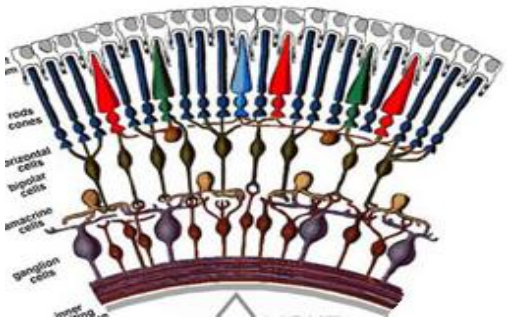
DISTURBI ACUTI DI VISIONE

Marcello Romano

ORIGINE NERVO OTTICO



Cellule ganglionari:

- possono ricevere informazioni da 1 a 300 fotorecettori Ý campionamento retinico: 1/300 nella periferia retinica, 1/1 nella fovea Ý acuità visiva (massima nella fovea)

nella periferia retinica :

- grande soma (G. magnocellulari) e assone di grosso calibro (alta velocità di conduzione)
- responsive a basse frequenze temporali e spaziali, alle variazioni di luminanza

nella macula:

- piccolo soma (G. Parvocellulari) e assone di piccolo calibro (ridotta velocità di conduzione)
- responsive ad alte frequenze temporali e spaziali, alle variazioni di contrasto cromatico

ANAMNESI NEUROFTALMOLOGICA *GUIDATA*

1. Localizzazione: deficit visivo monolaterale o bilaterale ?

Monolaterale- Bilaterale → prechiasmatico vs chiasmatico-posteriore

Difetto omonimo : difetto da danno delle vie ottiche retrochiasmatiche , quindi bilaterale e con pattern specifico; ad esempio un danno della corteccia occipitale di sinistra determinerà un' emianopsia laterale omonima dx (difetto nel quadrante nasale OS e temporale OD)

RETINA vs NERVO OTTICO

ANAMNESI NEUROFTALMOLOGICA *GUIDATA*

2. Positivo/negativo le fotopsie e gli scotomi positivi sono più frequentemente associati a patologia retinica; gli scotomi negativi a neuropatia ottiche

3. Decorso → miglioramento (neurite ottica) vs stabilità / progressione (altre neuropatie/ retinopatie)

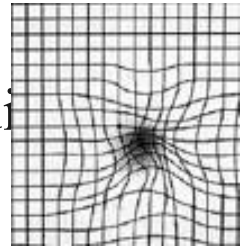
Descrizione del sintomo

4. Contesto del deficit visivo: febbre (neuropatie ottiche infettive/infiammatorie), trauma , familiarità (LHON)

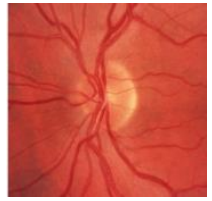
5. Sintomi associati

- Dolore ai movimenti oculari (neurite ottica)
- Cefalea (papilledema)
- Diplopia (patologia apice orbitario /regione sellare)

- Fotopsia /metamorfopsia (corioretinopatia)
- Nictalopia o cecità diurna /Emeralopia o cecità notturna (di
  retinica)

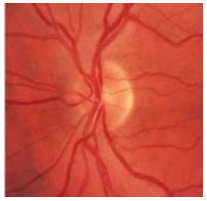


ESAME OBIETTIVO NEUROFTALMOLOGICO



- **Funzione visiva**
- **Attività pupillare**
- **Palpebre**
- **Regione orbitaria**
- **Motilità**
- **Segmento anteriore**
- **PIO**
- **Segmento posteriore**

Neuropatia ottica: DIAGNOSI CLINICA



↓ acuità visiva

↓percezione dei colori

APD: difetto afferente pupillare (forme monolaterali o bilaterali asimmetriche)

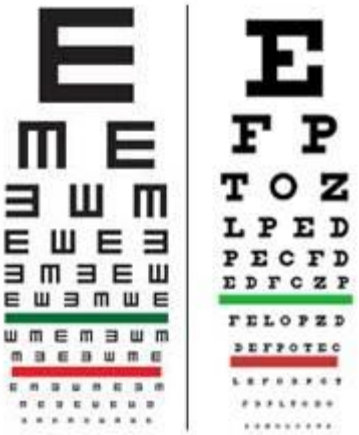
difetto perimetrico (deve essere ripetuto e verificato) : altitudinale o orizzontale, concentrico, scotoma centrale

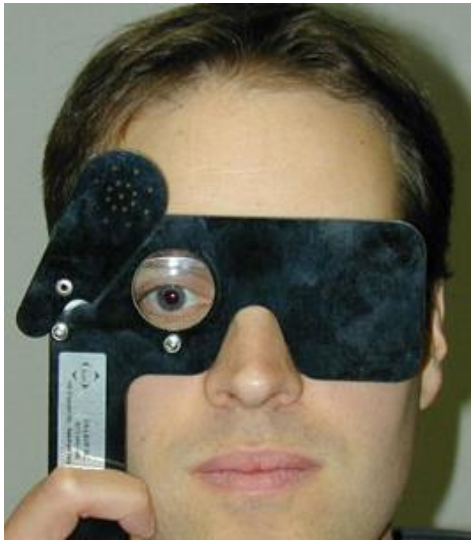
disco ottico: normale/edema/pallore

ESAME OBIETTIVO NEUROFTALMOLOGICO

Misurazione Acuita' Visiva

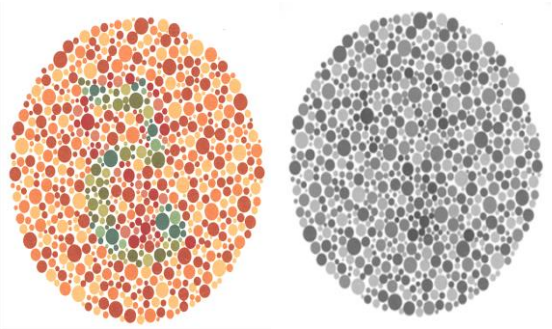
corretta (quando possibile!!) dato poco specifico per neuropatie ottiche





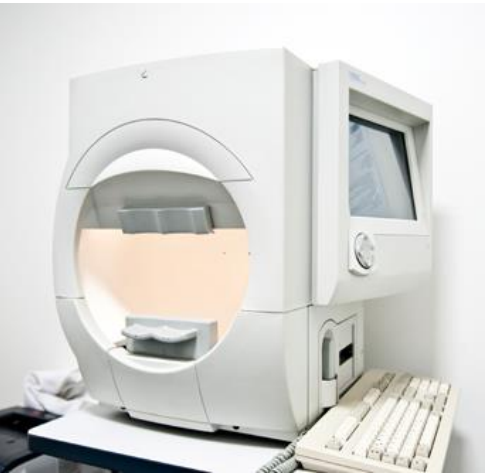
Valutazione Senso Cromatico

Test di Ishihara per identificare neuropatie ottiche/distrofie retiniche

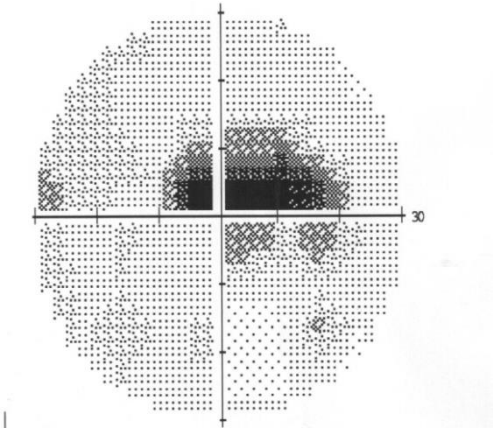


ESAMI STRUMENTALI
Perimetria Automatizzata Standardizzata

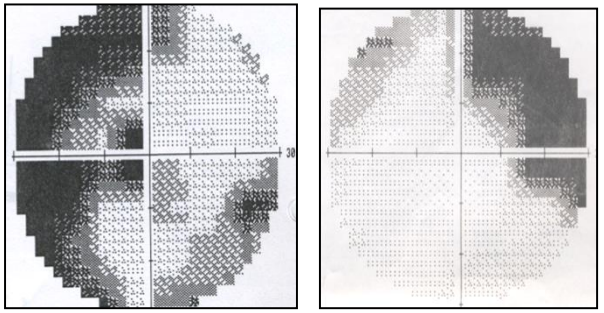
Localizzazione e quantificazione



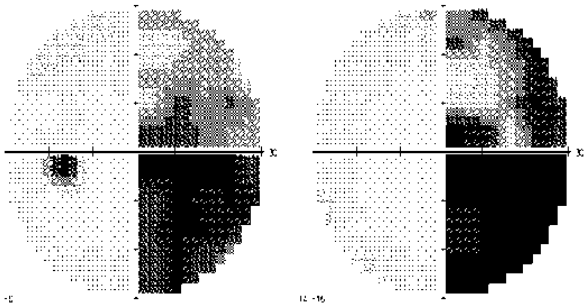
NEUROPATIE OTTICHE



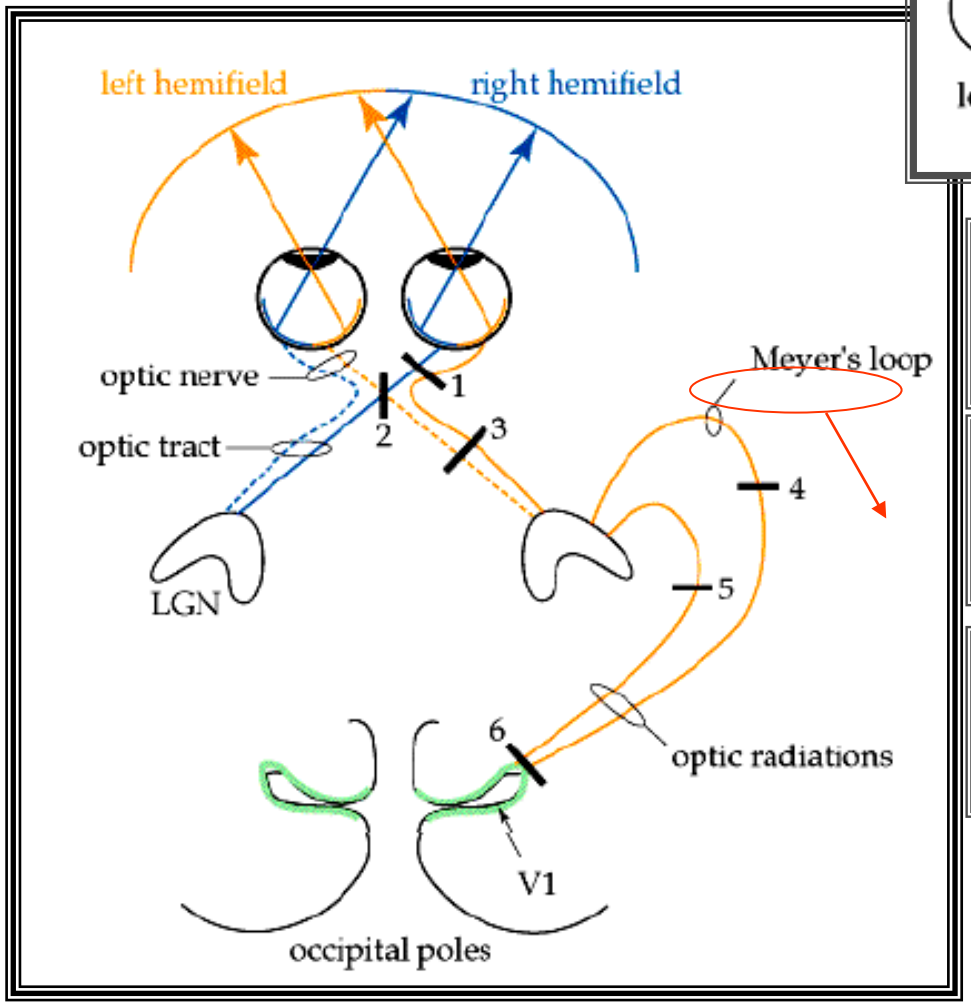
REGIONE CHIASMATICA

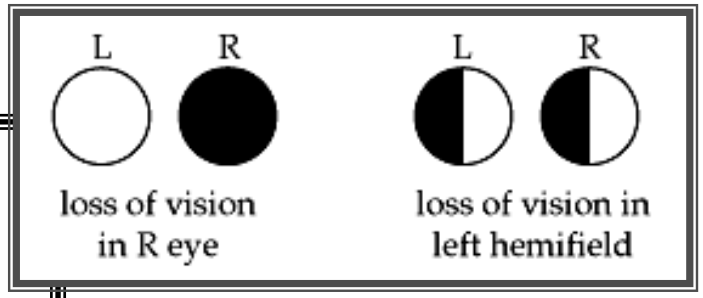


VIE OTTICHE RETROCHIASMATICHE

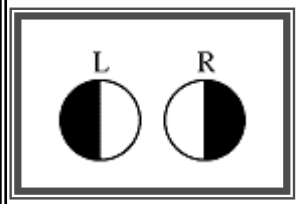


Visual Field

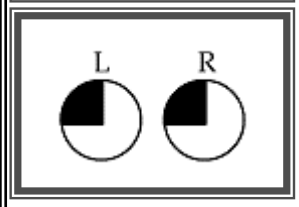




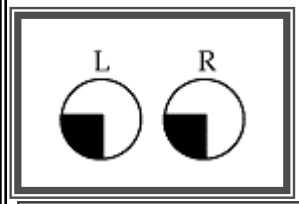
Optic Nerve
Optic Tract



Chiasmal Bitemporal



Themporal Lobe
"pie in the sky"



Parietal lobe
GAZE OPPOSITE

Homonimous hemanopia
Macular Sparing

RICORDA !!

