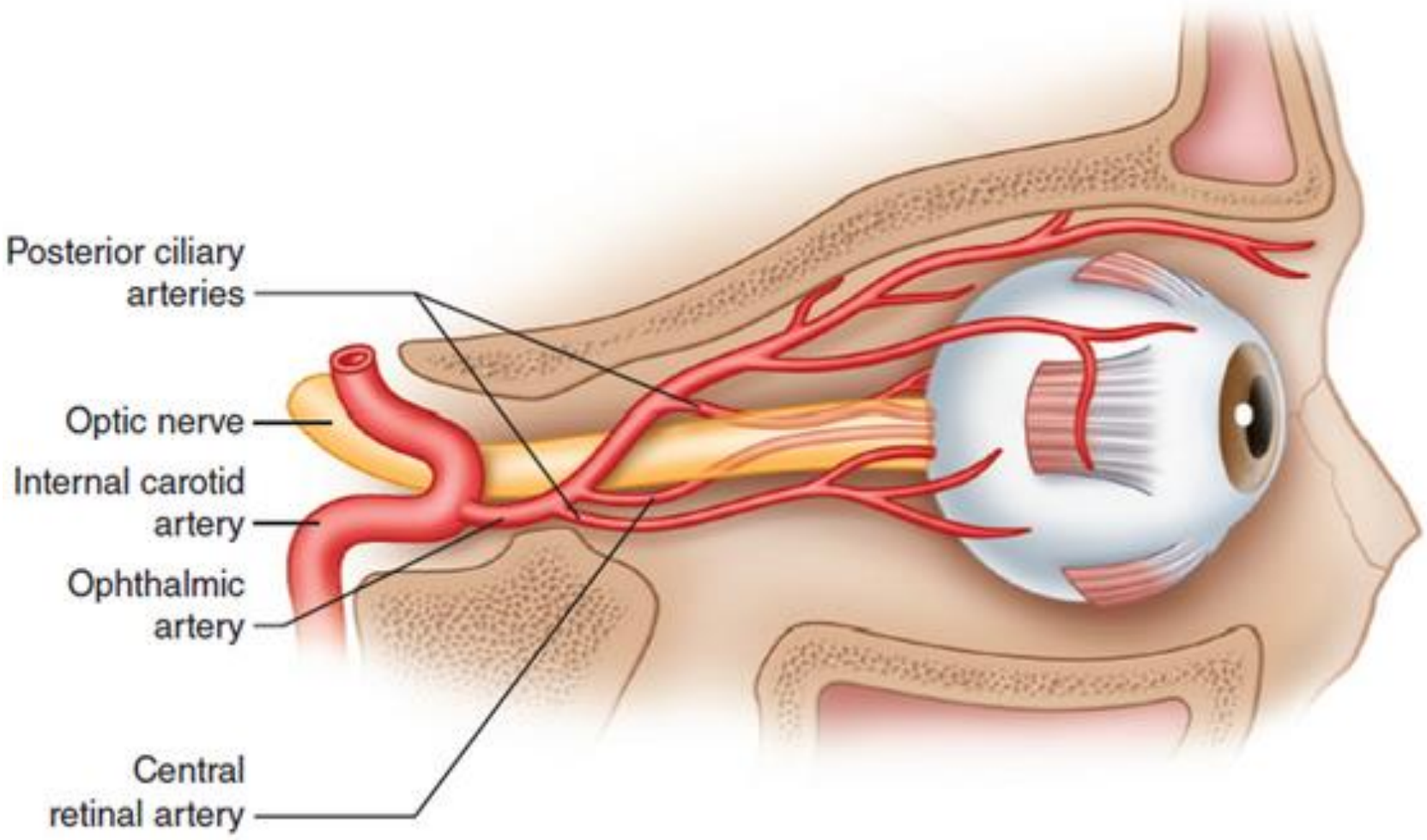
Ischemic Optic Neuropathy



Ischemic Optic Neuropathy



Blood supply of the optic nerve



Ischemic Optic Neuropathy:NAION

Risk factors

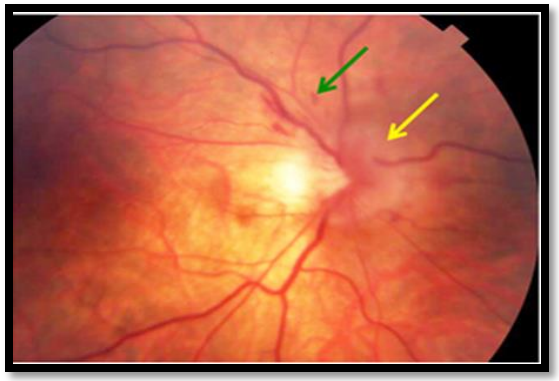
1. Structural crowding of the ONH
2. Hypertension
3. Diabetes Mellitus
4. Hypercholesterolemia
5. Sudden Hypotensive event
6. Sleep Apnoea Syndrome
7. Administration of sildenafil

Ischemic Optic Neuropathy:NAION

Clinical picture

1. Sudden onset visual loss
2. Painless
3. Monocular
4. Always discovered on awakening
5. Nocturnal Hypotension

Ischemic Optic Neuropathy:NAION

PARAMETER	FINDING
Visual Acuity	Often better than 20/100.
Visual Field	Typically **Inferior** Altitudinal defect.
Colour Vision	May be severely impaired when VA is good.
Ophthalmic Exam Findings 	Diffuse OR sectorial hyperaemic disc swelling associated with FEW peripapillary splinter-shaped haemorrhages.
	Small OR cupless disc in fellow eye.
	Swelling gradually resolves and pallor in 3-6 weeks after onset.
FA Finding	Acute Stage: localized disc hyperfluorescence, intense, eventually involves entire disc.
Laboratory Evaluation	No associated laboratory abnormalities.

Ischemic Optic Neuropathy:NAION

	NAION	Optic neurtis
Age	>50	<40
pain	Unusual	92%+
Pupil	APD+	APD+
VF	Altitudinal	Central
Optic disk	Edema 100% pale	Edema 33% hyperemic
Retinal Hge	Common	Unusual
F.A.	Delayed disk filling	No delayed
MRI	No optic nereve enhancement	enhancement

Ischemic Optic Neuropathy:NAION

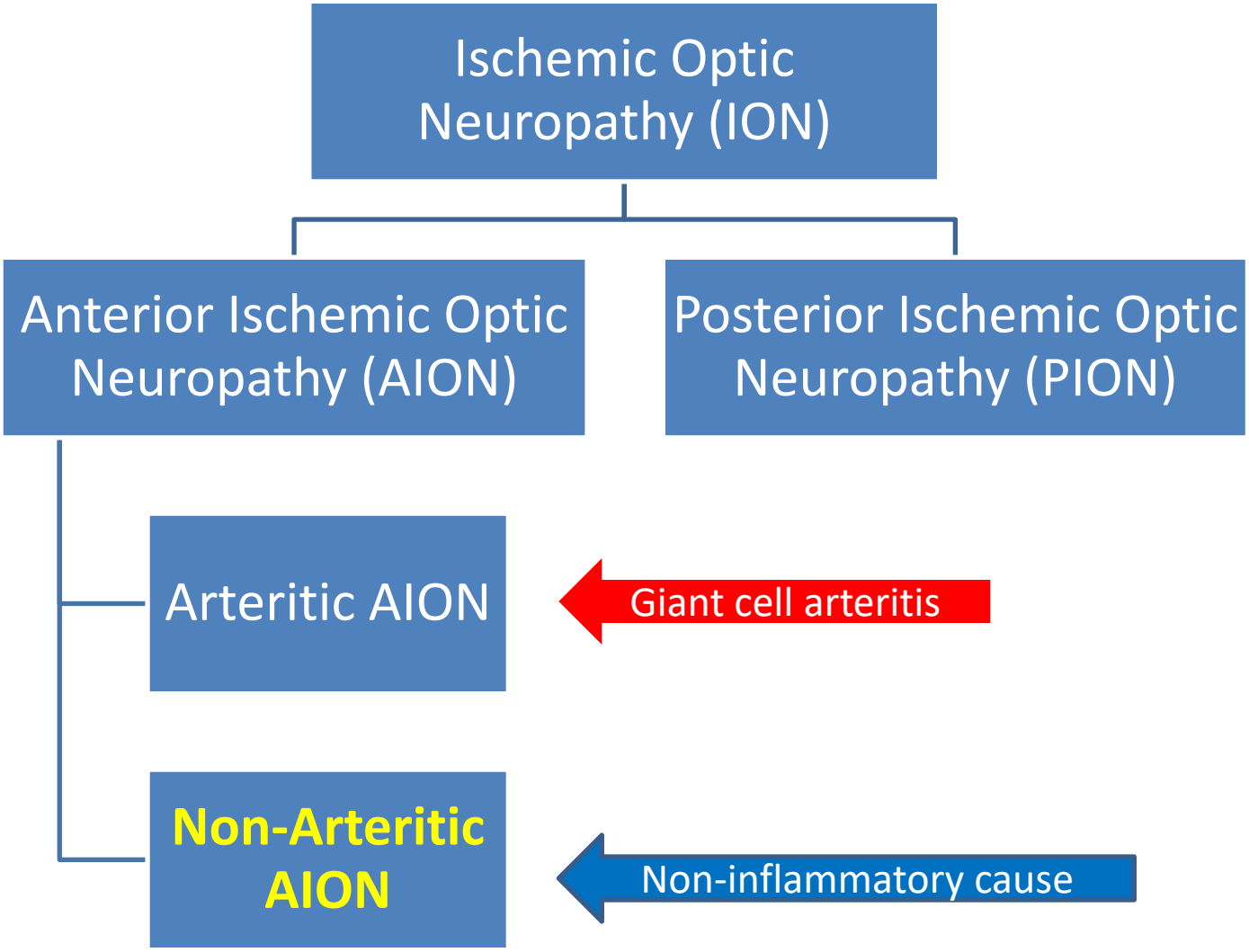
Treatment

- No definitive treatment.
- Aspirin is effective in reducing systemic vascular events.
- Aspirin does not reduce risk of involvement of the fellow eye.

