EUPO

European University Professors of Ophthalmology

Neuro-ophthalmology - Strabismus

25 years EUPO

Leuven, Belgium

June 29 - 30

www.eupo.eu

2012

The sequence of the EUPO courses

2012	Leuven	Neuro-ophthalmology - Strabismus
2011	Geneva (SOE)	Uveitis & Glaucoma
2010	Athens	Retina
2009	Amsterdam (SOE)	Cornea, Conjunctiva and Refractive surgery
2008	Geneva	Neuro-ophthalmology and strabismus
2007	Vienna (SOE)	Glaucoma and uveitis
2006	Ghent	Retina
2005	Berlin (SOE)	Cornea
2004	Nijmegen	Neuro-ophthalmology and strabismus
2003	Madrid (SOE)	Glaucoma and uveitis
2002	Erlangen	Retina
2001	Istanbul (SOE)	Cornea
2000	Leuven	Neuro-ophthalmology and strabismus
1999	Stockholm (SOE)	Glaucoma and uveitis
1998	Amsterdam (ICO)	Chorioretina
1997	Budapest (SOE)	Cornea, conjunctiva, lids, orbit
1996	Athens	Neuro-ophthalmology and strabismus
1995	Milano (SOE)	Uveitis, lens, glaucoma
1994	Montpellier	Retina
1993	Santiago de Compostella	The external eye
1992	Brussels (SOE)	Neuro-ophthalmology and strabismus
1991	Torino	Uveitis, lens, glaucoma
1990	Bonn	Chorioretina
1989	Leuven	The external eye and orbit
1988	Nijmegen	First EUPO course

Dear Colleague, Dear Friends,

I am very glad to welcome you to the EUPO 2012 (European University Professors in Ophthalmology) congress in Leuven from June 28 to June 30.

During the course, a highly esteemed faculty of national and international invited speakers will cover clinical topics in the field of **Neuro-ophthalmology and Strabismus**. I also want to thank the speakers for providing the course material, included in this course book.

The EUPO course takes place for the 25th time after the first organization in Nijmegen by Prof. Deutman. To celebrate this birthday, an academic session followed by a reception is organized on Thursday evening June 28 in the Hallen in the very city centre. This coming together of European colleagues in ophthalmology – younger and somewhat older – promises to be a remarkable event.

Please also note that the tradition of the EUPO party (on Friday evening) will be continued. This evening gives an informal and pleasant opportunity to meet with European residents in training, ophthalmologists and the course faculty of invited speakers in an atmosphere of good gastronomy.

With all these elements, I am convinced that this EUPO meeting has all opportunities for a scientific and social meeting of high standard. Let us hope for some nice sunny weather, which together with science and the typical local wining and dining, gives the guarantee of a memorable meeting in Leuven.

With my best personal regards,

Prof. Dr. Werner SPILEERS
Organizer EUPO 2012

available on **www.eupo.eu**

EUPO 2006
Retina

EUPO 2007
Uveitis

EUPO 2008
Neuro-Ophthalmology
and Strabismus

EUPO 2009
Cornea, Conjunctiva
and Refractive surgery

EUPO 2010
Retina

EUPO 2011
Uveitis and Glaucoma

EUPO 2012
Neuro-ophthalmology
and Strabismus

European University Professors of Ophthalmology

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PROGRAMME EUPO 2012 - Friday, June 29

Neuro-ophthalmology - Strabismus

Page

■ 08.00 - 09.00 Registration

■ 09.00 - 10.30 Session 1

10:30 Coffee break

■ 11.00 - 12.30 Session 2

12:30 Lunch break

■ 14.00 - 15.30 Session 3

14:00	7	Optic Neuropathy in Graves Orbitopathy *Antonella BOSCHI, Brussels*	67
14:30	8	Congenital optic nerve anomalies *Ingele CASTEELS, Leuven*	83
15:00	9	Inherited optic neuropathies *Marcela VOTRUBA, Cardiff*	107
15:30		Break	

■ 16.00 - 17.00 Session 4

16:00	10	Oculomotor palsies *Fion BREMNER, London*	111
16:30	11	Anisocoria *Aki KAWASAKI, Lausanne*	121
17:00		End of session	

17:30 Departure for EUPO Party, see page 10

PROGRAMME EUPO 2012 - Saturday, June 30

Neuro-ophthalmology - Strabismus

Page

■ 09.00 - 11.00 Session 5

11:00 Break

■ 11.30 - 13.00 Session 6

13:00 Lunch break

■ 14.00 - 16.00 Session 7

16:00 Closure

Welcome to the EUPO Party!

Venue: Jos Theys restaurant, Friday, June 29, 2012

You are a speaker or have registered to attend the EUPO Course 2012 in Leuven. The registration fee for the EUPO Course includes the EUPO Party.

Buses will take you from the Leuven University Hall directly to the party. Buses will leave at 17:30 and will return at 23:00.

The EUPO party will take place at the Jos Theys Restaurant, located in Holsbeek, at 10 km outside of Leuven.

A barbecue will be organized in this meet-and-eat farm where you will discover the taste of top quality beef and veal, and the class of an impressive wine cellar.

It will be an evening filled with food, drinks and music allowing the opportunity for social interaction and enjoyment between EUPO delegates, EUPO speakers and boardmembers.Don't forget to bring your ticket received upon registration.

Dress Code: Smart/Casual

Welcome!

Jos Theys Restaurant
Sluisbeekstraat 9
3220 Kortrijk-Dutsel (Holsbeek)
www.jostheys.be

About Leuven

Leuven is situated in the Dutch-speaking part of Belgium, at about 20 km east of Brussels. With a total population of 90.000 inhabitants, it could have been an ordinary little provincial town. Were it not that Leuven is known all over the world for its university (KULeuven), one of the oldest still existing catholic universities in the world, founded in 1425.

The city center looks like a very well preserved town with buildings from the 17th and 18th century. Unfortunately this is not due to a well organized protection but to a reconstruction of the old city. The center of Leuven was almost completely destroyed during the First World War and was carefully rebuilt afterwards.

Oude Markt

All through the year, the city of Leuven presents lively atmosphere because of the many students from all over Belgium. Especially in the evening, the many bars and students café, spread all over town, guarantee that there is always something happening. Very popular is the area around the 'Oude Markt' (Old Market).

Brewery

When brewing became a nationwide industry in the 19th century, Leuven became world famous for its beers, and today is still proud to be known as the beer capital of Belgium. Belgians will always associate the city of Leuven with one of the most famous and popular lager beer brands in Belgium: Stella Artois.

Fonske

"Fonske" is a statue near the centre of town. Its full name is Fons Sapientiae, Latin for "fountain of wisdom". The statue represents a university student who, while reading a book, lets wisdom flow into his head as liquid from a glass. Fonske is from time to time dressed in costumes appropriate for the occasion.

The town Hall

For those looking to find the most beautiful medieval building in the world: look no further! You will find it in the Belgian city of Leuven. The magnificent 15th century town hall of the city of Leuven alone is worth the trip.

University Library

The University Library on the Ladeuzeplein was a gift from the American people to Leuven after World War I during which the Germans burned down the original library, causing much outroar in the USA. Totem is a statue at the centre of the Ladeuzeplein; it is a work of the Belgian artist Jan Fabre. On a 23 meters high needle a giant jewel beetle shines against the clouds.

The Great Beguinage

The Great Beguinage is one of the world's best remaining examples of its architectural type. It was recognized by UNESCO as a World Heritage Site in 1998. It was founded in 1232 for ladies and girls from the city and the surrounding area. It was closed in 1796 by the French occupants, but shortly afterwards it was re-opened. By 1962, the original function had since long ended and the entire complex was bought by the university of Leuven. The old 16th and 17th century houses were transformed into modern flats for students and academic staff.