- **Anteriore al chiasma: difetto monolaterale**

- **Willebrandt's knee giuntional scotoma.**
  Fibre inferonasali prima di decussare il chiasma passano anteriormente verso il NO contolaterale prima di raggiungere il TO

- **Più posteriore al chiasma, più congruo il difetto cioè definito e omogeneo**

- **Retrochiasmatico: NO riduzione dell'acutezza visiva.**

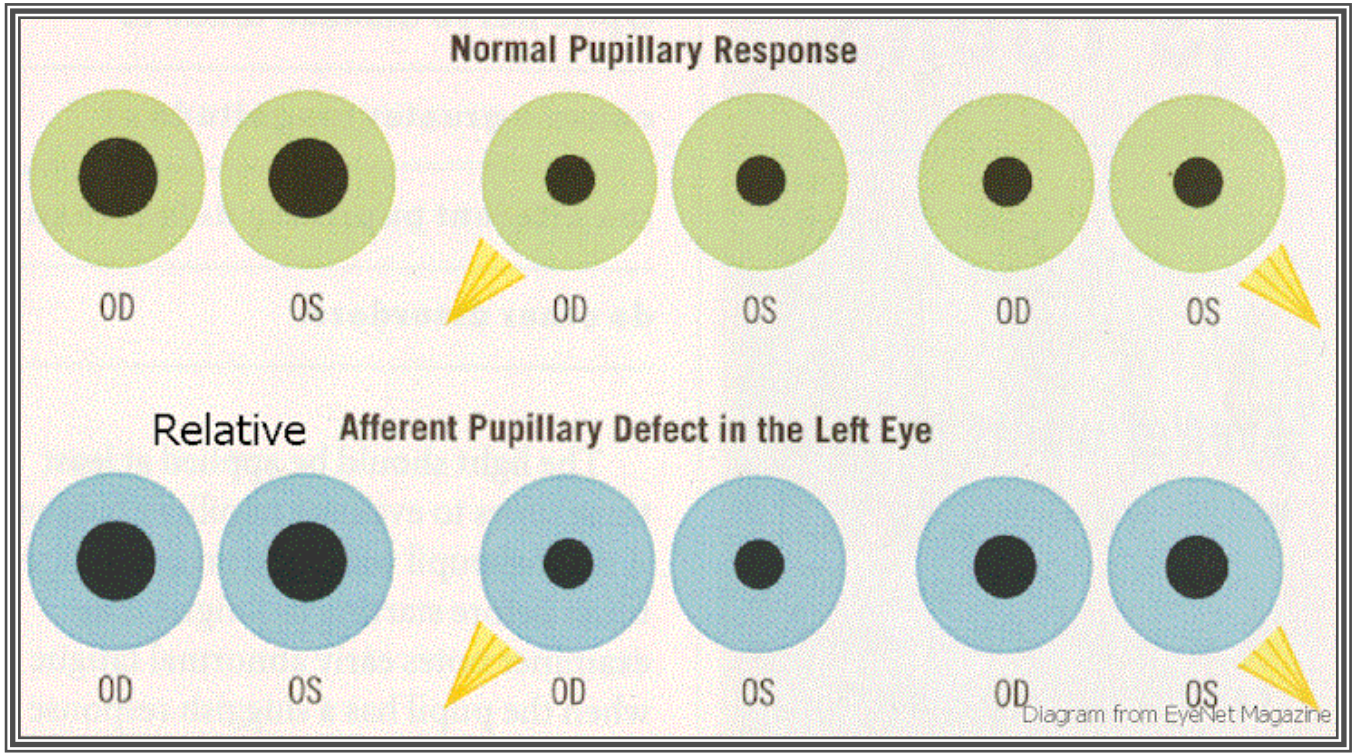
- **Riduzione dell'acuità visiva: lesioni al chiasma o anteriori**

Pre-Chiasmatic Defects

- Allargamento della Macchia cieca
- Arcuato, Altitudinale o orizzontale, Nasal Step, Nasal Depression
- Attraversamento dei meridiani orizzontale e verticale
- Centrale o Centrocaecale

- Papilledema, Drusen, Congenito, Neuriti Ottiche
- Glaucoma, Papilledema, Drusen Neuropatie. Retina
- Neuropatie Ottiche, Retina
- Maculopatie (acutezza visiva molto più ridotta del CV). Neuropatie Ottiche

PUPILLE



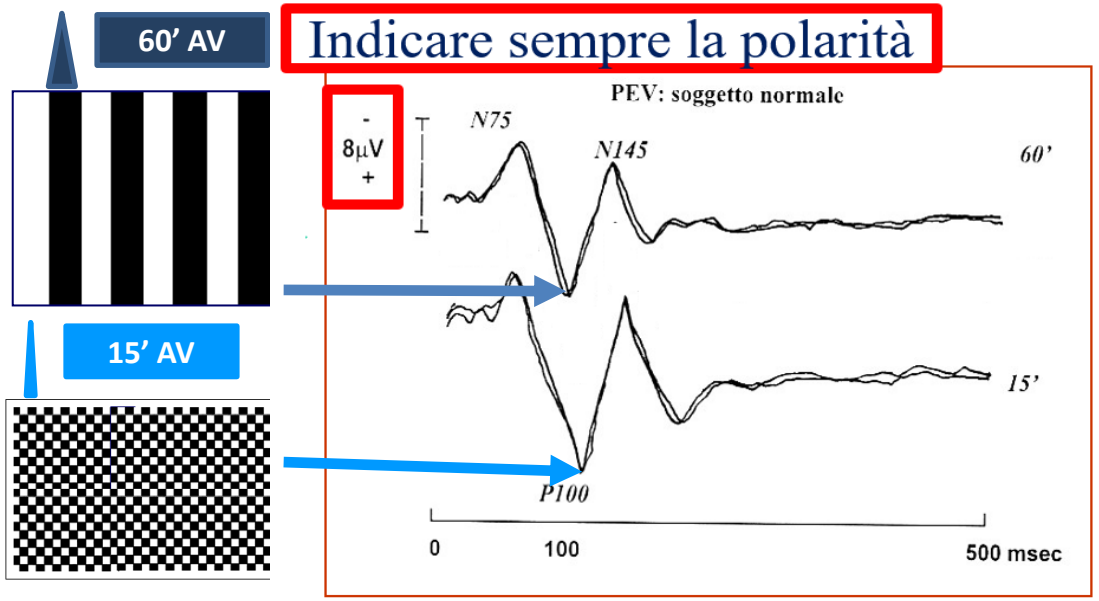
RICORDA !!!

RAPD + deficit visivo= Nervo Ottico

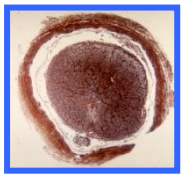
SEMEIOTICA

ELETTROFUNZIONALE DELLE VIE OTTICHE

PEV: stimolo visivo e risposte bioelettriche corticali



Basse frequenze spaziali (60’): risposta più “rapida” → assoni con più rapida velocità di conduzione → assoni di grosso calibro



Alte frequenze spaziali (15’): risposta + ritardata → assoni con più lenta velocità di conduzione → assoni di piccolo calibro

PEV+ PERG: il Tempo Retino-Corticale

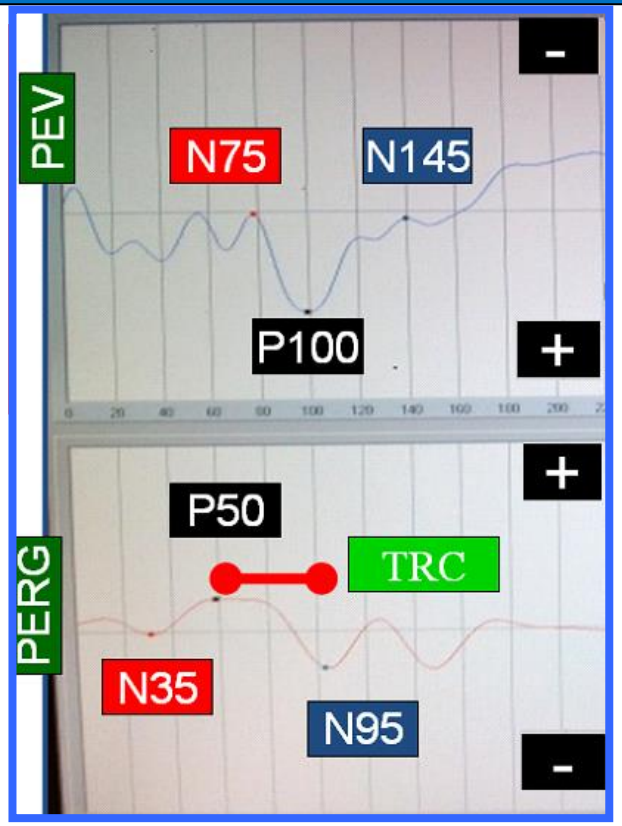
PEV P100 Tempo Implicito:
Risposta bioelettrica corteccia visiva

PERG P50 Tempo Implicito ed Ampiezza:
risposta bioelettrica delle cellule ganglionari

Differenza PEV P100- PERG P50 Tempi Impliciti è indicato come "Tempo Retinocorticale (TRC)"

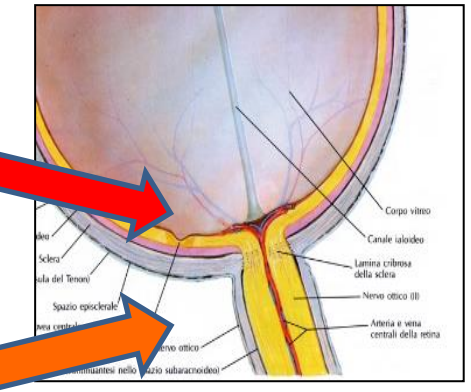
(indice elettrofisiologico della conduzione nervosa tra le cellule ganglionari e corteccia visiva) .

Celesia et al, IOVS, 1985.

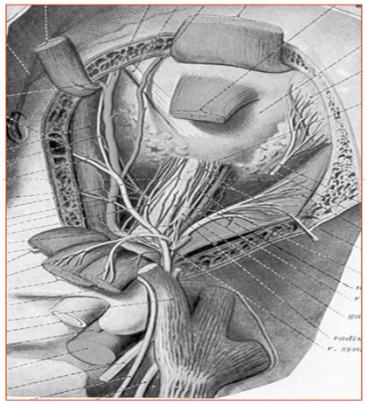


Le neuriti ottiche: aspetto oftlamoscopico

Papillite o neurite ottica anteriore:
rigonfiamento del disco ottico



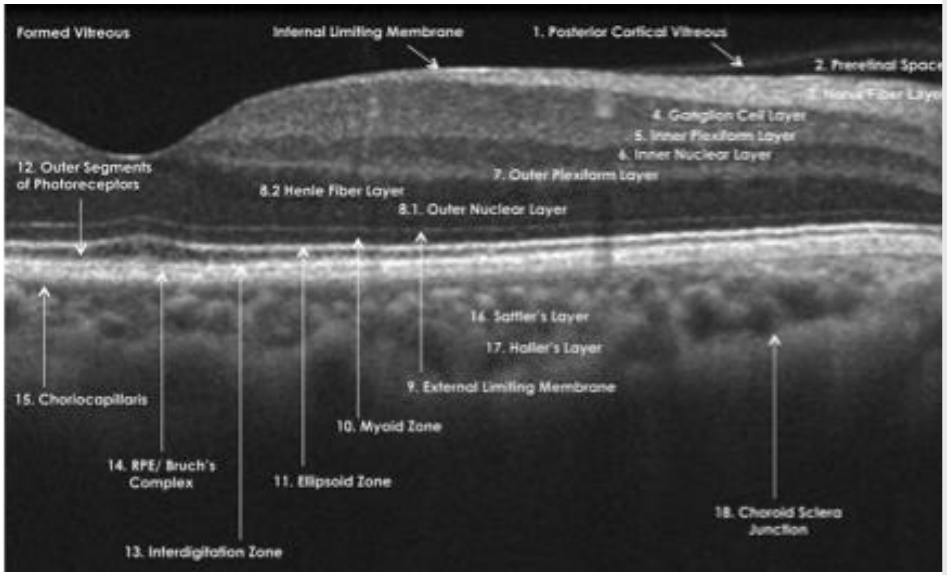
Neurite retrobulbare (intraorbitaria, canalicolare o intracranica):
assenza di rigonfiamento o altri segni del disco ottico



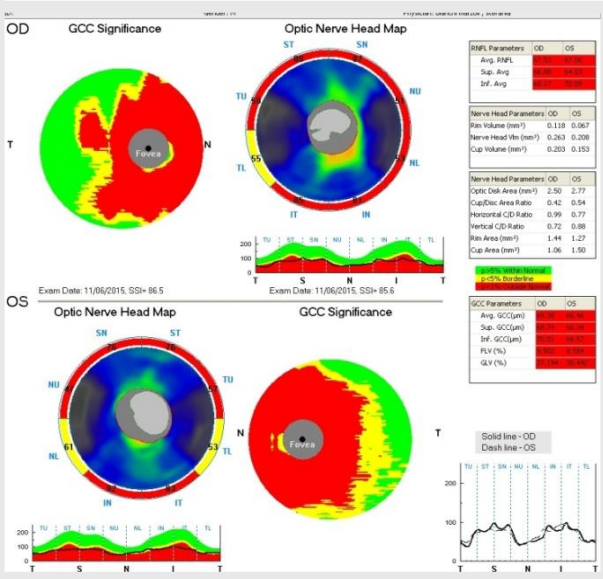
OCT

Informazioni strutturali qualitative : integrità delle strutture dei diversi strati retinici

Informazioni quantitative: spessore retinico ed analisi segmentale (spessore dei diversi strati retinici)



- Spessore complesso cellule ganglionari retiniche (GCC)
- Spessore strato delle fibre nervose intraretiniche (RNFL)

