Double vision- Differentials and work up

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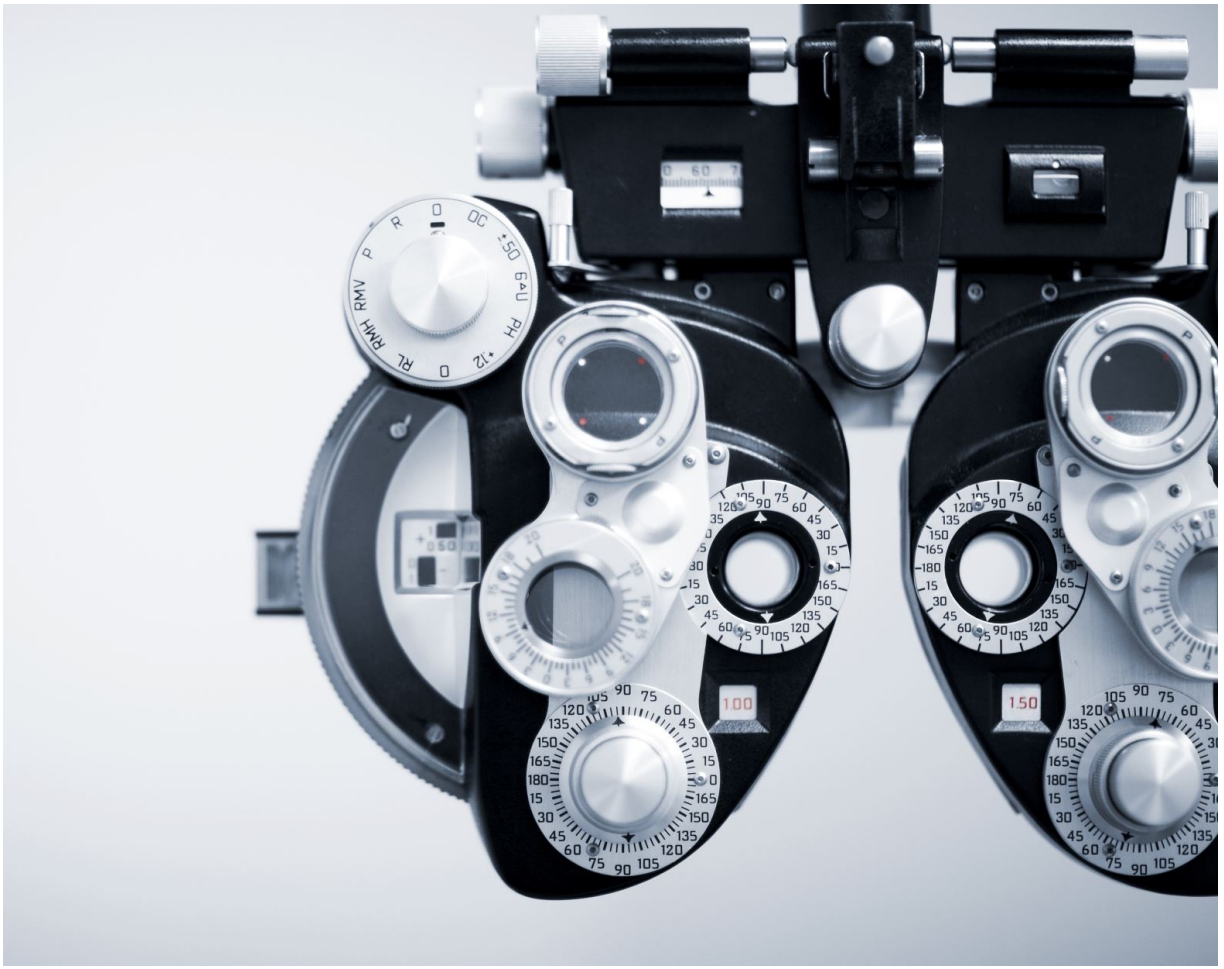

Disclosures

No Disclosure

Objectives

1. Review the patterns of cranial neuropathies causing double vision.
2. Review differentials of double vision etiologies.
3. Review supra nuclear causes and neuro muscular causes of double vision.
4. Review the evaluation and management of diplopia.
5. Review when to consider an urgent work up versus routine work up.

Approach to Diplopia

Is it double vision or blurry vision?

Diplopia- Questions to ask ?

Does it go away?

Monocular Diplopia

Still have diplopia

Resolves with pin hole

Binocular Diplopia

Orbital

Intracranial

Diplopia is gone

Pattern recognition is Vital !!

Helps in identifying the location of the problem

Its all about localization !

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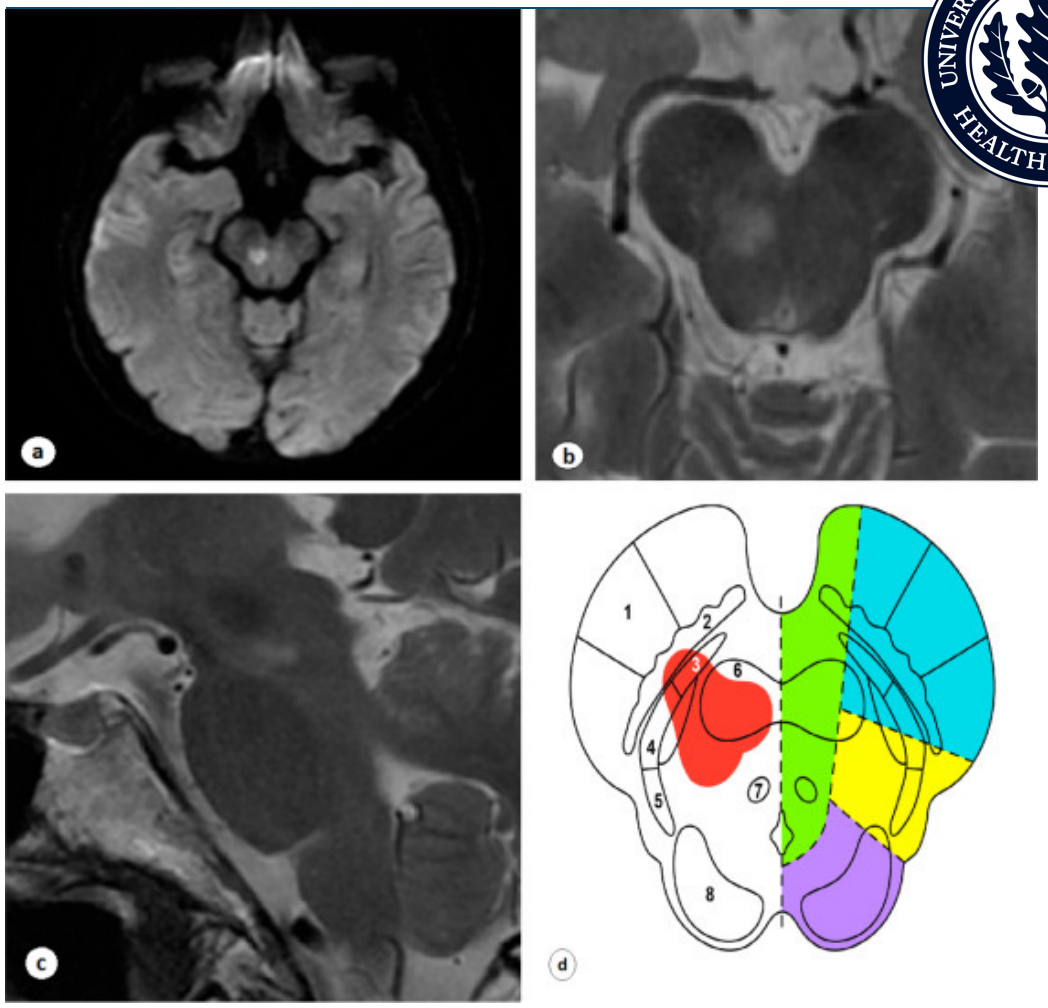
Its all about localization!

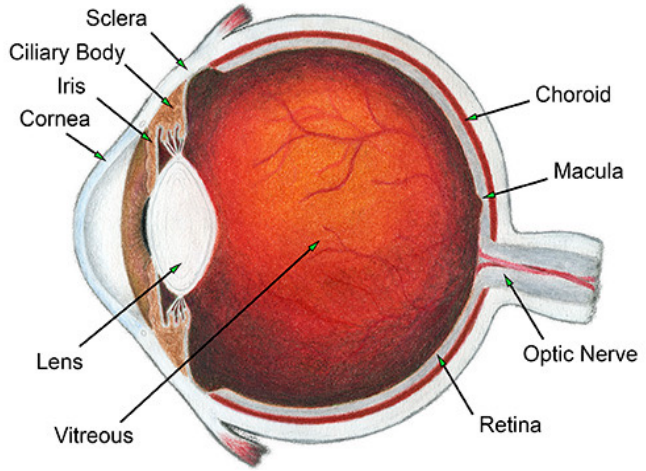


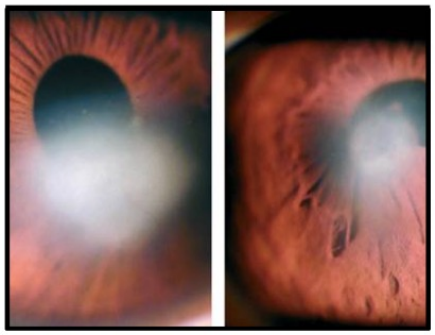
Does it look like a zebra or a unicorn?

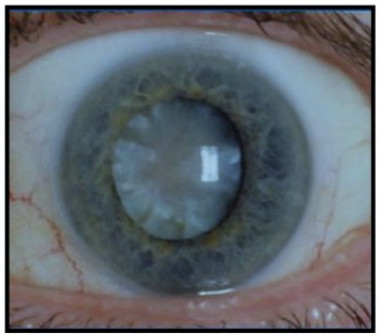
Localization !!!

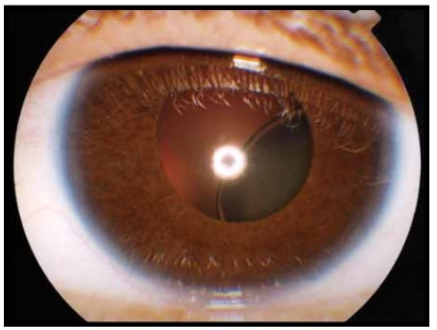
Localization –Afferent Pathway

- Globe
  - Cornea
  - Lens
  - Retina
- Optic nerve
- Chiasm
- Optic tract
- Optic Radiation









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- **Optic nerve**
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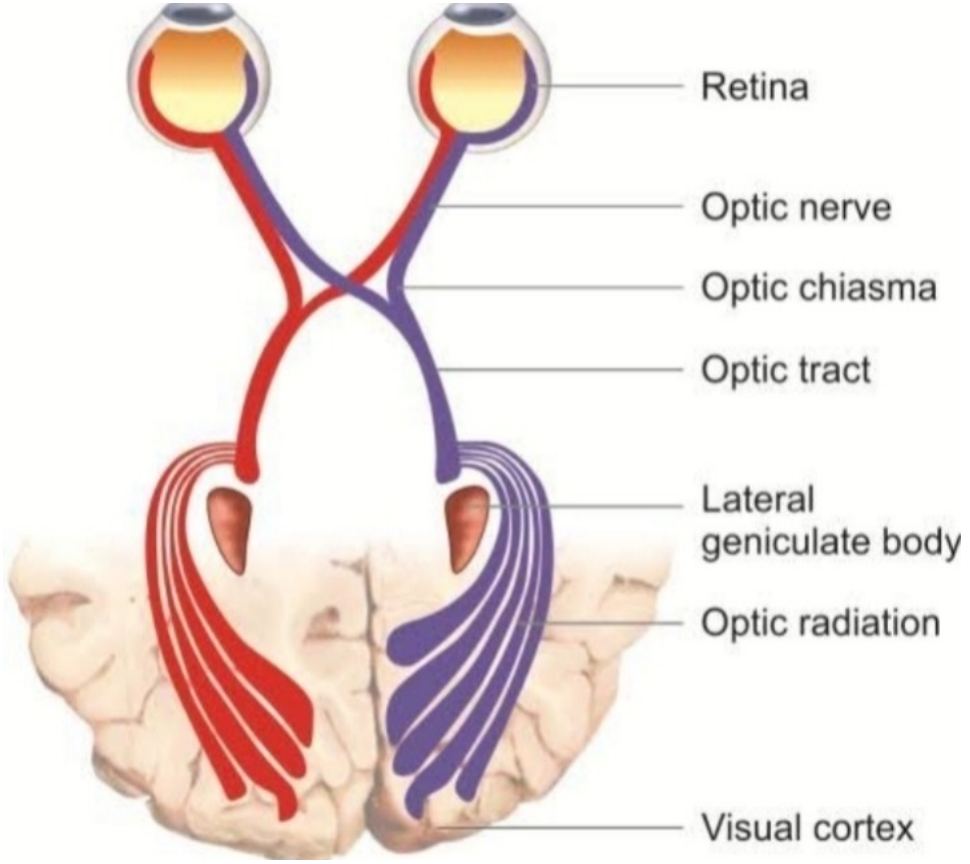
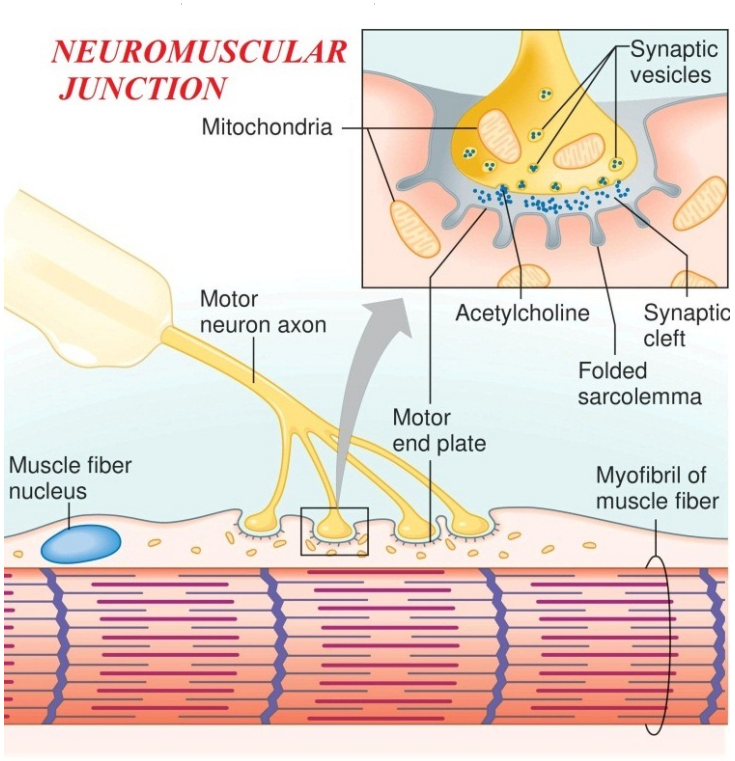


Localization –Efferent Pathway

- Muscle
- NM junction
- Nerve
  - Orbit
  - Orbital Apex
  - Cavernous Sinus
  - Subarachnoid space
  - Brainstem
- Nucleus
- Internuclear
- Supra nuclear



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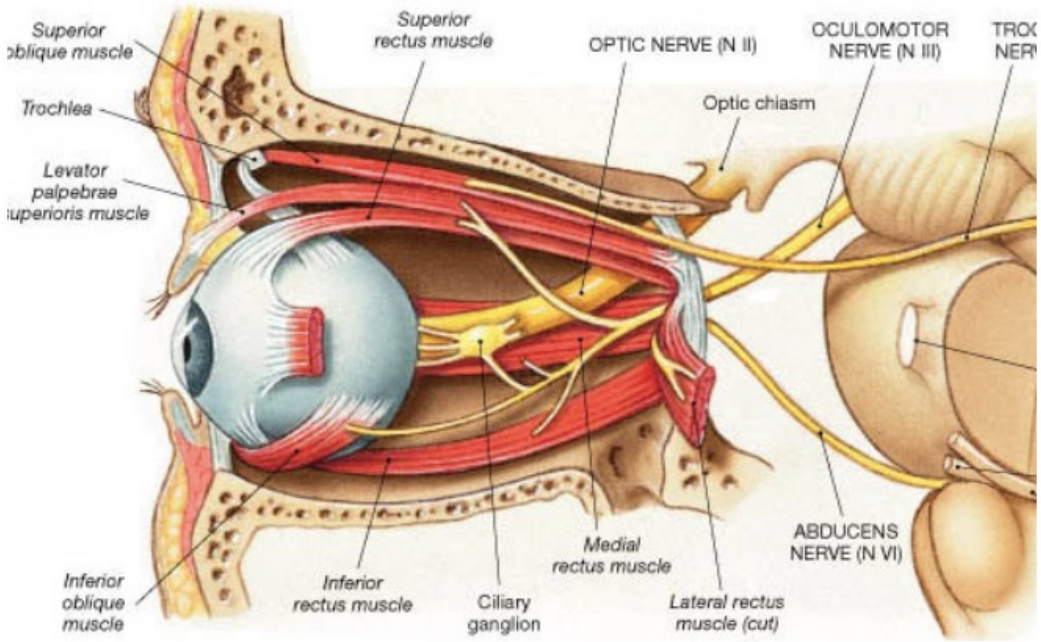