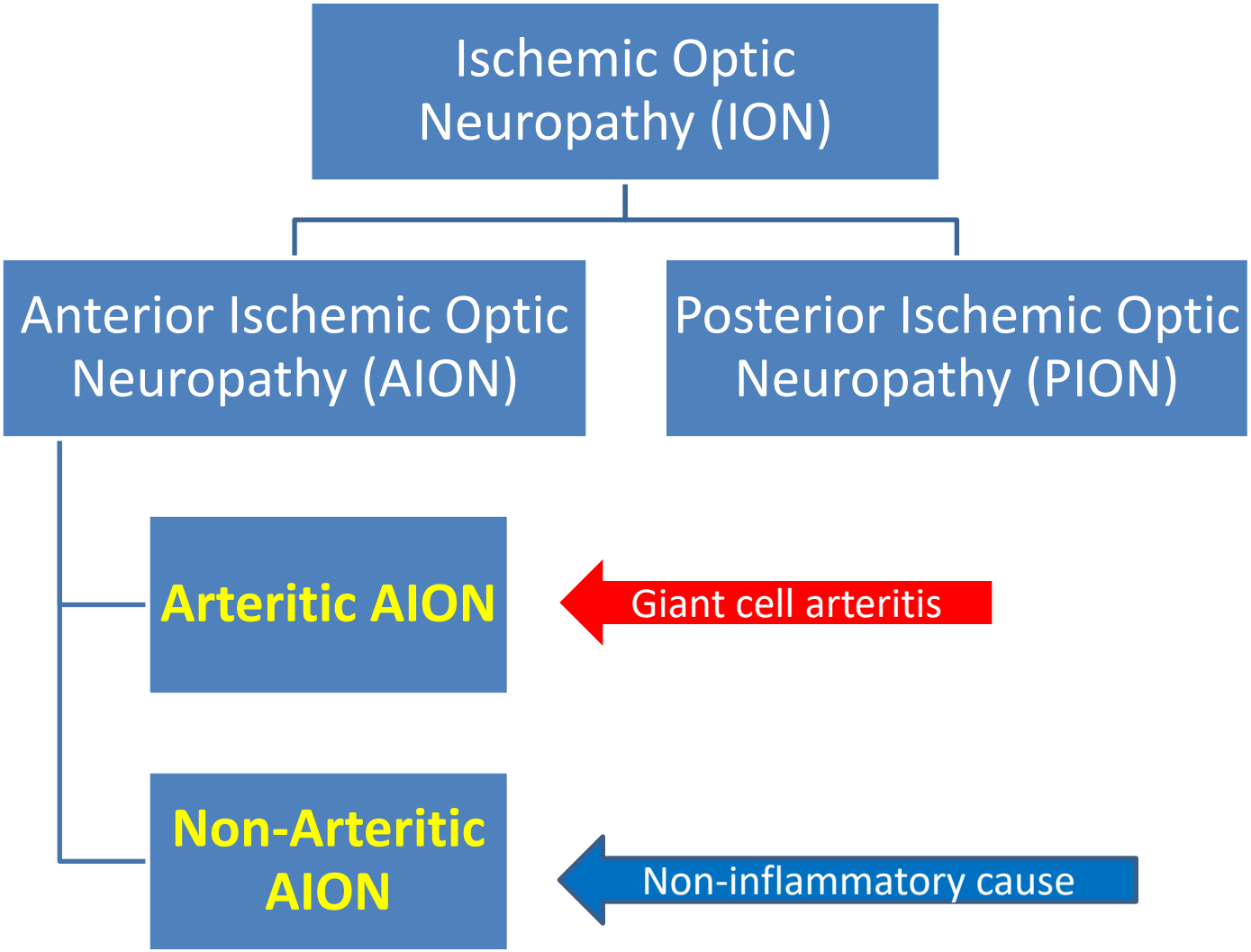
Ischemic Optic Neuropathy:NAION

Condition	Prognosis
No further loss of vision	Very small percentage
Recurrences in the same eye	~6%
Involvement of the FELLOW eye	~10% after 2 years
	~15% after 5 years
2 Important Factors caused involvement of FELLOW eye	Poor VA in 1st eye
	DM
Signs of FELLOW eye involvement	1 eye optic atrophy

Ischemic Optic Neuropathy



Ischemic Optic Neuropathy



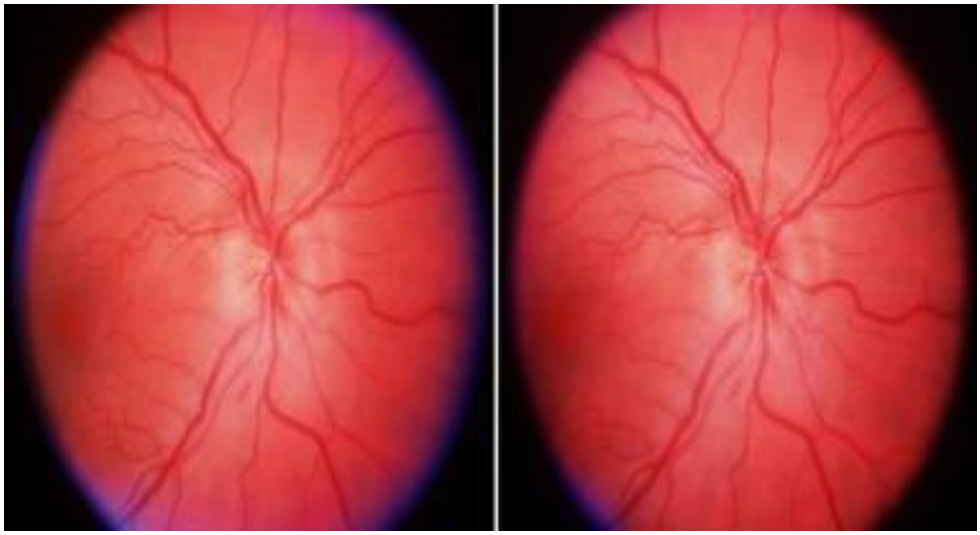
Ischemic Optic Neuropathy: AAION

Symptoms:

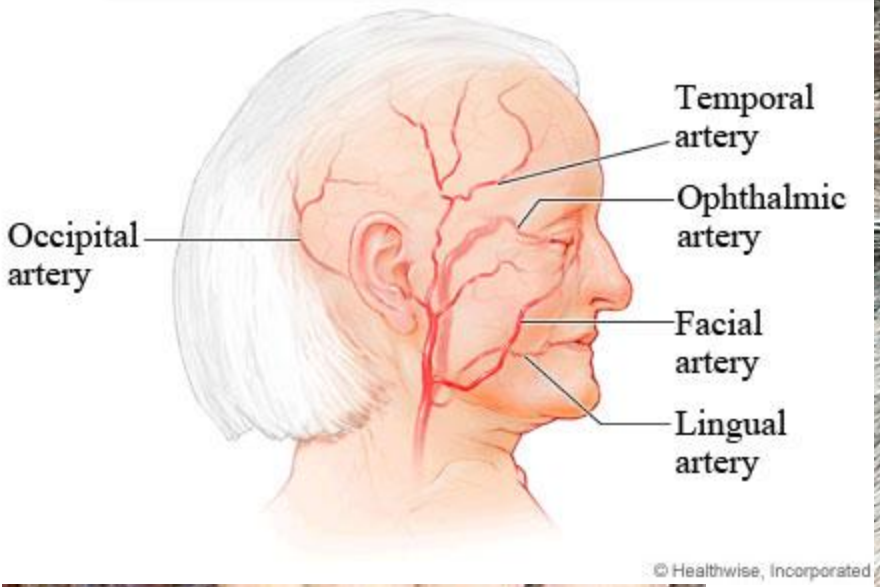
- Acute vision loss one or both eyes
- Painless

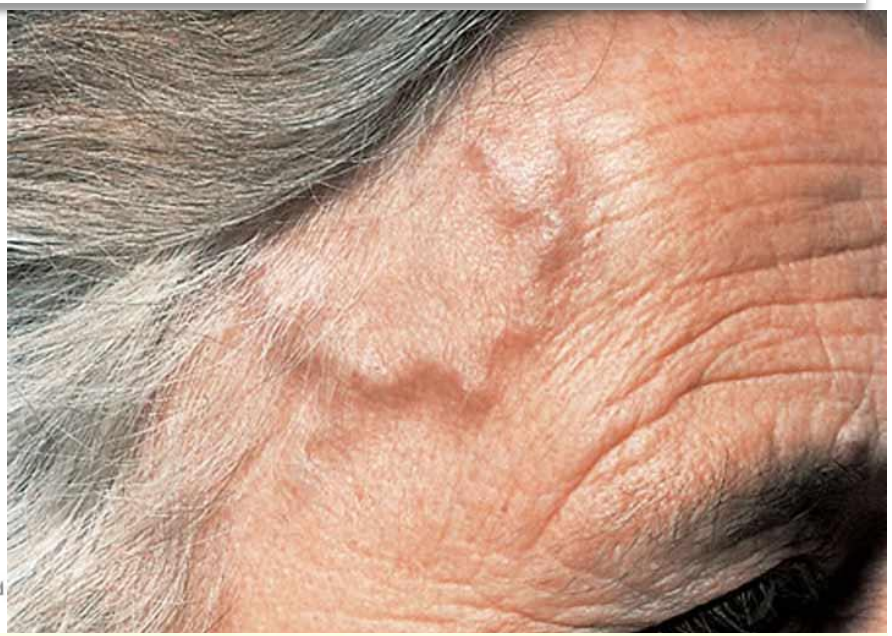
Signs:

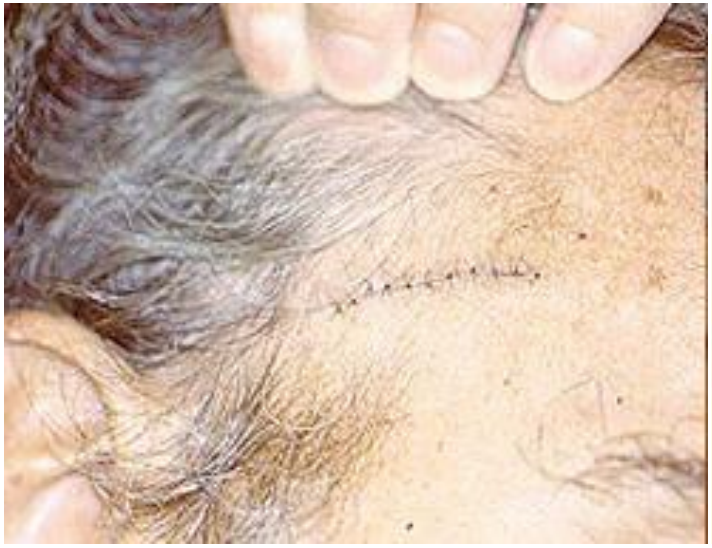
- VF loss
- RAPD +ve
- Swollen Optic Disc (AION) + flame haemorhage



Ischemic Optic Neuropathy: AAION







Giant cells (arrow) within a granuloma (circle) of granulomatous inflammation

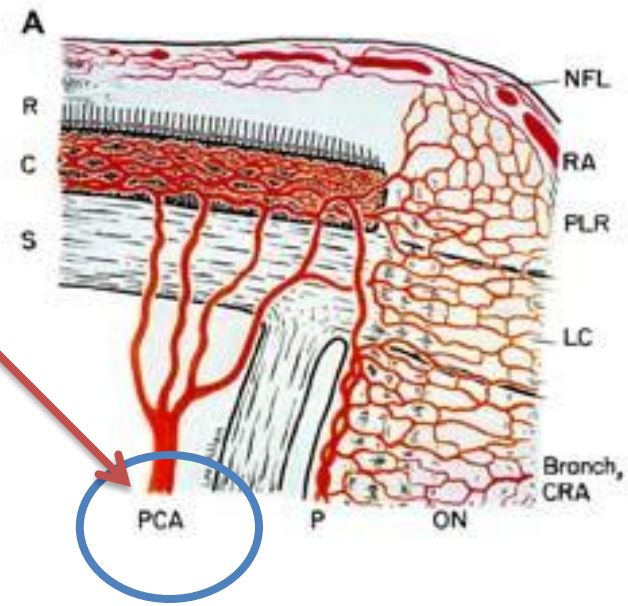
Ischemic Optic Neuropathy: AAION

Posterior ciliary artery is the main source of blood supply to the optic nerve head

Occlusion of the posterior ciliary artery results in infarction of a segment or the entire optic nerve head

Depending upon the area of the optic nerve head supplied by the occluded posterior ciliary artery

Results in development of A-AION and in massive visual loss.



Ischemic Optic Neuropathy: AAION

Age: Fifty years of age or older at onset.

Gender : 3 times more common in women than in men

Race: Common among Caucasians > other races

Giant cell arteritis

New onset of localized headache.

Temporal artery pulse.