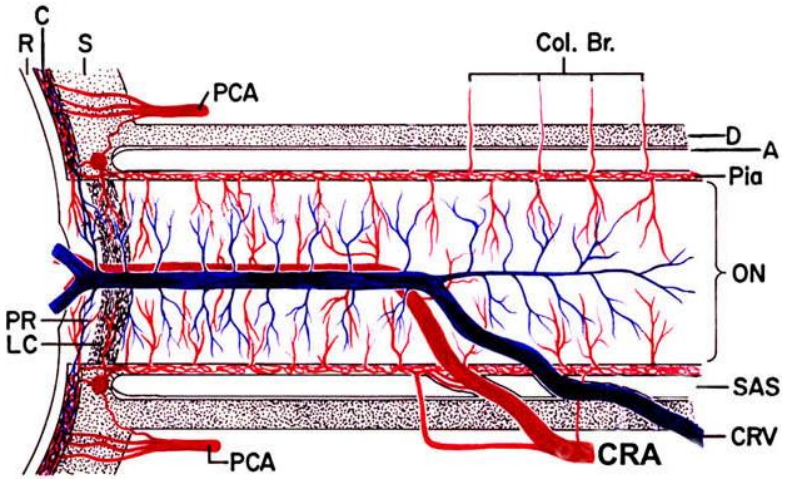


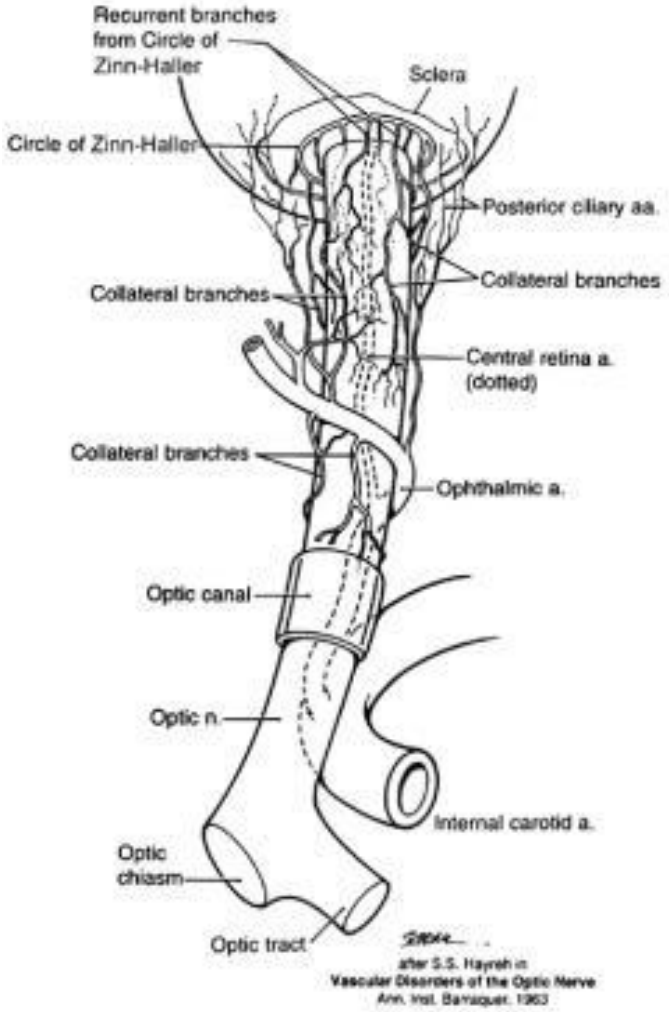
Neuropatia Ottica Ischemica ION

Patologia del <u>circolo ciliare posteriore</u> che irrora la testa del NO (anello di Zinn-Haller, parte esigua della retina e coroide

- ❖Anteriore
- ❖Posteriore (molto rara)

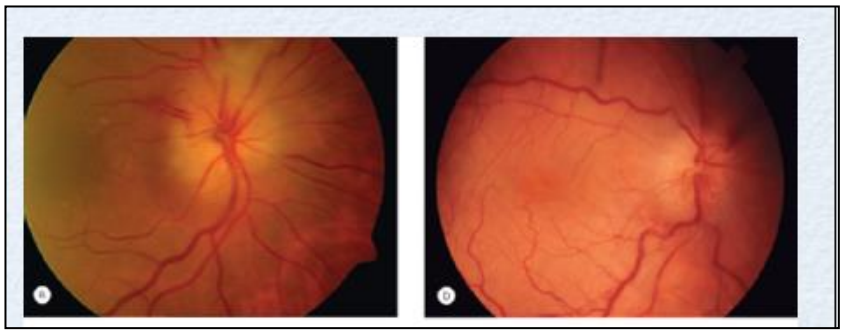
- ❖Non arteritica **NAION**
- ❖Arteritica **AION**

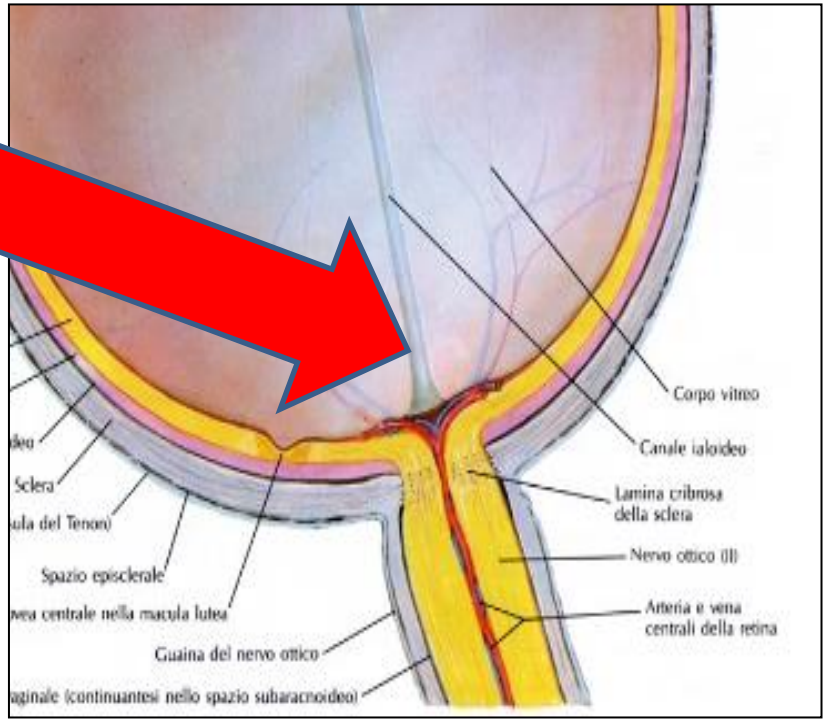




LE NEURITI OTTICHE

a)Anteriore

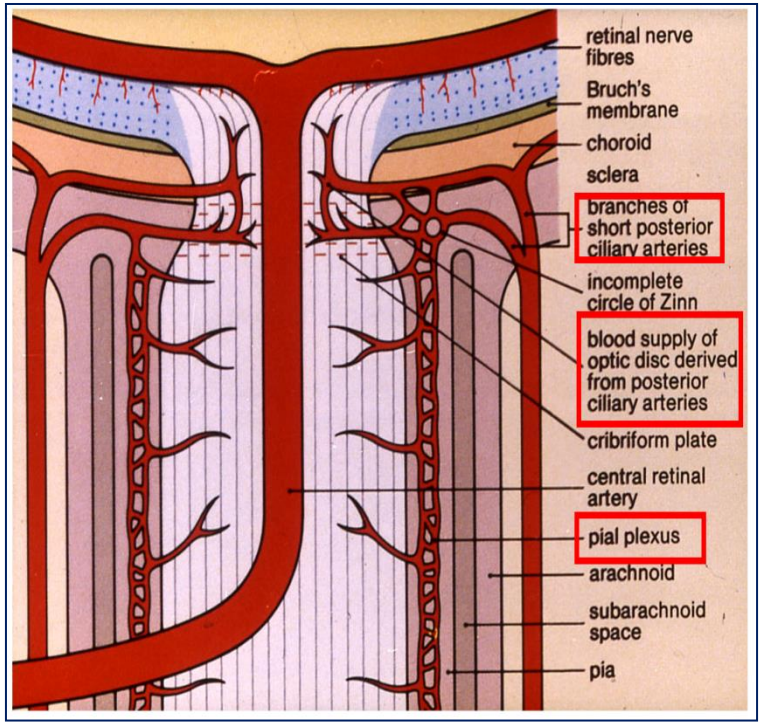




NEUROPATIA ISCHEMICA ANTERIORE (NOIA)

Patogenesi

Infarto **nella regione prelaminare**
(irrorata da rami dell'arteria
centrale della retina),
laminare
(irrorata dalle arterie ciliari posteriori)
e immediatamente retrolaminare
(irrorata dal plesso piale) del n. ottico



NEUROPATIA ISCHEMICA ANTERIORE (NOIA)

Fattori di rischio

- FORMA NON ARTERITICA

-ipertensione arteriosa,

- diabete mellito

-Fumo

-Ipercolesterolemia

-Iperomocestinemia

-Iperfibrigenemia

-Sleep Apnea Syndrome

- insufficienza carotide comune per aterosclerosi

- FORMA ARTERITICA

- Malattia di Horton
- LES
- Artrite reumatoide
- Panarterite nodosa

NEUROPATIA ISCHEMICA ANTERIORE (NOIA)

Insorgenza: 5-7 decade, prevalentemente nel sesso femminile

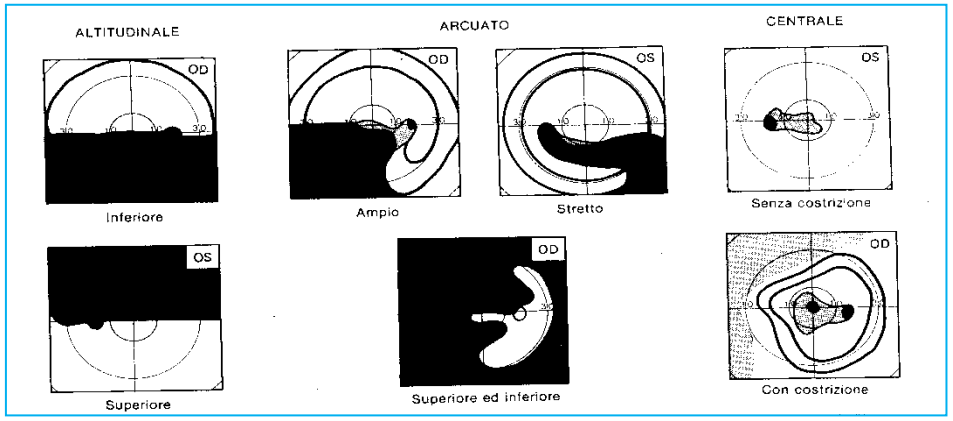
• Sintomatologia soggettiva: notevole riduzione del visus acuta o progressiva

- ***NOIA non arteritica:*** prima ore del mattino/ sovradosaggio farmaci ipertensivi

- occhio controlaterale 25-50 % dei casi entro i 5 anni

- ***NOIA arteritica:*** perdita della funzione visiva mono o bilaterale

• **deficit campimetrici**

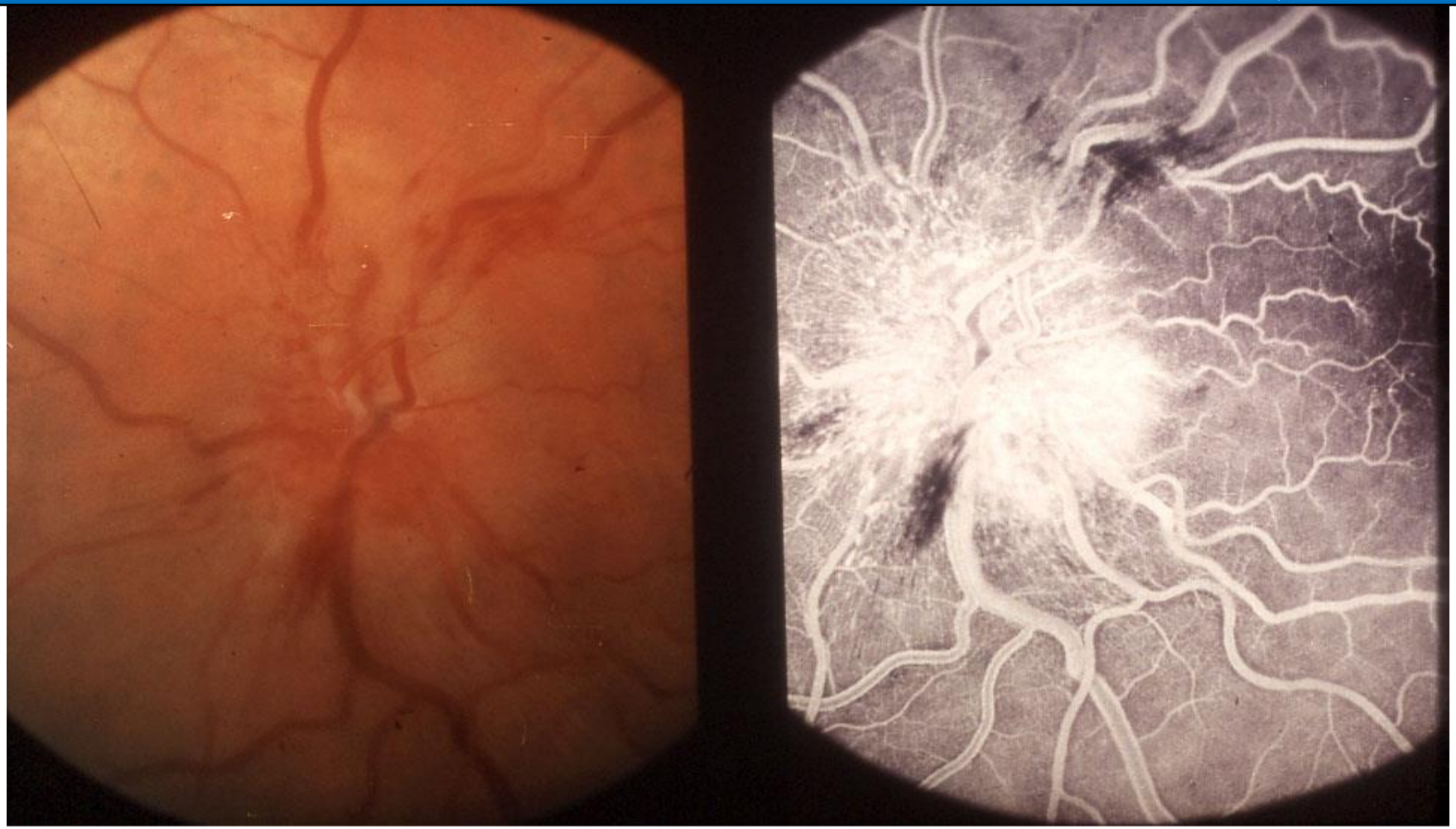


NEUROPATIA ISCHEMICA ANTERIORE (NOIA)