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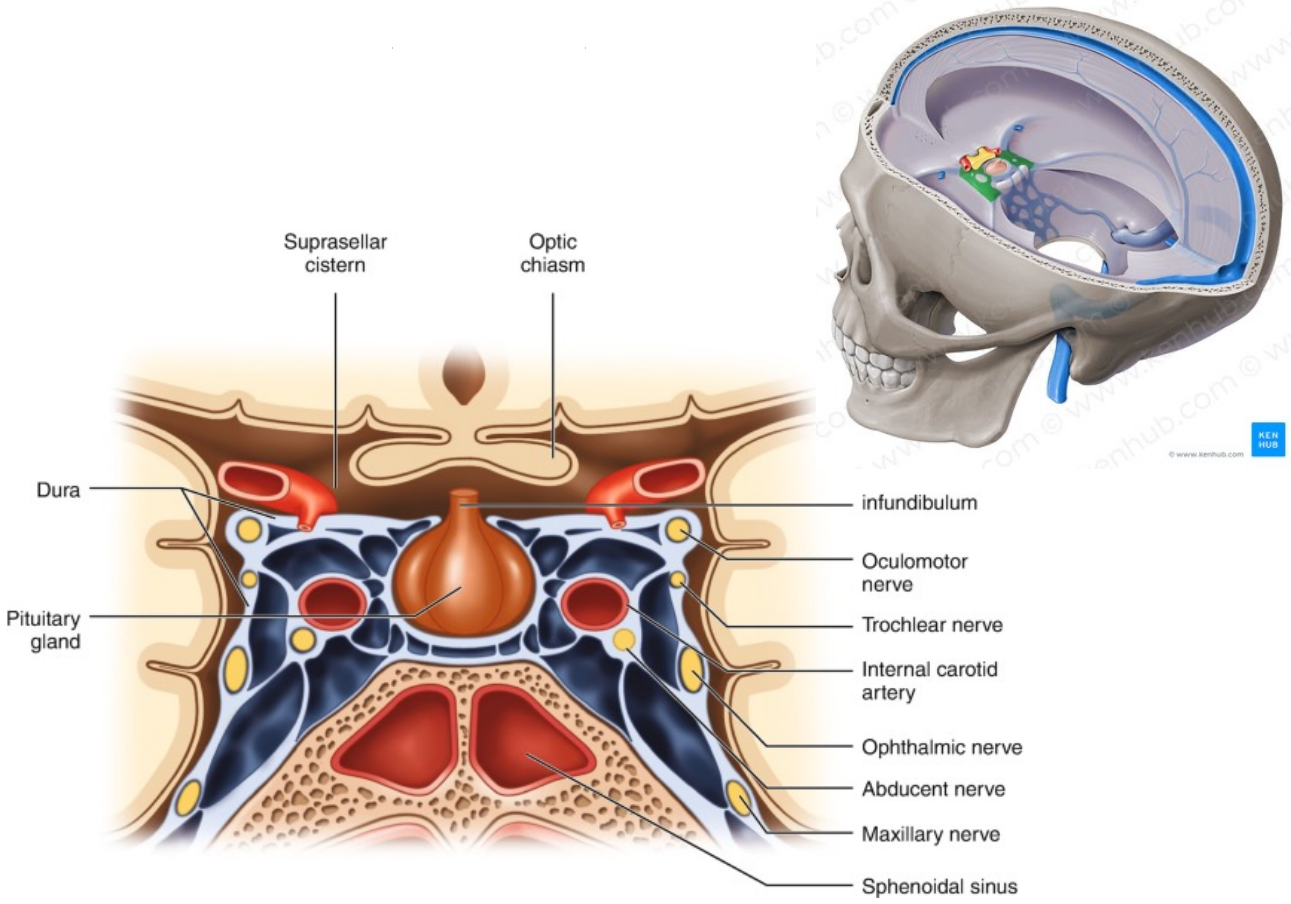

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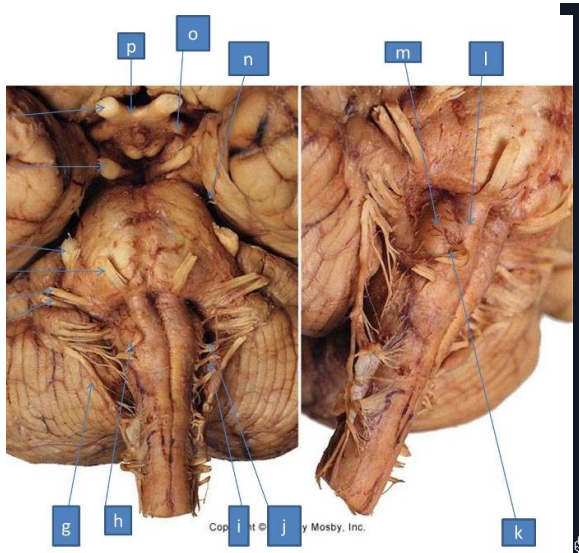
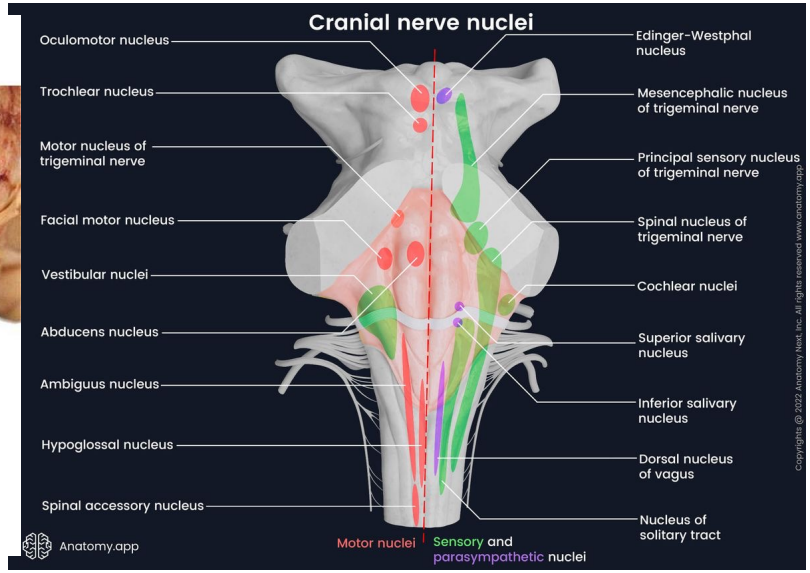
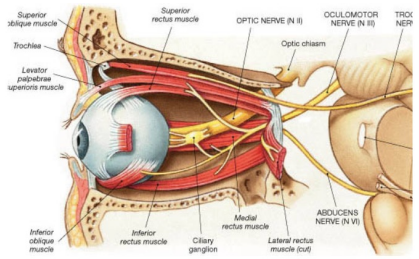
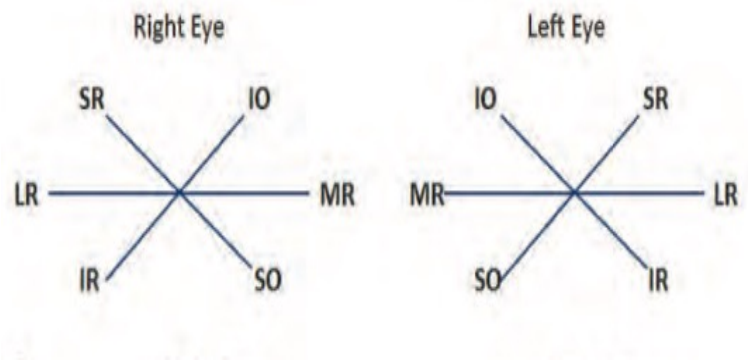


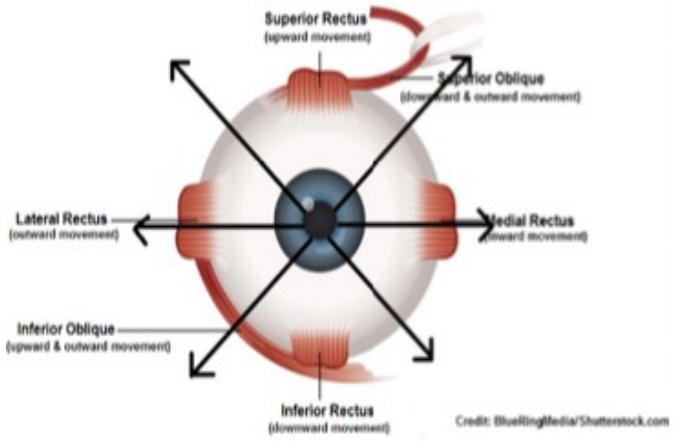




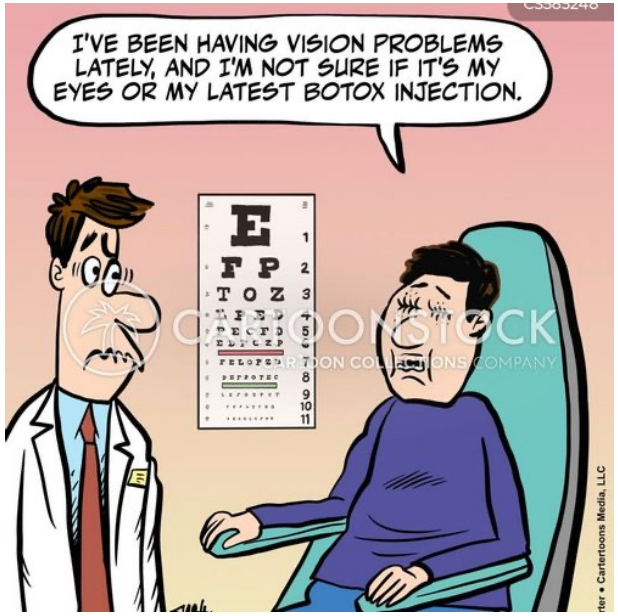
Extra ocular muscles and actions

Extraocular Muscle	Primary Action	Secondary Action	Tertiary Action
Lateral rectus	Abduction	None	None
Medial rectus	Adduction	None	None
Superior rectus	Elevation	Inclycotorsion	Adduction
Inferior rectus	Depression	Excyclotorsion	Adduction
Superior oblique	Incyclotorsion	Depression	Abduction
Inferior oblique	Excyclotorsion	Elevation	Abduction





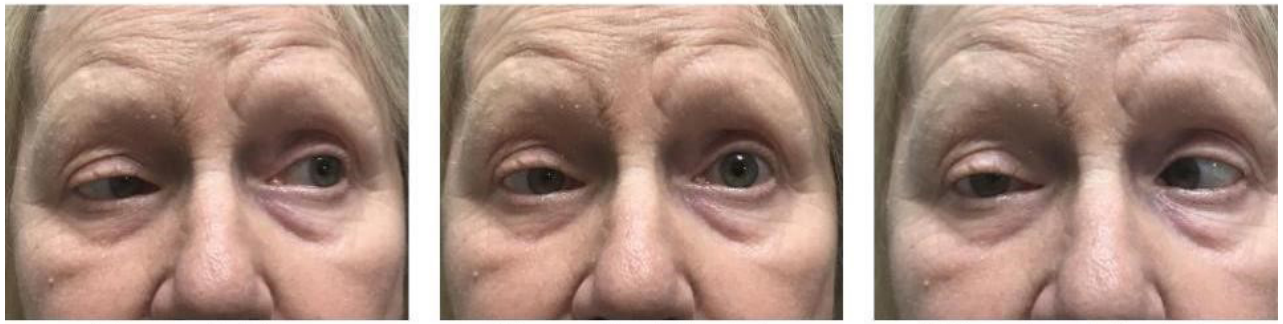
Detective work – Called history taking !
A Neuro –ophthalmology superpower !



"... Well, maybe you have double vision because you keep ordering doubles."

Diplopia –what questions to ask?

- Acute vs Chronic vs subacute
- Constant vs intermittent
- Horizontal/vertical/diagonal
- Limitation with eye movement
- Diplopia that changes with different gazes
- Is it worse at distance or at near?
- What brings it on ?
- Pain on eye movements
- Associated neuro symptoms – Dizziness , gait difficulty
- Fatigability, ptosis, SOB, change in voice
- Headaches, weight loss, chills/fever



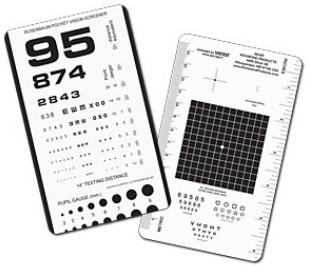
Left gaze: no deviation | Primary position: right esotropia | Right gaze: larger right esotropia

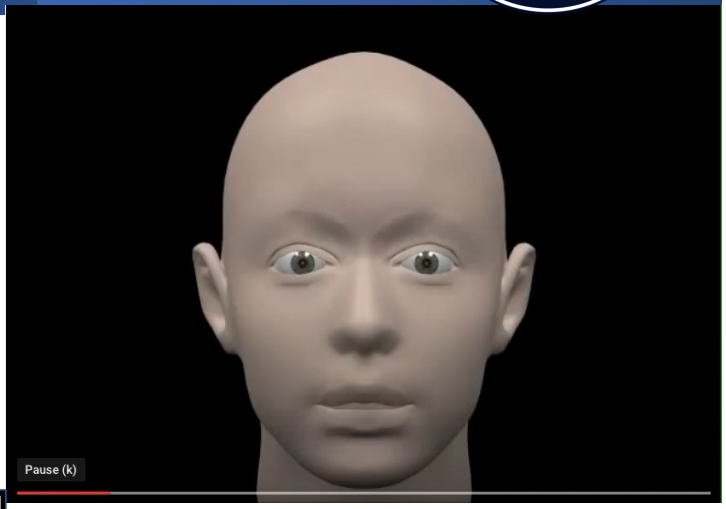
History

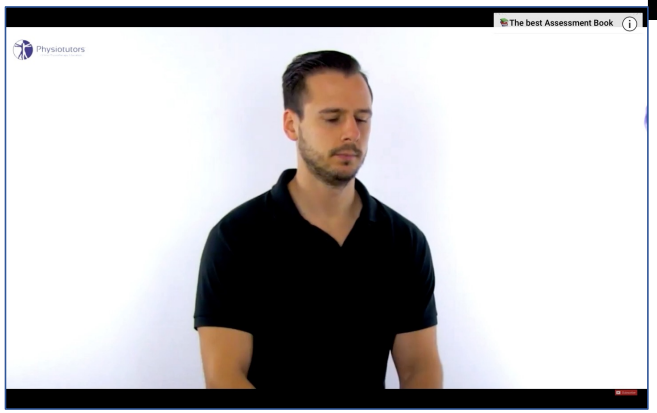
- Age
- PMH
  - Diabetes/HTN/HLD/smoking
  - Other neurologic PMH- MS, Parkinsons, Hx of stroke
  - Trauma – MVA/ TBI , ocular trauma
  - Hx of immunosuppression
- Ocular Hx
  - Hx of myopia
  - Hx of childhood strabismus /strabismus surgery
  - Ocular trauma-orbital wall/floor fracture
- PSH: /cataract or retinal/orbital surgery

Examination

- Visual acuity/Pin hole
- Stereo vision
- Duction and version
- Saccades and smooth pursuit
- Cover uncover testing
- Maddox rod
- Prism measurements

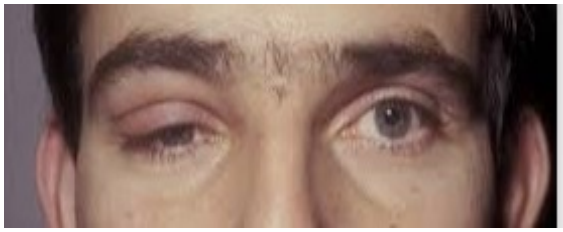


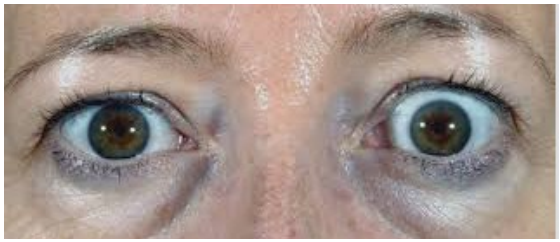


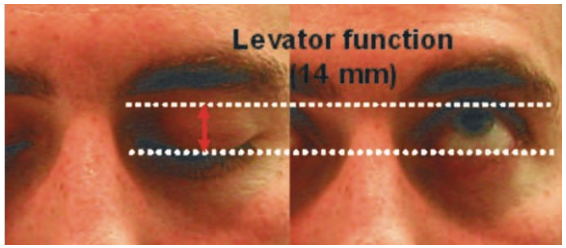


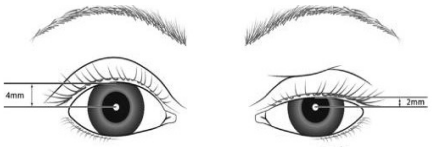
Examination – Eyelid /Globe

- External -Gaze preference , head tilt/turn , Conjunctival injection
- Eyelid: Retraction or ptosis
- Proptosis, enophthalmos