Museum M

Leuven is a creative and dynamic city also on a cultural level. There are several museums to visit, for instance the Museum M. The museum M maintains a number of exhibition spaces and a collection that grew historically.

Botanical Garden

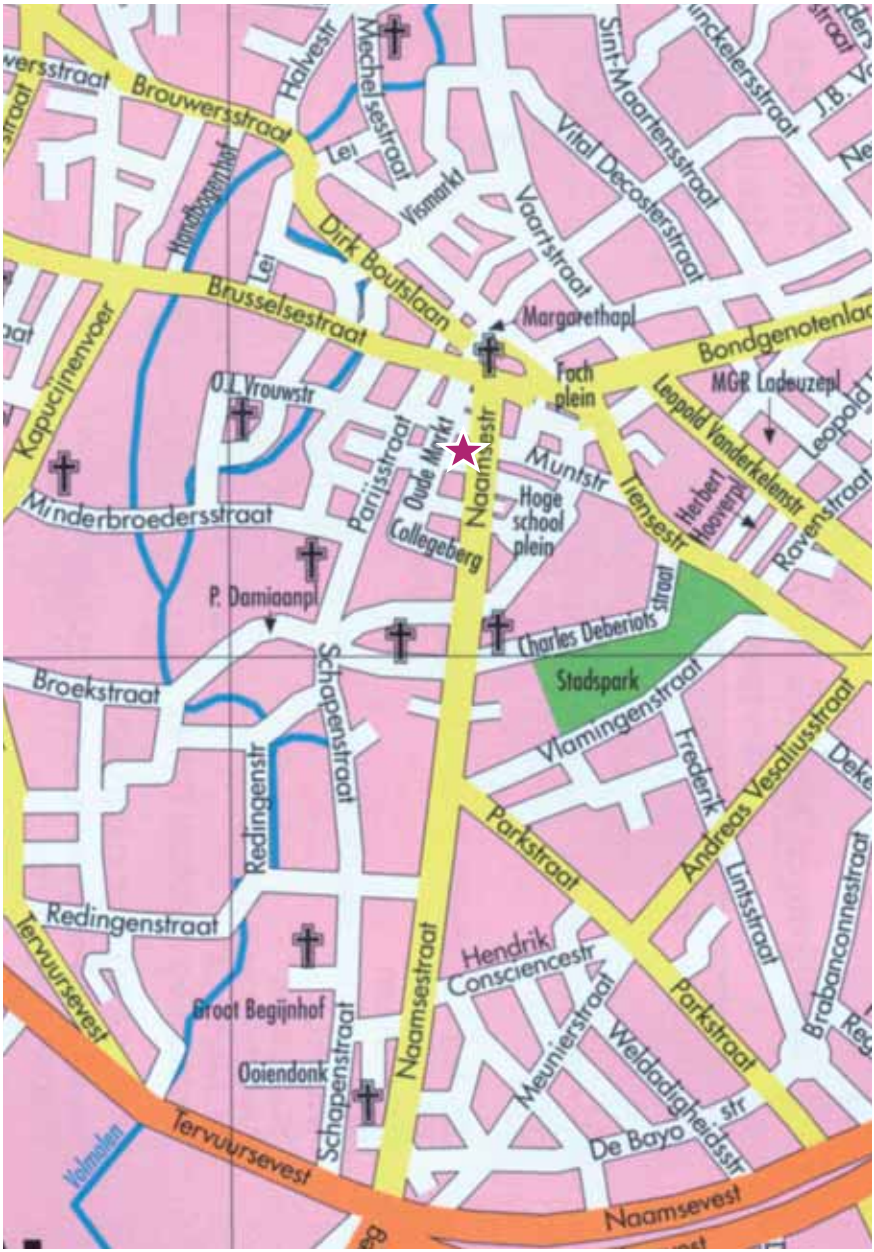
The herbal gardens of Leuven are the oldest in Belgium. The Leuven university created a first herbal garden in 1738 for its medical students. Besides the scientific and educational value of the plant collection, the visitors will enjoy the heavenly beauty of the place. In July and August the garden is the backdrop for "Summer in the Herbal garden", an outdoor exhibition with national and international works of art.

St. Peter's Church

Saint Peter's Church is the oldest church in Leuven. It was presumably founded in 986. The first church burnt down in 1176. A new Romanesque church was built with a crypt, an extension, at the back of the choir. The church is situated on the city's Grote Mark (Old Market)t, right across the ornate Town Hall. Built mainly in the 15th century in Brabantine Gothic style, the church has a cruciform floor plan and a low bell tower that has never been completed.

Map of Leuven

★ EUPO 2012 Venue



Railway station

1. The investigation of unexplained visual loss

- Werner SPILEERS, Leuven, Belgium

The investigation of unexplained visual loss

Werner SPILEERS
University Hospitals Leuven

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Neuro-ophthalmology

- Believe your clinical examination !

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The Neuro-Ophthalmic Examination

- Visual acuity, colour vision, …
- Pupillary function (and eyelid position)
- Ocular motility
- …
- *Visual electrophysiology: pVEP, fERG, …*
- Visual field testing
- *Neuro-imaging*

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Unexplained visual loss: optic neuropathy ?

- Challenge: diagnosis of visual loss when no structural abnormalities in the eye are apparent

- Concept: optical disturbances
  (refractive error, abnormalities of ocular media)

versus

neuroretinal disturbances
(retina, optic nerve,chiasm, optic tract, optic radiations, visual cortex)

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Unexplained visual loss

- If subnormal acuity:

  acuity tested at distance and at near
  perform (or repeat) a skilled refraction !

- BCVA

- If no further improvement can be obtained:

  perform potential acuity test

PINHOLE TEST

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Pinhole test

- Improves acuity if caused by optical factors

  uncorrected refractive errors
  (-5 D to +5 D)
  tear film abnormalities
  corneal abnormalities
  lenticular abnormalities

- Finds a clear optical path
- Use multiple holes (diam 1.5 mm)

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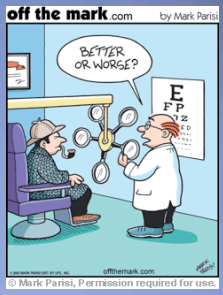
- We measure only: central resolution at high contrast:

VISUAL ACUITY



- One simple test does a pretty good job in detecting (most) visual dysfunction

TABLE 2. Visual Acuity in Different Notations

Visual Angle (min)	Snellen Fraction			Decimal Notation	logMAR
	Feet	Meters	NAS Standard		
0.5	20/10	6/3	4/2	2.0	−0.3
0.75	20/15	6/4.5	4/3	1.5	−0.1
1.0	20/20	6/6	4/4	1.0	0.0
1.25	20/25	6/7.5	4/5	0.8	0.1
1.5	20/30	6/9	4/6	0.7	0.2
2.0	20/40	6/12	4/8	0.5	0.3
2.5	20/50	6/15	4/10	0.4	0.4
3.0	20/60	6/18	4/12	0.3	0.5
4.0	20/80	6/24	4/16		0.6
5.0	20/100	6/30	4/20	0.2	0.7
6.0	20/120	6/36	4/24		0.8
8.0	20/150	6/45	4/32		0.9
10.0	20/200	6/60	4/40	0.1	1.0
20.0	20/400	6/120	4/80	0.05	1.3

Unexplained visual loss

- If acuity is **not** fully improved by pinhole test:

perform *swinging light pupil test*

relative afferent pupillary defect

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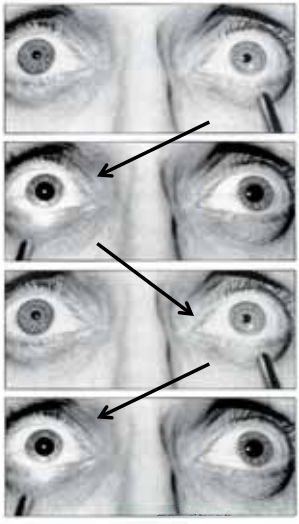

Fig. 13.7 This patient has a large afferent defect in the right eye. It is best demonstrated by alternating the light from eye to eye at a steady rate. The light should be kept just below the visual axis and one to two inches from each eye. Each eye should be illuminated for about 1 full second and then the light switched quickly to the other eye; this allows comparison of the initial direct contraction to light in each eye. If the examiner prefers to look for pupillary escape, the light should be held on each eye for 3 seconds and pupillary dilatation observed before switching to the other eye.