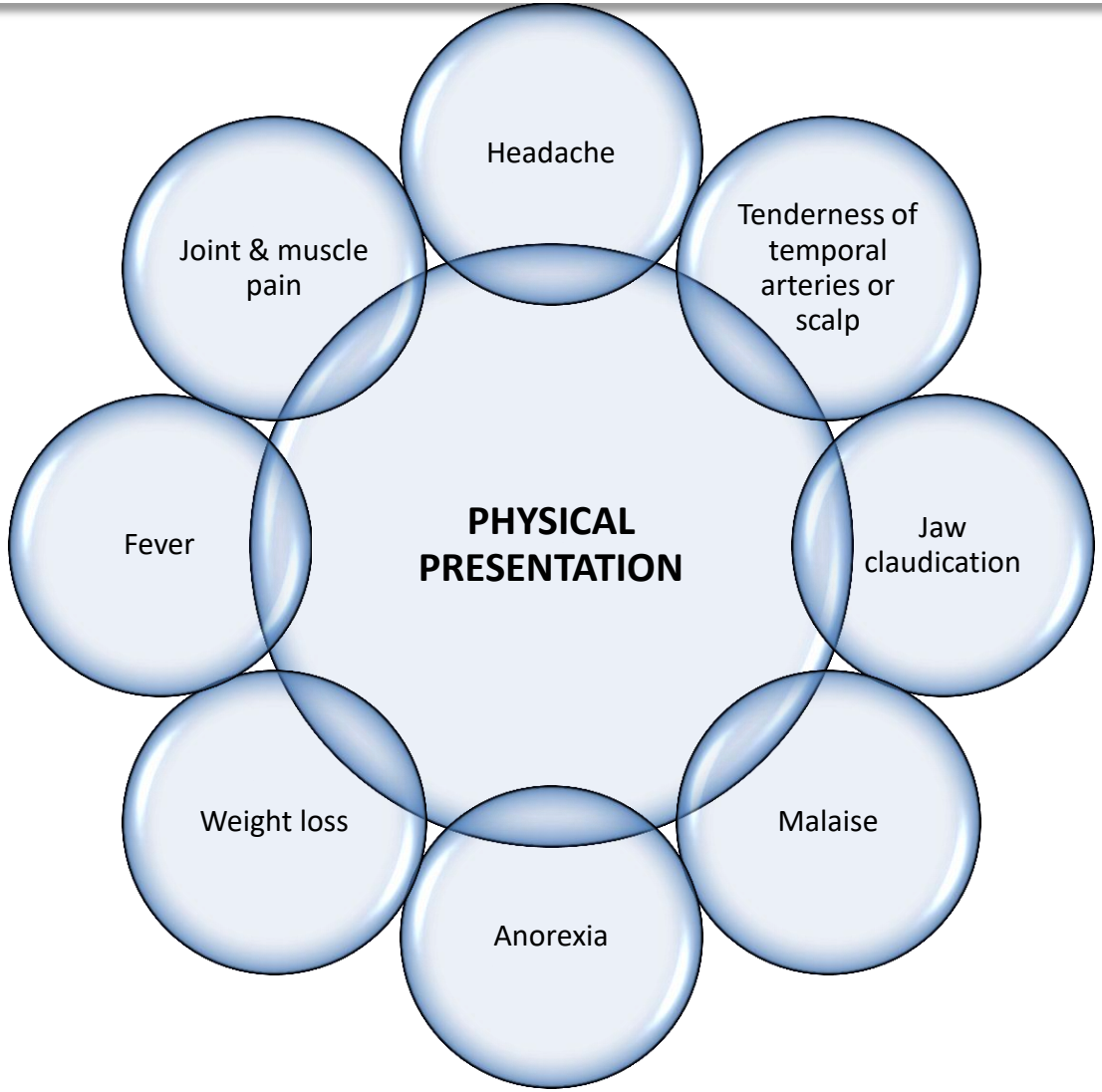
Elevated ESR.

Positive temporal artery biopsy.

60–70% will have a new headache
50% will have constitutional symptoms
50% will have jaw claudication
40–50% will have symptoms of polymyalgia rheumatica
15% will have partial or complete loss of vision
4–15% will have arm claudication

Source: Salvarani C et al., 2002.[13]

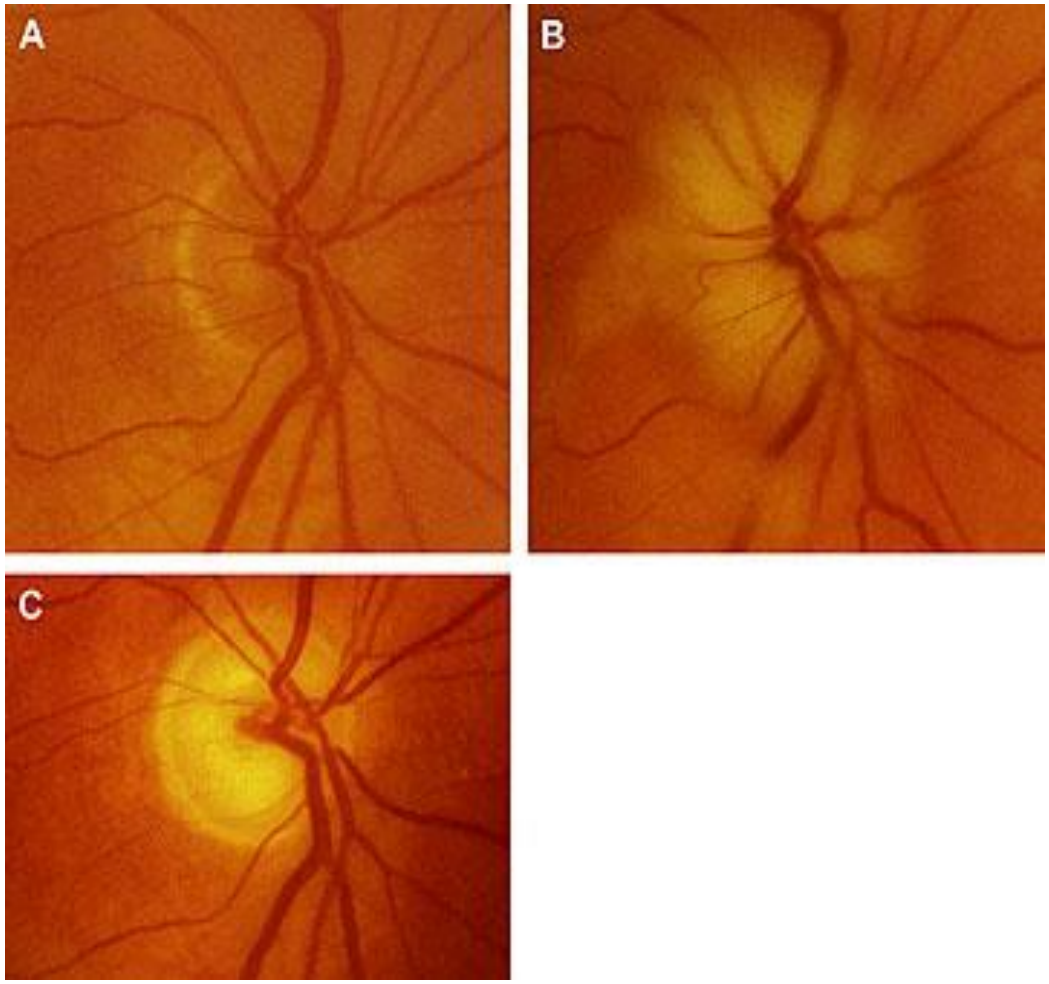
Ischemic Optic Neuropathy: AAION



Ischemic Optic Neuropathy: AAION

VA	• Sudden • Unilateral visual loss (↓ VAthat is typically severe (<6/60) in over 60% of the patients
RAPD	• Positive
Visual Field	• Visual field defect (altitudinal & inferior), more extensive than NAION
Colour vision	• Dyschromatopsia
Pain	• Periocular pain + flashing
Optic Disc	• Pale & swollen optic disc (swollen diffusely) • Chalky mark • Hyperemic swelling

Ischemic Optic Neuropathy: AAION



Fundus photographs of right eye with A-AION:

(A) Before developing A-AION

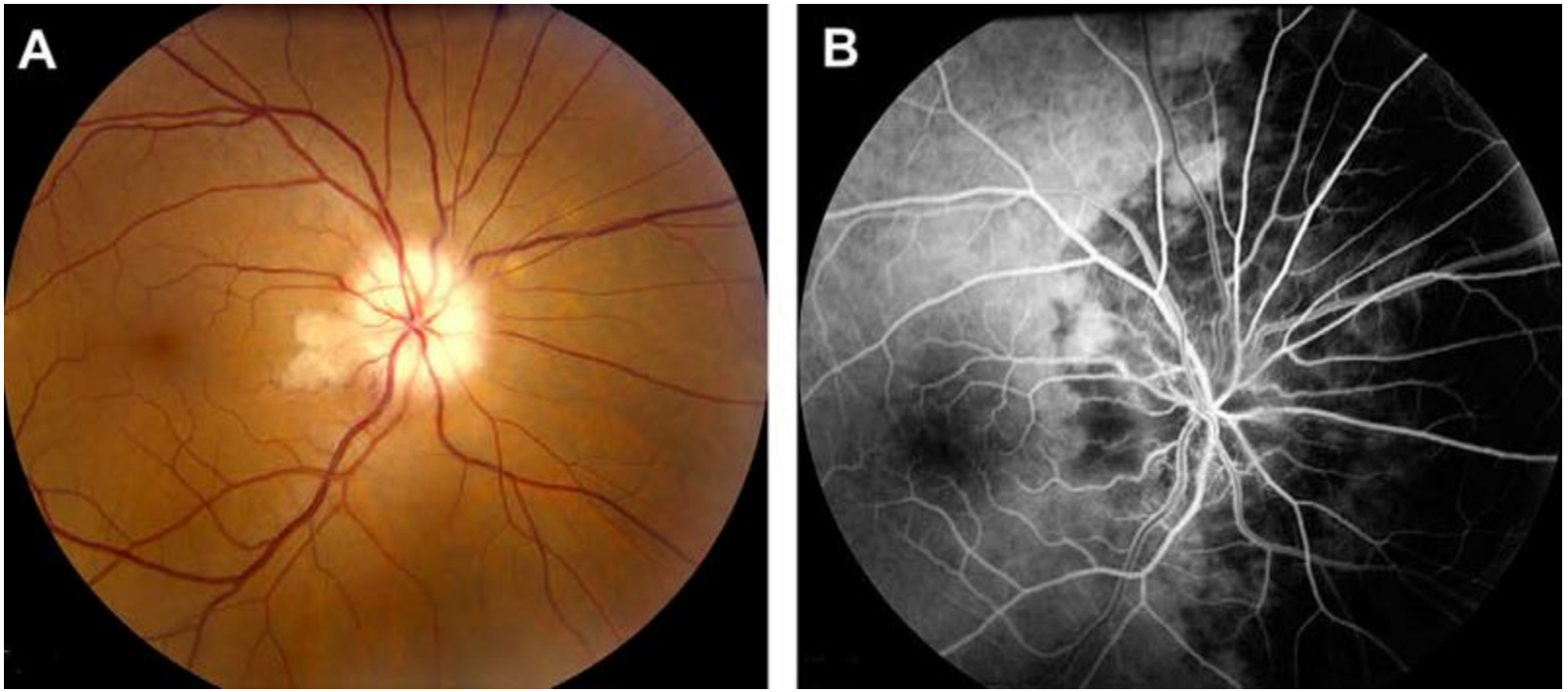
(B) One week after developing A-AION with chalky white optic disc edema and

(C) 4 months later showing optic disc cupping with a cup/disc ratio of 0.8 (note no cup in **A**)

Hayreh SS (2009) Ischemic optic neuropathy. Progress in retinal and eye research 28: 34-62