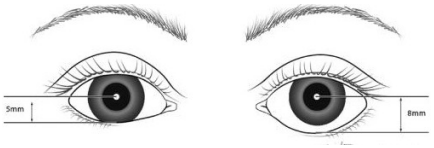




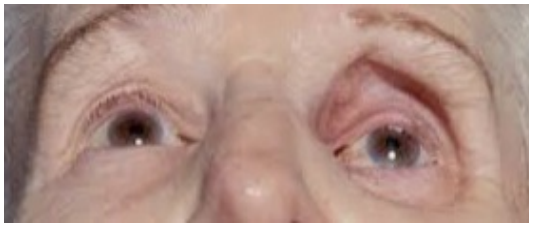


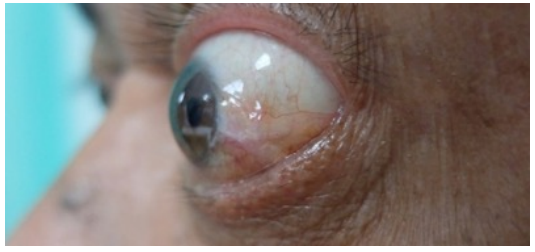


Marginal Reflex Distance 1

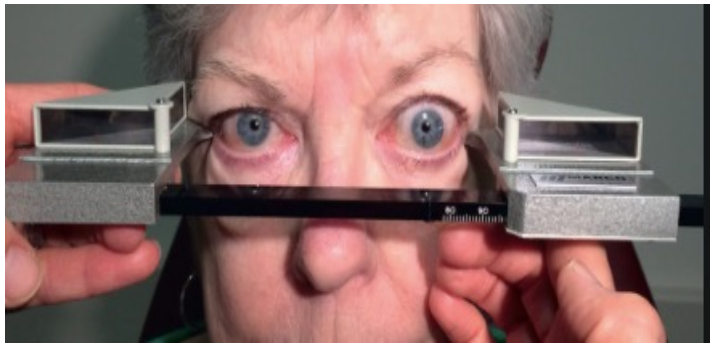


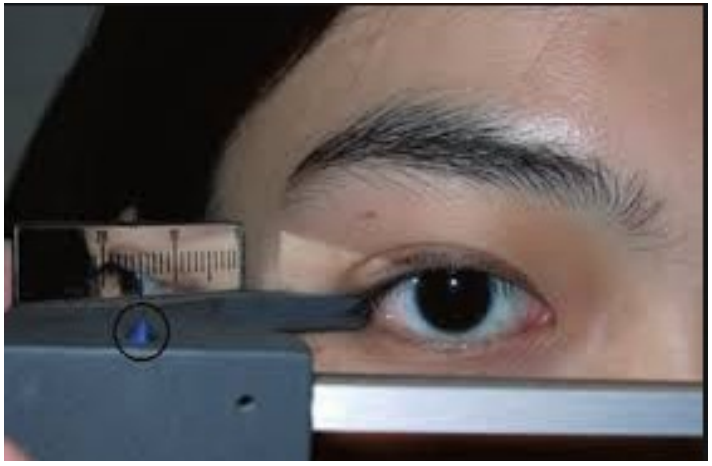
Marginal Reflex Distance 2

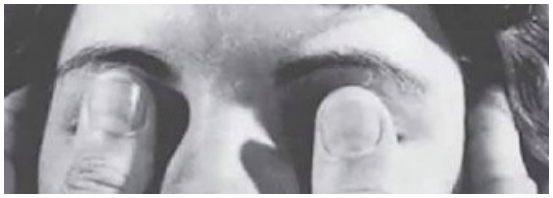




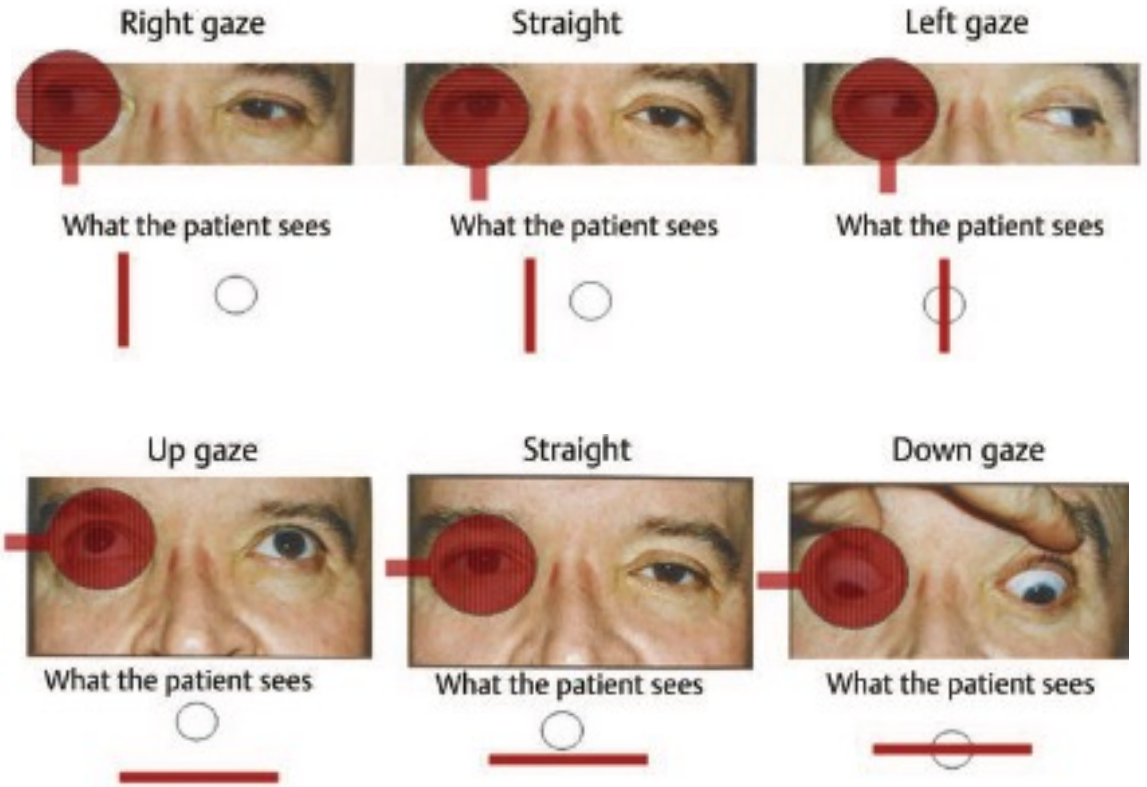
Examination – Proptosis



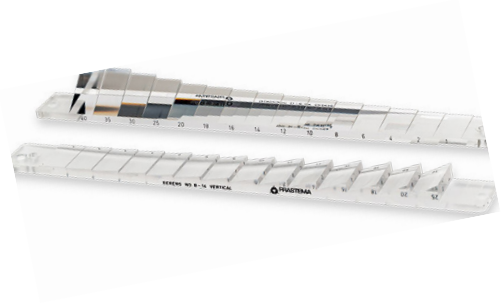


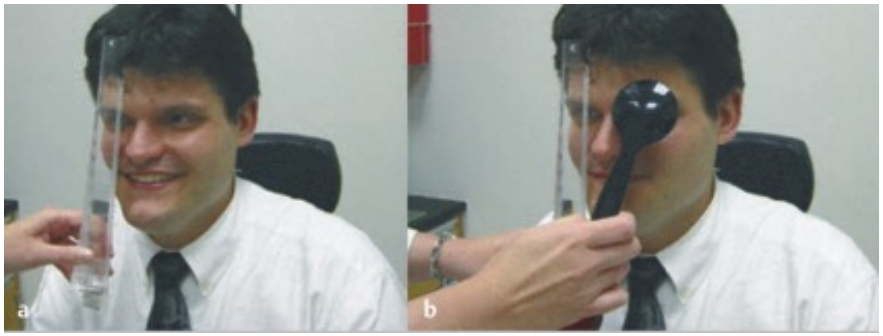


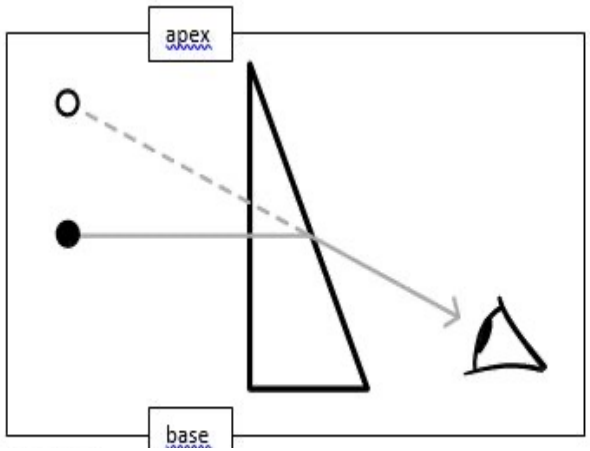
Examination- Maddox Rod test

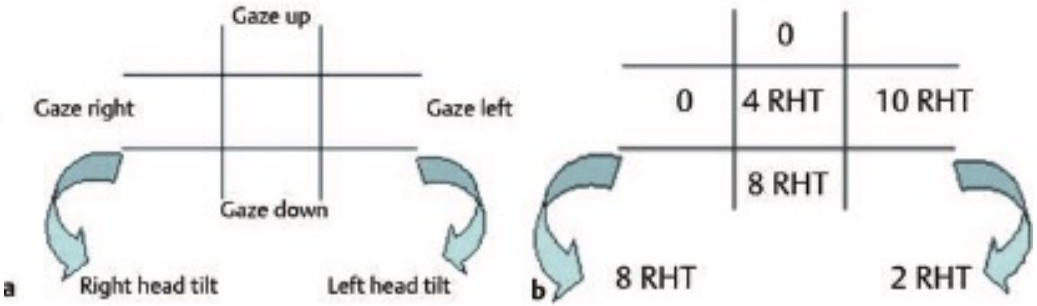


Examination- Prism measurement









Final conclusions and plan based on the clinical findings in each case..

"I AGREE, LAUGHTER IS THE BEST MEDICINE . . . UNFORTUNATELY, YOUR INSURANCE DOESN'T COVER THAT!"

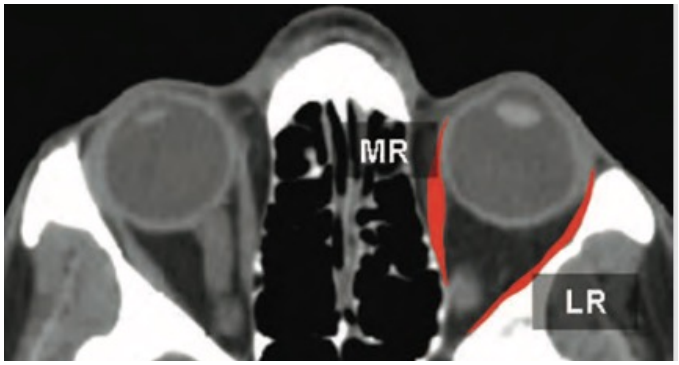
Etiology of *Binocular* Diplopia

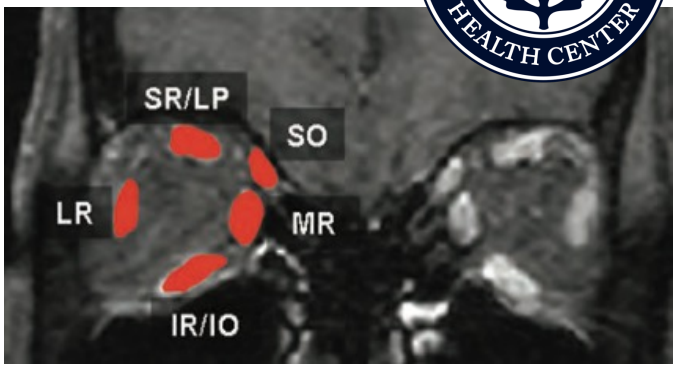
- Convergence/accommodation
- Breakdown of ocular muscle imbalance
- Trauma
- Muscular: Strabismus, Thyroid, Myasthenia, Myositis
- Orbital: Cellulitis, sinusitis, intra-orbital tumor
- 3rd : DM, Vasculopathic, pituitary tumor, orbit pseudotumor, trauma
- 4th : congenital, DM, vascular, trauma
- 6th : DM, Vasculopathic,, herpes, tumor, IIH
- Supranuclear: INO, stroke, skew, migraine, Wernicke's
- Hemifield slip

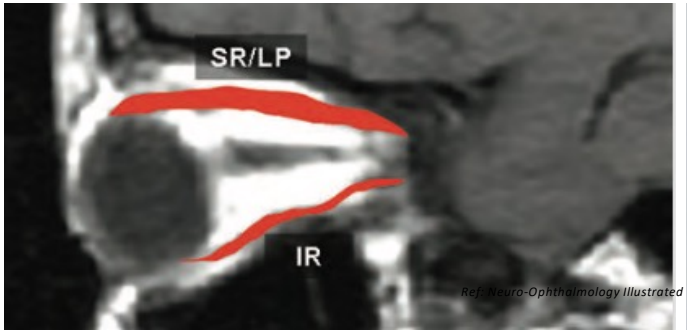
Every case needs to be tailored

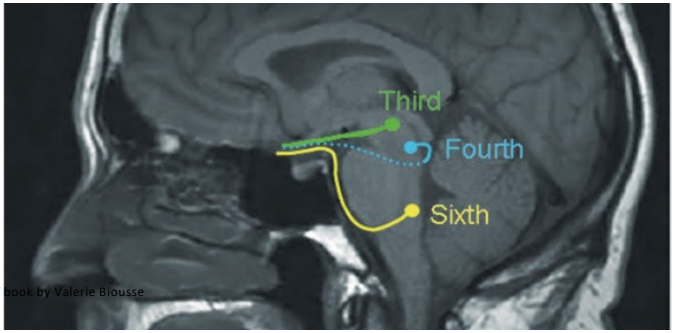
- Family photos , old photos
- Old doctor's records
- Labs
- MRI Brain
- MRI orbit
- MRA if needed – PCOM aneurysm
- CT orbit – TED
- EMG – Single fiber

Extra-ocular muscles on CT/MRI









Ref: *Neuro-Ophthalmology Illustrated* book by Valerie Biousse

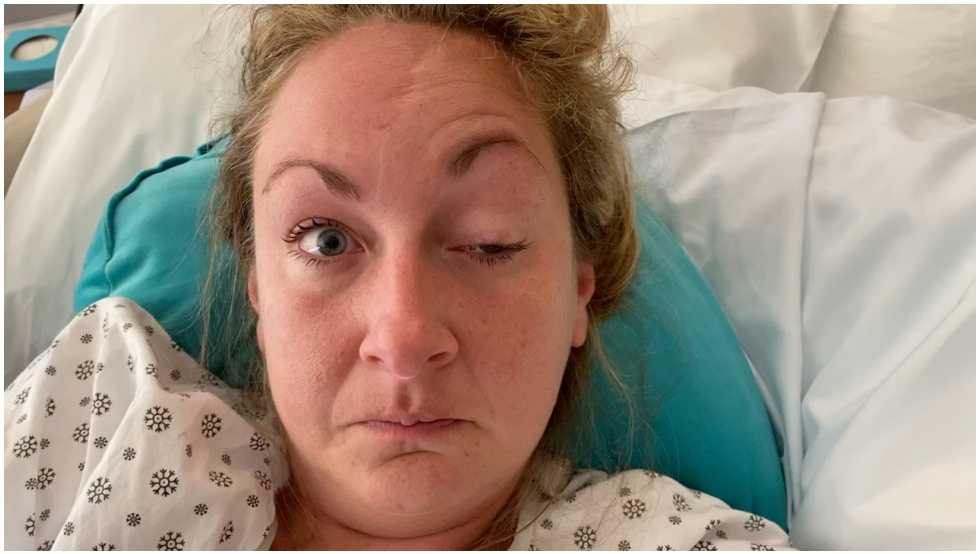
Clinical Cases

Basic cranial nerve patterns

Clinical Cases

31-year-old Caucasian woman with a history of MS.

Initial diagnosis of MS was made 2 years before this presentation when she presented with bilateral upper extremity paresthesia, blurry vision, and diplopia secondary to a left sixth nerve palsy.

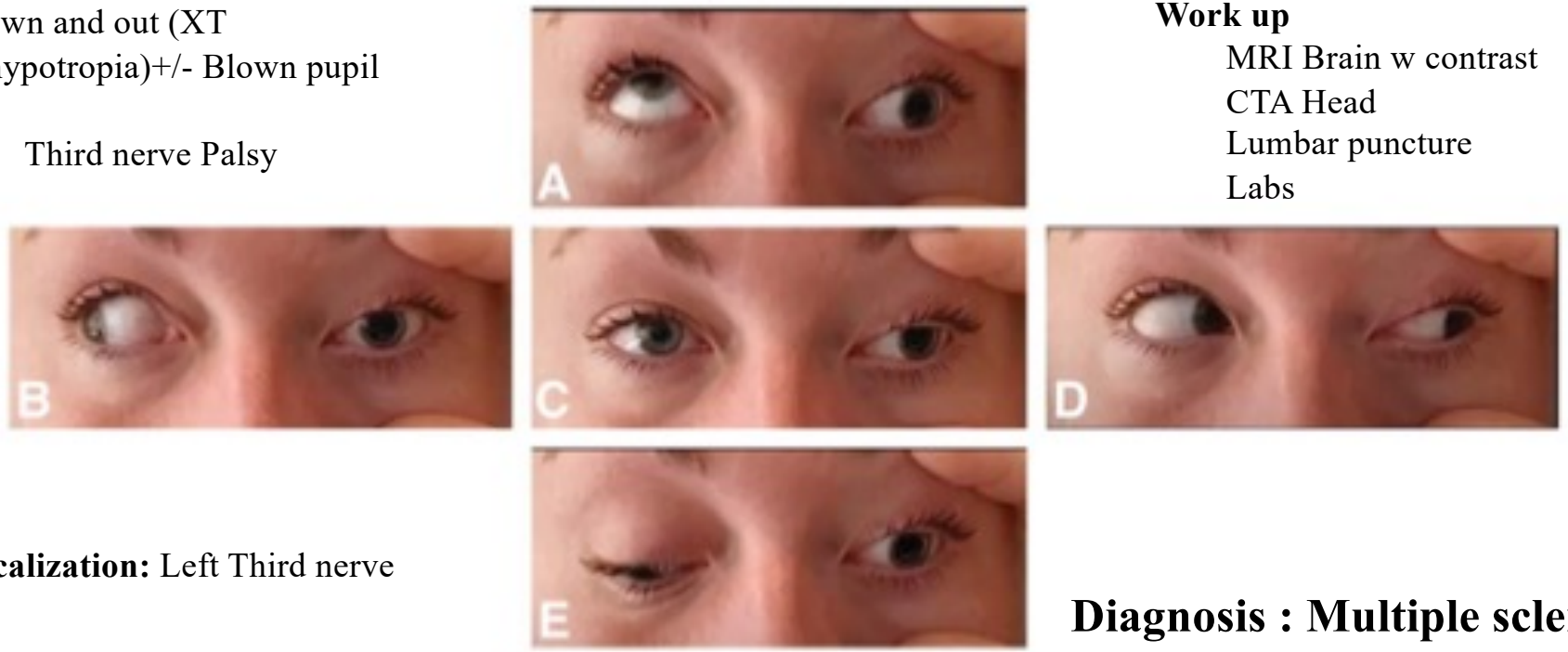


Clinical Cases

URGENT

Pattern: Ptosis , with eye down and out (XT +hypotropia)+/- Blown pupil

Third nerve Palsy



Work up

MRI Brain w contrast
CTA Head
Lumbar puncture
Labs

Localization: Left Third nerve

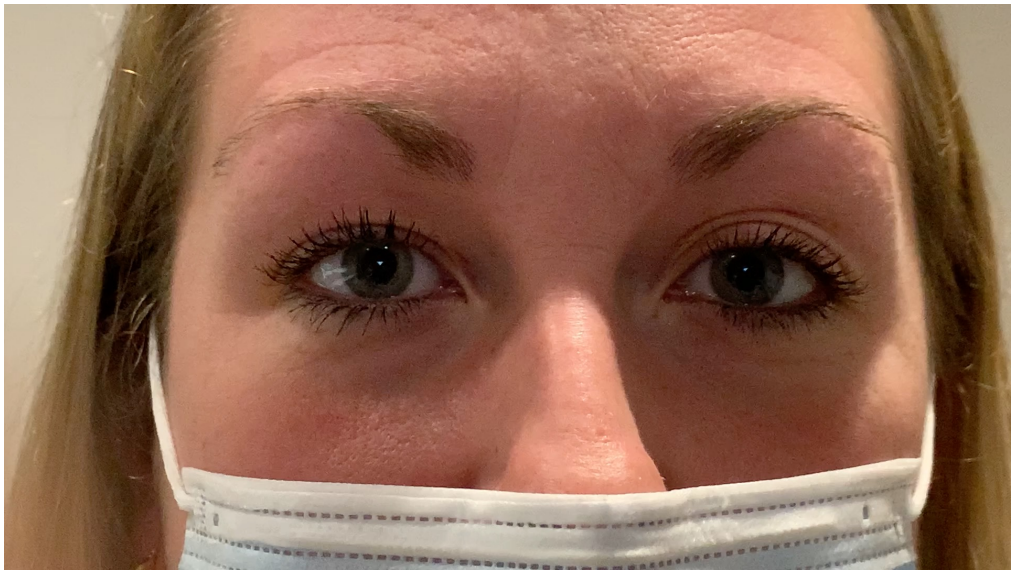
Diagnosis : Multiple sclerosis

Clinical Cases - Pearls

Isolated cranial nerve palsies are rare as initial presentations of MS and even rarer presentations of relapse.