Relative afferent pupillary defect

- Reliable and sensitive indicator of asymmetrical **optic nerve dysfunction**
- Absence of RAPD should prompt reevaluation of a working diagnosis of optic neuropathy or consideration of bilateral involvement
- A relatively small lesion of the optic nerve results in a large RAPD

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Testing for RAPD

- Dim ambient lighting
- Patient fixates at distance; bright light source
- Move the light source rapidly when alternating

- Bilateral optic neuropathy may show no relative difference between the two eyes when both pupils are equally impaired
- A prominent RAPD is possible even in the presence of normal acuity
- RAPDs do not result in anisocoria

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Relative afferent pupillary defect

- A *retinal* lesion must be substantially larger: retinal artery occlusion; widespread chorioretinal lesions; retinal detachment:
  R/ eye fundus examination !
- *Chiasmal* lesion if fibers of optic nerves are involved asymmetrically
- *Optic tract* lesion: mild RAPD in contralateral eye (= eye with temporal field loss) due to more crossed fibers

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Relative afferent pupillary defect

- LGN, radiatio optica, cortical lesion: no RAPD
- An RAPD should never be attributed to media opacities only
- (amblyopia: only very mild RAPD possible, versus important acuity loss)
- NO RAPD in functional visual loss

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Optic nerve versus macular disease

- Clinical picture: Amsler chart, eye fundus, …
- Optical coherence tomography
- pVEP ?
- pERG ?
- Flash ERG ?

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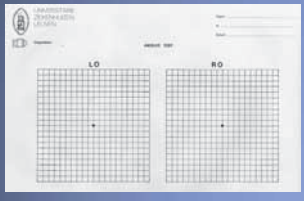
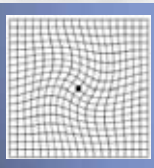
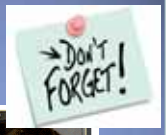
Amsler chart

- Metamorphopsia points to macular disease





Fundoscopy !



90 diopter lens, …

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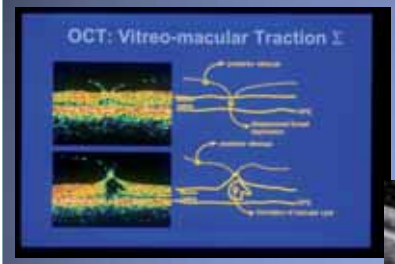
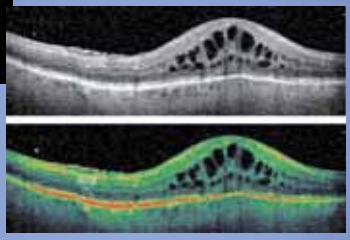
Optical coherence tomography





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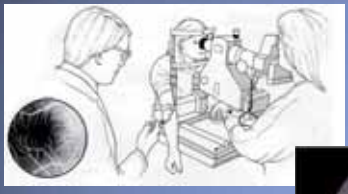
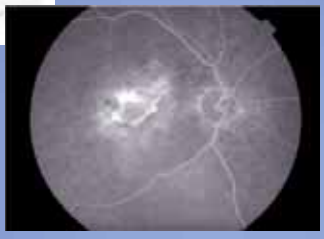
Fluorescein angiography





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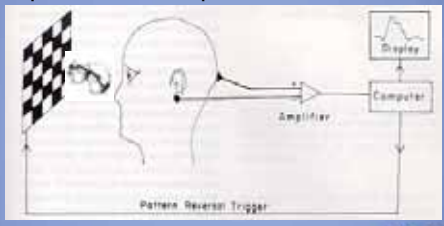
Pattern VEP

- Pattern reversal
- Low reversal rate
- High contrast checkerboard stimulus at different check sizes
- Use optimum optical correction !!
- Needs fixation and cooperation of the patient



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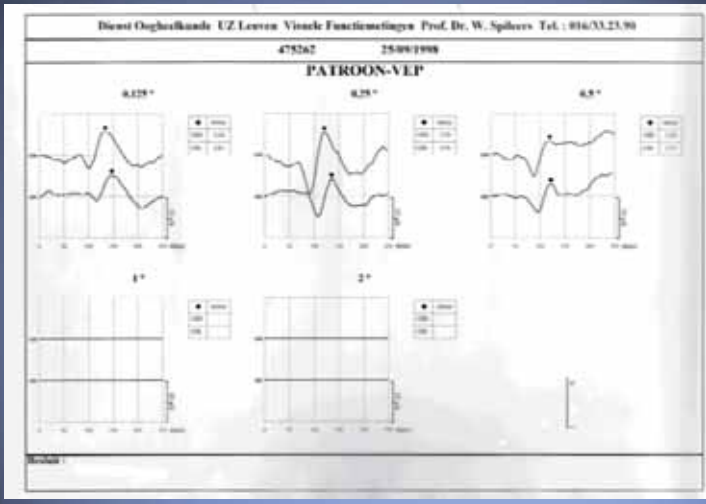

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Pattern VEP

- Investigates the functional integrity of the visual system
- Does NOT depict the localisation of the deficit
- Needs to be evaluated in conjunction with the full clinical picture

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Macular disease

Affects the VEP response !!

Optic nerve disease

Affects the VEP response

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Pattern ERG

- Small retinal response
- Technically demanding
- High contrast checkerboard
- Optical correction needed
- Active fixation
- Binocular recording

- **P50**: 2.5-5.0 microV
- **N95**: 3.5-6.5 microV

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If pVEP is abnormal

- PERG: P50 nl (and N95 reduced)

  optic nerve disease

- PERG: P50 reduced

  macular disease ?

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Flash - ERG

- mass retinal response
- photoreceptors, bipolar and Mueller cells contribute to the response
- rod and cone activity can be separated
- NO ganglion cell contribution

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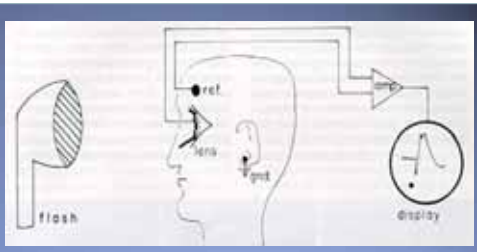

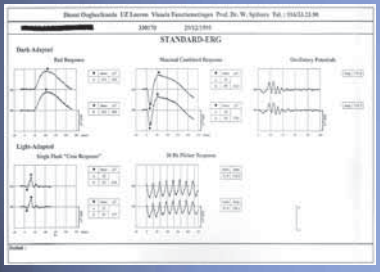

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Flash-ERG: optic nerve and ganglion cell disease

- *Normal* flash ERG

Flash-ERG: macular disease

- *Normal* flash ERG

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Unexplained visual loss

- If no full improvement with pinhole
- If **RAPD +:**

visual field examination

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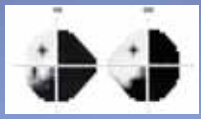
Visual field testing !!