Ischemic Optic Neuropathy: AAION

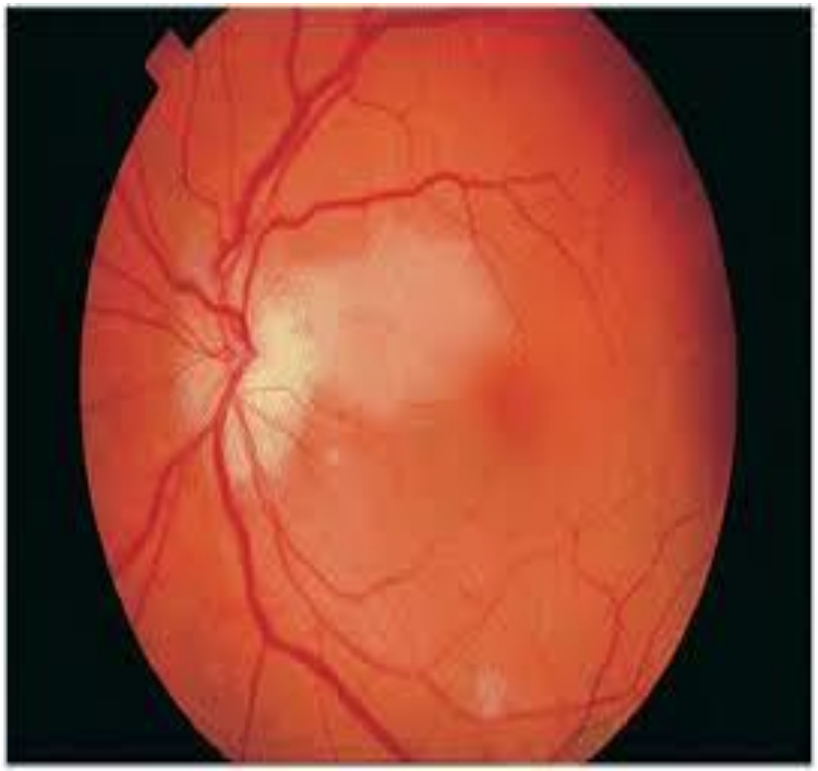
WORK UP: FFA finding



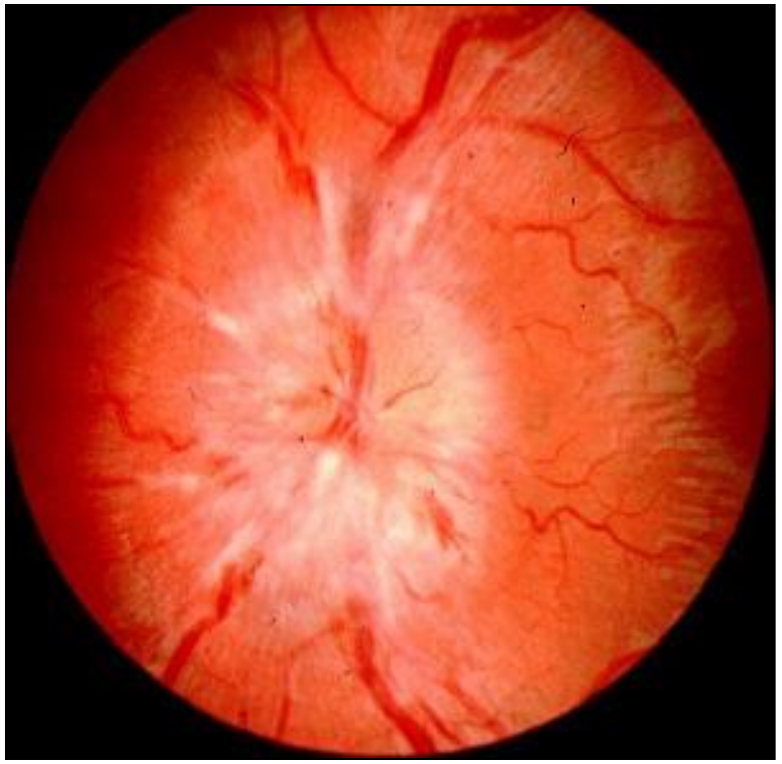
Fundus photograph (**A**) and fluorescein fundus angiogram (**B**) of right eye with A-AION and cilioretinal artery occlusion during the initial stages. (**A**) Fundus photograph shows chalky white optic disc edema with retinal infarct in the distribution of occluded cilioretinal artery. (**B**) Fluorescein fundus angiogram shows evidence of occlusion of the medial posterior ciliary artery and no filling of the cilioretinal artery.

Hayreh SS (2009) Ischemic optic neuropathy. Progress in retinal and eye research 28: 34-62

Ischemic Optic Neuropathy: AAION



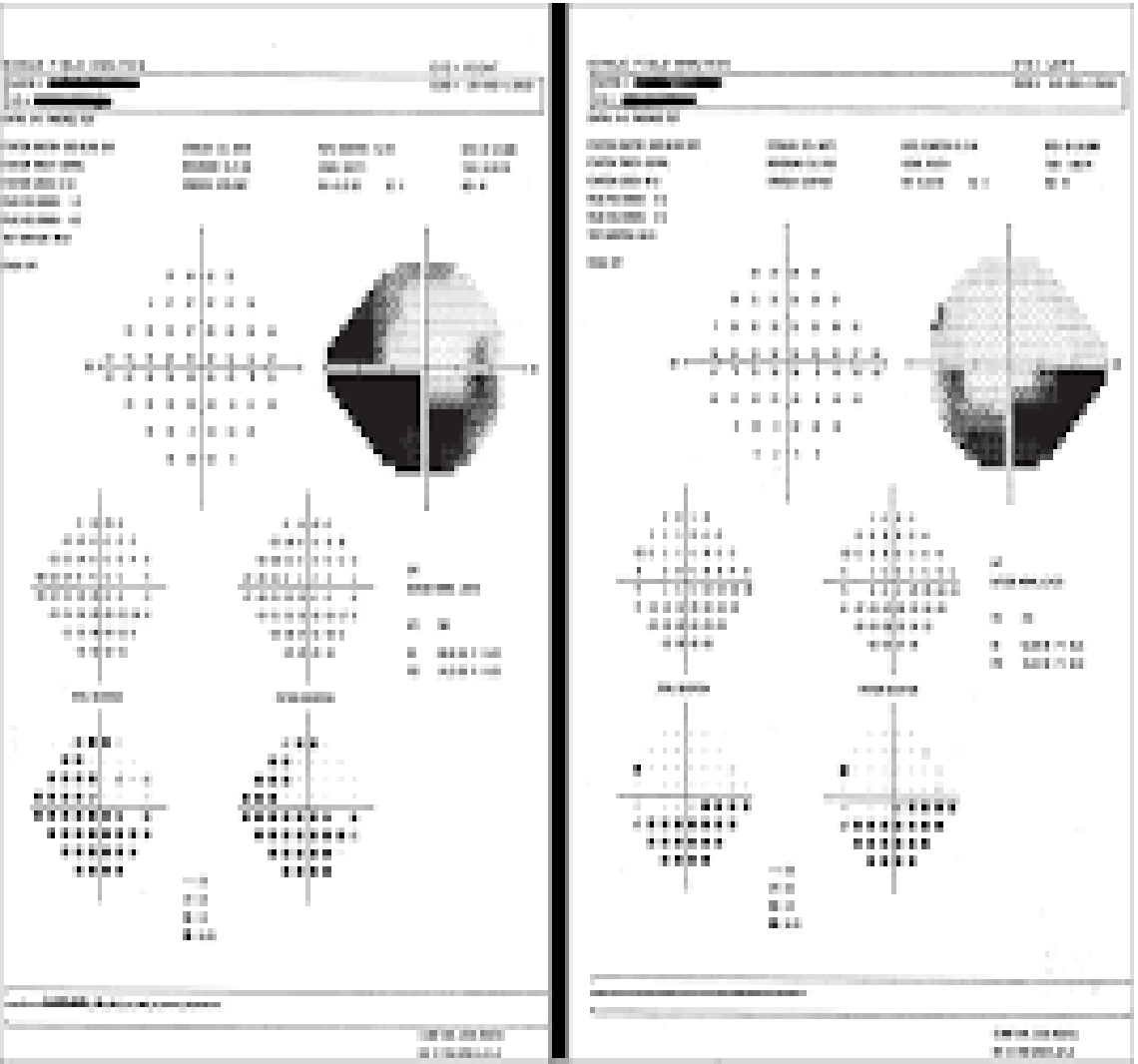
Pale optic disc edema with adjacent retina infarcted

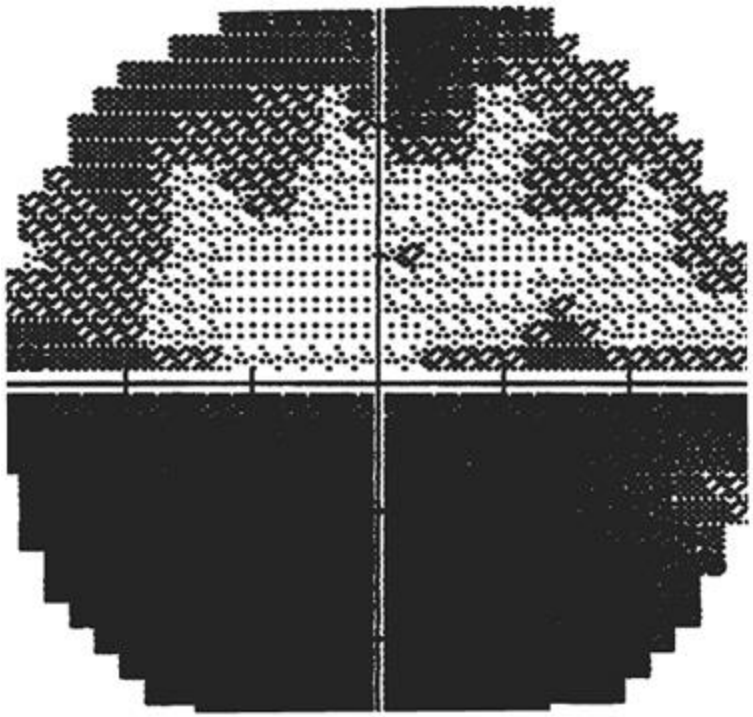


Chalky white pale,swollen and hyperemic optic disc

Ischemic Optic Neuropathy: AAION

Visual field defect (Altitudinal & inferiorly)





Ischemic Optic Neuropathy: AAION

Diagnostic work up

1. Erythrocyte sedimentation rate (ESR) >47mm
2. C-reactive protein >2.45 MG/DL
3. Fluorescein fundus angiographic (FFA): Critical diagnostic test for A-AION during the early stages → shows thrombosis and occlusion of the posterior ciliary artery in GCA
4. Jaw Claudication
5. Neck pain

(Kanski, 2003 & Hayreh, 2011)

Ischemic Optic Neuropathy: AAION

- AAION is **EMERGENCY** case.
- Early treatment is essential.
- Aim of treatment: To prevent blindness of the fellow eye.
- Treatment: (steroid therapy)
  - High dose systemic corticosteroid (IV methylprednisolone & oral prednisolone) for several months.
  - Temporal artery biopsy- within 3 days of treatment
- Duration of treatment: ~1 to 2 years

Ischemic Optic Neuropathy: AAION

- Prognosis-POOR
- Visual loss is usually permanent.
- Visual recovery of the affected eye that has treatment is poor with a 15-34% improvement rate.