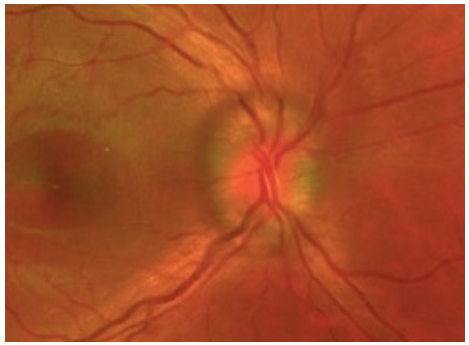
Although the literature discussing cranial nerve palsies in MS is limited, MS has been found as a cause of isolated cranial nerve palsies in 1.7% in a few retrospective studies.

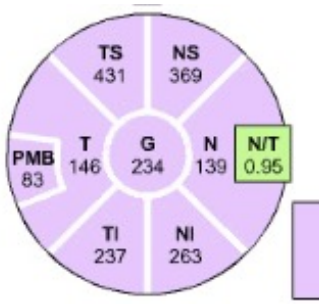
Third nerve palsies, if present, are more commonly present on initial presentation than relapse.



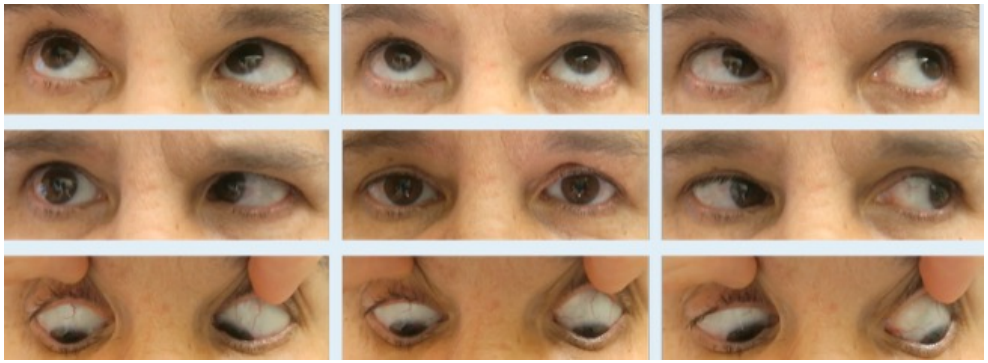
Clinical Cases – 6th nerve palsy

35 YOF with subacute positional headaches, tinnitus , and blurry vision





Right			Left		
-2	0	0	0	0	0
-2		0	0		0
-2	0	0	0	0	0



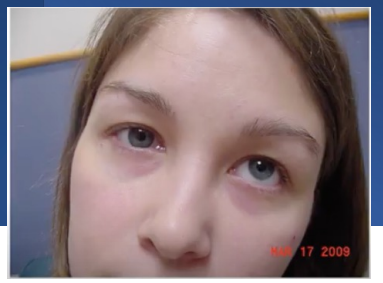
Pattern: Diplopia worse on right gaze w/ R LR restriction

Localization: R 6th Nerve Palsy

Work up: MRI Brain w/ wo contrast , MRV, LP

Diagnosis : Idiopathic intracranial Hypertension

Clinical Cases – 4th nerve palsy



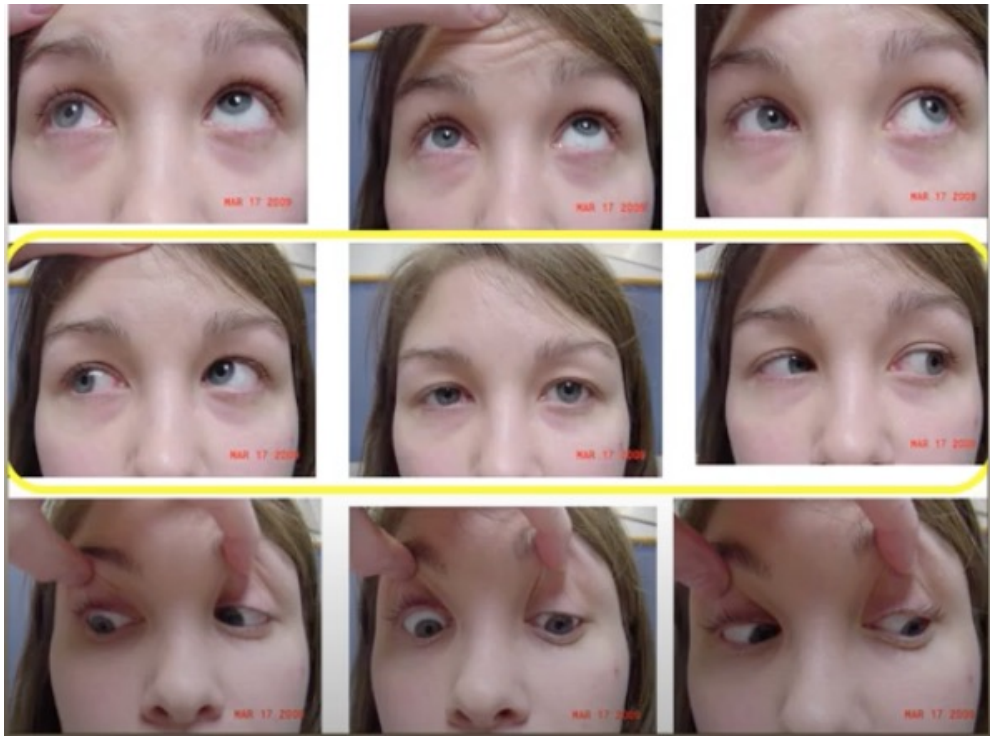
20 YOF with vertical diplopia after a head trauma/MVA whiplash

Pattern: Vertical Diplopia- Left Hypertropia worse on right gaze , and left head tilt.

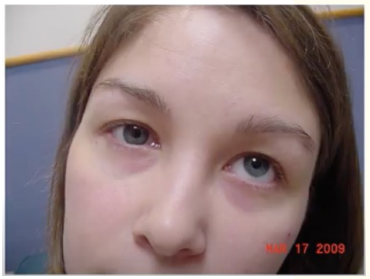
Localization: Left 4th nerve palsy- Midbrain/orbit?

Work up: MRI Brain w/wo contrast
Labs for diplopia- MG /TED – less likely

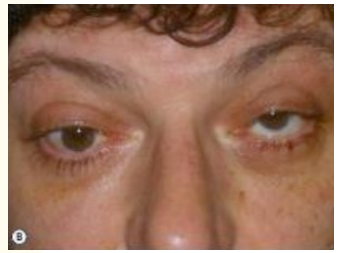
Diagnosis: Left Fourth Nerve Palsy



4th N Palsy vs Skew Deviation



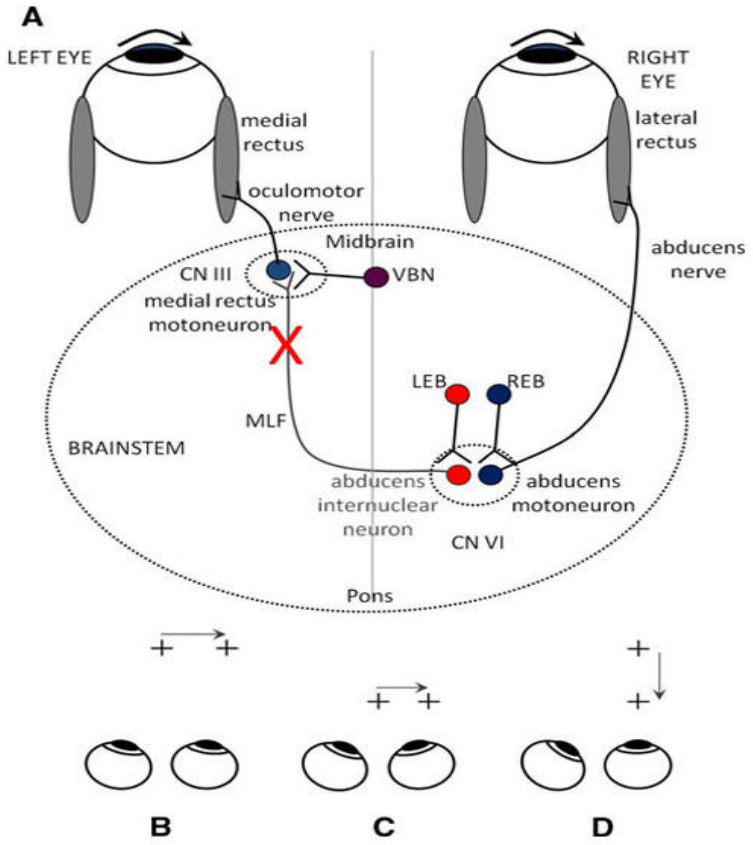
Trochlear nerve palsy	Skew deviation
1. Hypertropia in primary position	1. Hypertropia in primary position
2. Incomitant: hypertropia worse on gaze to opposite side acutely; may become comitant with time	2. Incomitant, comitant, or alternating
3. Hypertropia worse on ipsilateral head tilt	3. Hypertropia may or may not change with head tilt
4. Compensatory head tilt contralateral to the hypertropic eye	4. Pathologic head tilt contralateral to the hypertropic eye
5. Excyclotorsion of the hypertropic eye	5. Incyclotorsion of the hypertropic eye if present (and excyclotorsion of the hypotropic eye)
6. Usually no other neurologic signs (unless caused by brain trauma or lesions in brainstem)	6. Usually has other neurologic signs (eg, gaze-evoked nystagmus, gaze palsy, dysarthria, ataxia, hemiplegia)



Skipping over the cranial nerves …

Clinical Cases

38 yo AAM with diplopia. Hx of MS



Clinical Cases

Pattern: Limited EOM of Left lateral rectus and right Medial rectus

Bilateral in this case

Diagnosis : Inter-nuclear ophthalmoplegia

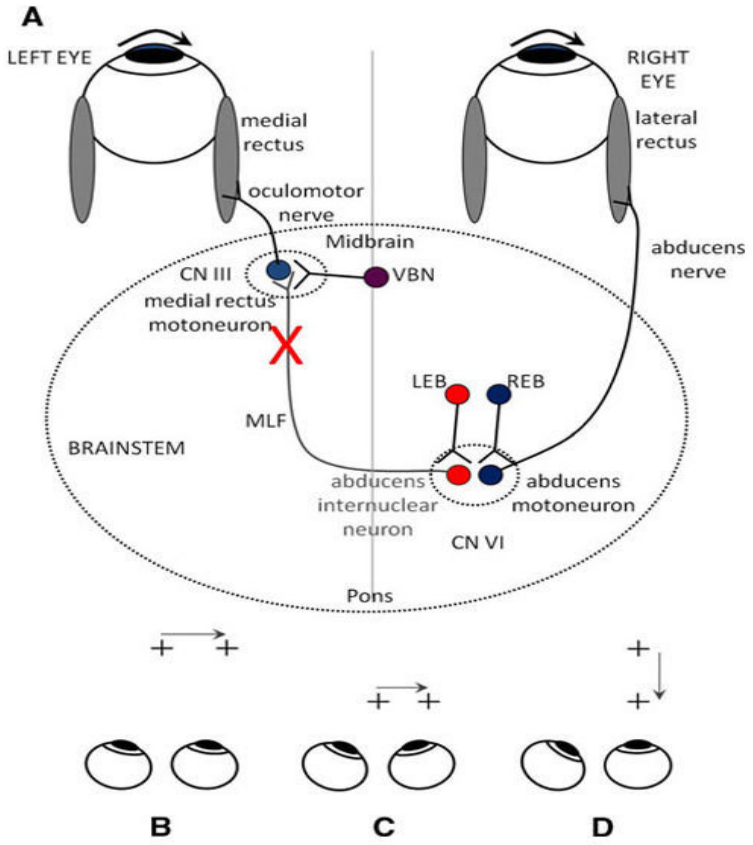
INO is due to MLF disruption
– An **internuclear cause** of diplopia

Localization : Midbrain - Medial Longitudinal Fasciculus

Work up

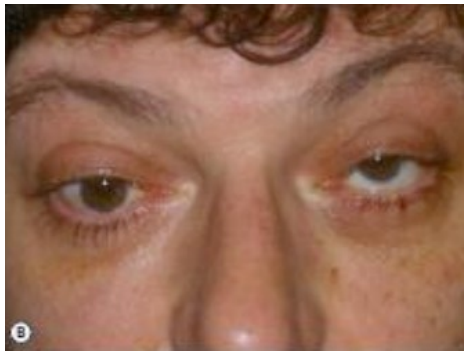
MRI Brain and orbit w/wo contrast
No repeat LP required here.

Final diagnosis: MS Relapse

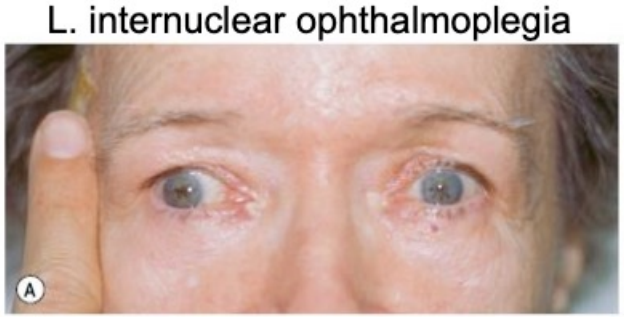


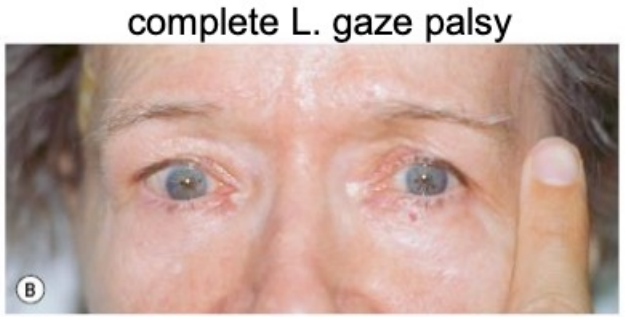
Clinical Cases
-Other Supra nuclear reasons of diplopia

- Stroke
- Wernicke's
- Migraine
- Skew



Hypertropia
Not mapping to IVth NP





L eye neither abducts nor adducts (1) + R eye does not addcut(1/2)
Diagnosis : One and half syndrome
Pattern- Gaze palsy +INO
Localization -Vith Nucles or PPRF and MLF

Muscles disease

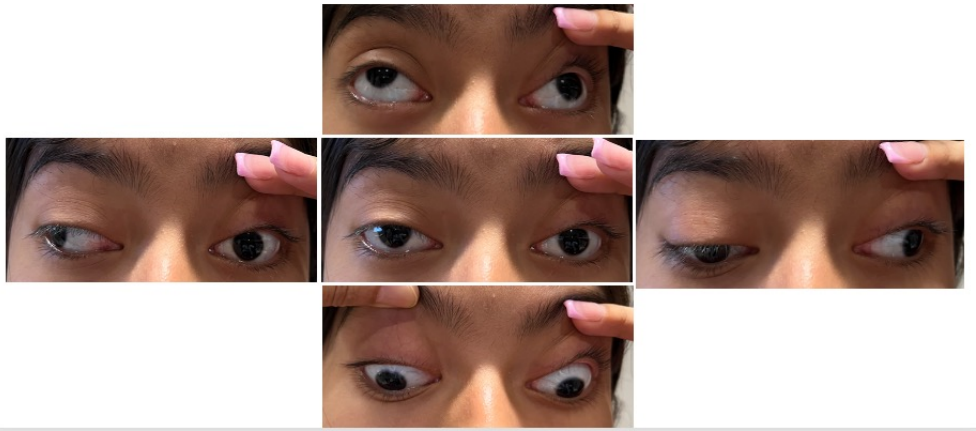
Clinical Cases

15 yoF with double vision and bilateral ptosis since 7 yrs of age at least. S/p two blepharoplasties OU , now with recurrence.

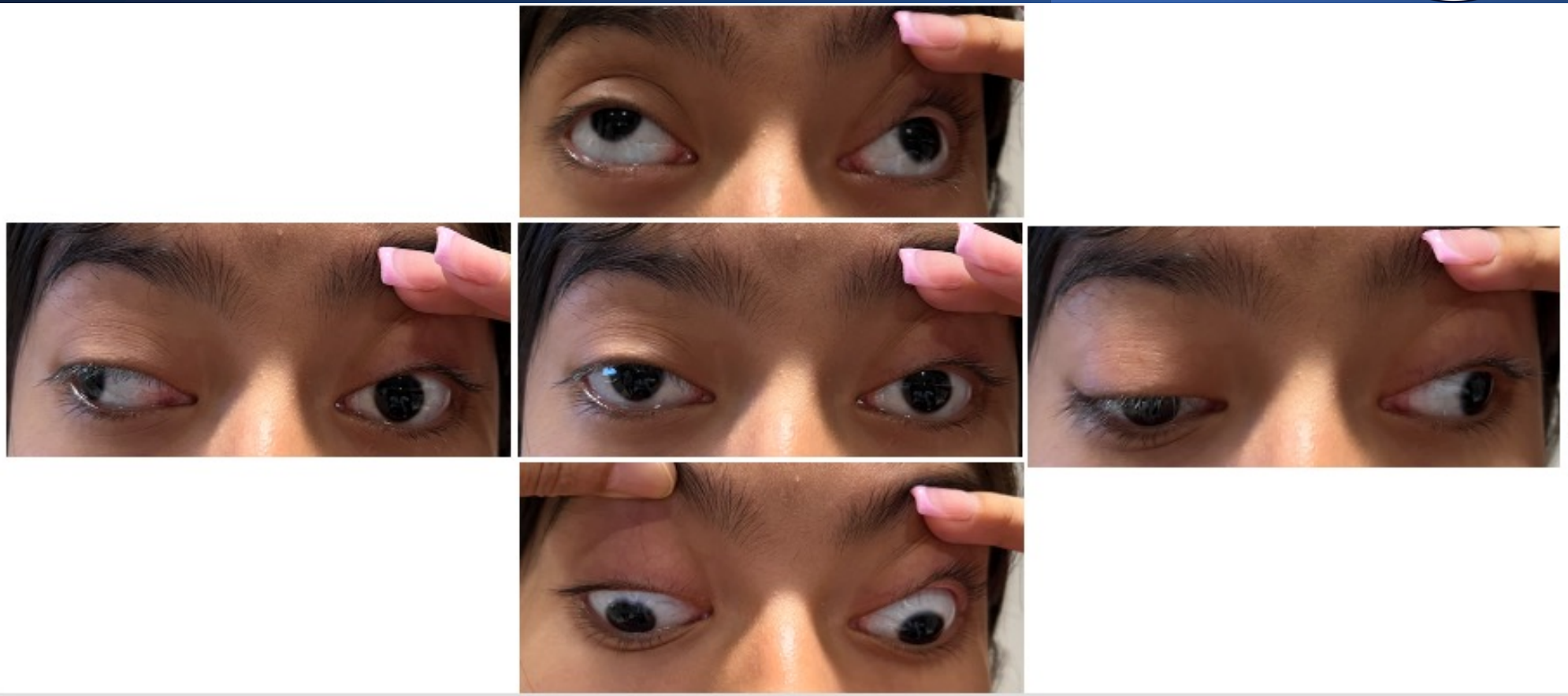
MG serology – negative.
Thyroid function normal.