- Of both eyes !!



- Localises the lesion ! ⟹ IMAGING of the ophthalmologist

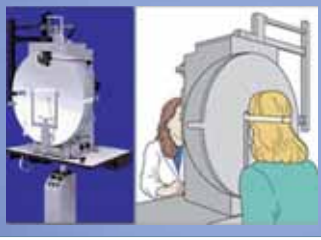


Figure 9.1. Schematic illustration of the visual pathway and visual field defects produced by lesions in various areas of the pathway. ON, optic nerve; CH, chiasm; OT, optic tract; LGB, lateral geniculate body; ML, Meyer's loop; OR, optic radiations.

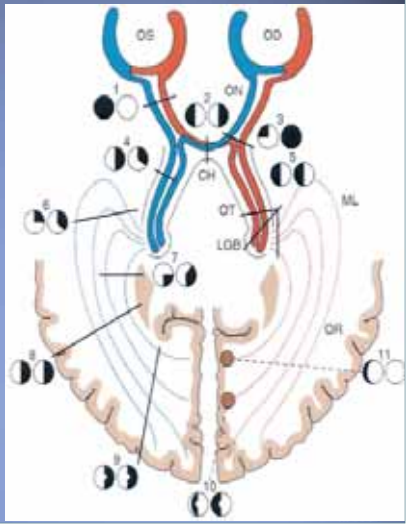
1. Compromise of the left optic nerve results in a central scotoma in the left eye, with a normal right visual field.

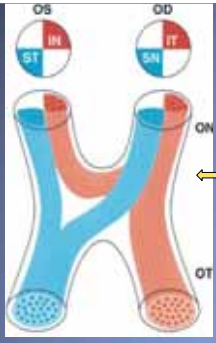
2. A lesion of the optic chiasm may cause a bitemporal hemianopia.

3. A lesion at the junction of the right optic nerve and the chiasm results in a central scotoma in the right eye and a superior visual field defect that respects the vertical meridian in the left eye. This effect results from compromise of the inferior nasal crossing fibers from the left eye, which extend into the prechiasmal portion of the right optic nerve (i.e., Wilbrand's knee). The resulting visual field defect is known as a junctional scotoma, which is localized at the junction of the optic nerve and chiasm.

4. Complete interruption of the optic tract produces a homonymous hemianopic field defect. Subtotal lesions produce highly incongruous homonymous hemianopias.

5. Complete interruption of the optic tract, lateral geniculate body, and optic radiations results in a total contralateral homonymous hemianopia.





⇦ ***Wilbrand's knee***

Figure 9.7. Schematic illustration of crossing fibers in the optic chiasm. The inferior nasal fibers from the left eye extend into the prechiasmal right optic nerve, forming **Wilbrand's knee**. ON, optic nerve; OT, optic tract; IN, inferior nasal; ST, superior temporal; IT, inferior temporal; SN, superior nasal. (Modified from Glaser JS. Anatomy of the visual sensory system. In: Tasman W, Jaeger EA, eds. Clinical ophthalmology, vol 2. 1994:4.)

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6. Fibers originating in the ipsilateral inferior temporal retina and the contralateral inferior nasal retina sweep anteriorly and laterally around the temporal horn (i.e., Meyer's loop) before transversing posteriorly. As a result, lesions of the temporal lobe characteristically produce superior, often incongruous homonymous quadrantanopias.

7. Parietal lobe lesions may interrupt visual pathway fibers from the superior retinas pursuing a more direct posterior course. This results in an inferior homonymous quadrantanopia.

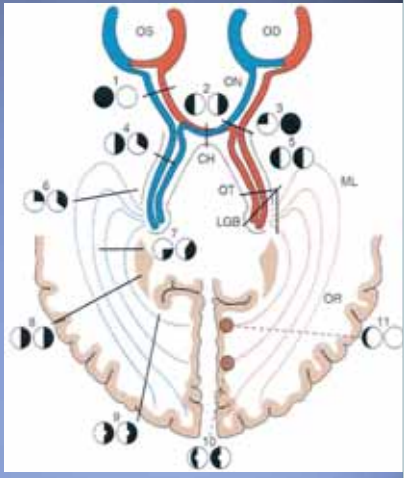
8. Complete interruption of the optic radiations results in contralateral total homonymous hemianopia.

9. Posterior occipital lobe lesions result in homonymous hemianopic defects, which may spare the macula. Subtotal occipital lesions produce exquisitely *congruous* visual field defects because the fibers are more highly segregated in the occipital area.

10. Lesions affecting the posterior portion of the occipital lobe may spare the more anteriorly placed unpaired crossing peripheral nasal retinal fibers, resulting in a preserved temporal crescent in an otherwise congruous homonymous hemianopia.

11. Focal lesions involving the anterior-most portion of the occipital lobe may affect the receptive area for the unpaired crossing fibers from the contralateral nasal retina, resulting in a unilateral peripheral temporal visual field defect.

(Modified from Harrington DO, Drake MV. The visual fields: Text and atlas of clinical perimetry. 6th ed. St. Louis: CV Mosby; 1990, with permission.)



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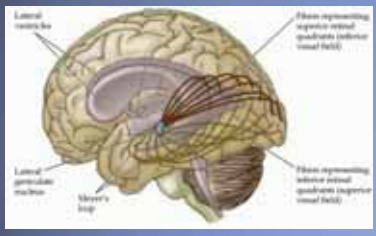
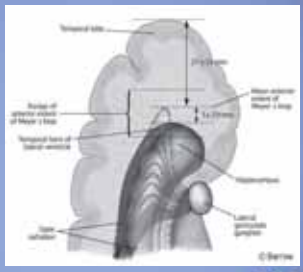
Meyer's loop in radiatio optica





Cfr Jager, 2005

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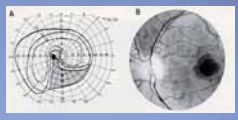
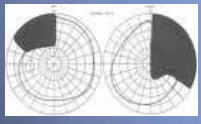
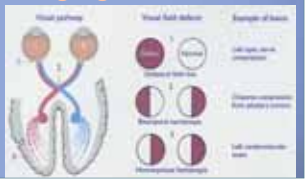
Visual field loss

non hemianopic defect (nerve fiber bundle configuration): prechiasmal lesion: (mass lesion very unlikely)



hemianopic defect: junction optic nerve and chiasm; chiasm, optic tract: compressive lesion is very probable: neuro-imaging !!

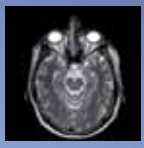




EUPO2012

Unexplained visual loss

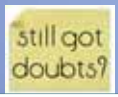
- Neuro-imaging !! MRI (or CT)



Information to neuroradiologist should include at least the expected location of the pathology and the suspected differential diagnosis

"*ORBITOBRAINOGRAM" ???:*
inappropriate images are worse than no images at all !!

CT: nl



Non-organic visual loss

- ***Functional visual loss***; malingering, hysteria, …
- Malingering: … willful alteration of subjective symptoms and responses on examination …
- Hysteria: …may be considered in patients who are not clearly seeking secondary gain …

EUPO2012

Clinical presentation

- !! As many as half of the patients with functional visual loss have this superimposed upon organic pathology !!

EUPO2012

Functional visual loss ??