DIFFERENTIATION :

AAION FROM NAAION

1. Systemic symptoms GCA : Patients with NA-AION have no systemic symptoms of giant cell arteritis.
2. Visual symptoms: Amaurosis fugax is highly suggestive of AAION and is extremely rare in NA-AION.
3. Hematologic abnormalities:Elevated ESR and CRP, particularly CRP, is helpful in the diagnosis of GCA. Patients with NA-AION do not show any of these abnormalities.
4. Early massive visual loss: Extremely suggestive of A-AION.
5. Chalky white optic disc edema: This is almost diagnostic of A-AION and is seen in 69% of AAION eyes. In NAAION, chalky white optic disc edema occurs only very rarely with embolic occlusion of the posterior ciliary artery.
6. AAION associated with cilioretinal artery occlusion . This is almost diagnostic of AAION.
7. Fluorescein fundus angiography: Evidence of posterior ciliary artery occlusion in AAION.
8. Temporal artery biopsy.

Optic Neuropathies : Causes

- **Demyelinating**
- **Inflammatory**
- **Non-arteritic Ischemic**
- **Arteritic Ischemic**
- Traumatic

Rapid onset

- Infiltrative
- Compressive
- Hereditary
- Radiation
- Paraneoplastic
- Toxic/nutritional

Gradual onset

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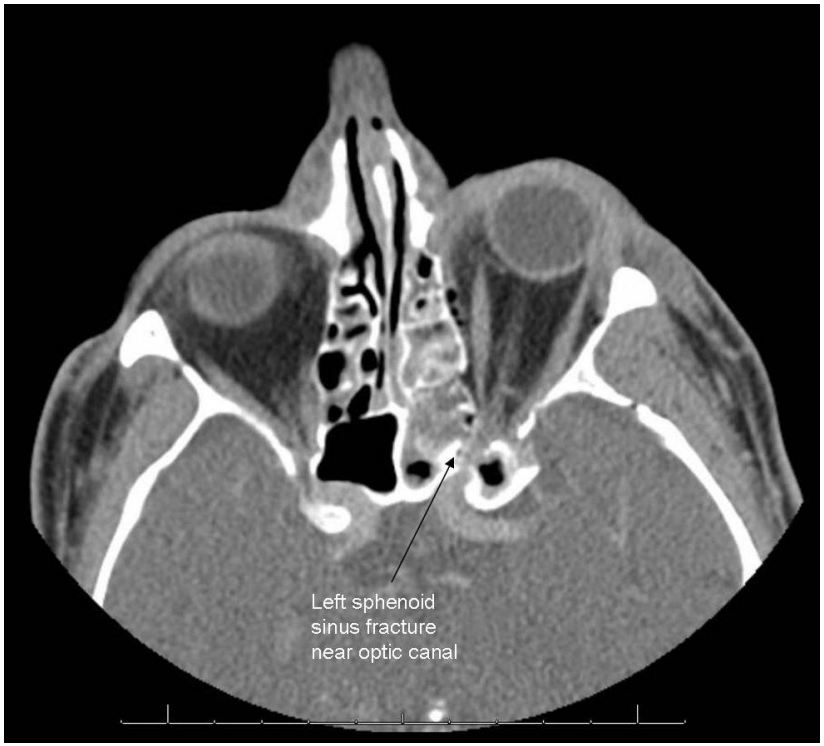
Traumatic Optic Neuropathy

- Patients usually had suffered craniofacial trauma but occasionally mild orbital or eye injury.

- A RAPD is the main clue to the diagnosis.

Traumatic Optic Neuropathy

- CT scan of the orbit is recommended to detect any bony fractures, fractures of the optic canal, and acute orbital hemorrhages.



Traumatic Optic Neuropathy

High-dose steroid therapy

- Was adopted as a treatment because of their beneficial effect in studies on spinal cord injuries.

- May be harmful to the optic nerve if started 8 hours after the injury

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Infilterative Optic Neuropathy

- Systemic malignancies such as lymphoma, leukemia, multiple myeloma, and carcinoma.
- The optic disc can be swollen or normal in appearance.
- MRI of the brain and orbit may show meningeal and optic nerve enhancement.

Infilterative Optic Neuropathy

- Spinal tap is recommended in cases of suspected CNS malignancy but more than one spinal tap may be needed to detect malignant cells.
- In case of localized optic nerve infiltration with no evidence of systemic disease, histopathological diagnosis may require direct optic nerve sheath biopsy.

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Compressive Optic Neuropathy

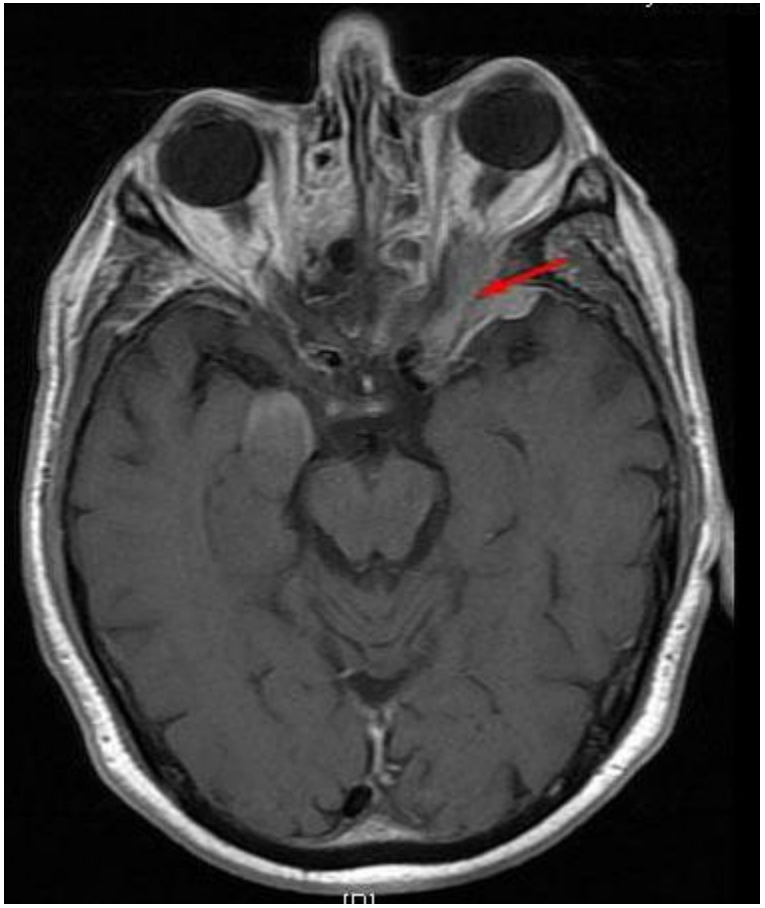
- Common causes include orbital and intracranial meningiomas, pituitary adenomas, intracranial aneurysms, craniopharyngiomas, and gliomas of the anterior visual pathway.

- Vision loss, however, can be fast and dramatic in pituitary apoplexy, or ruptured aneurysm.

- Visual field testing aids in the localization of the lesion.

Compressive Optic Neuropathy

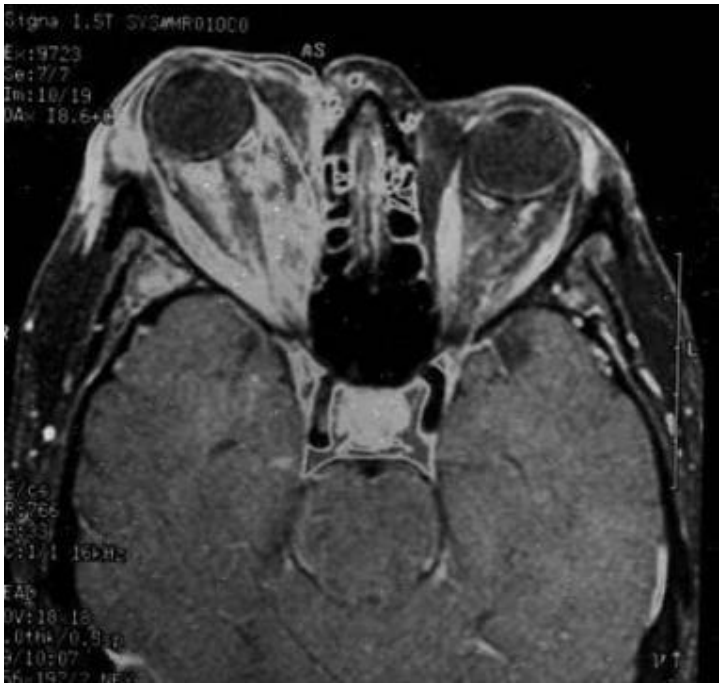
- Neuroimaging study (MRI of brain and orbits) revealed an extensive meningioma involving the left orbital apex (arrow)



Compressive Optic Neuropathy

- Thyroid eye disease and can present as asymmetric progressive visual loss.

- This will require prompt therapy (orbital radiation, orbital decompression, high-dose systemic steroids).



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Hereditary Optic Neuropathy

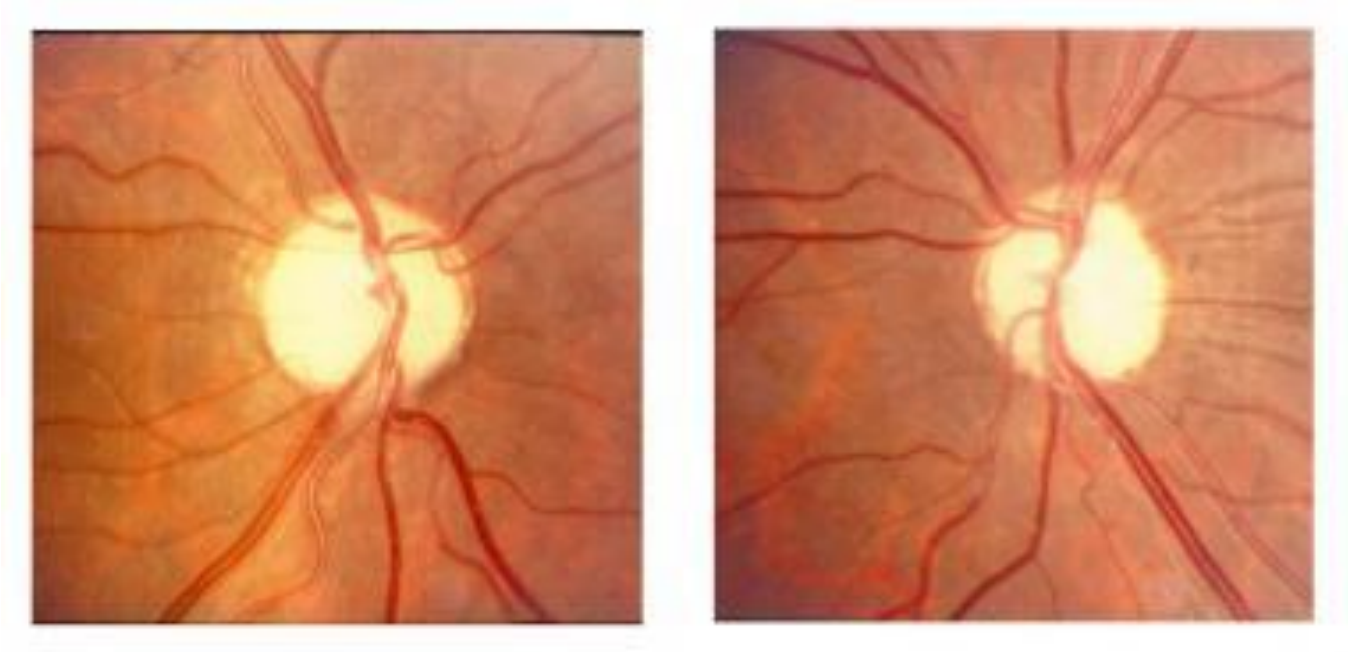
- AD
- AR
- XL
- MT

Hereditary Optic Neuropathy: AD (Kjers' type)

- There various responsible genetic mutations occur in the OPA1 gene located on the chromosome 3 q region
- 1st decade of life
- Bilateral symmetric visual loss.
- Bilateral central or cecocentral scotomas.
- Color vision deficit along the tritan (blue-yellow) axis.