EMG positive with multiple jitters.

Failed steroids and Mestinon

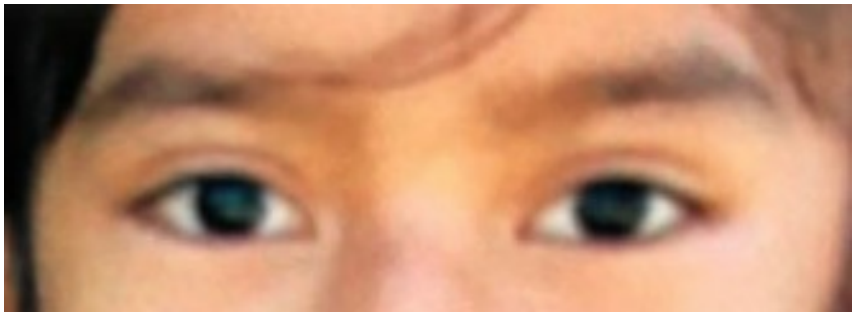


Clinical Cases



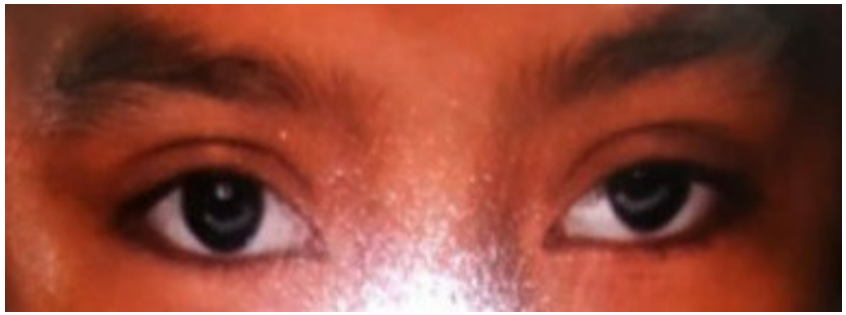
Clinical Cases – Old images

Age 4– LE ptosis early

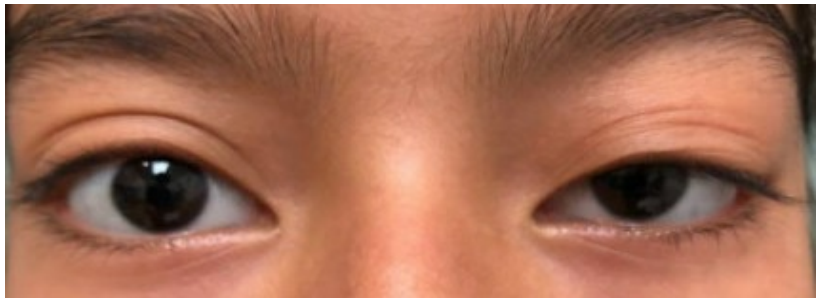


5th/6th grade (age 10-11)-severe ptosis covering her left pupillary reflex and left eye esotropia

Age 7– left HT and mild XT



Age 11- LE ptosis, Left HT and Left XT



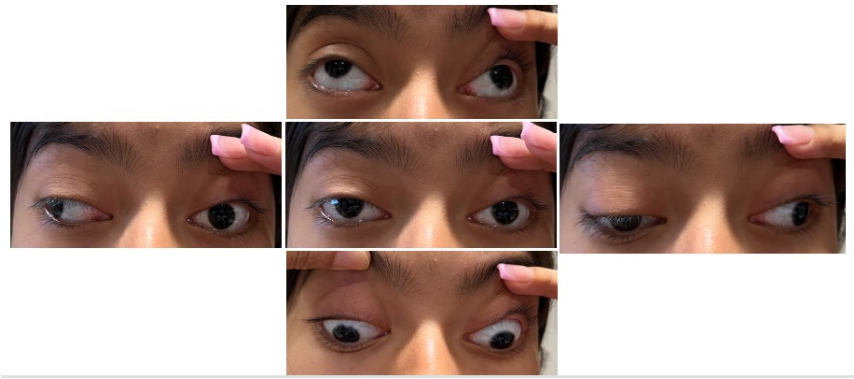
Clinical Cases – whole genome sequencing

m.10132_15439del in the mitochondrial genome (NC_012920.1)

- Heteroplasmic deletion including m.10132_15439 encompassing the following genes:*MT-ND3, MT-TR, MT-ND4L, MT-ND4, MT-TH, MT-TS2, MT-TL2, MT-ND5, MT-ND6, MT-TE, and MT-CYB of the mitochondrial genome was identified
- Has not been previously published as a pathogenic variant in association with a primary mitochondrial disorder or as a benign variant to our knowledge

We interpret this as a Pathogenic Variant.

Diagnosis: CPEO



Clinical Cases — Pearls

- Up to 60% cases of mitochondrial CPEO are due to mitochondrial DNA (mtDNA) deletions (ranging from 1.3 to 1.9 kb).
- Other cases however are due to nuclear DNA (nDNA)-related defects of mtDNA maintenance (e.g., *POLG1, ANT, C10orf2/twinkle* or *POLG2)*.
- Sporadic cases of CPEO suggest de novo mutations in mtDNA while autosomal dominant or recessive inheritance patterns point to nDNA mutations.

Treatment

- ❖ No definitive cure for CPEO
- ❖ Control of symptoms
- ❖ Prism lenses for diplopia
- ❖ Surgical correction for strabismus (may reoccur)
- ❖ Surgical ptosis correction-
  - Good levator -advancement or resection of LPS
  - Poor levator function - eyelid suspension to the frontalis muscle with autogenous or synthetic sling material

Other neuro-muscular junction disorder

	Myasthenia	Lambert Eaton	Botulism
Defect	Ach R (post synaptic)	Ca ++ channel (pre synaptic)	Ach release (pre-synaptic)
Lids	ptosis	ptosis	ptosis
EOMS	ophthalmoplegia	Not prominent	ophthalmoplegia
Pupil	spared	spared	Poorly reactive
Strength	decrements	increments	
Other symptoms		autonomic	constipation
Associations		paraneoplasic	

Vascular causes

Clinical Cases

29 yo RH, AAF with new onset diplopia on extreme lateral gazes.

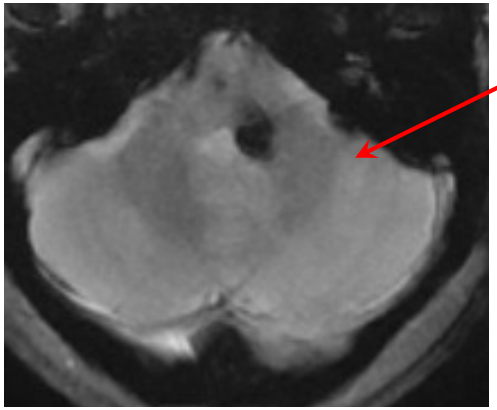
Facial sensation was intact to light touch but had documented Left side facial droop during her hospital stay.

Pattern: Left MR Palsy +
Right abduction nystagmus +
Left 6 LR palsy

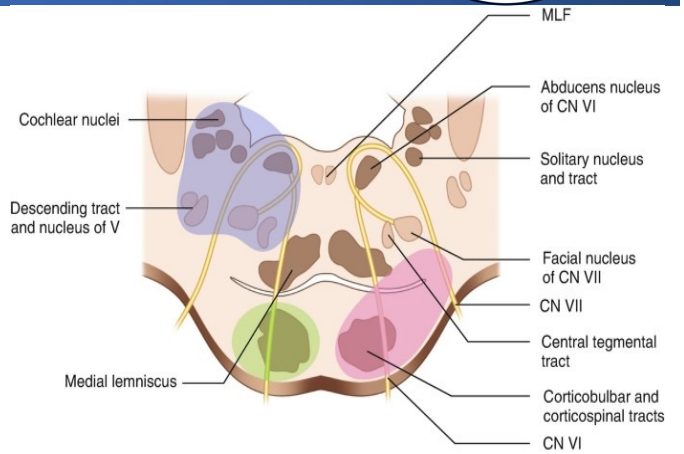
Localization: Left 6th nerve
+MLF? + left Facial nerve
= Pons /Midbrain

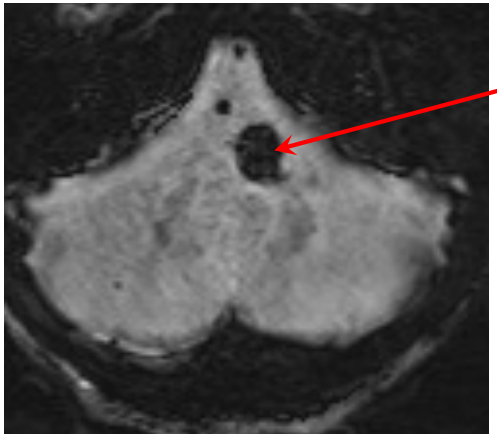
Diagnosis: Pontine Cavernoma

Clinical Cases - Comparison of MRI - GRE sequence -2018 to 2020



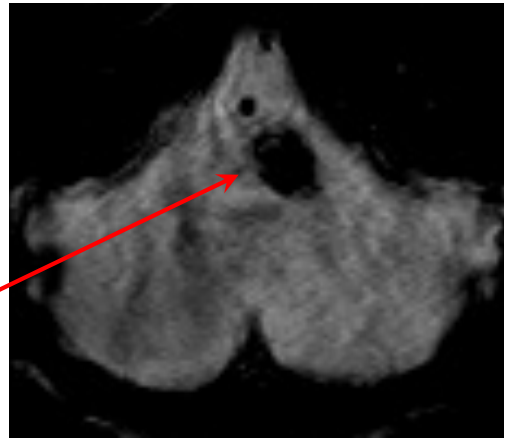
7/2018: Small left dorsal pontine cavernoma and adjacent hemorrhage (possibly obscuring another cavernoma) with mild surrounding edema in the medial aspect of the left middle cerebellar peduncle





2/25/2020: Susceptibility artifact is larger now but still on the left side.

9/23/20: Susceptibility artifact is now MUCH larger. It now crosses the midline and extends much closer to the ventral pons



Clinical Cases -Pearls

- A cavernoma is a cluster of abnormal blood vessels, usually found in the brain and spinal cord.
- Also known as cavernous angiomas, cavernous haemangiomas, or cerebral cavernous malformation (CCM).
- They may leak blood and lead to hemorrhage in the brain or spinal cord or mass effect causing a variety of neurologic symptoms
- The purpose of cavernoma removal is to release pressure to the brainstem and prevent rebleeding
- **Radical resection of the cavernoma** while preserving the surrounding normal brainstem during the subacute phase from the first or second rebleeding is the best surgical strategy in elderly patients
- For elderly patients, **stereo tactic radiosurgery** might be a suitable alternative treatment.

Symptomatic Brainstem Cavernoma of Elderly Patients: Timing and Strategy of Surgical Treatment. Two Case Reports and Review of the Literature .Tetsuya Negoto1, Shota Terachi1, Yuko Baba1, Shin Yamashita2, Terukazu Kuramoto2, Motohiro Morioka1

Clinical Cases

71-year-old woman with progressive diplopia and left sided ptosis

- Exam: **Complete left ptosis, blown pupil, with partial left sided third and fourth nerve palsies**
- MRA brain- no aneurysm
- Diagnosed as Ocular myasthenia
  - Serology negative
  - acetylcholinesterase antibody
  - No EMG records
- Mestinon trial
- Excision of a thymoma
- Symptoms slowly resolved

But 5 months later ..

New left eye proptosis, chemosis of left eye inferiorly with corkscrewing of conjunctival blood vessels and a positive ocular bruit

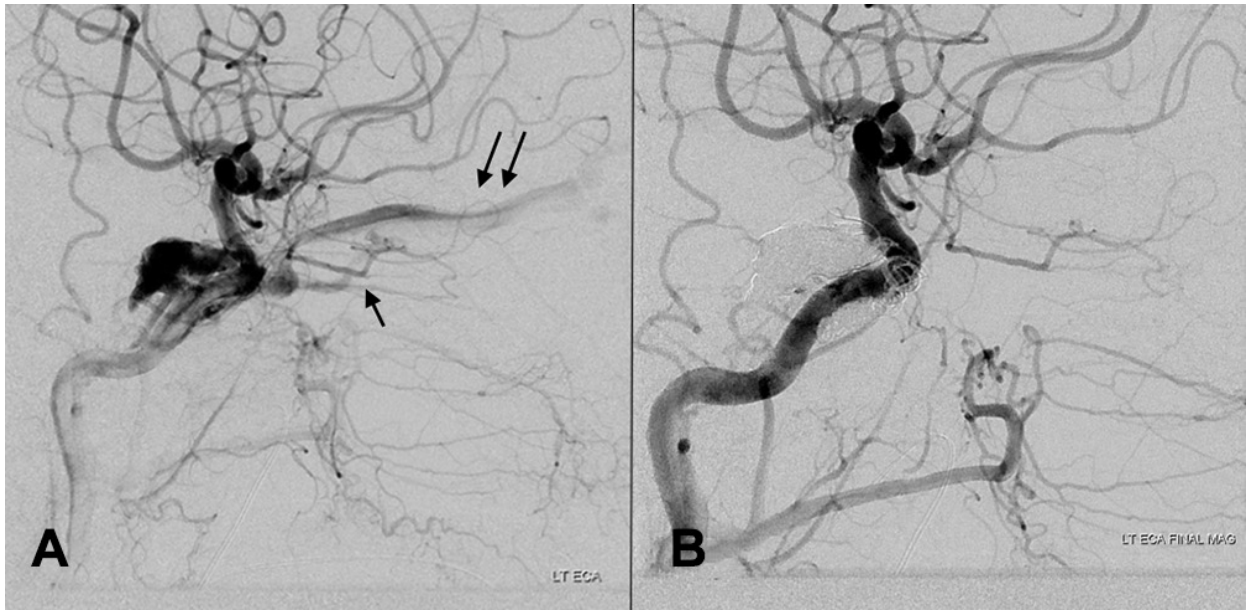
Clinical Cases

URGENT Neuro IR referral

Pattern: Proptosis, chemosis, Bruits, any cranial neuropathy

Work up

MRI Brain
CTA Head
Diagnostic Angiogram



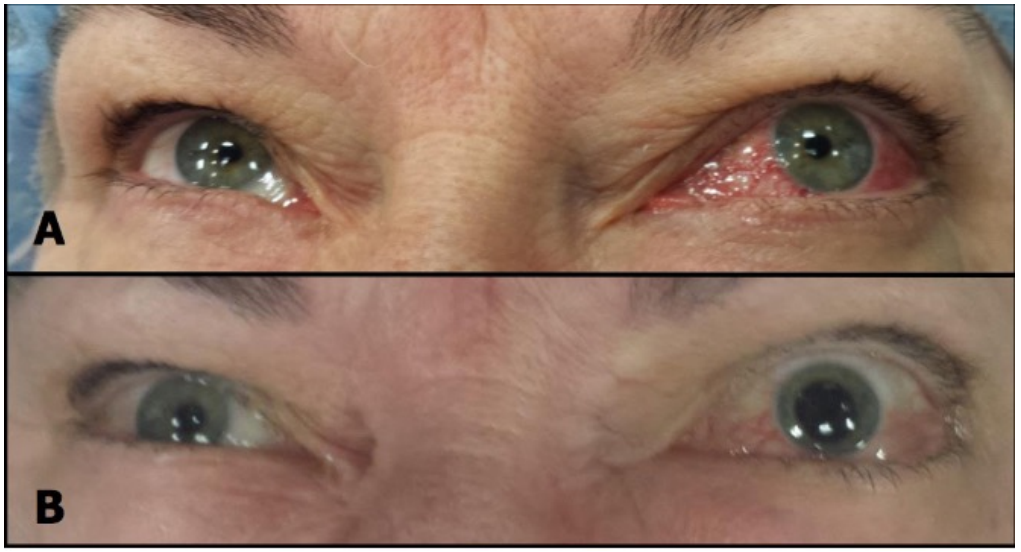
Diagnosis : Indirect CCF fistula

Clinical Cases

Injected eye w/ ophthalmoplegia

Things to rule out

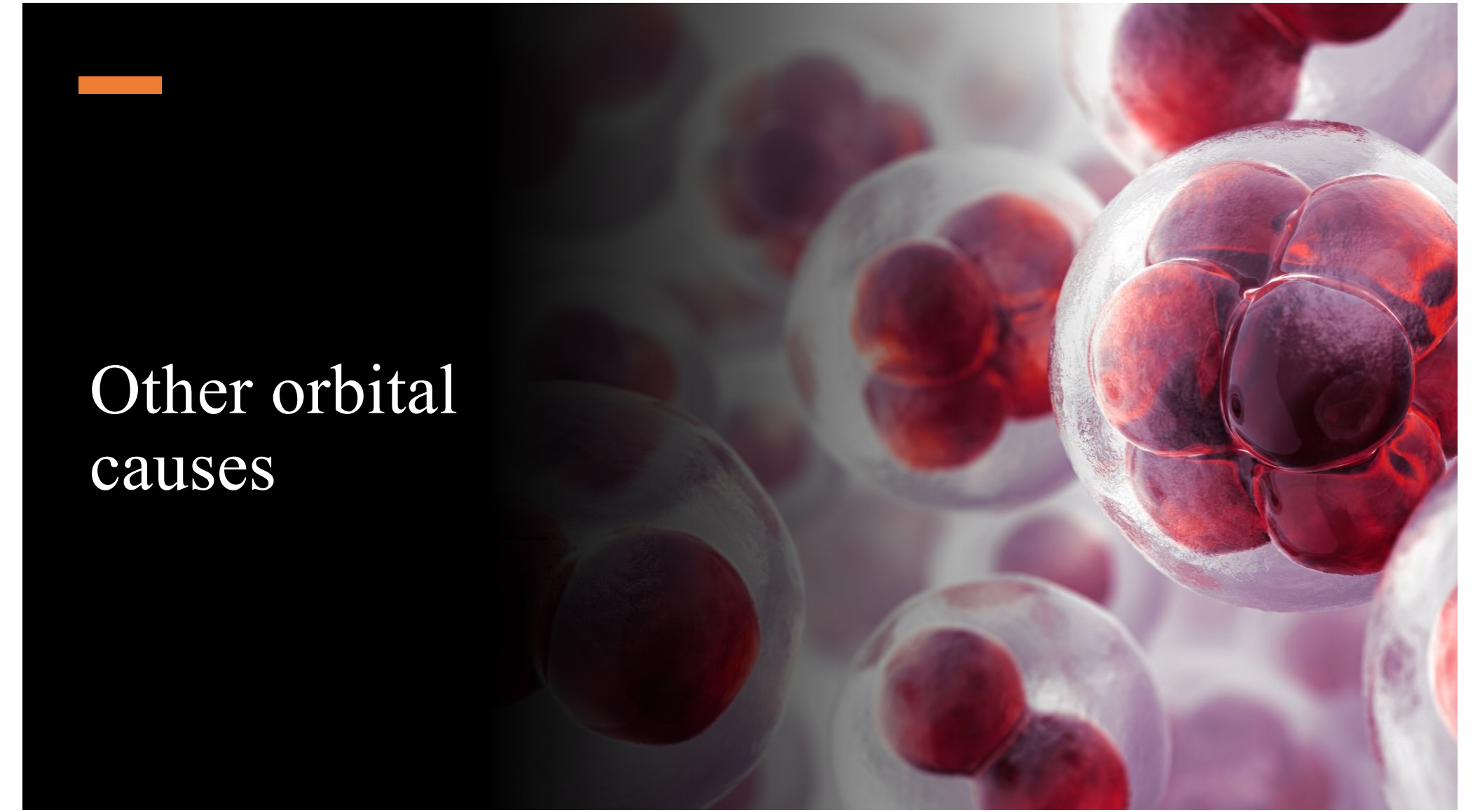
- Thyroid eye disease
- Idiopathic orbital inflammation spectrum
- Carotid cavernous fistula
- Cavernous sinus thrombosis
- Orbital mass