- Diagnosis per exclusionem !
  High degree of suspicion is needed
- Follow-up is frequently needed even if the “suspicion” is high
- Try to make diagnosis early to avoid “unnecessary” investigations (e.g. CT or MRI)

EUPO2012

Functional visual loss

- Children: (pubescent girl aged 9-11 years)
  difficult relationships with parents or peers at school …
  usually bilateral symptoms and restricted to the visual system
- Adults:
  for financial gain after injury at work, an assault, …or to support a claim for disability benefit
  may have additional functional symptoms such as headache, back pain, …

EUPO2012

Diseases often misdiagnosed as functional visual loss

- Pituitary tumors with early compressive signs
- Leber's hereditary optic neuropathy
- Bilateral retrochiasmal disease
- Early cone dystrophy or Stargardt's disease
- Retrobulbar optic neuropathies
- CAR, MAR, …
- Small occipital infarcts

EUPO2012

Unexplained visual loss

- First exclude organic visual loss !!
- Be aware of clues that a patient's visual loss may be non-organic:

RAPD ?!

EUPO2012

Perimetry

- Do not forget the manual perimeter of Goldmann !!
- (automated perimetry)

EUPO2012

Functional visual loss ??

Goldmann visual field testing:

eg: nonphysiologic spiraling:
the field spirals to the center

eg: generalized constriction: each stimulus is associated with approximately the same size visual field

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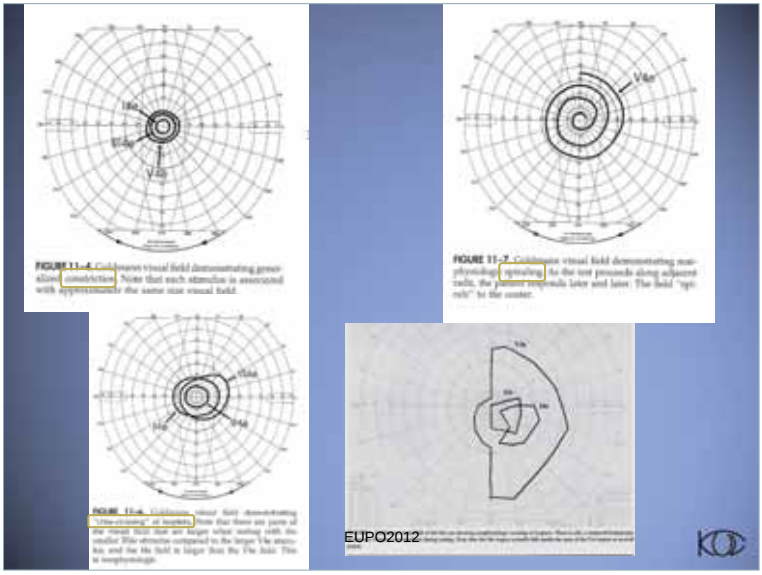
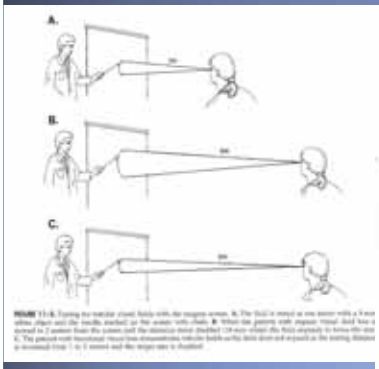


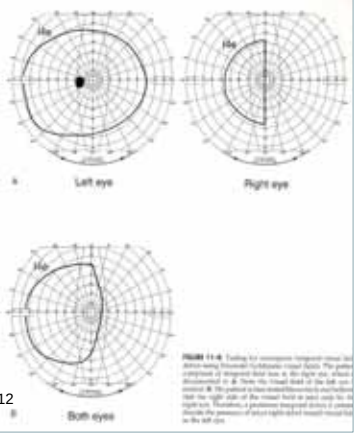
Constricted visual field in one or both eyes

- Tangent screen visual field at one and two meters

  The size of the VF should expand at the 2 meter distance
  in functional VF constriction, it is frequent to see the VF remain the same size or actually shrink

EUPO2012





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Central visual field

- Central sotoma:

  perform careful fundoscopy, OCT, angiography, ERG to rule out subtle maculopathy

  if no maculopathy: perform neuroimaging:

  most patients with central sotoma on VF testing, have organic pathology !

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- CAVE: real visual pathway disease being misdiagnosed as non-organic

- Follow-up until you can demonstrate either organic or non-organic disease

EUPO2012

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2. Visual Electrophysiology in Neuro-ophthalmology

• Graham HOLDER, London, United Kingdom

Electrophysiological testing provides objective data regarding the function of the visual pathways and is thus indispensable to neuro-ophthalmic practice. After a brief review of the techniques routinely available in clinical practice ie electroretinography (ERG), pattern electroretinography (PERG), multi-focal electroretinography (mfERG) and the visual evoked potential (VEP), a case-based approach will be used to demonstrate the use of these tests.

In non-organic visual loss the role of electrophysiology is to demonstrate normal function in the presence of symptoms that suggest otherwise. The use of the VEP in the objective determination of visual system resolution will also be discussed.

The normal pattern electroretinogram (PERG) contains two main components. There is a positive component at approximately 50ms (P50) and a later, larger negative component at approximately 95ms (N95). Although much of the PERG arises in the retinal ganglion cells, and N95 objectively assesses central retinal ganglion cell function, P50 is driven by the macular photoreceptors and acts objectively as a measure of macular function. The pattern visual evoked potential shows delay in most optic nerve diseases but is also commonly delayed in macular dysfunction. The presentation will show how use of the PERG enables an improved interpretation of the pattern VEP and thus facilitates the distinction between optic nerve disease and macular disease.

The presentation will also address those retinal disorders most likely to be mistaken for optic nerve dysfunction. The disorders addressed will include paraneoplastic retinopathies; autoimmune retinopathy; AZOOR (acute zonal occult outer retinopathy) and others where the clinical presentation may masquerade as possible optic nerve disease.

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3. Visual Field testing in neuro-ophthalmology

• John WILD, Cardiff, United Kingdom

4. Is this optic neuritis? Differential diagnosis

• Dan MILEA, Angers, France

Optic neuritis is typically characterized by acute, painflul visual loss, associated with color vision dysfunction, involving the central region of the visual field, and occurring in a young adult. Its diagnosis is usually straightforward, based on clinical arguments, but other conditions of the optic nerve or of the retina can mimick optic neuritis. More rarely, functional visual loss, especially if occuring in children and young adults, can be mistaken as optic neuritis.

The typical neuro-ophthalmological findings of optic nerve involvement include color vision impairment, presence of a relative afferent pupillary defect, and central or ceco-central visual field defect with a normal or swollen optic disc

Other optic neuropathies

Several optic neuropathies can mimick optic neuritis : compressive optic neuropathy, ischemic optic neuropathy, Leber's hereditary optic neuropathy, traumatic optic neuropathy and radiation-induced optic neuropathy. The optic disc appearance may be helpful to distinguish optic neuritis from other optic neuropathies, although some of the features can be overlapping between these two conditions. In optic neuritis, the optic disc is usually normal, disc edema occurring clinically in one third of the cases. In older patients, acute visual loss related to an oedematous optic neuropathy is usually associated with anterior ischemic optic neuropathy. Altitudinal swelling, pallor, arterial attenuation, and hemorrhages are found more commonly in anterior ischemic optic neuropathy than in optic neuritis.

In the acute phase of traumatic and radiation-induced optic neuropathy, the optic disc is usually normal; as in optic neuritis, optic disc pallor does not occur before several weeks after the onsent of symptoms. Optic disc cupping, due to enlargement of the physiological excavation, is another pathological disc change occurring in some chronic optic neuropathies.

Retinal conditions

Retinal conditions (especially maculopathies and especially in case of unilateral involvement) can mimick optic neuritis because of the central vision deficit. The main clinical elements which help distinguishing a maculopathy from optic neuritis are the following : lack of pain on eye movements, a relative afferent pupillary deficit, color vision dysfunction. In optic neuritis, color vision perception is usually altered or even absent, while in macular disease it can be moderately impaired. An exception are the cone-rod dystrophies, in which color vision can be abnormal. The photostress test (measurement of the vision recovery time after exposure to a bright light) is a useful method to detect a maculopathy. This time is prolonged in a maculopathy, but within normal limits in an optic neuropathy.