Hereditary Optic Neuropathy: AD (Kjers' type)

- The optic disc : temporal pallor and in some cases severe excavation and cupping.



Hereditary Optic Neuropathy

AR (Wolfram syndrome)

- 1st year of life
- It can be associated with diabetes mellitus, diabetes inspidus, and deafness.

XL

- Xp11.4–Xp11.2 (OPA2)

Hereditary Optic Neuropathy

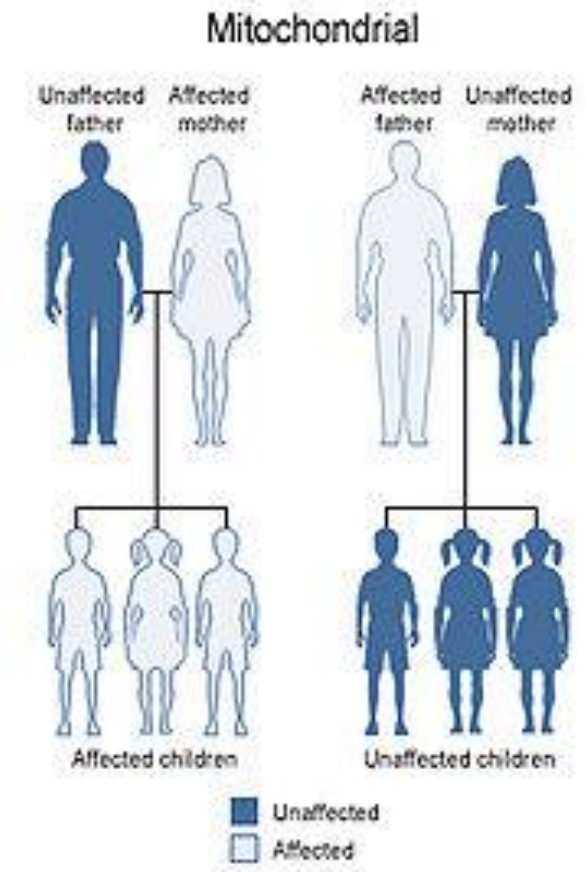
Optic neuropathy can also occur in neurological conditions such as:

Spinocerebellar degeneration

Olivo-ponto-cerebellar atrophy.

Hereditary Optic Neuropathy: LHON

- LHON has 4 primary mitochondrial genome mutations; G11778A, G3460A and T14484C and T10663C.
- M>F
- The frequencies of mutation may vary across different countries
- Newer mutations have been described worldwide



Hereditary Optic Neuropathy: LHON

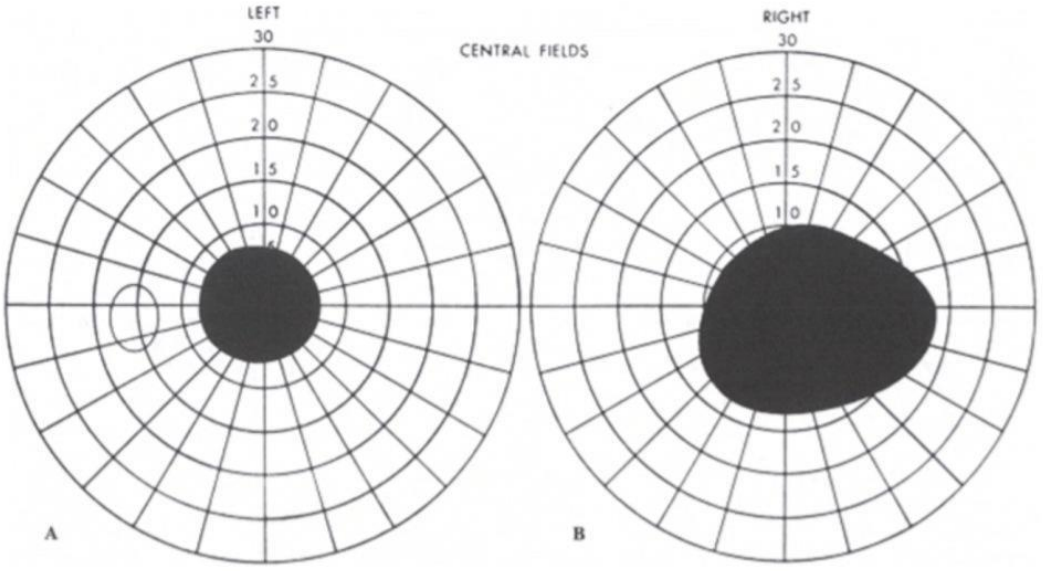
- Acute unilateral, painless, visual loss.
- some cases may stay asymptomatic or have a chronic course
- Sequential bilateral involvement may occur weeks or months later.
- Some patients may demonstrate neurological manifestations such as peripheral neuropathy, ataxia, dystonia and cardiac conduction defects

Hereditary Optic Neuropathy: LHON

- Occasionally, optic nerve pallor can be seen initially. Because of the wide age range (6–80 years old) at which LHON may present, it is frequently misdiagnosed
- Young patients are often diagnosed as optic neuritis and older patients as ischemic or infiltrative optic neuropathy.

Hereditary Optic Neuropathy: LHON

- Visual filed defects tend to be central or cecocentral as the papillo-macular bundle is first and most severely



Hereditary Optic Neuropathy: LHON

- Fundoscopy may show disk swelling, thickening of the peripapillary retinal nerve fiber layer

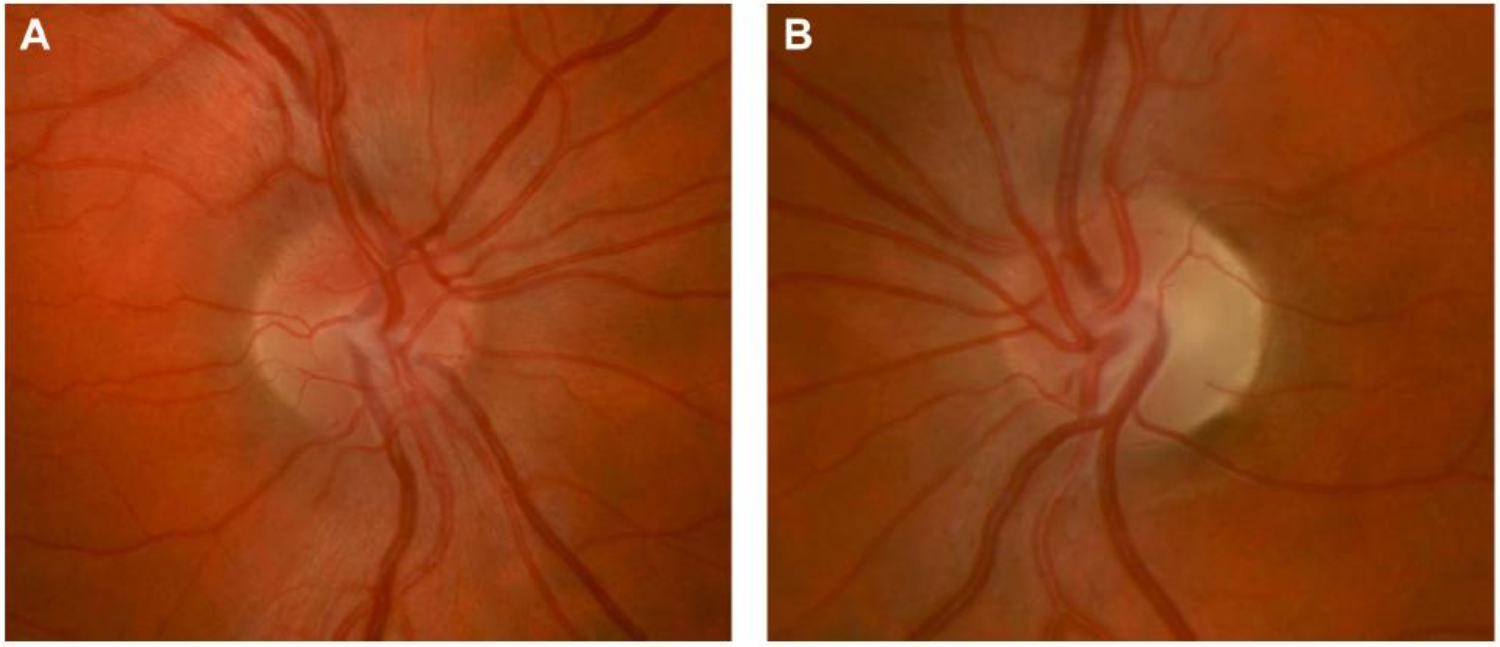
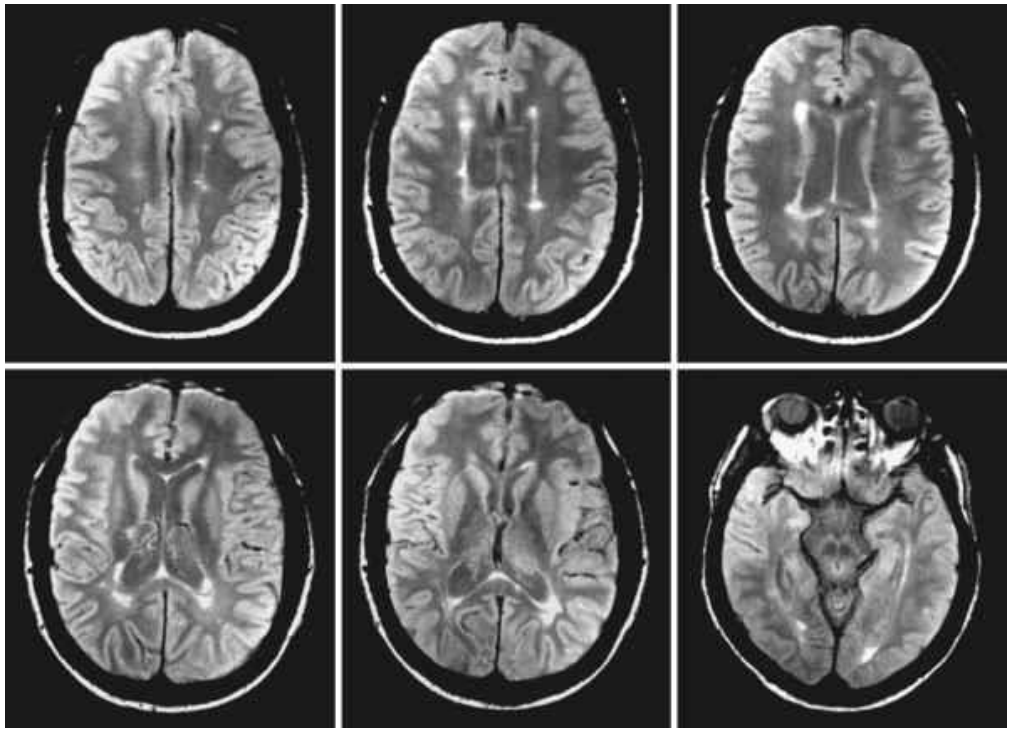


Figure 2 Right optic nerve (**A**) of a patient with acute LHON-related vision loss showing mild hyperemia, blurring of the disc margin, and elevation of the optic nerve head from swelling of the peripapillary retinal nerve fiber layer. LHON-related vision loss in the left eye had occurred 6 months prior leading to prominent temporal optic nerve pallor (**B**) from atrophy of the retinal nerve fiber layer.
Abbreviation: LHON, Leber hereditary optic neuropathy.