Clinical Cases – Red Flags suggesting CC Fistula

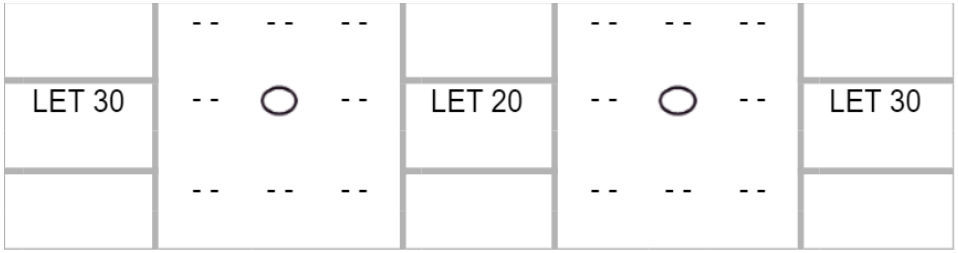
- Classic triad: Proptosis, chemosis, and pulsatile tinnitus
- Indirect, low flow fistulas more challenging to diagnosis
- Look for arterialization of conjunctival vessels
- Look for bruits
- Non-invasive vascular imaging not sensitive.

Other orbital causes

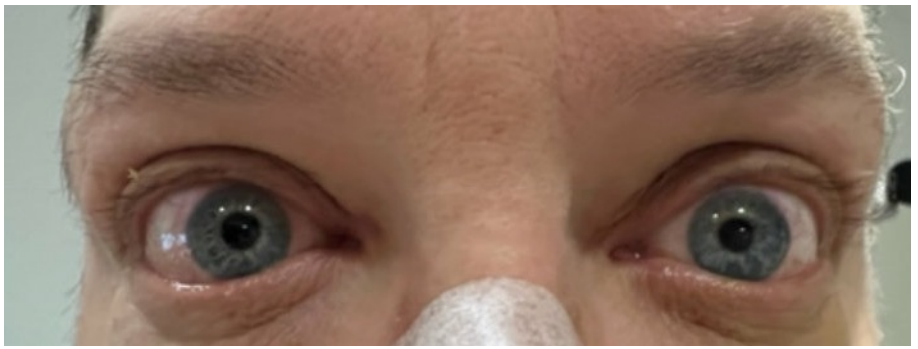


Clinical Cases

41 YOM with diplopia



Right			Left		
-1	0	0	0	0	-1
-1		0	0		-1
-1	0	0	.5	0	-.5



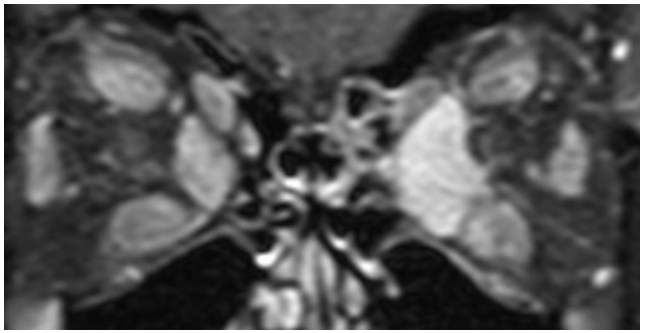
Pattern: (2021)
Restricted EOM – Bilateral 6 nerve deficits L> R
Exophthalmos, dry eyes , conjunctival chemosis, Lid retraction

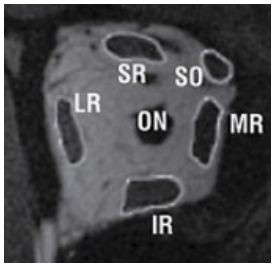
Localization: Orbit

Work Up :
Ocular prism measurement, Thyroid labs
MRI Brain/Orbit w/ wo contrast , CT orbit w/ wo contrast

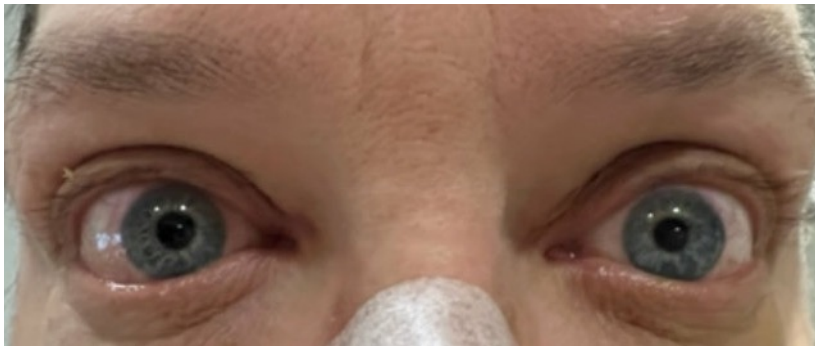
Clinical Cases

MRI 2021 Before Tepezza infusion

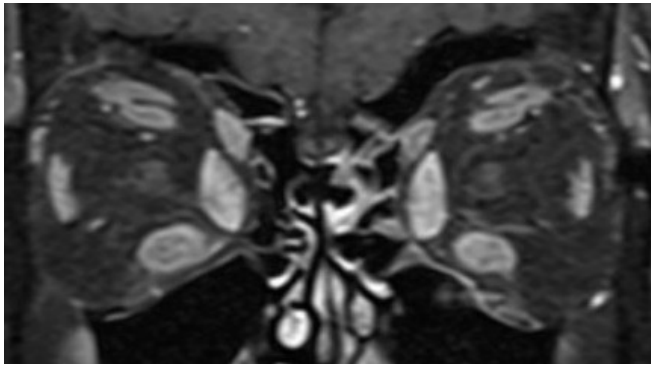




2022 After Tepezza infusion

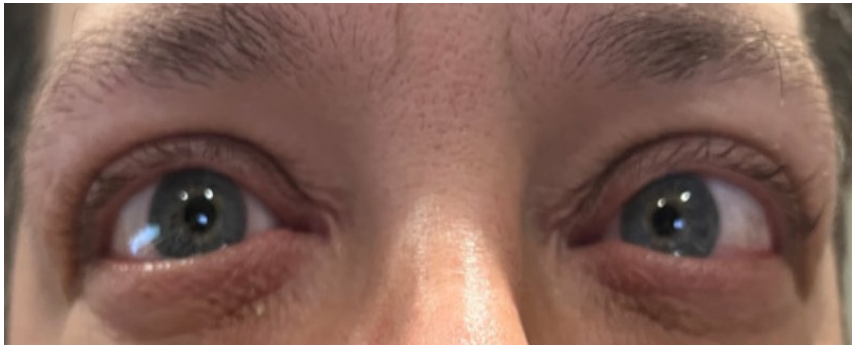


MRI Orbit 2022 after Tepezza infusion



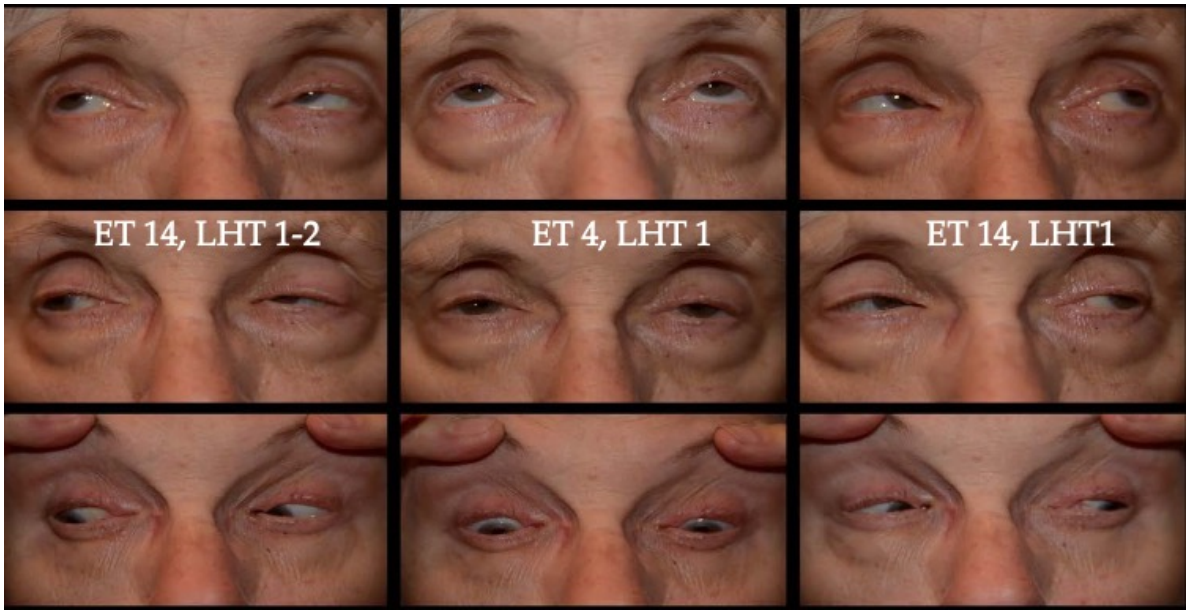
Diagnosis: Thyroid Eye disease

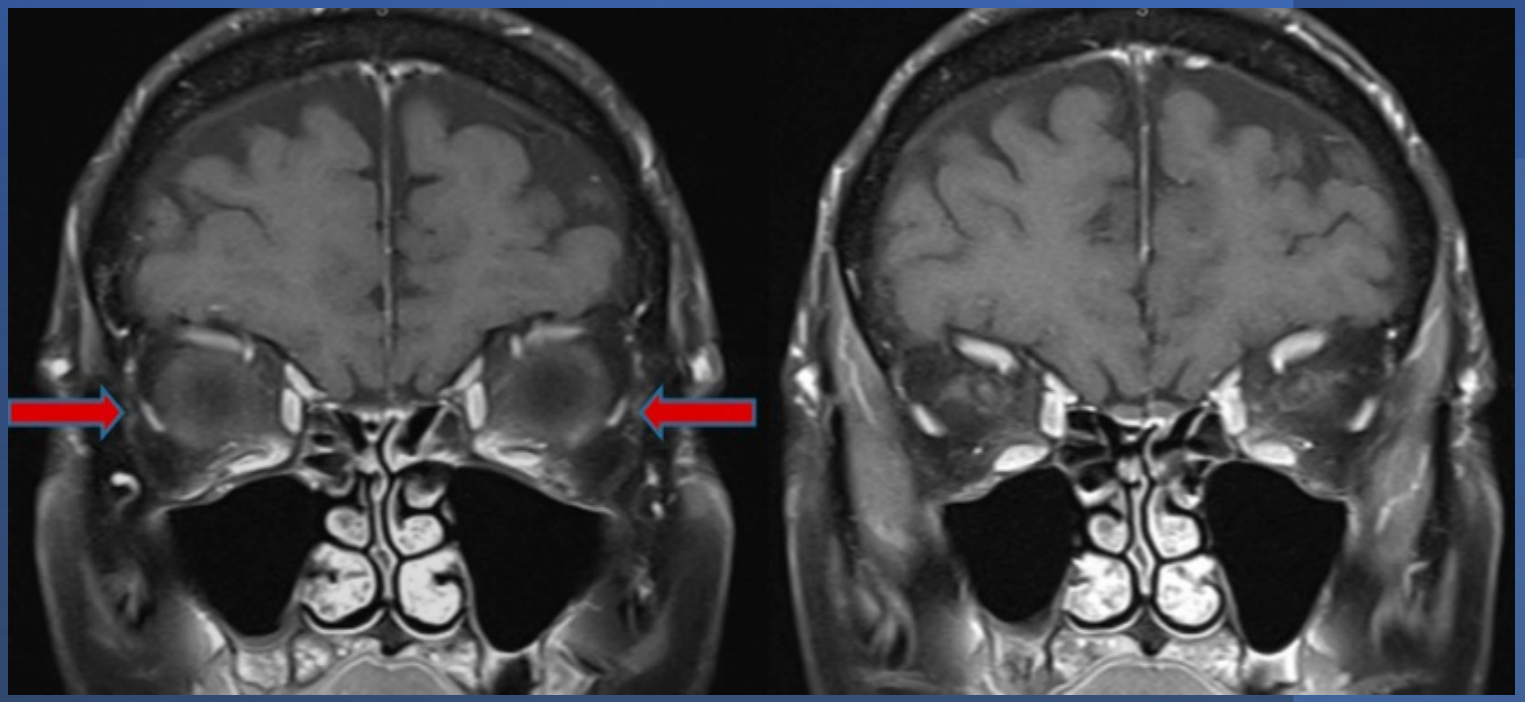
2023 residual esotropia



Clinical Cases

- 77 yo Female
- Intermittent binocular horizontal diplopia for 6 months
    - Only present at distance
    - Increases in latera gaze
- PMH: Osteroporosis

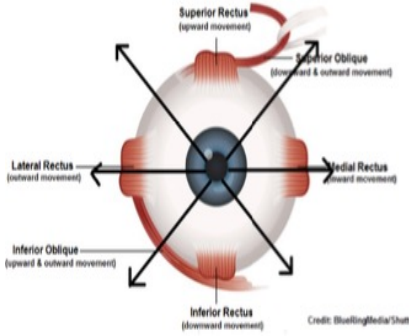


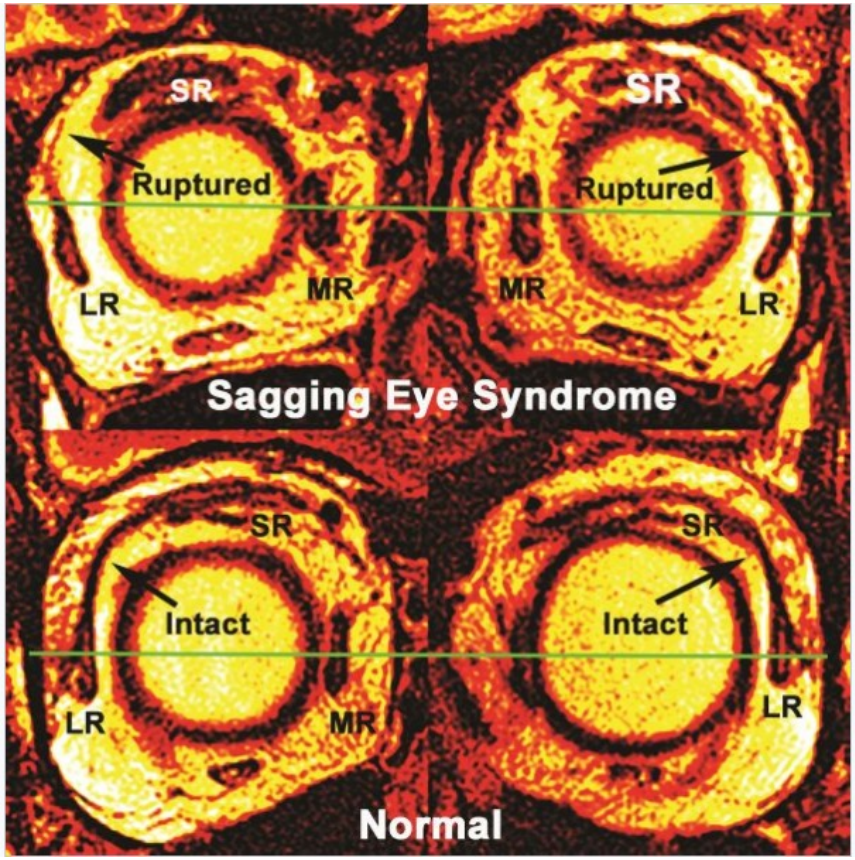


Inferior displacement of the lateral rectus muscles consistent with Sagging Eye Syndrome

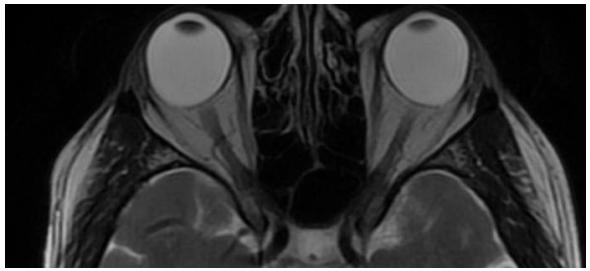
Clinical Cases – Sagging eye syndrome

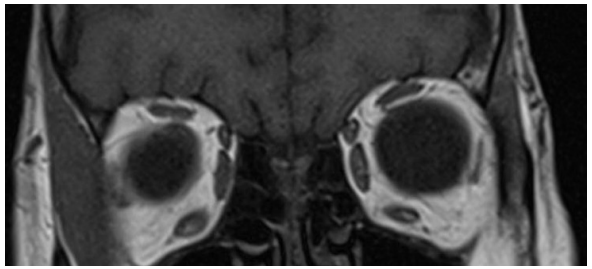
- Age related changes in EOM and orbital connective tissue
- Laxity or rupture of the SR+LR connective tissue bands results in inferior displacement of lateral rectus pulley complexes
- Associated involutional ptosis , deep superior sulci
- Explains conditions in elderly divergence insufficiency and broken down phoria.