- **Aspetto oftamoscopico:** rigonfiamento del disco ottico, edema, emorragie, essudati. Evoluzione in pallore diffuso o localizzato (atrofia o subatrofia)

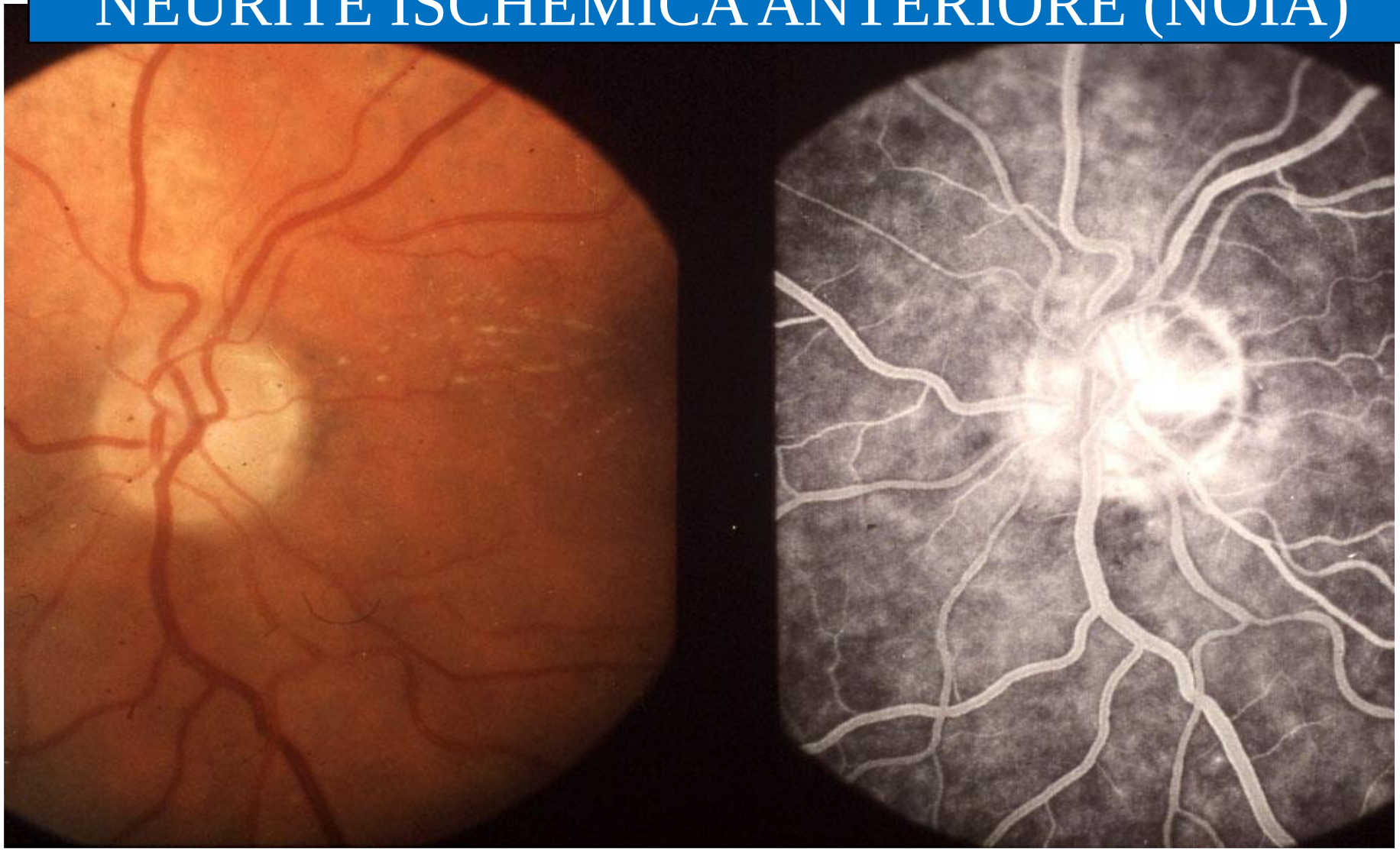
- Modificazione del senso cromatico
- PEV con aumento dei tempi di conduzione e ridotti di ampiezza,
- ERG normale.
- Riduzione della sensibilità al contrasto

NEUROPATIA ISCHEMICA ANTERIORE (NOIA)

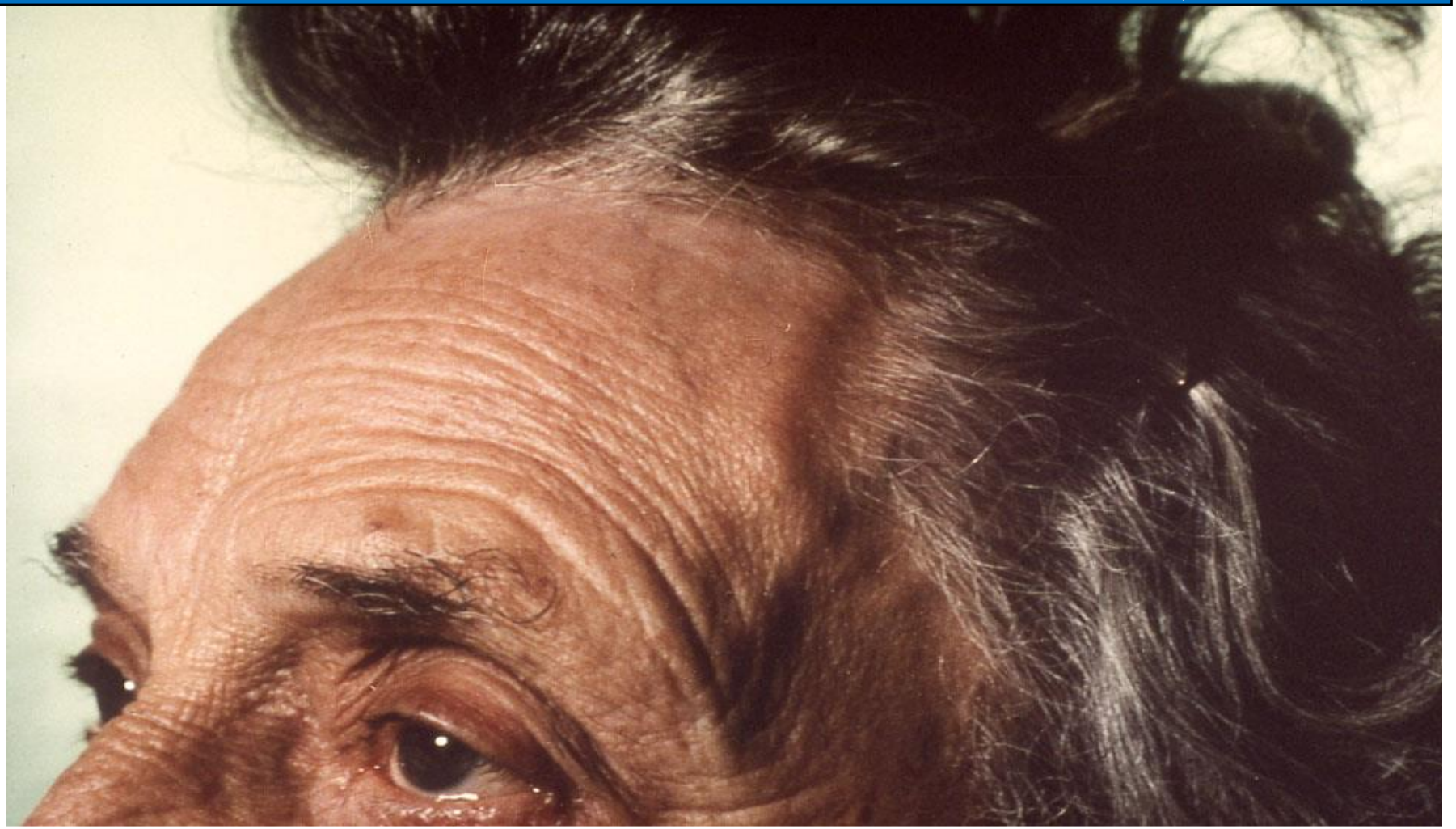


Ischaemic papillopathy

NEURITE ISCHEMICA ANTERIORE (NOIA)



NEURITE ISCHEMICA ANTERIORE (NOIA)



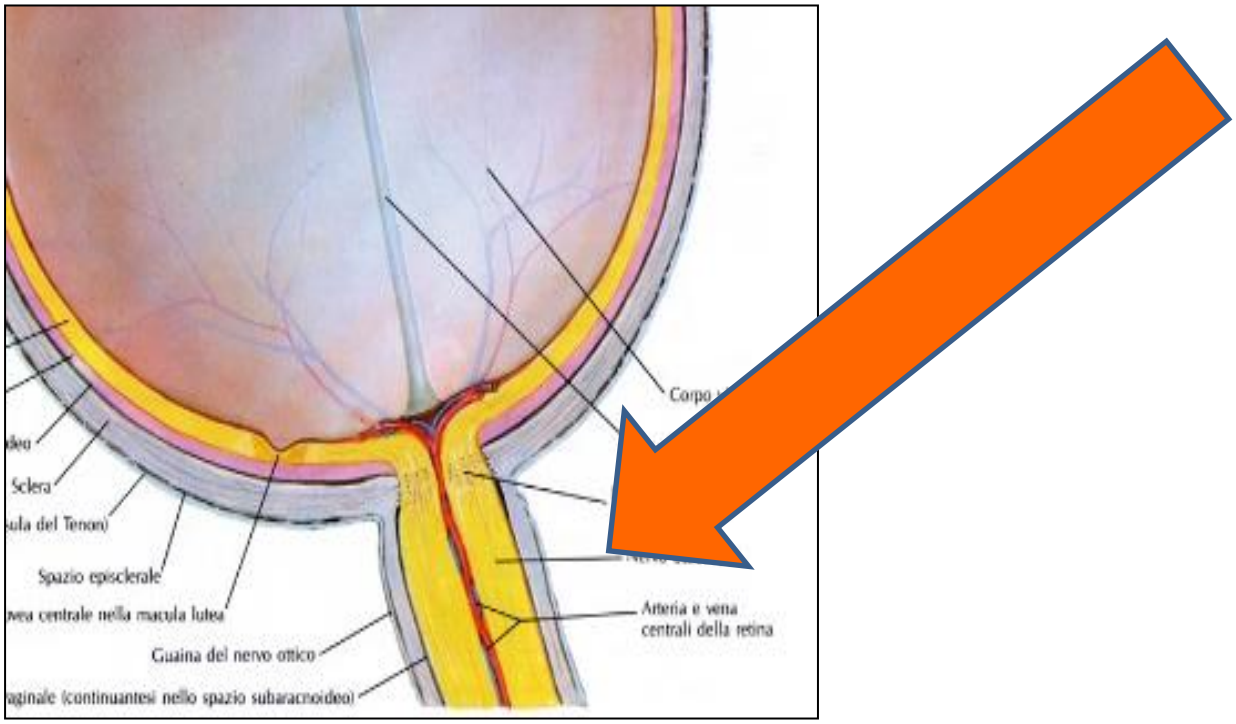
NEUROPATIA ISCHEMICA ANTERIORE (NOIA)

Terapia

- **1-3 giorni:** Metilprednisolone1-2d/die ev in 3-4 somministrazioni
- **4-15 giorni:** prednisone 1mg/Kg/die
- riduzione del predisone del 10% ogni settimana successiva
- **Controllo:** glicemia, pressione arteriosa
- **Associare:** gastroprotettori, vasodilatatori cerebrali, antiaggreganti piastrinici

LE NEURITI OTTICHE

b)Retrobulbare



NEURITE OTTICA RETROBULBARE (NORB)

"inspiegabile perdita acuta o progressiva del visus"

Caratterizzata da:

- alterazione del riflesso pupillare
- deficit del campo visivo
- modificazione del senso cromatico prevalentemente nell'asse giallo-blu e verde-rosso
- modificazione della sensibilità al contrasto
- dolore ai movimenti oculari

NEURITE OTTICA RETROBULBARE (NORB)

Esame obiettivo: alcun segno di rigonfiamento (edema), essudati, emorragie, modificazione del colorito del disco ottico. Il pallore successivamente.