Hereditary Optic Neuropathy: LHON

- MRI may show optic nerve enhancement and white matter lesions, which may add to the diagnostic difficulties



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Radiation-induced Optic Neuropathy

- Patients with RON can present with vision loss, months or years following history of radiation exposure to the brain or orbit.
- The risk ↑ +chemotherapy
- The mechanism of RON is ischemia caused by endothelial cell injury from radiation.
- MRI of the orbit may show optic nerve enhancement with gadolinium

Radiation-induced Optic Neuropathy

- The optic disc is usually normal but can be swollen.
- Patients may also have radiation retinopathy with retinal hemorrhages, cotton wool spots, exudates and macular edema.
- There is no treatment of proven efficacy for RON.
- Hyperbaric oxygen, steroids, antiplatelet drugs, and anticoagulants have all been used with limited success .
- The visual prognosis is poor with 45% of eyes ending with no light perception visual acuity

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Gradual onset

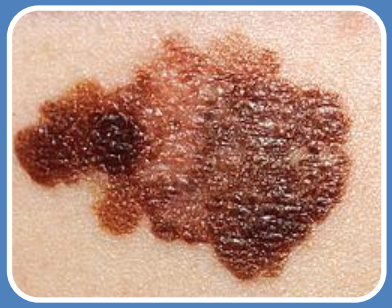
Paraneoplastic Optic Neuropathy

- Cancer-associated retinopathy (CAR)
- Melanoma-associated retinopathy (MAR)
- Paraneoplastic optic neuropathy (PON)
- Patients with car typically present with progressive loss of vision and photopsia

Paraneoplastic Optic Neuropathy

CAR

- Small-cell lung cancer (SCLC),gynecologic tumors
- Autoantibodies against calcium-binding photoreceptor protein that participates in the transduction of light.



MAR

- Photopsias
- Autoantibodies against the bipolar cells of the retina

PON

- Progressive visual loss and optic disc edema,
- Autoantibodies against
- collapsin-responsive mediator protein-5
- (CRMP-5, also called anti-CV2)

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Gradual onset

Metabolic Optic Neuropathies

The three subcategories of metabolic optic neuropathies are

- Heredodegenerative (such as leber's hereditary optic neuropathy).
- Nutritional deficiencies (such as vitamins B12 or folic acid).
- Toxicities (such as ethambutol or cyanide).

Metabolic Optic Neuropathies

TABLE 5-1 Expected Clinical Characteristics of Most Toxic, Nutritional, and Hereditary Optic Neuropathies

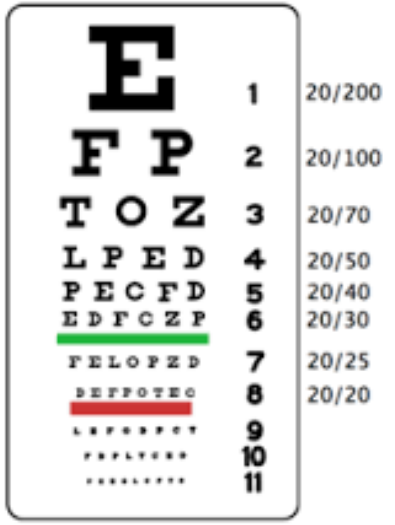
- Gradual, symmetric progression
- Painless onset
- Dyschromatopsia (loss of color perception)
- Central/cecocentral visual field loss
- Visual acuity greater than hand motion
- No optic disc swelling
- No macular symptoms (eg, metamorphopsia, light sensitivity, micropsia)
- Improvement after removing the offending agent or nutritional repletion

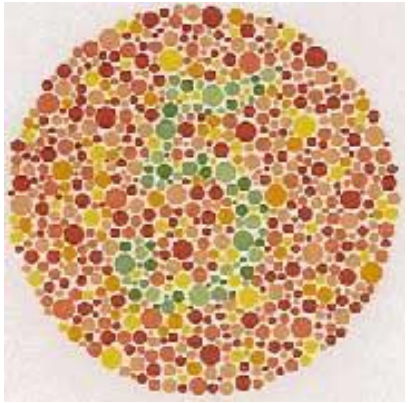
Toxic Optic Neuropathies

Symptoms
Diminution of vision: bilaterally symmetrical, painless, gradually progressive
Dyschromatopsia
Signs
Pupils: sluggish, no RAPD
Optic disc: normal, swollen, or hyperemic in early stages: temporal optic disc pallor later
Visual field defect: centrocaecal scotoma

Toxic Optic Neuropathies

- Visual acuity may vary from minimal reduction to no light perception (NLP) in rare cases.
- Most patients have 20/200 vision or better.
- Color vision should be assessed because dyschromatopsia is a constant feature in these conditions.



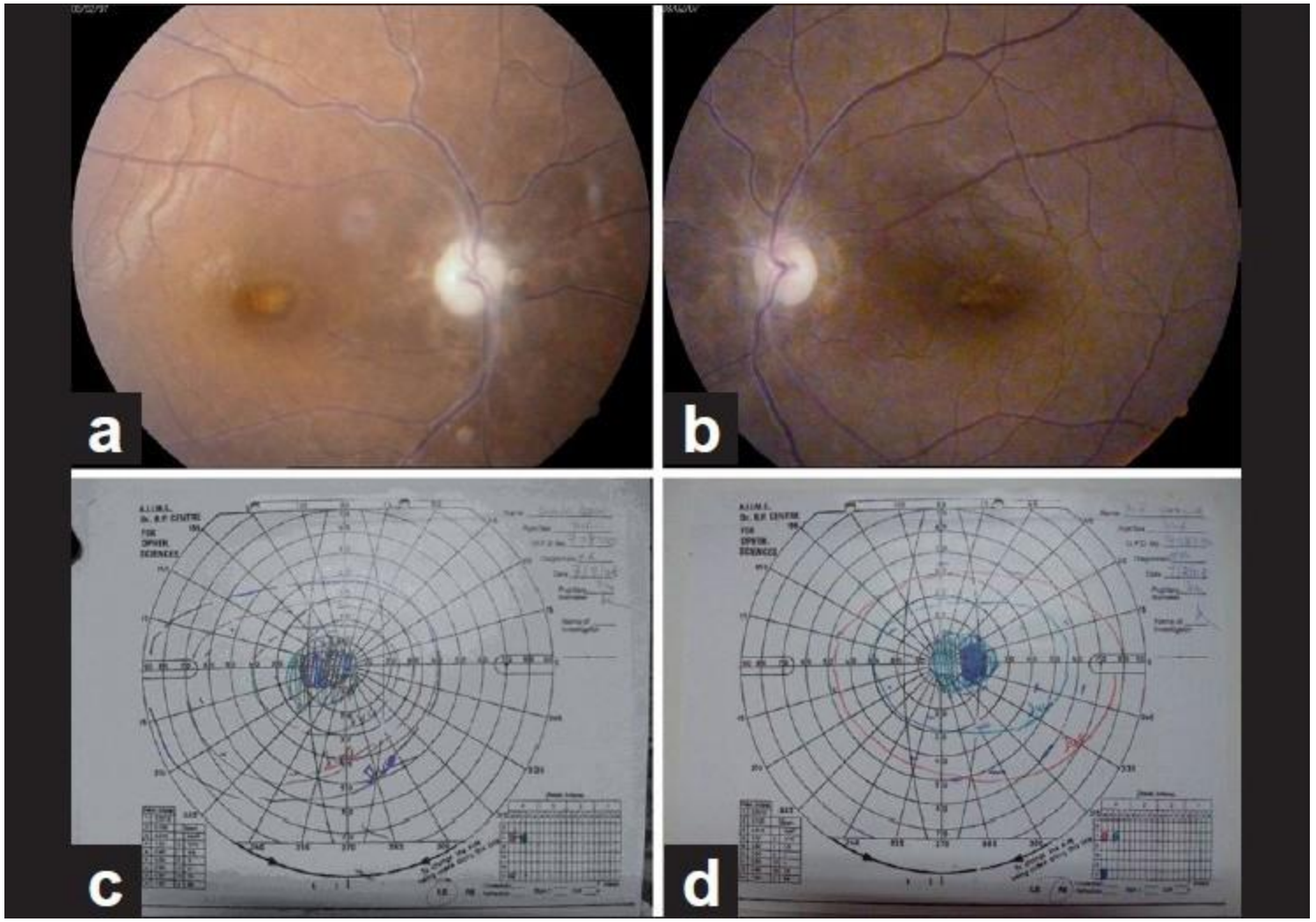


Toxic Optic Neuropathies

- In the early stages of toxic optic neuropathies, most patients also have normal-appearing optic nerves, but disc edema and hyperemia may be seen in some intoxications, especially in acute poisonings.

- Papillomacular bundle loss and optic atrophy develop after a variable interval depending on the responsible toxin.

Toxic Optic Neuropathies



Toxic Optic Neuropathies

Alcohols: Methanol, ethylene glycol (antifreeze)

Antibiotics: Chloramphenicol, sulfonamides, linezolid

Antimalarials: Chloroquine, quinine

Antitubercular drugs: Isoniazid, ethambutol, streptomycin

Antiarrhythmic agents: Digitalis, amiodarone

Anticancer agents: Vincristine, methotrexate

Heavy metals: Lead, mercury, thallium

Others: Carbon monoxide, tobacco

Toxic Optic Neuropathies

- In the workplace, industrial locations, and related to intentional or accidental poisonings, optic nerve toxicity has been reported to result from

✓ Methanol

✓ Ethylene glycol (antifreeze)

✓ Lead

✓ Mercury

✓ Thallium

✓ Carbon monoxide.

Toxic Optic Neuropathies

- Among the many causes of TON, the top 10 toxins include:

Medications

- Ethambutol, rifampin, isoniazid, streptomycin
- Linezolid
- Chloramphenicol
- Isoretinoin
- Cyclosporin

Acute Toxins

- Methanol
- Ethylene glycol

Nutritional Optic Neuropathies

The clinical presentation and basic pathophysiology are similar to TON.

Most often, they present as a non-specific retrobulbar optic neuropathy.

Currently, the treatment is limited to the intensive use of vitamins with variable results in individual cases, and to the implementation of preventive measures, when feasible.

Nutritional Optic Neuropathies

- Optic disc may be normal or slightly hyperemic in the early stages.
- In a small group of patients with hyperemic discs, small splinter hemorrhages on or off the disc.
- Several months to years later , papillomacular bundle dropout and temporal disc pallor, followed by optic atrophy.

Nutritional Optic Neuropathies

Deficiency of

- Thiamine (vitamin B1)
- Cyanocobalamin (vitamin B12)
- Pyridoxine (vitamin B6)
- Niacin (vitamin B3)
- Riboflavin (vitamin B2)
- Folic acid

Nutritional Optic Neuropathies

Tobacco Alcohol Ambylopia (TAA)

- TAA is an old term for a constellation of elements that can lead to a mitochondrial optic neuropathy.
- The classic patient is a man with a history of heavy alcohol and tobacco consumption.