Clinical Cases – Heavy eye syndrome





HES is the result of LR and SR shifts caused by the elongated posterior portion of the eyeball due to high myopia.

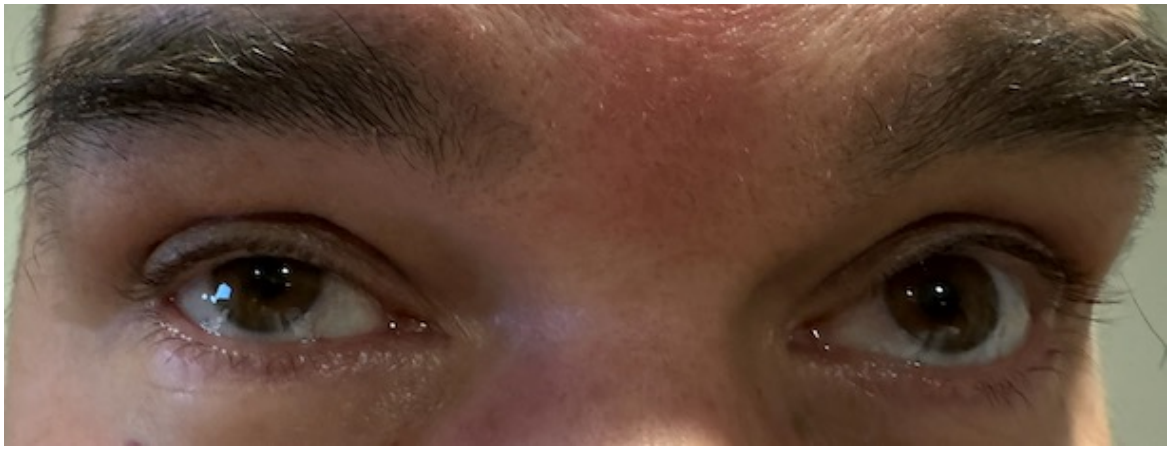
Nasal shift of SR causes reduced supraduction and increased adduction.
Consequently, HES shows esodeviation and hypo-deviation due to increased adduction, reduced abduction, reduced supraduction with an increased infra-duction

Heavy eye syndrome vs Sagging eye syndrome

	Heavy eye syndrome	Sagging Eye syndrome
Presentation	Progressive **esotropia and hypotropia** with **limitation of abduction and elevation**	Esotropia worse at distance, associated with **limited supraduction but full abduction**, along with degenerative changes such as bilateral **blepharoptosis, and deepening of the lid sulci**
Etiology	LR and SR shifts caused by the elongated posterior portion of the eyeball due to high myopia	Degeneration of the lateral rectus-superior rectus (LR-SR) band due to aging
MRI	• Inferior lateral rectus displacement and medial superior rectus displacement • Degeneration of the LR- SR band • Severe supero-temporal prolapse of myopic globe	• Inferior displacement of the lateral rectus • Degeneration of the LR- SR band • No appreciable globe prolapse

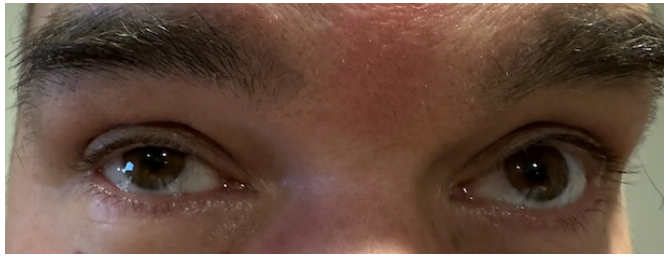
Clinical Case

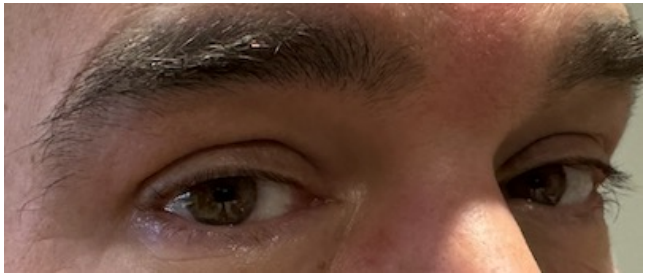
- 58 yo M with PMH of HTN, HLD , hypothyroidism, with diplopia.
- Exam: Partial right third nerve palsy w/o pupillary involvement
- Right eye upper lid swelling in the lacrimal area.

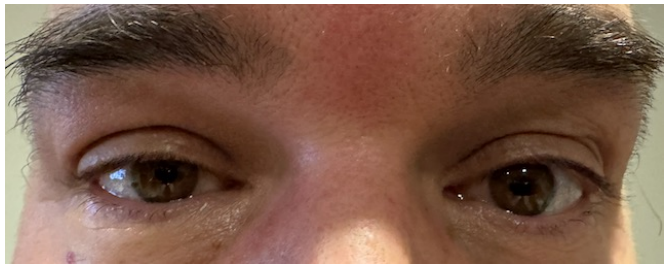


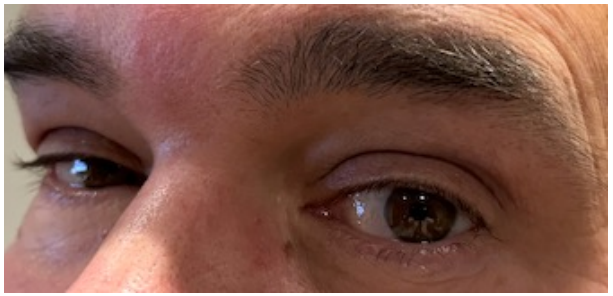
	-1	-1	-1	LHT 8	0	0	0	
Ortho	0	◯	0	Ortho	0	◯	0	Ortho
	0	0	0	Ortho	0	0	0	

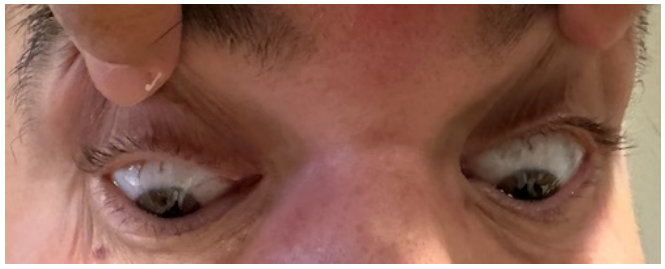
Clinical Case



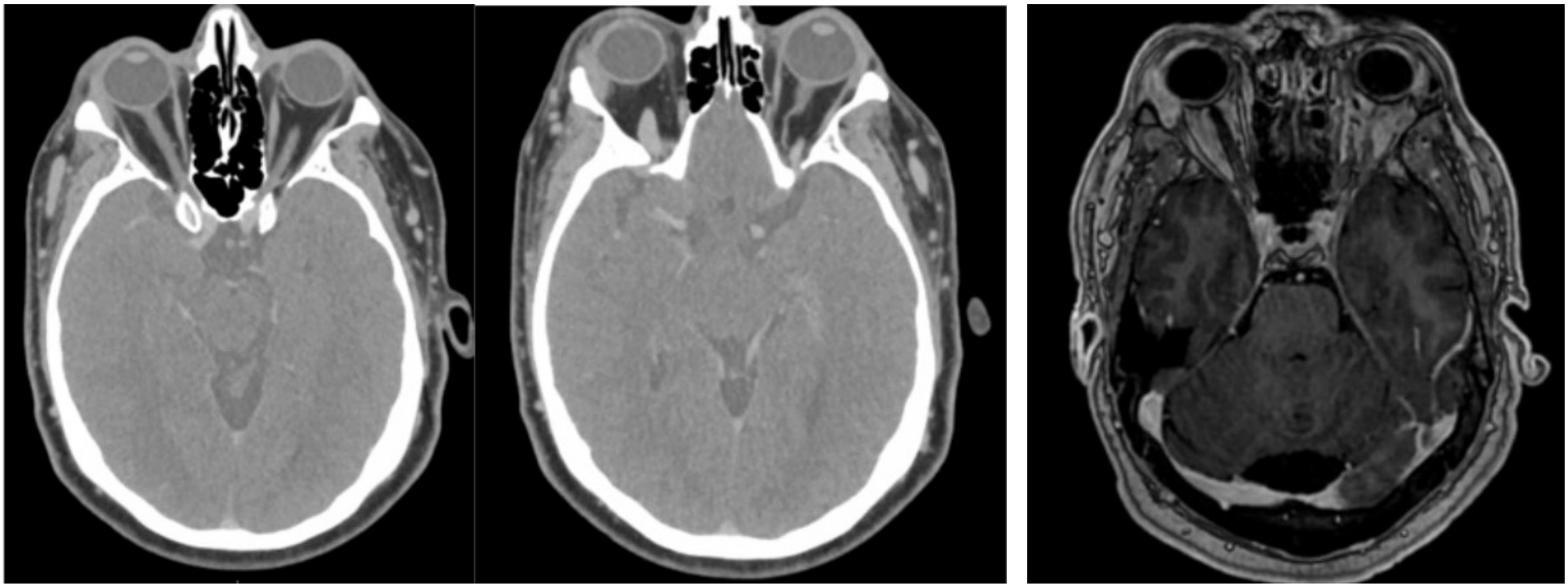








Clinical Case



MRI Orbit: Nonspecific enlargement and hyperenhancement of the right lacrimal gland.

Clinical Case

Biopsy of lacrimal gland: Benign glandular tissue with chronic inflammation.

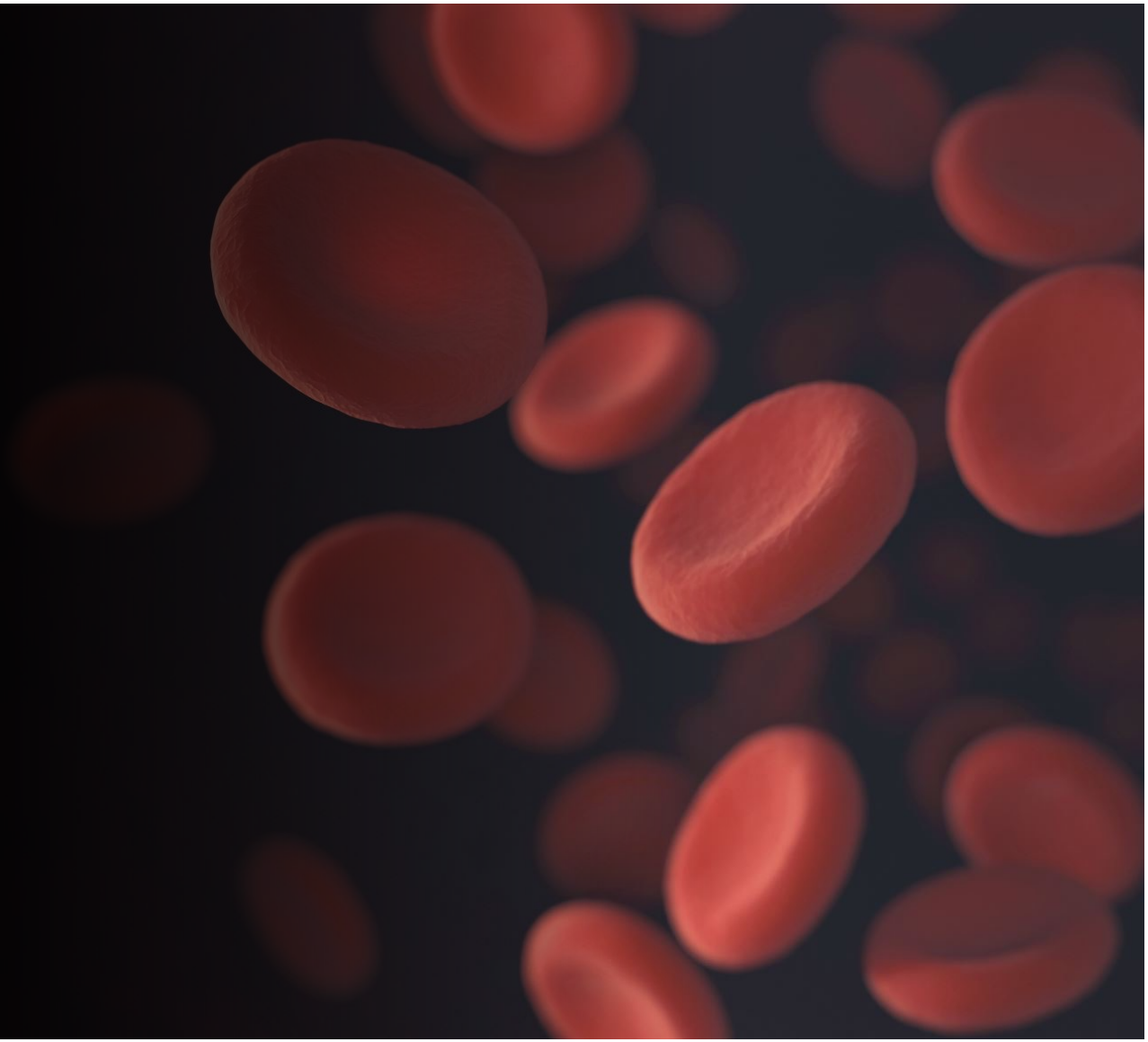
Negative for lymphoma, Ig G4

CT Chest : No evidence of sarcoid

CTV- No cavernous sins thrombosis but has nonspecific prominence of the superior ophthalmic veins bilaterally

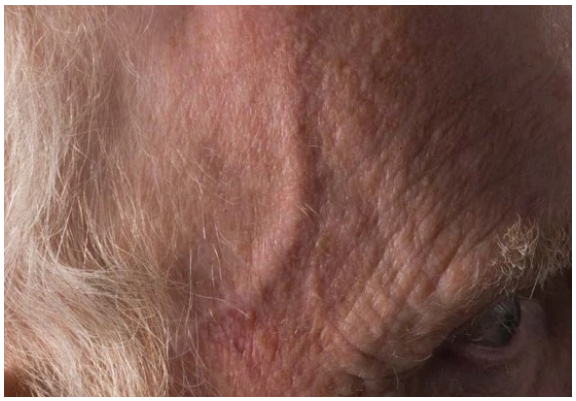
Treated with high dose prednisone.

Other Etiologies

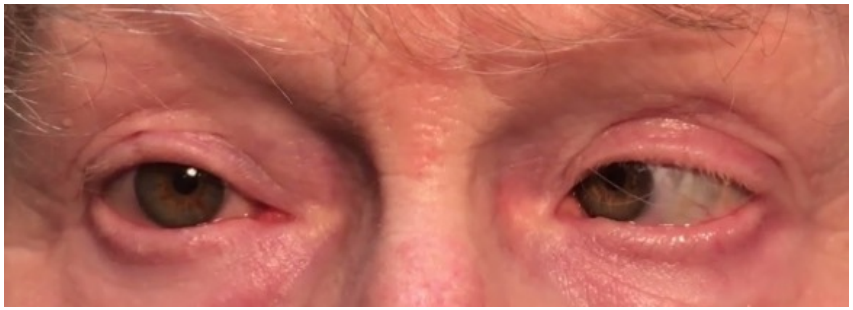


Clinical Case

78 y.o. Caucasian, male with a PMH of HTN, DM II diagnosed a week back presenting with horizontal binocular diplopia.
Exam: left 6th nerve palsy, VA 20/20 OU , normal VF and optic nerves
Other complaints: Headaches + , generalized fatigue with jaw claudication, weight loss .
CRP 176.7
ESR: 72
TFT normal

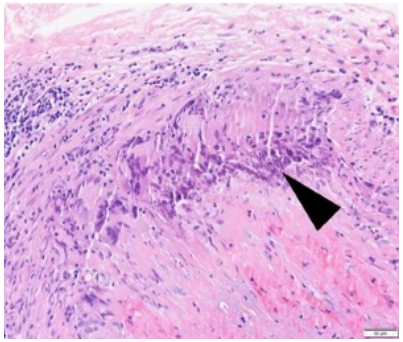


	0	0	0	LET 2	0	0	-1	
Ortho	0	◯	0	LET 2	0	◯	-1	LET 4
	0	0	0	LET 2	0	0	-1	



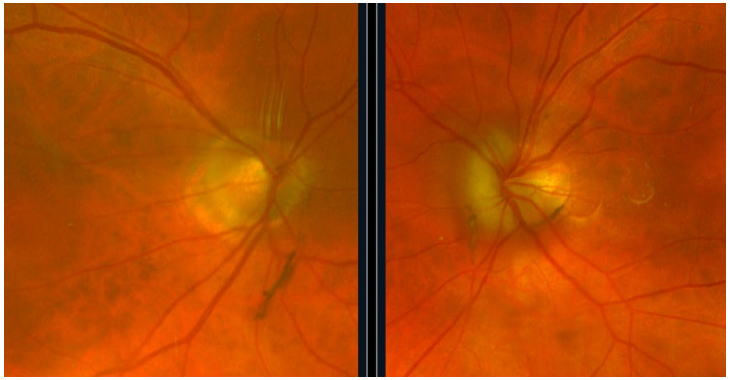
Clinical Case

Temporal artery Biopsy a week later was positive.