- **Semeiotica strumentale:**

PEV con aumento dei tempi di conduzione e ridotti in ampiezza (ritardo della conduzione nervosa lungo le vie ottiche)

ERG normale

- **PERG** alterato:

indice di degenerazione retrograda

NEURITE OTTICA RETROBULBARE (NORB)

Eziologia:

a) Ischemiche: alterazioni arteriosclerotiche o aterosclerotiche delle arterie cerebrali anteriori

b) Infettive: teteno, brucellosi, rosolia, influenza, varicella, tubercolosi, sifilide. Isolate o associate a sepsi focale (tonsillite , carie ecc..)

c) Traumatiche (per compressione diretta, fenomeni trombotici, spasmo arterioso)

d) Da radiazioni (da radioterapia per tumori intracranici o dei seni paranasali)

e) Aracnoidite otticochiasmatica: in associazione a:
meningite basale, traumi cranici, tumori intracranici,
sindrome della sella vuota,
per: strozzamento del tessuto nervoso,
necrosi post-infiammatoria delle fibre, occlusione vascolare

NEURITE OTTICA RETROBULBARE (NORB)

Eziologia:

f) Lesioni compressive:

- tumori intraorbitari e intracranici, lesioni infiammatorie dei seni paranasali, aneurismi, emorragie orbitarie spontanee o traumatiche

- affezioni primarie dell'osso (osteopetrosi, displasia fibrosa, displasia craniometafisaria)

- idrocefalo congenito o acquisito

- - meningiomi della parte anteriore della falce del cervello

- Tumori ipofisari

g) Forme tossiche e carenziali

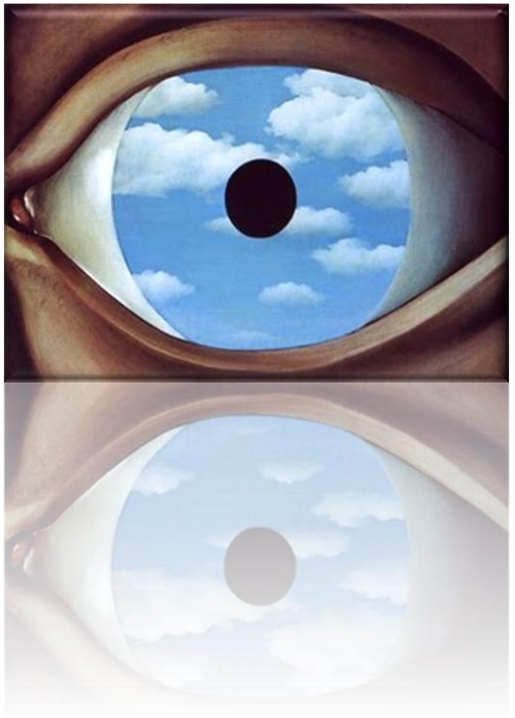
- ambliopia nutrizionale (Vitamina B1, B2, B6, B12, Acido nicotinico, acido folico

- ambliopia tropicale (associata ad atassia ed acufeni)

- farmaci

h) Forme infiltranti: leucemie e linfomi

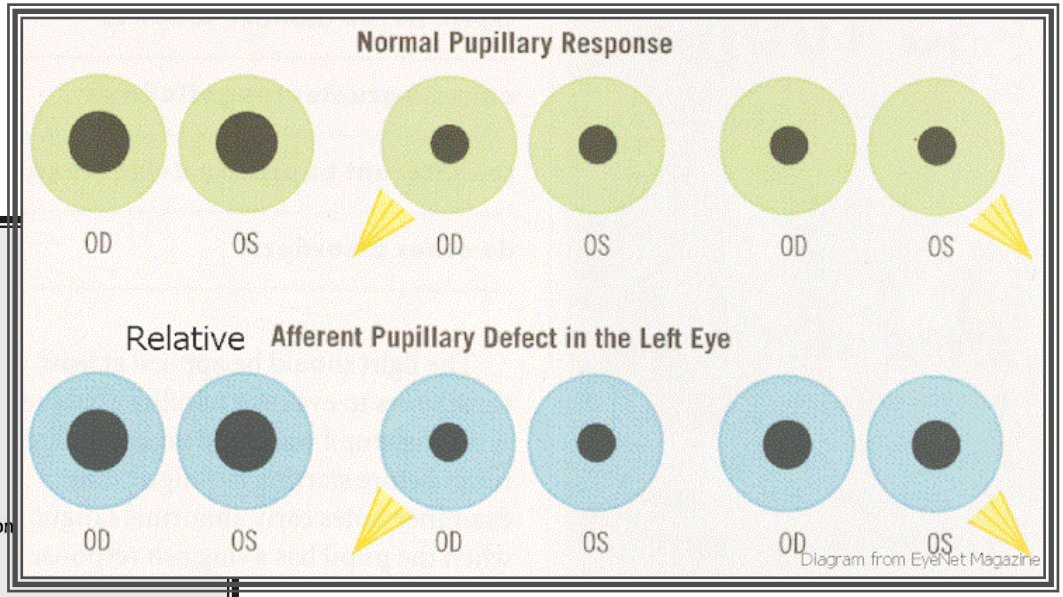
Neurite Ottica Acuta

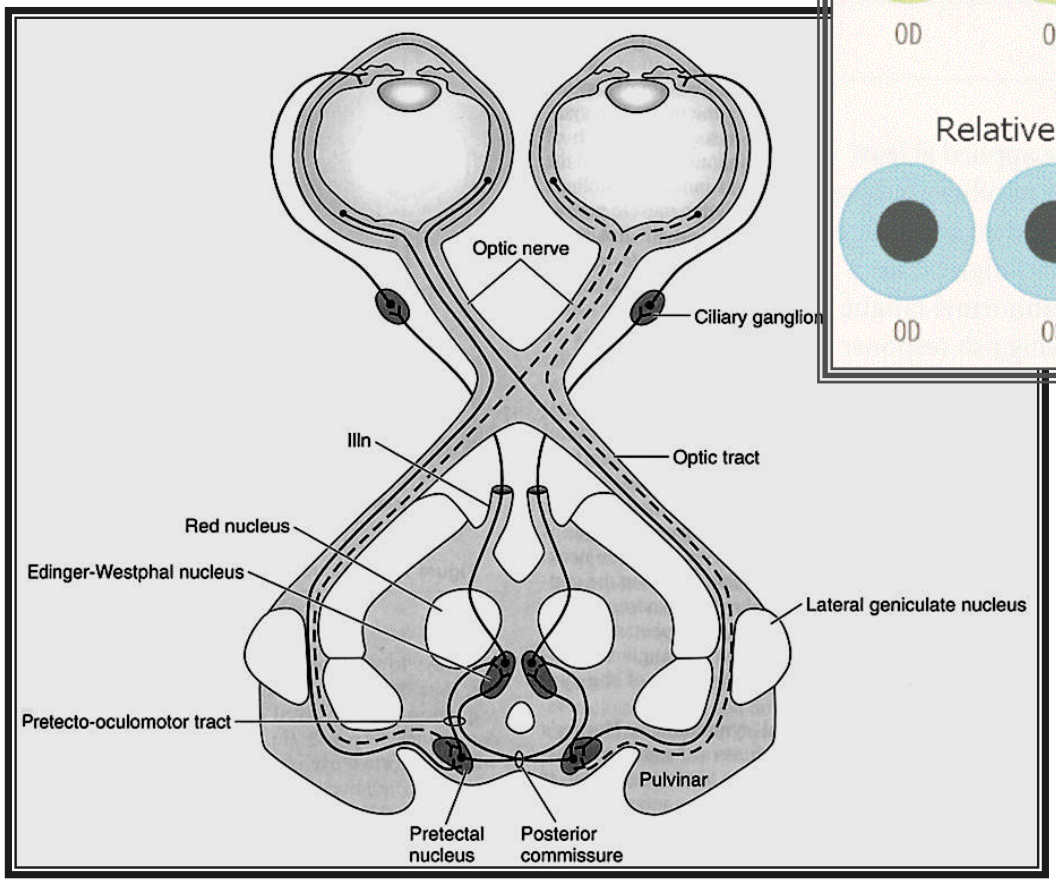


a) Sclerosi multipla

- Insorge nel 20-60 % dei soggetti che sviluppano SM
- Età: 3-4 decade
- Sesso: prevalente femminile
- Dolore <90% : non correlato alla SM
- Deficit visivo unilaterale
- Durata 7-10 giorni
- Non legato alla razza o al luogo di nascita
- NO normale o poco congesto
- Difetti CV
- BT 101 (tipizzazione linfocitaria) dal 34 al 70 % dei casi
- IgG oligoclonale nel LCS
- Sintomo di Uhthoff
- PEV aumento latenza P100

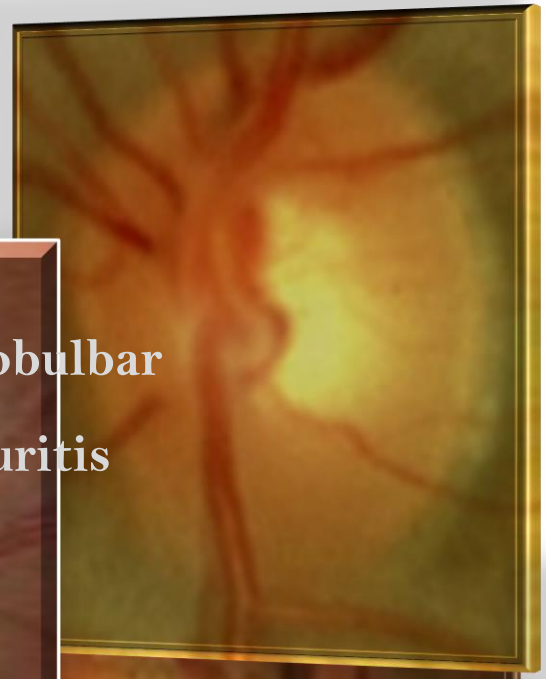
Pupille

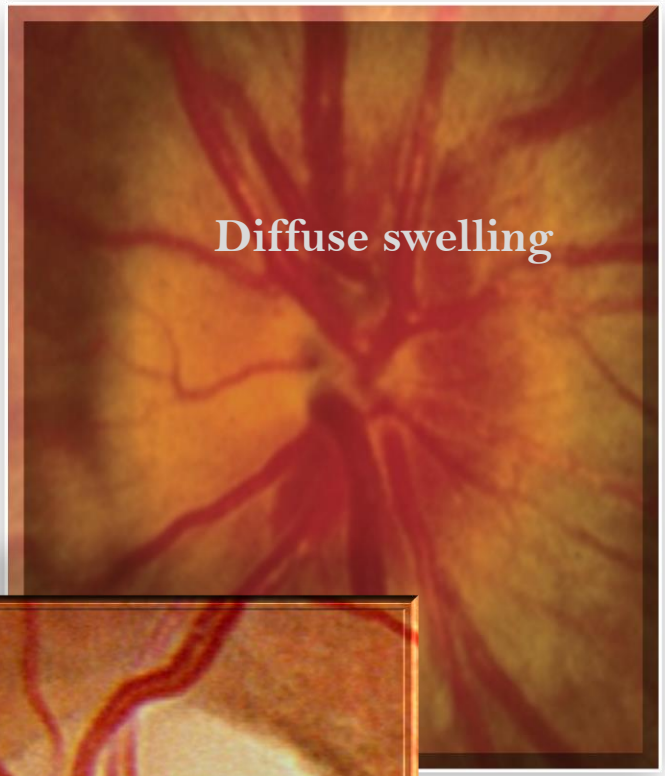




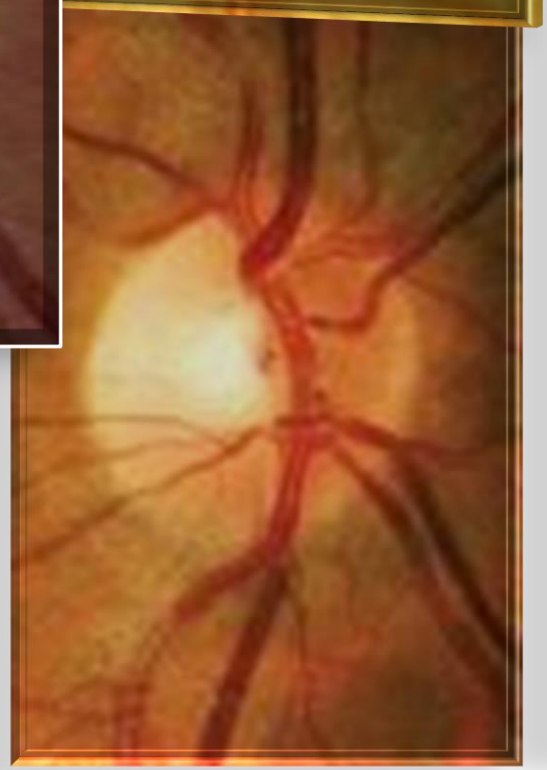
APD + deficit visivo acuto= Neurite Ottica

Retrobulbar neuritis

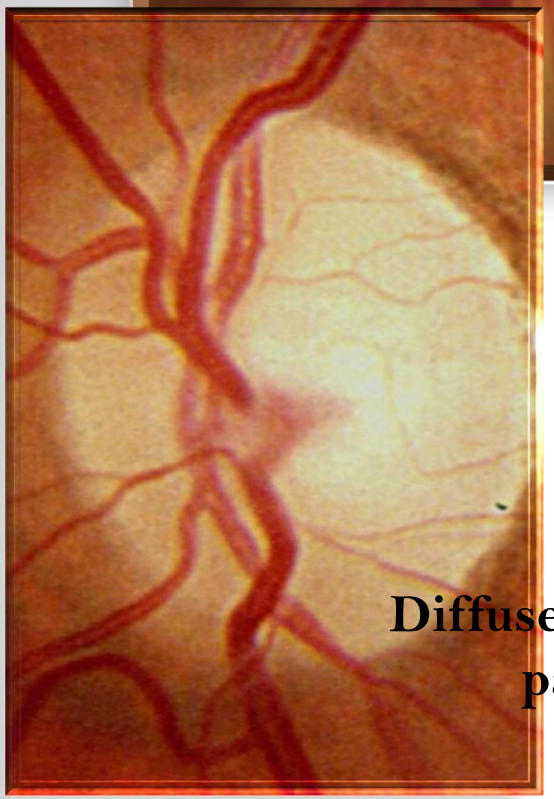




Diffuse swelling



Temporal Pallor



Diffuse neurorim pallor

OCT NMSOD VS MULTIPLE SCLEROSIS

MULTIPLE SCLEROSIS JOURNAL | MSJ

Topical Review

Neuromyelitis optica and multiple sclerosis: Seeing differences through optical coherence tomography

JL Bennett, J de Seze, M Lana-Peixoto, J Palace, A Waldman, S Schippling, S Tenembaum, B Banwell, B Greenberg, M Levy, K Fujihara, KH Chan, HJ Kim, N Asgari, DK Sato, A Saiz, J Wuerfel, H Zimmermann, A Green, P Villoslada and F Paul with the GJCF-ICC&BR[a]

Abstract: Neuromyelitis optica (NMO) is an inflammatory autoimmune disease of the central nervous system that preferentially targets the optic nerves and spinal cord. The clinical presentation may suggest multiple sclerosis (MS), but a highly specific serum autoantibody against the astrocytic water channel aquaporin-4 present in up to 80% of NMO patients enables distinction from MS. Optic neuritis may occur in either condition resulting in neuro-anatomical retinal changes. Optical coherence tomography (OCT) has become a useful tool for analyzing retinal damage both in MS and NMO. Numerous studies showed that optic neuritis in NMO typically results in more severe retinal nerve fiber layer (RNFL) and ganglion cell layer thinning and more frequent development of microcystic macular edema than in MS. Furthermore, while patients' RNFL thinning also occurs in the absence of optic neuritis in MS, subclinical damage seems to be rare in NMO. Thus, OCT might be useful in differentiating NMO from MS and serve as an outcome parameter in clinical studies.