Nutritional Optic Neuropathies

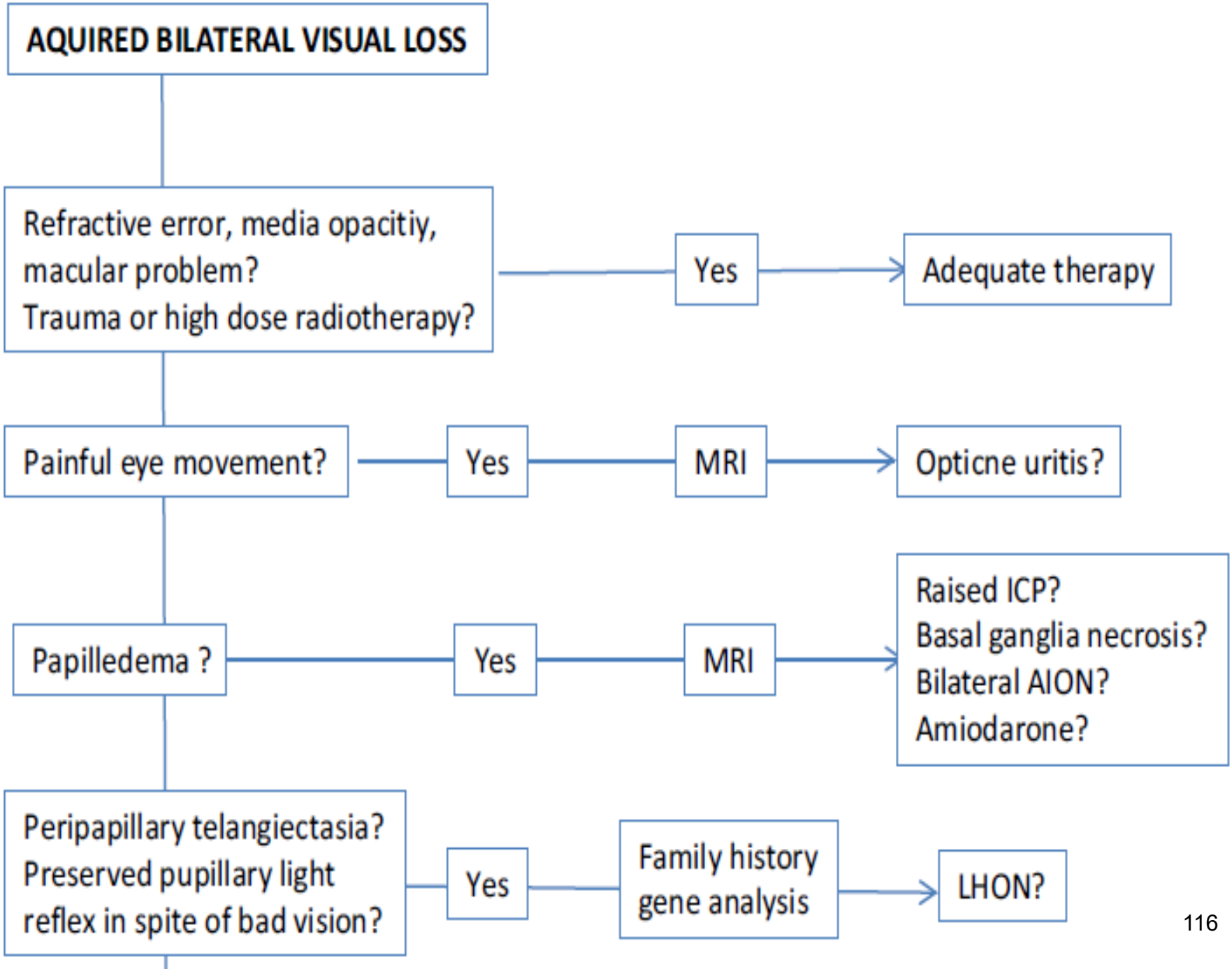
Tobacco Alcohol Ambylopia (TAA)

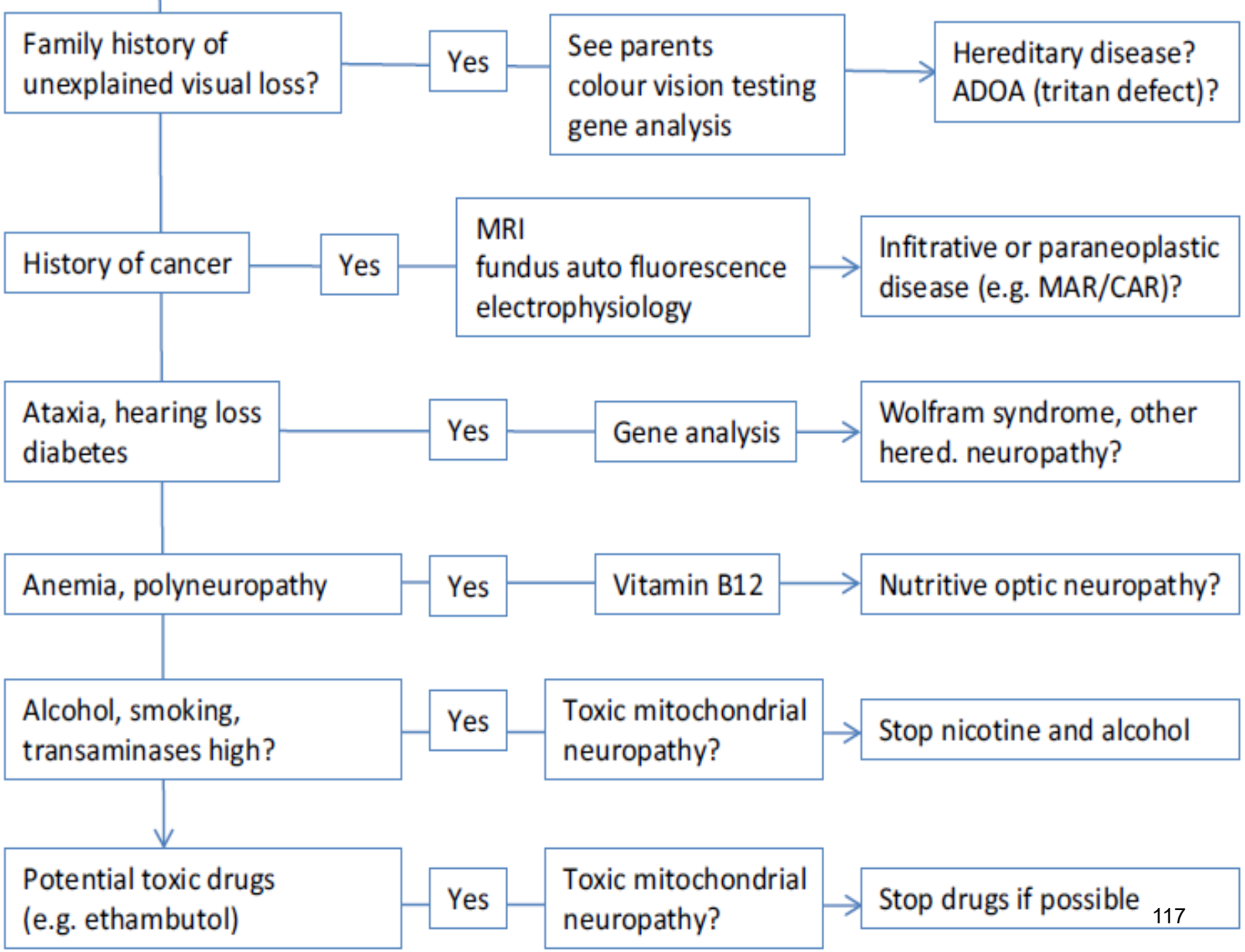
- Combined nutritional mitochondrial impairment, from vitamin deficiencies (folate and B-12) classically seen in alcoholics, with tobacco-derived products, such as cyanide and ROS.
- It has been suggested that the additive effect of the cyanide toxicity, ROS, and deficiencies of thiamine, riboflavin, pyridoxine, and b12 result in TAA

Toxic Optic Neuropathies: Other agents

- Hypovitaminosis A – night blindness (nyctalopia), keratomalacia.

- Hypervitaminosis A – yellow skin and conjunctiva, pseudotumor cerebri (papilledema), retinal hemorrhage.


AQUIRED BILATERAL VISUAL LOSS
Refractive error, media opacitiy, macular problem? Trauma or high dose radiotherapy?
Yes
Adequate therapy
Painful eye movement?
Yes
MRI
Opticne uritis?
Papilledema ?
Yes
MRI
Raised ICP? Basal ganglia necrosis? Bilateral AION? Amiodarone?
Peripapillary telangiectasia? Preserved pupillary light reflex in spite of bad vision?
Yes
Family history gene analysis
LHON?


Family history of unexplained visual loss?
Yes
See parents
colour vision testing
gene analysis
Hereditary disease?
ADOA (tritan defect)?
History of cancer
Yes
MRI
fundus auto fluorescence
electrophysiology
Infitrative or paraneoplastic disease (e.g. MAR/CAR)?
Ataxia, hearing loss diabetes
Yes
Gene analysis
Wolfram syndrome, other hered. neuropathy?
Anemia, polyneuropathy
Yes
Vitamin B12
Nutritive optic neuropathy?
Alcohol, smoking, transaminases high?
Yes
Toxic mitochondrial neuropathy?
Stop nicotine and alcohol
Potential toxic drugs (e.g. ethambutol)
Yes
Toxic mitochondrial neuropathy?
Stop drugs if possible

Type of optic neuropathy	Onset	Pattern of visual field loss	Ophthalmoscopic findings	Additional features
Demyelinating	Acute	Central, cecocentral, arcuate	75% normal disc (retrobulbar)	Neurological signs of brain stem (diplopia, ataxia, weakness) or spinal cord involvement (leg weakness, bladder symptoms, paresthesias, abnormal MRI)
Non-arteritic Ischemic	Acute	Arcuate, altitudinal	Swollen disc (usually sectoral) with disc hemorrhages	Crowded (anamalous) disk, systemic vascular risk factors (diabetes, hypertension, hyerlipedemia)
Arteritic Ischemic	Acute	Arcuate	Pallid swelling of the disc	Headache, jaw claudications, transient visual loss or diplopia, myalgias, fever, weight loss, High ESR and CRP
Inflammatory	Acute, sub-acute	Arcuate, central, cecocentral	Swollen disc	Features of auto-immune diseases (skin rash, arthritis, Raynaud's phenomenon), exquisite responsiveness to systemic steroids

Type of optic neuropathy	Onset	Pattern of visual field loss	Ophthalmoscopic findings	Additional features
Hereditary	Chronic (dominant and recessive), acute or subacute (Leber's)	Central, cecocentral	Pale (dominant and recessive) or mildly swollen with peripapillary telengiectatic vessels (Leber's)	Onset in childhood with positive family history, Mitochondrial DNA testing may reveal Leber's mutataion
Traumatic	Acute	Arcaute, central or hemianopic	Normal	Head or facial trauma
Radiation	Acute	Arcuate, hemianopic	Normal	History of radiation to the brain or orbit, MRI may show enhancement of the optic nerve with Gadolinium
Paraneoplastic	Subacute, chronic	Central	Swollen disc	Associated small-cell lung carcinoma, CRMP-5 marker may be positive, paraneoplastic cerebellar syndrome

Type of optic neuropathy	Onset	Pattern of visual field loss	Ophthalmoscopic findings	Additional features
Infiltrative	Acute, subacute	Arcuate, hemianopic	Normal or swollen disc	Systemic malignancy may be present, MRI may show optic nerve or meningeal infiltration
Compressive	Chronic	Arcuate, hemianopic	Normal or pale disc	MRI will show a compressive mass
Toxic/nutritional	Acute, subacute or chronic	Central, cecocentral	Normal or mildly swollen disc	History of drug use (ethambutol, alcohol)

Optic Neuropathies : Causes

- Demyelinating
- Inflammatory
- Non-arteritic Ischemic
- Arteritic Ischemic
- Traumatic

Rapid onset

- Infiltrative
- Compressive
- Hereditary
- Radiation
- Paraneoplastic
- Toxic/nutritional

Gradual onset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THANK YOU