Optic neuritis is commonly associated withcentral or cecocentral scotoma, although arcuate, altitudinal or even generalized defects can also occur; on th opposite, in macular conditions visual field defects are usually central.

Ophthalmoscopy is crucial in differentiating central retina involvement from an optic neuritis. In more difficult cases, macular and peripapillar OCT, more rarely of electrophysiological tests (MfERG and VEP) may be performed. Autofluorescence and/or fluorescein angiography are more rarely used these days than in the past, in order to detect retinal or choroidal changes, occurring in progressive photoreceptor dystrophies and in central serous retinopathy.

If visual loss is related to macular cone dysfunction, ophthalmoscopic examination of the retina may be normal or it may show minimal changes of the macular appearance or pallor of the temporal optic disc. The diagnosis of these diseases may be difficult, sometimes requiring electrophysiological examination with multifocal electroretinography. Central serous chorioretinopathy (CSC), white dots syndromes (WDS) and some autoimmune rétinopathies may also mimick optic neuritis. The white dots syndromes represent a group of idiopathic retinal and choroidal diseases affecting mainly young women. These conditions include multiple evanescent white dot syndrome (MEWDS), acute idiopathic blind spot enlargement (AIBSE), acute zonular occult outer retinopathy (AZOOR), multifocal choroiditis (MFC), punctate inner choroiditis (PIC) and acute macular neuroretinopathy. Due to the normal appearance of the retina and choroid on fundoscopy, the clinical picture of some of these diseases can be similar to that of optic neuritis. In these cases, the diagnosis may be obtained with fluorescein and ICG angiography and ERG testing.

Nonorganic visual loss

Optic neuritis can also be mimicked by functional, non-organic visual loss which frequently occurs in young subjects. The diagnosis of functional visual loss is based on the inconsistency of results on subjective visual function tests and on the absence of objective signs of afferent pathways dysfunction.

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5. Ischemic optic neuropathies

• François BORRUAT, Lausanne, Switzerland

Introduction

Ischemic events to the optic nerve result in variable degrees of visual loss, affecting visual acuity, color vision, and visual field. The purpose of this talk is to summarize the actual concepts of the principal mechanisms and etiologies of ischemic optic neuropathies (ION): non-arteritic ION, diabetic papillopathy, arteritic ION, perioperative ION, and radiation-induced ION.

1. Non-arteritic ischemic optic neuropathy

Non-arteritic ION is the most frequent cause of acute optic neuropathy in patients aged over 50. The prelaminar-laminar portion of the optic nerve is involved in more than 90% of cases and the optic nerve appears swollen, with papillary hemorrhages. Visual acuity is decreased and visual field loss is often altitudinal, more frequently inferiorly *(Figure 1)*. Visual prognosis is poor although 40% of patients benefit from some visual improvement over the first 6 months following the ischemic event.

Cardiovascular risk factors (systemic hypertension, diabetes mellitus, hypercholesterolemia) are found in 60% of non-arteritic ION patients. Non-arteritic ION patients are thought to develop an ischemic event because they present a disc-at-risk, i.e. a small optic disc with a cup-disc ratio < 0.3. The possible role of nocturnal hypotension and sleep apnea has been emphasized by some authors.

Treatment options include corticosteroids and aspirin, but are subject to controversies. Thus far, there is no evidence-based medicine (EBM) to support treatment or not. A common attitude is to discuss the corticosteroid therapy if visual acuity is <3/10 and visual loss occurred within 2 weeks. New therapeutic modalities have been recently proposed: intravitreal injection of triamcinolone or anti-VEGF, erythropoietin, but further studies are needed to validate them.

The exact physiopathology of non-arteritic ION is still unknown. Recently, both a murine and a primate model of non-arteritic ION have been developed. Recent experimental results suggest that an inflammatory reaction occurs within the ischemic optic disc, possibly explaining the progressive visual loss following the initial loss in some non-arteritic ION patients. A specific anti-inflammatory therapy might be proposed in the future.

There is a suggestion that some medication could induce an acute anterior optic neuropathy, presumably ischemic, in some patients. Incriminated medications include amiodarone and phosphodiesterase-5-inhibitors, but the incidence of such visual loss is very rare. It might represent an idiosyncratic response.

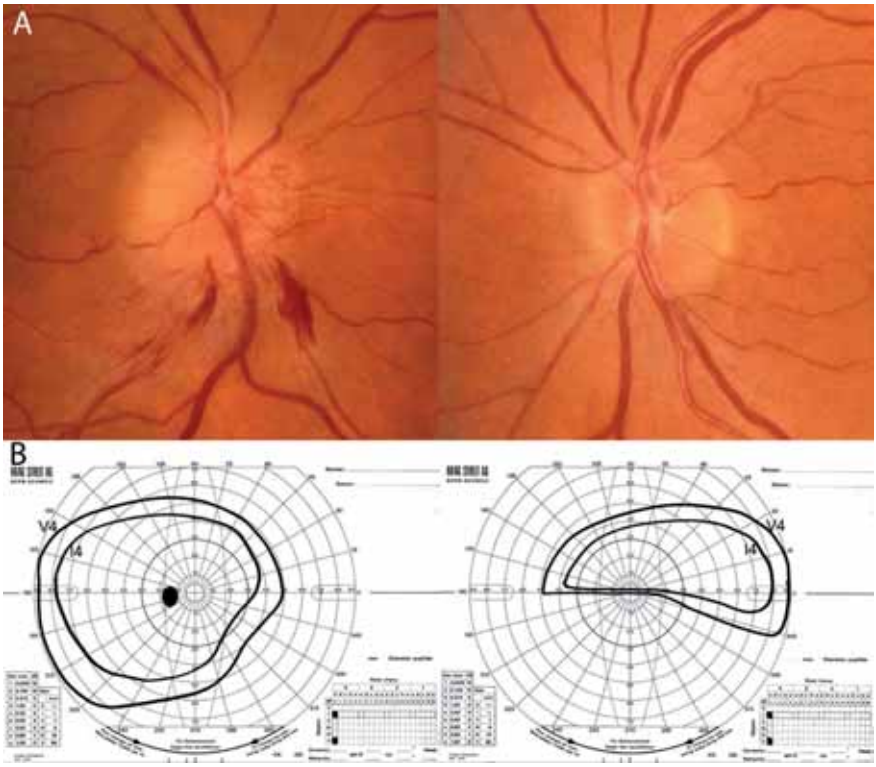

Figure 1

Top – Non arteritic anterior ION. Swollen right optic disc with flame-shaped hemorrhages and superior hypoperfusion of the right optic disc. The left optic disc is of small diameter, non excavated, so-called disc-at-risk

Bottom – Altitudinal inferior visual field loss of the right eye corresponding to the non perfused superior right optic disc.

2. Diabetic papillopathy

Symptomatic or asymptomatic disc swelling, mostly bilateral, can occur in diabetic patients. Initially it was reported only in young type 1 diabetic patients but is now known to happen also in older type 2 diabetic patients. It is however a rare event, recent studies revealing an incidence of 5/10'000 patient-years. Visual prognosis is overall better than for non-arteritic ION patients.

Diabetic papillopatjhy is thought to represent a mild form of non-arteritic ION *(Figure 2)*. The exact physiopathology of this relatively indolent ION is not known, but is clearly associated with a rapid decline in HbA1c levels.