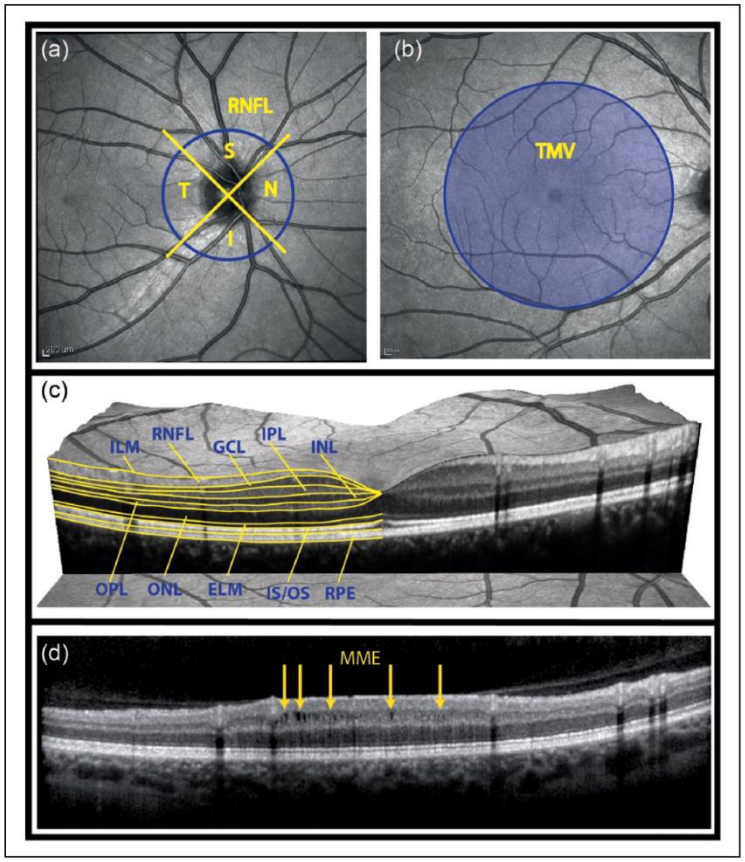


Figure 1. Retinal parameters acquired by OCT.
(a) Fundus image showing the acquisition of the peripapillary RNFL thickness. OCT records a ring scan of 3.4 mm diameter around the optic nerve head, which is divided into quadrants. (b) The total macular volume is derived from a volume scan and contains all retinal layers in a 6 mm diameter cylinder around the fovea centralis. (c) Intra-retinal layer segmentation in a spectral domain OCT image. (d) MME in a patient with optic neuritis. MME locations are marked by yellow arrows.
OCT: optical coherence tomography; RNFL: retinal nerve fiber layer; S: superior; N: nasal; I: inferior; T: temporal; TMV: total macular volume; GCL; ganglion cell layer; IPL: inner plexiform layer; INL: inner nuclear layer; OPL: outer plexiform layer; ONL: outer nuclear layer; ELM: external limiting membrane; IS/OS: inner segments/outer segments of the photoreceptor layer; RPE: retinal pigment epithelium; MME: microcystic macular edema.

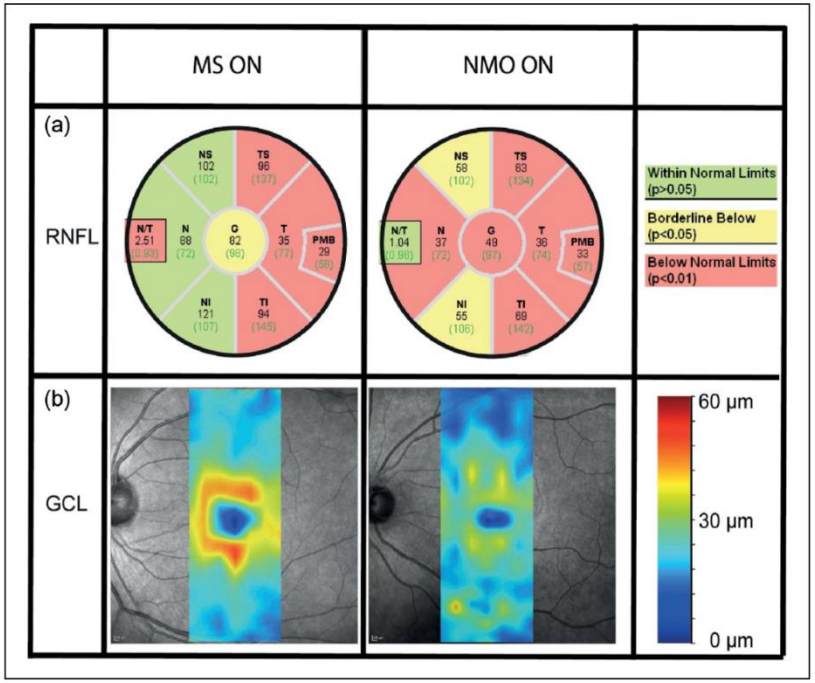
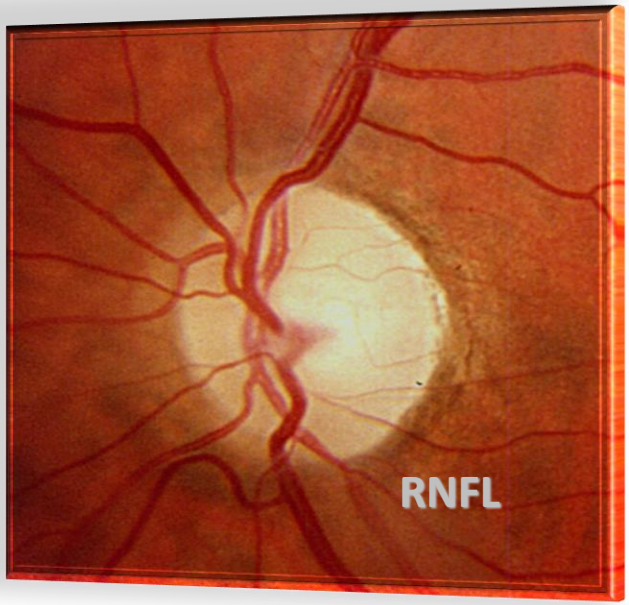
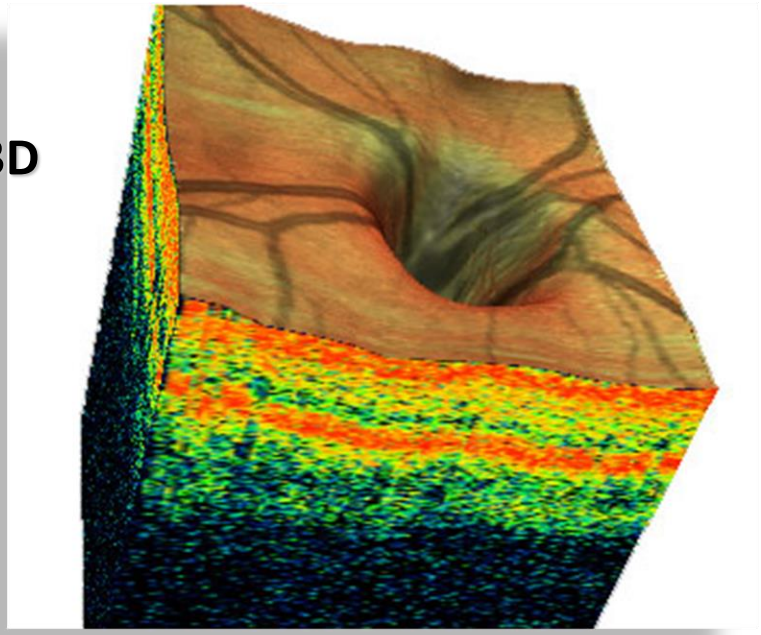


Figure 2. Typical differences in retinal damage between NMO-ON and MS-ON.
(a) RNFL thickness values for different locations of the peripapillary ring scans including comparison to a healthy reference group. (b) Thickness map of the retinal GCL, derived with help of a semiautomatic segmentation software. The NMO-ON patient shows more severe thinning both in the RNFL and GCL.
MS: multiple sclerosis; ON: optic neuritis; NMO: neuromyelitis optica; RNFL: retinal nerve fiber layer; GCL: ganglion cell layer.



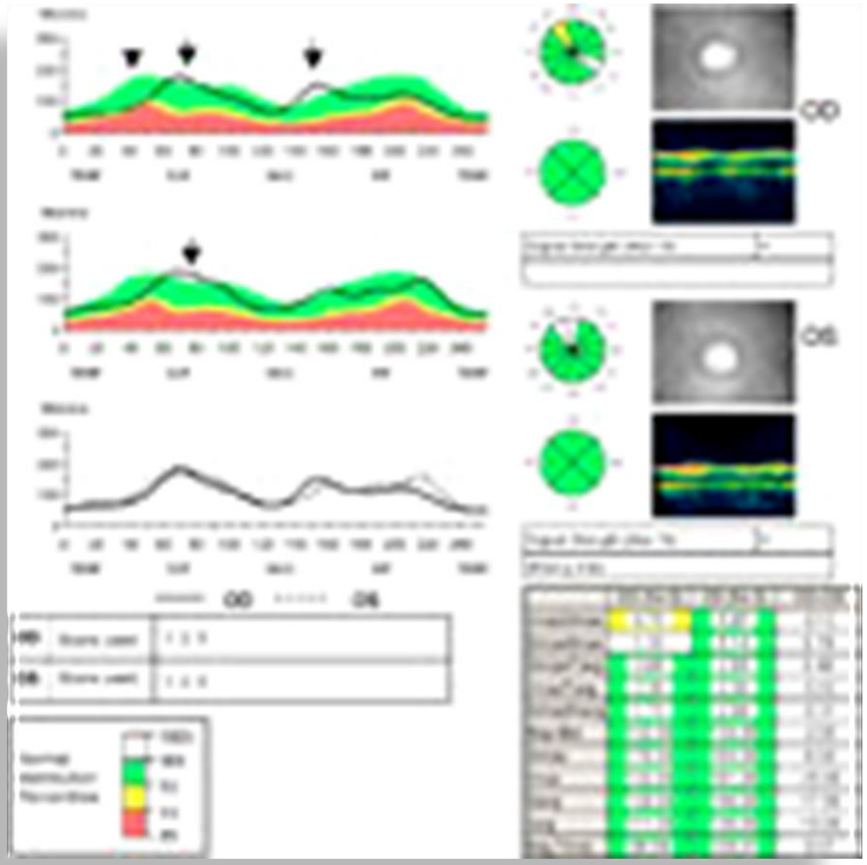


Ocular Coherence Tomography

Retinal Nerve Fiber Layer Thickness

Surrogate Marker of Neurodegeneration

AP Handerson& DH Miller Brain 2008



Section Editor: Fiona Costello, MD, FRCP(C)

From the Section Editor: The next two installments in the JNO "Disease of the Year: Multiple Sclerosis" series focus on lessons that can be learned form the afferent visual pathway, as a putative model of MS. In their article entitled, "Visual evoked potentials as a biomarker in multiple sclerosis and associated optic neuritis" Leocani and colleagues highlight the role of visual evoked potential (VEP) testing as a means of capturing the effects of demyelination, remyelination, and associated neuroaxonal injury in the central nervous system (CNS). Conjointly, Horton and Bennett discuss the acute management of optic neuritis, which is aptly described as an "evolving paradigm." In their state-of-the art overview of the topic, these authors explore the spectrum of inflammatory optic neuropathies, with emphasis on clinical features, neuroimaging findings, and serological markers that help refine diagnosis, and target appropriate treatment strategies. When considered holistically, these reviews prompt us to consider how VEP and other surrogate endpoints can be used to differentiate subtypes of optic neuritis that may ultimately herald a wide variety of CNS inflammatory disorders.

Visual Evoked Potentials as a Biomarker in Multiple Sclerosis and Associated Optic Neuritis

Letizia Leocani, MD, Simone Guerrieri, MD, Giancarlo Comi, MD

OCT - VEP INDEX

SCIENTIFIC REPORTS

OPEN

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In vivo structural and functional assessment of optic nerve damage in neuromyelitis optica spectrum disorders and multiple sclerosis

Marco Vabanesi[1,2], Marco Pisa[1,2], Simone Guerrieri[1,2], Lucia Moiola[2], Marta Radaelli[2], Stefania Medaglini[2], Vittorio Martinelli[2], Giancarlo Comi[1,2] & Letizia Leocani[1,2]

Early detection of neuromyelitis optica spectrum disorders (NMOSD), especially after optic neuritis, a presenting manifestation commonly observed also in multiple sclerosis (MS), is crucial for timely treatment and prognosis. Integrated visual pathway assessment with optical coherence tomography (OCT) and visual evoked potentials (VEP) may help in this task, showing *in vivo* different pathophysiological backgrounds. We evaluated combined VEP and OCT in a cross-sectional, single-centre study assessing 50 consecutive NMOSD patients, 57 MS patients and 52 healthy controls. After optic neuritis, VEP were more frequently absent in NMOSD compared to MS; most NMOSD eyes with recordable VEP showed prolonged latency, but extreme latency delays were less common than in MS. OCT showed predominantly axonal involvement in NMOSD, with 88% eyes (95% CI: 69–97%) displaying retinal nerve fibre layer thickness $<60\,\mu m$ even after first optic neuritis episode. Accuracy of OCT was further enhanced by combination with VEP into a new Z-score derived OCT-VEP index, measuring prevalence of axonal damage or demyelination. Our results suggest that integrated optic nerve assessment may elucidate differences in optic neuritis pathophysiology; conduction slowing with relatively preserved nerve fibre layer suggests MS, while severe neuroaxonal loss after optic neuritis, often hindering VEP response, characterizes NMOSD.