Diagnosis: Giant cell arteritis

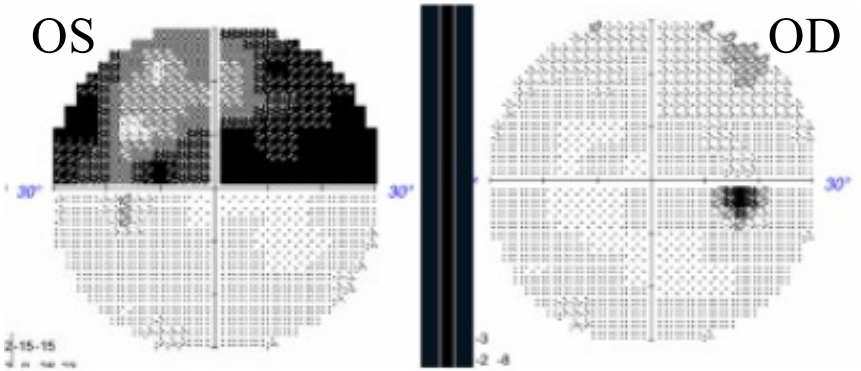
OD



OS

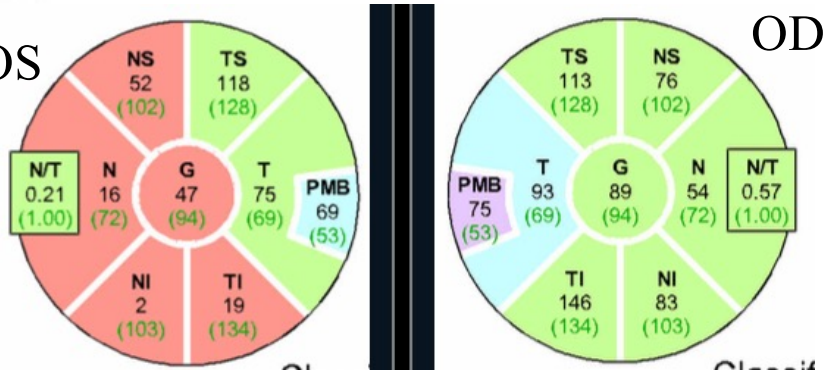
Humphrey Visual field testing & OCT

OS



OD

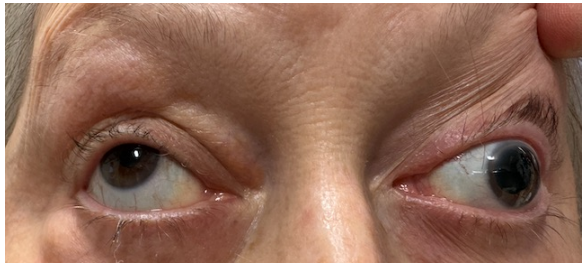
OS

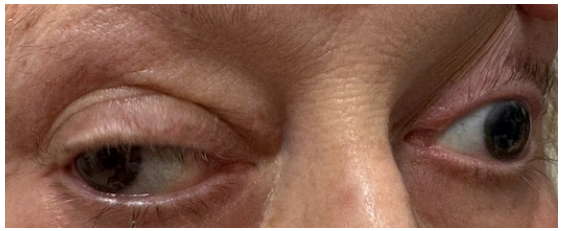


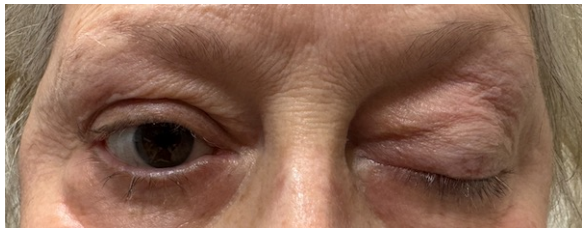
OD

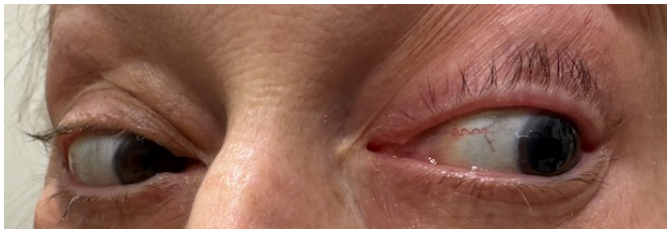
Clinical case

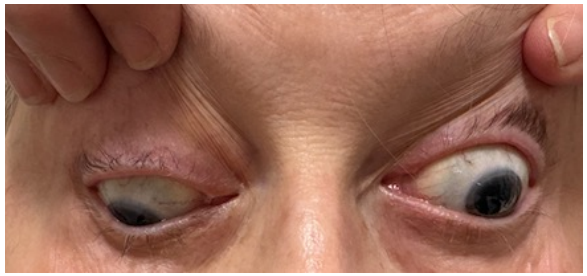
60 yo F with hx of breast cancer with diplopia











Localization: Left Third nerve

Pattern: Ptosis , with eye down and out (XT +hypotropia)+/- Blown pupil

Third nerve Palsy

Work up

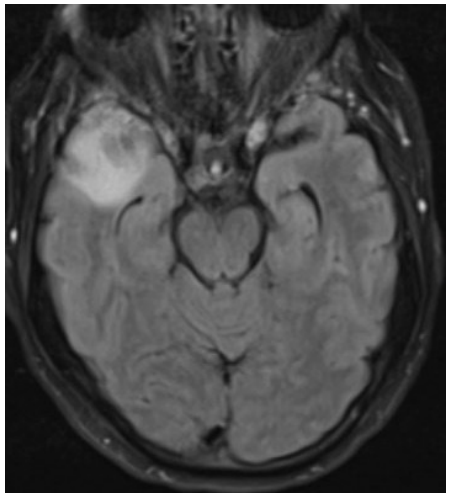
MRI Brain w contrast

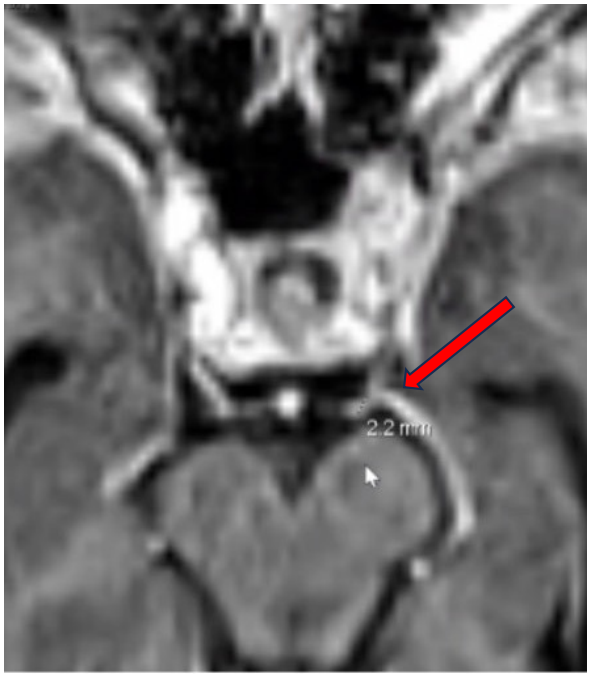
CTA Head

Clinical case

- MRI Brain – Metastasis to the brain No midbrain involvement
- CTA –no PCOM aneurysm
- MG/TED work up neg
- Repeat MRI shows left third nerve enhancement

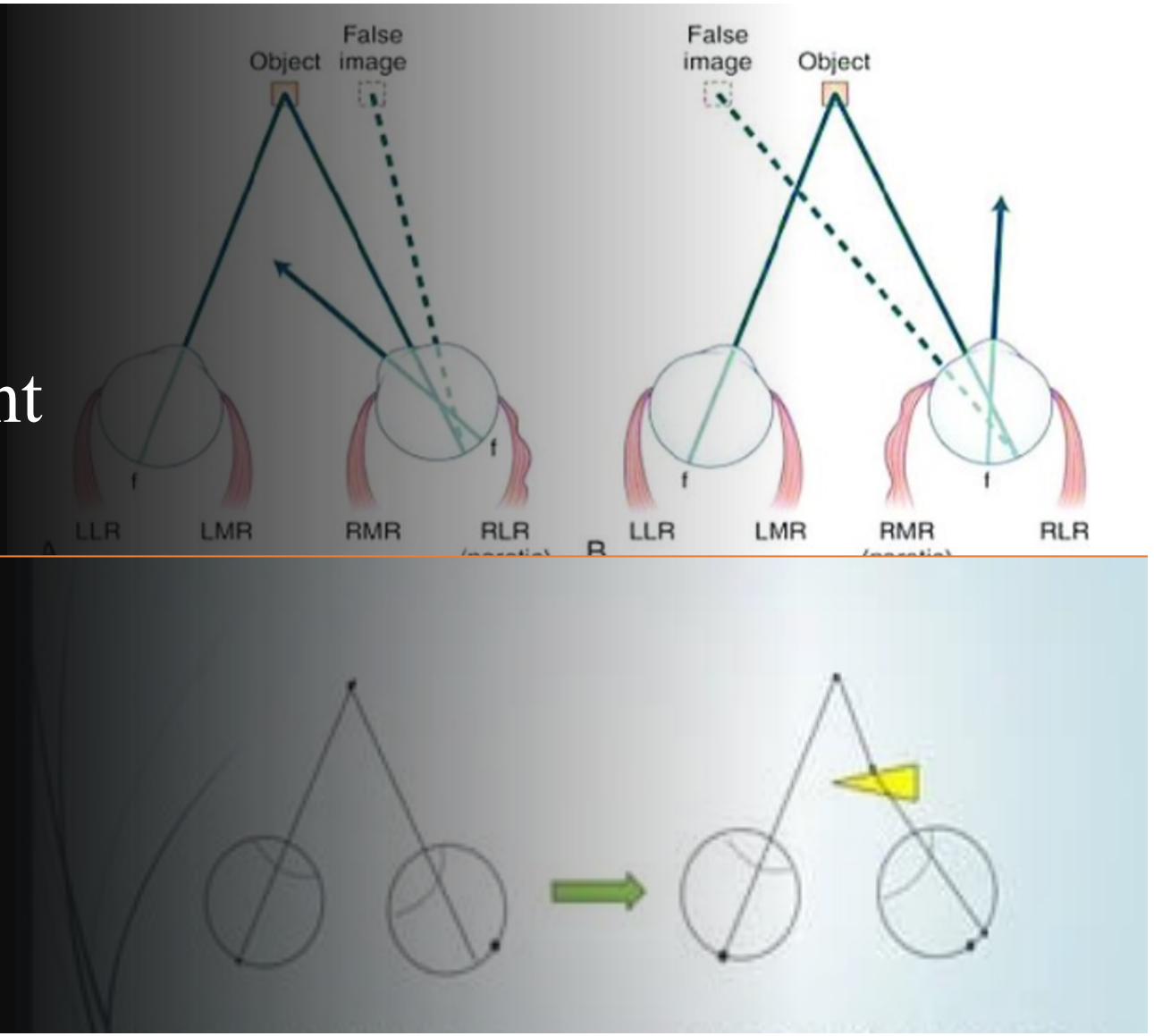
Diagnosis : Brain Metastasis w/ Left 3rd n involvement



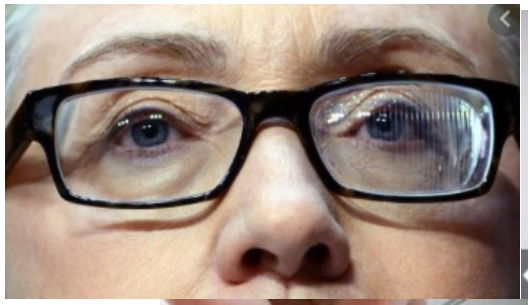


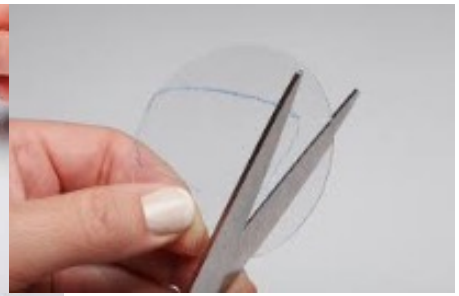
Management of diplopia

Prisms – The Light Benders



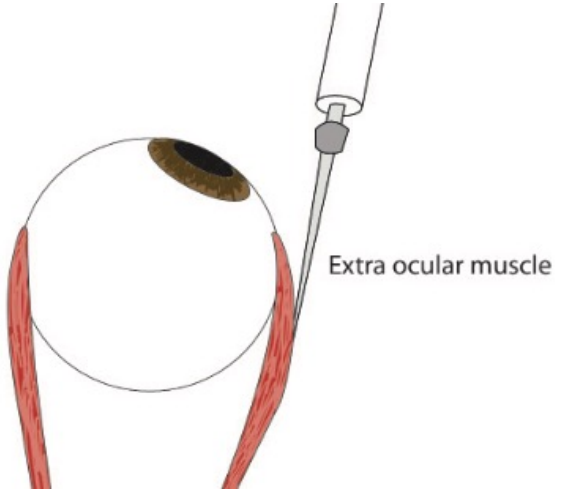
Management- Prism glasses– Fresnel & Grounded prisms

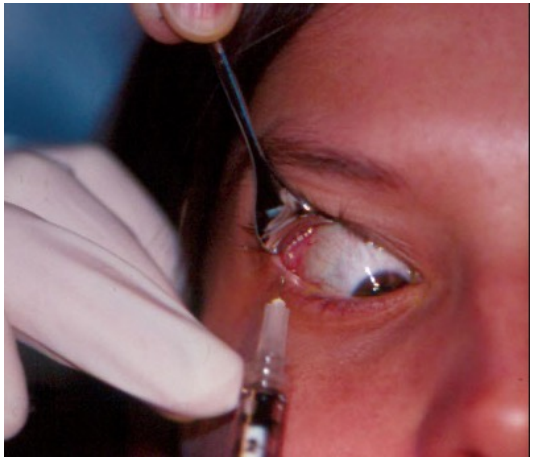


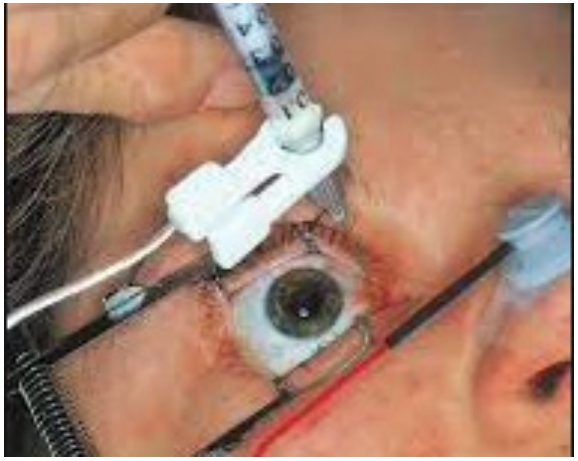


Management

Botox injection in the eye muscle

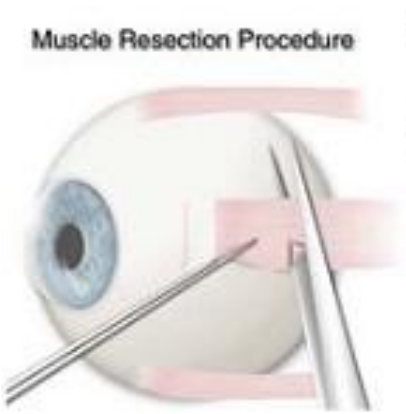


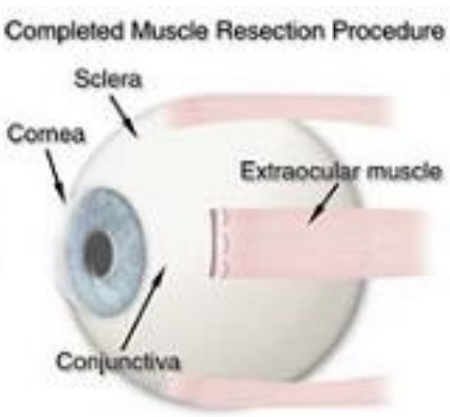


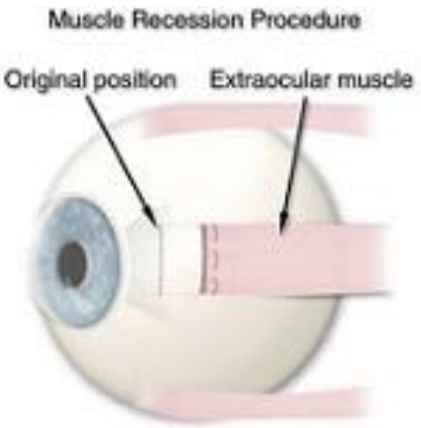


Management

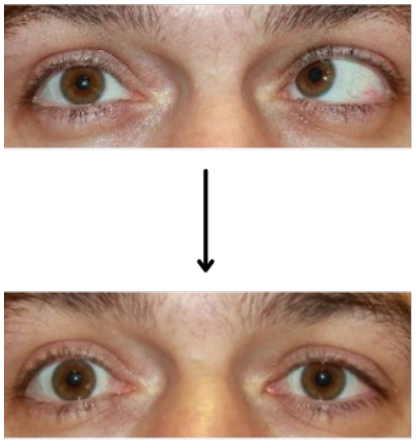
Surgery



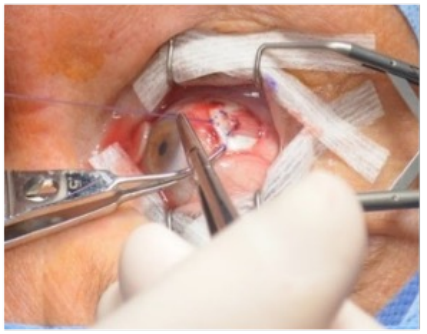




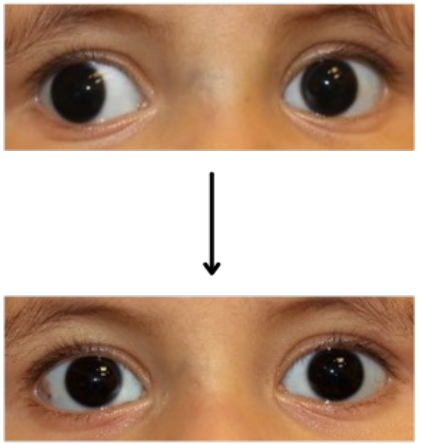
Esotropia (ET)



After Surgical Repair



Exotropia (XT)



After Surgical Repair

Summary

- Good history and examination holds clues to the diagnosis
- External appearance often holds clues to the diagnosis
- Pattern recognition and localization is key to solving the problem
- Beware of chronic red eye
- Learn to recognize cases that need urgent work up
- All cases need to be tailored for work up
- Treatment needs to be tailored as well

Thank you