There is no EBM for the treatment of diabetic papillopathy, which is relatively benign in the majority of cases. Intravitreous injection of triamcinolone or anti-VEGF has resulted in rapid resolution of optic disc swelling and visual loss in isolated cases.

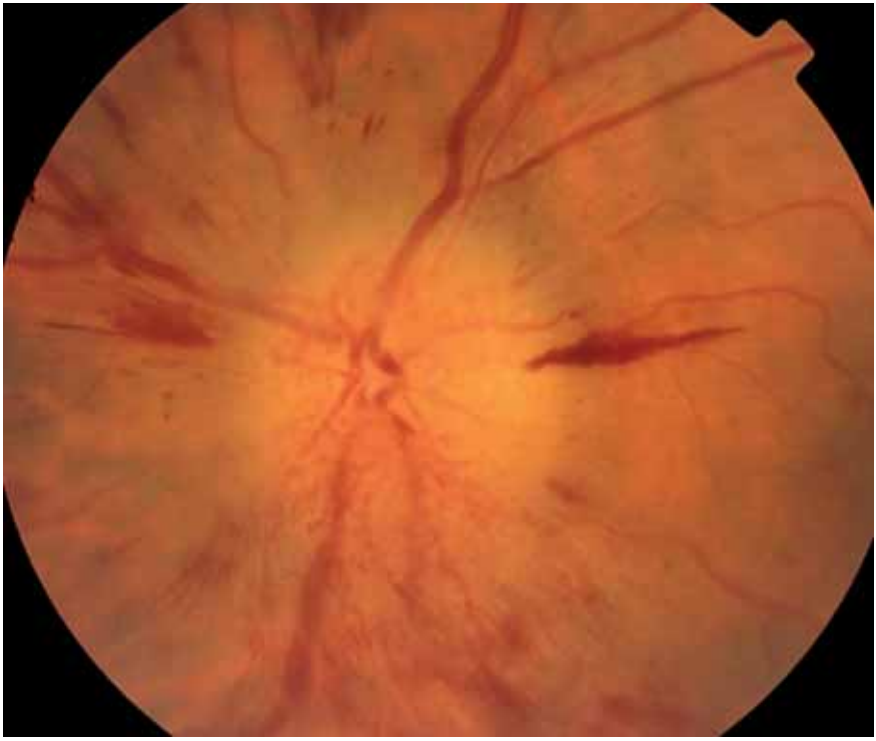

Figure 2

Diabetic papillopathy. The fundus appearance is similar to non arteritic anterior ION but exhibits more florid parapapillary hemorrhages and optic disc telangiectasias-

3. Arteritic ischemic optic neuropathy

An arteritic form of ION is encountered less frequently than its non-arteritic counterpart. Visual loss in arteritic ION is usually more profound and the swollen optic disc frequently exhibits a chalky-white appearance (Figure 3). Untreated, there is a great risk of bilateral involvement within a few days. There is no association with the presence of a disc-at-risk, cup-disc ratio being usually >0.3.

Arteritic ION has been reported in several inflammatory disorders, namely relapsing polychondritis, rheumatoid arthritis, Takayasu's arteritis, herpes zoster, PAN, SLE, Churg-Strauss, Behçet's, Crohn's, Birdshot chorioretinopathy. However giant cell arteritis (GCA) is by far the commonest cause of an arteritic ION.

GCA is a disease of the elderly, occurring only rarely before the age of 60, its incidence increasing markedly with increasing age. Systemic signs and symptoms of GCA (headaches, unexplained fever, weight loss, nocturnal sudation, proximal joint pain, scalp tenderness, and jaw claudication) are absent in 20-30% of patients, the so-called occult form of GCA. Laboratory studies are usually positive (elevated ESR and CRP, thrombocytosis, elevated fibrinogen), but a non-elevated ESR is found in 15-25% of cases. In the presence of visual symptoms (transient or permanent) fluorescein angiography is helpful, often revealing delayed perfusion of several territories (optic nerve, retina, choroid) *(Figure 3)*.

Transient diplopia or transient episodes of visual loss occur relatively frequently before the onset of permanent visual loss. Such transient symptoms are present in approximately 25% of cases and are frequently overlooked at presentation. GCA should always be suspected in patients aged > 60 years presenting transient symptoms, and adequate work-up should always be performed even when the episode has resolved.

Imaging of the temporal artery is now available with Doppler studies, MRI/MRA and angio-CT. However, the gold standard to confirm a suspicion of GCA remains the temporal artery biopsy (TAB). There is no evidence that bilateral TAB is beneficial.

The visual prognosis of patients with GCA has drastically improved with the use of corticosteroids. Steroids should be administered as early as a clear suspicion of GCA is present, before the results of TAB. High doses are necessary, but both the optimal dosage and the route of administration (oral versus intravenous) are unknown, due to the lack of dedicated studies (there is no EBM for the treatment of visual loss in GCA). Prednisone 1mg/kg/day is considered to be the minimal standard initial dosage and several institutions recommend intravenous methylprednisolone (250-1000mg/day/3-5 days) in case of acute or impending visual loss. Bed rest is also recommended in order to improve perfusion pressure at the level of the optic disc. Aspirin has been recommended as it decreases the level of interferon-γ, and decreases the risk of stroke.

If GCA is a disorder of the elderly, and the inflammatory mechanisms are well described, the trigger of this disorder is unknown. Recent experimental research and preliminary studies in humans suggest a possible infection with a bacterial infection (Burkholderia Pseudomallei). Studies are on-going and their results might have an impact of the future management of GCA.

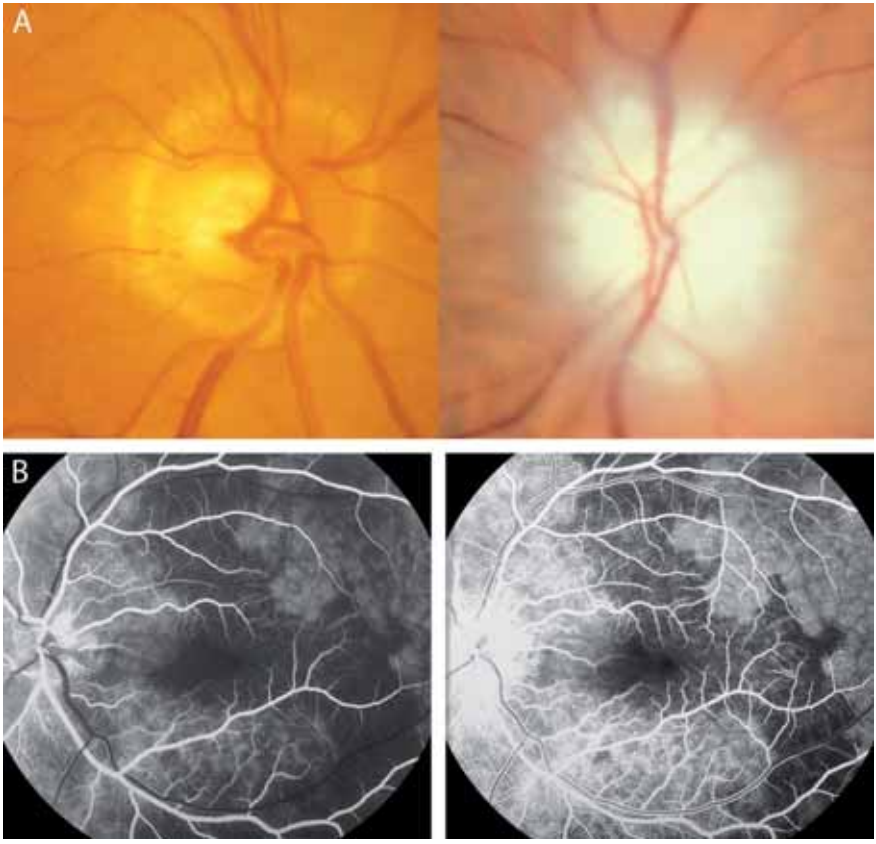

Figure 3

Top – Arteritic anterior ION. The left optic disc exhibits marked swelling and pallor, so-called chalky white swelling. The right optic disc has a normal size and cupping.
Bottom – Fluorescein angiography revealed an extensive patch of delayed choroidal perfusion

4. Perioperative ION

Visual loss can result from ION when surgery is performed at distance from the visual pathways. Whereas this rare but unfortunate complication is unpredictable, it is worth recognizing this possibility. Perioperative ION can be anterior *(Figure 4-5)* or retrobulbar. In the case of retrobulbar ION, normal fundus appearance will be initially present, evolving into optic atrophy after 4-6 weeks.