OCT - VEP INDEX

La accuratezza di OCT è stato ulteriormente migliorata dalla combinazione con VEP in un nuovo indice Z score OCT-VEP capace di misurare la prevalenza di danno assonale o demielinizzazione.
I nostri risultati suggeriscono che la la valutazione integrata del nervo ottico può chiarire le differenze nella fisiopatologia della neurite ottica; un rallentamento della conduzione con uno strato di fibre nervose relativamente conservato suggerisce la SM, mentre una grave perdita neuroassonale dopo neurite ottica, che spesso ostacola la risposta VEP, caratterizza NMOSD

Leocani 2019 Scientific reports

RMN

E' il miglior esame prognostico per l'evoluzione in MS

1) **NO Isolate & RMN normale=25% rischio MS a 15Y**
2) **NO&3 o più lesioni alla RMN=78% rischio MS a 15Y**

Recupero Visivo

- Pallore temporale
- Riduzione del senso luminoso
- Ridotta sensibilità al contrasto
- Discromatopsia (R/G)
- Fenomeno di Uthoff
- Fenomeno di Pulfrich Illusione visiva di movimento (pendolare-ellittico)
- Rischio di ricorrenza 28% a 5 anni; 35% at 10 anni

Condizioni associate alla NORB

b) Neuromielite ottica (malattia di Devic)

- NORB bilaterale associata a mielite trasversa
- Ambo i sessi, a tutte le età
- Rigonfiamento modesto del disco ottico
- Grave compromissione visiva
- LCS: pleocitosi, cellule polimorfonucleate, aumento della concentrazione proteica

c) encefalite periassiale diffusa (Malattia di Schilder)

d) Malattie dei seni (sfenoidale ed etmoidale

e) Encelfalomieliti acute

f) Malattia di Creutzfeld-Jakob

g) Sindrome di Guillain-Barrè

NEURITE OTTICA RETROBULBARE (NORB)

Terapia:

Scopo di accelerare il recupero ma non l'entità

- **1-3 giorni:** Metilprednisolone1-2d/die ev in 3-4 somministrazioni
- **4-15 giorni:** prednisone 1mg/Kg/die
- riduzione del prednisone del 10% ogni settimana successiva
- Controllo: glicemia, pressione arteriosa
- Associare: gastroprotettori

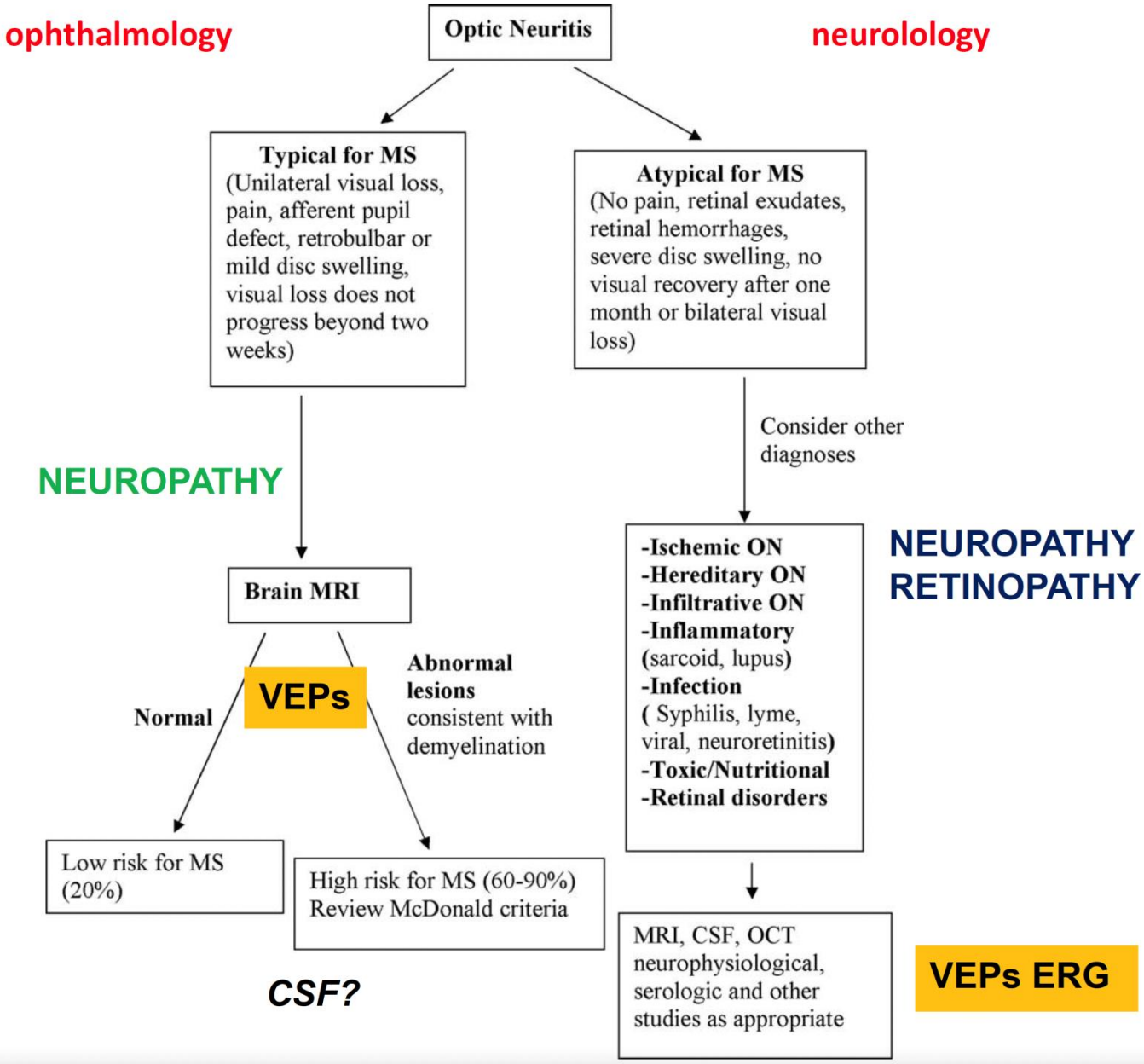
ATYPICAL OPTIC NEURITIS

	Typical	Atypical
Age	Young adult	Age >50 years or <12 years
Ethnic origin	White	African, Asian, or Polynesian descent
Laterality	Unilateral symptoms	Bilateral simultaneous or rapidly sequential
Pain	Mild periocular pain; worse on eye movement	Severe periocular pain waking patient from sleep, painless visual loss, pain persisting longer than 2 weeks
Vision	Mild to moderated uniocular visual loss followed by spontaneous improvement	Severe visual loss (worse than 6/60 or 20/200), no recovery starting within 3 weeks of onset, progression of visual loss for more than 2 weeks
Appearance	Normal or swollen optic disc	Severe optic disc swelling, macular star (neuroretinitis), optic disc haemorrhages, anterior—posterior segment inflammation, marked retinal exudates
Other	Uhthoff's phenomenon, Pulfrich effect, previous self-limiting neurological episodes	Family history, neoplastic history

WORK-UP: blood test for syphilis, sarcoidosis, Bartonella henselae, Lyme disease, HIV, CRP, ESR, ANA, ANCA, vitamin B12, folate, AQP4 and MOG, LHON

INFLAMMATORY OPTIC NEUROPATHY

- **Subacute, painful loss of central vision** (variable degrees) that may progress for 7-10 days
- **Pain** exacerbated by eye movements
- **Colour vision abnormalities** usually more prominent than visual acuity loss
- **Prominent RAPD** in the affected eye
- Optic nerve **normal in retrobulbar optic neuritis/swollen in papillitis**
- Leakage of fluorescein at FAG for papillitis


ophthalmology
Optic Neuritis
neurolology
Typical for MS
(Unilateral visual loss, pain, afferent pupil defect, retrobulbar or mild disc swelling, visual loss does not progress beyond two weeks)
Atypical for MS
(No pain, retinal exudates, retinal hemorrhages, severe disc swelling, no visual recovery after one month or bilateral visual loss)
NEUROPATHY
Consider other diagnoses
Brain MRI
Normal
VEPs
Abnormal lesions consistent with demyelination
Low risk for MS (20%)
High risk for MS (60-90%) Review McDonald criteria
CSF?
-Ischemic ON
-Hereditary ON
-Infiltrative ON
-Inflammatory (sarcoid, lupus)
-Infection (Syphilis, lyme, viral, neuroretinitis)
-Toxic/Nutritional
-Retinal disorders
NEUROPATHY
RETINOPATHY
MRI, CSF, OCT neurophysiological, serologic and other studies as appropriate
VEPs ERG

Case Reports in Ophthalmology

Case Rep Ophthalmol 2019;10:349–356

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Published online: October 23, 2019

Case Report

Three Cases of Creutzfeldt-Jakob Disease with Visual Disturbances as Initial Manifestation

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Yoshihito Sakanishi[a] Atsushi Mizota[b] Nobuyuki Ebihara[a]

[a]Department of Ophthalmology, Urayasu Hospital, Juntendo University, Chiba, Japan;
[b]Department of Ophthalmology, Teikyo University, Tokyo, Japan

Table 1. Summarized data of the Heidenhain variant of 3 CJD cases

	Case 1	Case 2	Case 3
Sex and age	male, 61 years	male, 65 years	male, 77 years
Initial visual symptom	progressively blurred vision and visual field defect (left homonymous hemianopia)	blurred vision and visual field defect (central sensitivity down in both eyes)	progressively blurred vision and visual field defect (right homonymous hemianopia)
Initial visual acuity	20/40 OD 20/25 OS	20/40 OD 20/40 OS	20/600 OD 20/400 OS
Time of referring to neurology from onset of visual symptoms	5 weeks	4 weeks	5 weeks
DWI findings	high signal intensity in the cortex and occipital lobes on the right side	high signal intensity in the right temporal lobes and the parietal lobe	high signal intensity in the cortex and occipital lobes bilaterally
Time to onset of neurological symptoms from onset			
Progressive dementia	5 weeks	4 weeks	5 weeks
Myoclonus	5 weeks	5 weeks	5 weeks
Pyramidal symptom	6 weeks	5 weeks	6 weeks
Extrapyramidal symptom	6 weeks	5 weeks	6 weeks
Cerebellar symptom	5 weeks	5 weeks	5 weeks
Akinetic mutism	6 weeks	5 weeks	5 weeks
Memory disturbance	5 weeks	4 weeks	5 weeks
Mental/intellectual impairment	6 weeks	4 weeks	5 weeks
CSF (14-3-3/tau)	+/+	+/+	+/+
EEG	PSD	PSD	PSD
ERG	reduced b-wave	inoperative	inoperative

CJD, Creutzfeldt-Jakob disease; CSF, cerebrospinal fluid; DWI, diffusion-weighted magnetic resonance imaging; EEG, electroencephalography; ERG, electroretinogram; PSD, periodic synchronous discharge.

Case Reports in
Ophthalmology

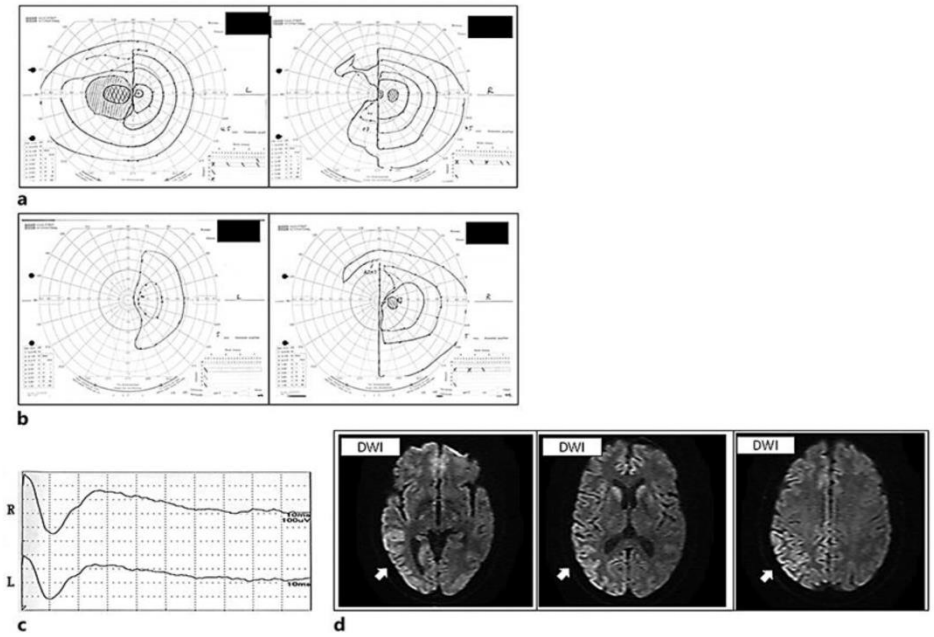


Fig. 1. **a–d** Goldmann visual field tests. Dark-adapted bright flash ERGs and DWI in case 1. **a** The visual field at the first examination was left homonymous hemianopia. **b** The visual acuity and visual field defect has worsened on the next medical examination after 2 weeks. **c** The b-wave amplitude of ERG was reduced. **d** The DWI showed high signal intensity in the cortex and occipital lobes on the right side (arrows). DWI, diffusion-weighted magnetic resonance imaging; ERG, electroretinogram.

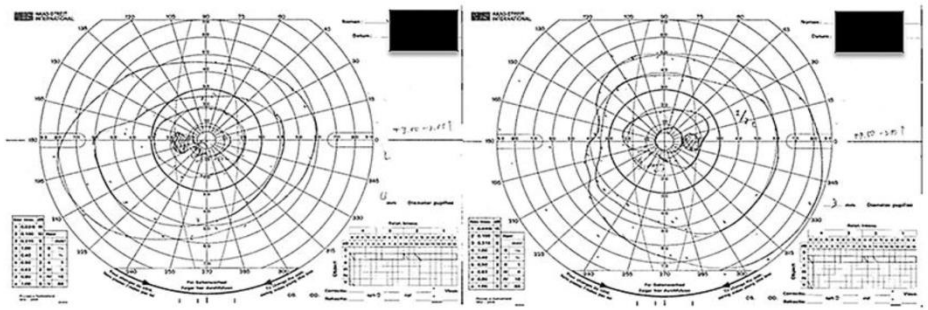


Fig. 2. Goldmann visual field test in case 2. The central sensitivity of visual fields was slightly depressed in both eyes.

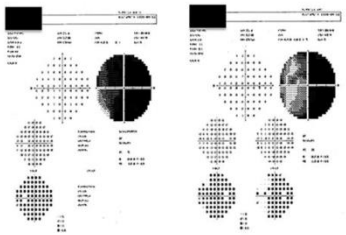


Fig. 3. Humphrey visual field test in case 3. The visual field testing showed right homonymous hemianopia, and the right eye was especially poor.

LHON

Leber's Hereditary Optic Neuropathy (LHON)

- **Maternally inherited**: over 90% of cases carry a **mtDNA** point mutation affecting complex I at nps 11778/ND4 (Wallace et al. 1988), 3460/ND1, and 14484/ND6
- **Male prevalence** (M: F=4:1), higher for 14484/ND6 mutation
- **Variable penetrance** despite most LHON maternal lineages are homoplasmic mutant (risk of being affected around 50% in males and 10% in females)

- **Acute/subacute central vision** loss (papillomacular bundle) in young/adults

- **Retinal ganglion cell death** (tissue specificity)

LHON

2) Acute stage:

- **Acute/subacute central vision loss PAINLESS** at eye movements, **bilateral at onset in 25-50%** of cases associated with central scotoma
- In **unilateral presentation** the second eye becomes affected usually in 6-8 weeks (max within 1 year), even though rare unilateral cases are reported
- Visual loss progression in the first weeks with **nadir usually reached in 4-6 weeks**

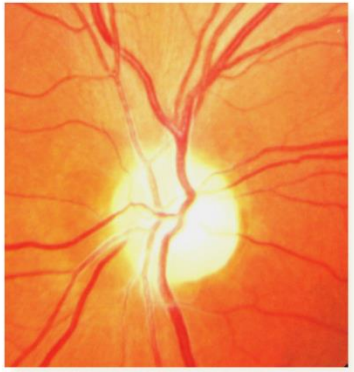
- **Fundus oculi** can show **teleangectasias, microangiopathy and retinal nerve fiber swelling (PSEUDOEDEMA)** **but in 20% of cases is normal**

- At difference with inflammatory papillitis **FAG is normal** (**no fluorescein leakage**)
- **Brain MRI is usually normal** except for in rare cases optic nerve hyperintensity
- **Peak of disease onset between 15 and 30 years** even though very early and late cases are reported

LHON

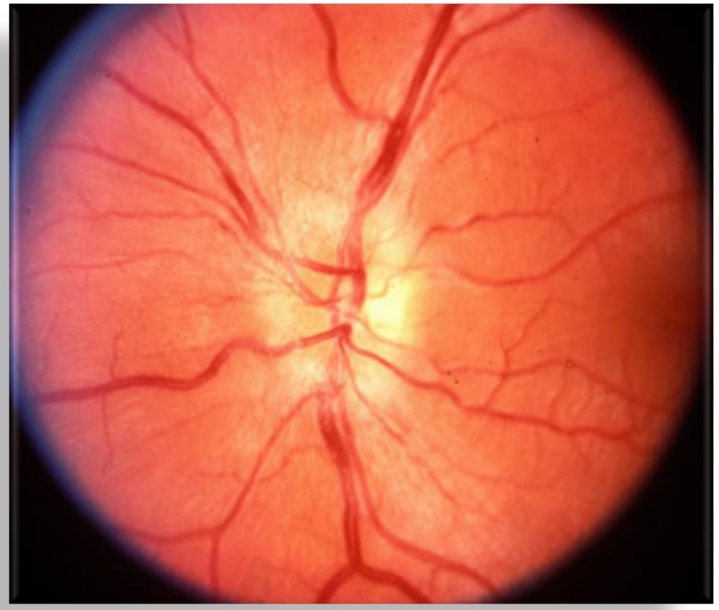
3) Chronic stage:

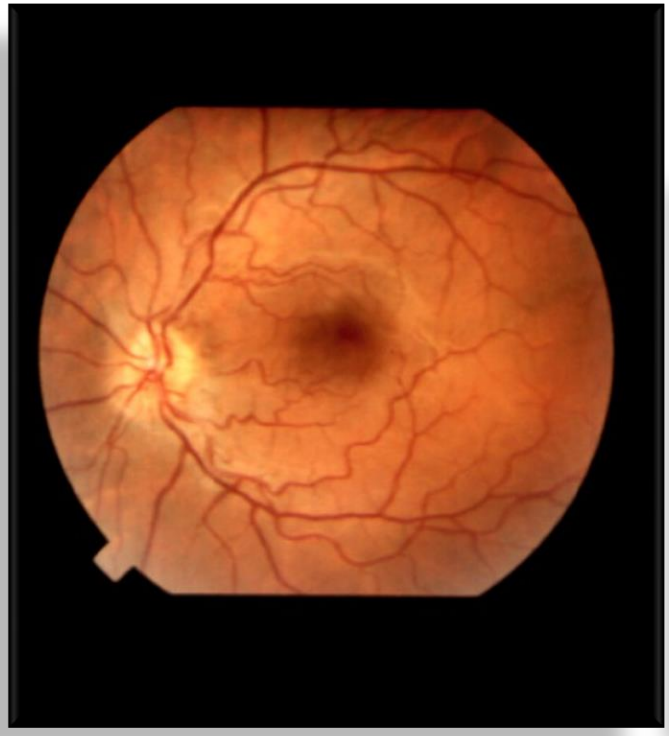
- In about **6 weeks <u>optic nerve pallor is evident</u>**, starting from the temporal sector
- In **<u>advanced stages the presence of optic disc cupping is possible (d.d. with glaucoma)</u>**
- **<u>Visual fields</u>** show enlargement of the central defect to a generalized defect
- **<u>Partial visual recovery possible</u>** in some cases with higher probability with the 14484/ND6 (60-80%), lower for 11778/ND4 and 3460/ND1 mutations (20%, usually after the 1st year of the disease but also late recovery possible

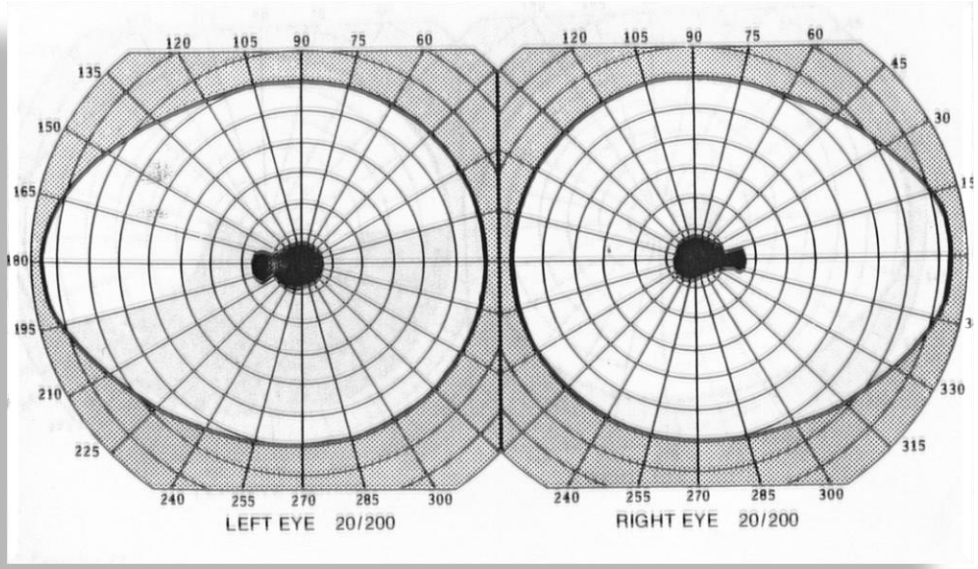


- ***<u>Positive prognostic factors:</u>***
  - *Age before 20 years*
  - *Big optic disc size*
  - *14484/ND6 mutation*

LHON



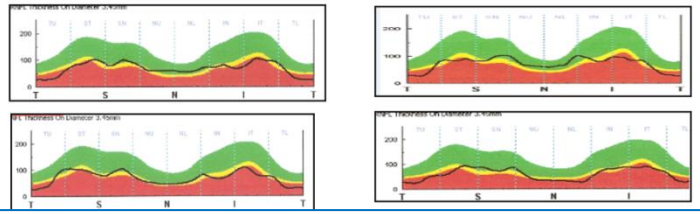



120 105 90 75 60
135
150
165
180
195
210
225
240 255 270 285 300
LEFT EYE 20/200
120 105 90 75 60
45
30
330
315
240 255 270 285 300
RIGHT EYE 20/200

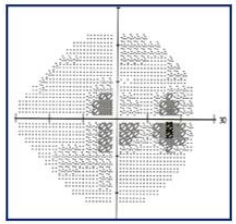
Neuropatie Ottiche Ereditarie

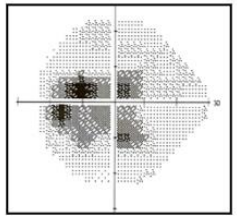
Neuropatia ottica di Leber

• Riduzione dello spessore delle fibre nervose peripapillari



• Scotoma centrale e paracentrale





LHON

When suspect LHON:

- **Bilateral Acute/subacute visual loss without pain**
- Brain MRI negative for demyelinating lesions
- Absence of leakage at FAG
- **In the acute phase evidence at fundus oculi of microangiopathy, optic disc hyperemia and pseudodema**
- **Maintenance of the PLR**
- **Absence of recovery after steroid therapy**
- **Family history positive for acute visual loss along the maternal line**

What to do:

- **Search for the most common mtDNA LHON mutations (LHON 11778/ND4, 3460/ND1 and 14484/ND6**
- If negative and the clinical suspicion is high send the 24-hr urine for the **complete mtDNA sequence** looking for rare mtDNA mutations

CONCLUSIONI

"Riduzione del visus in assenza di difetti refrattivi o patologie del segmento anteriore o della retina"

- Anamnesi/ età/ sesso
- Esame del fondo: NOIA/NORB
- Esame di: riflessi pupillari, CV, Senso Cromatico, ERG, PEV, PERG
- RM, TAC, esame neurologico,
- esame del LCS
- Terapia immediata

CONCLUSIONI

GDS di Neuroftalmologia della SIN

Per aderire

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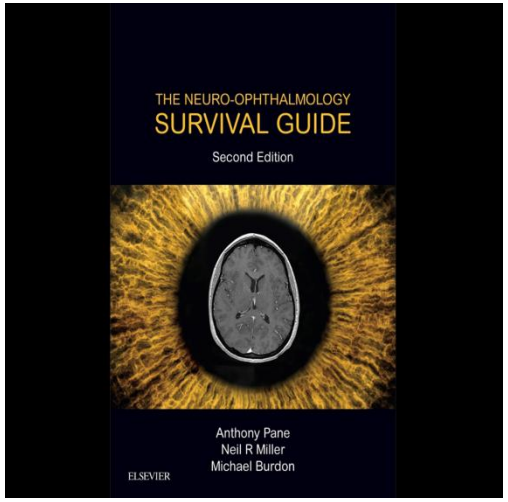
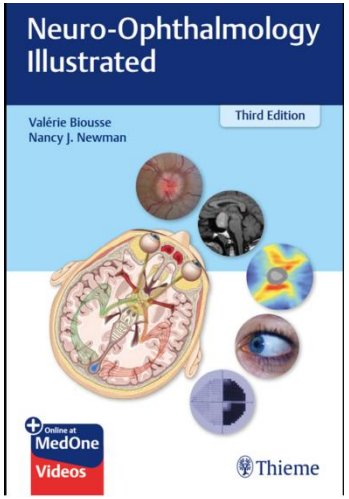
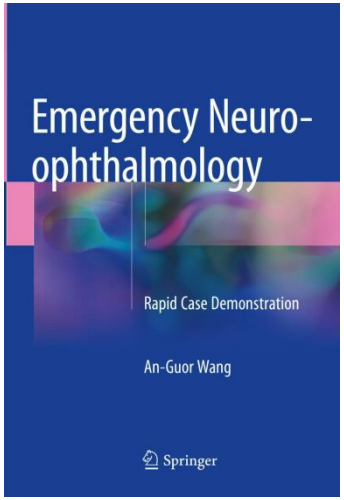
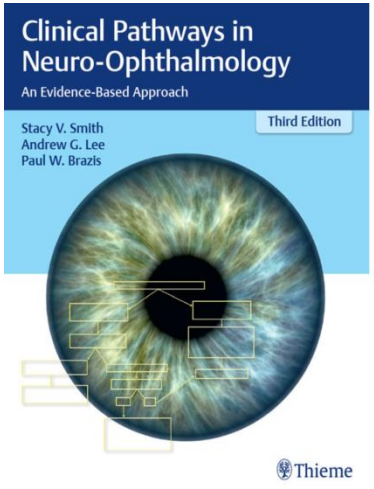








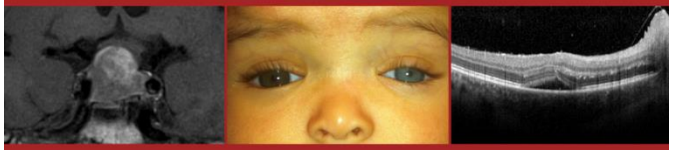
Third Edition

Enhanced DIGITAL VERSION Included. Details inside.

LIU, VOLPE, AND GALETTA'S

NEURO-OPHTHALMOLOGY

DIAGNOSIS AND MANAGEMENT



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