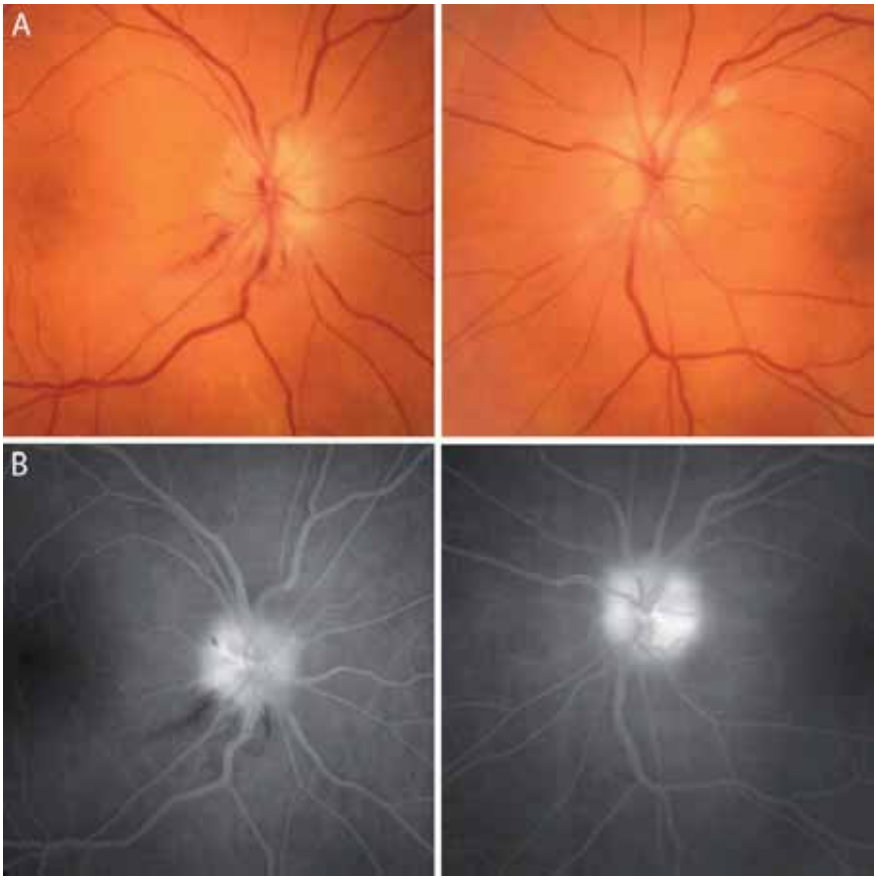

Figure 4

Perioperative anterior ION. Following an uncomplicated orthopedic procedure this patient presented bilateral anterior ION. Fundus appearance is similar to non arteritic anterior ION. Fluorescein angiography showed normal retinal and choroidal perfusion, but diffuse papillary leakage in both eyes.

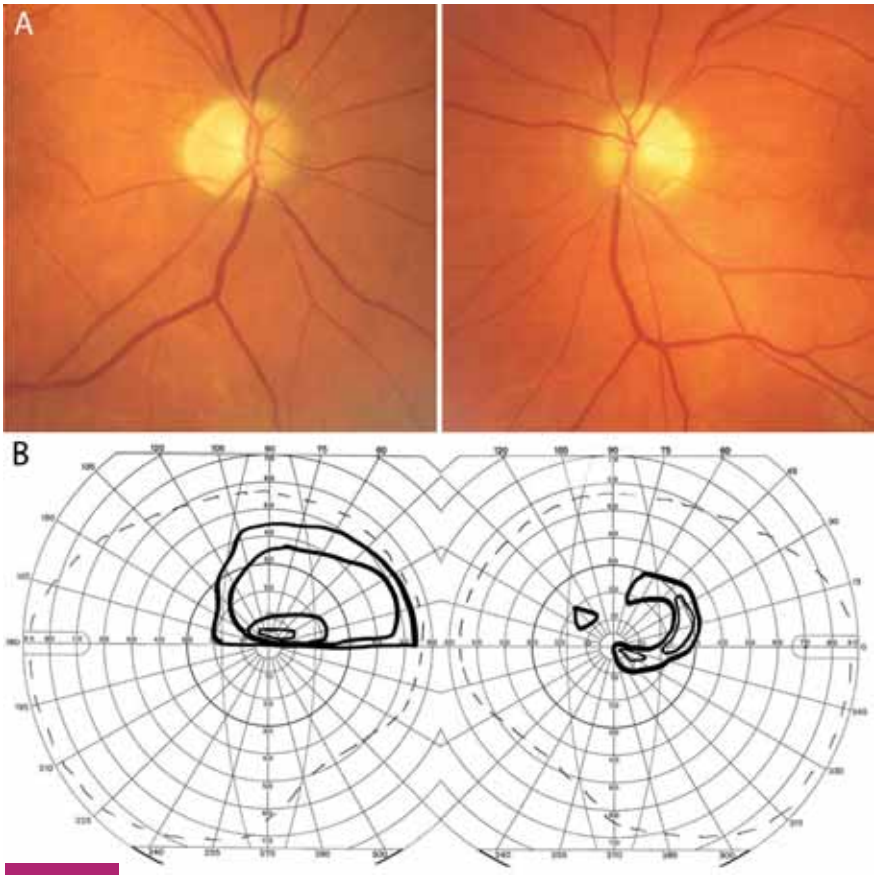

Figure 5

Perioperative anterior ION (same patient as in Figure 4). Three months later, bilateral optic atrophy was present. Visual field defect was permanent in both eyes.

Perioperative ION has been initially associated with spine surgery but has now been reported after cardiac, gastrointestinal, neck and orthopedic procedures. The majority of these procedures are characterized by a long surgical time, peri-postoperative anemia, peri-postoperative systemic hypotension. However, these data do not differ significantly when perioperative ION patients are compared with patients who did not lose vision. Recent studies showed that perioperative ION after spine surgery is associated with the following risk factors: male, obese, prone position in a Wilson frame.

There is no EBM for the treatment of perioperative ION. Early diagnosis is mandatory as it is suggested that an early normalization of anemia and/or blood pressure might improve the visual prognosis.

5. Radiation-induced optic neuropathy (RON)

RON is a delayed complication of radiotherapy, occurring at a median of 13 months after irradiation. The intracranial optic nerve is most frequently involved, as radiotherapy is frequently used to treat residual tumor in the vicinity of the optic chiasm. A safe dosage of radiotherapy (50Gy in daily doses <2Gy) should protect the optic nerve but cases of RON have been reported with "safe" dosage of irradiation. RON is unpredictable but fortunately very rare.

Diagnosis is supported by MRI showing a swollen optic nerve/optic chiasm, enhancing with Gadolinium, in the absence of tumor compression/infiltration *(Figure 6-7)*.

Visual prognosis is very poor, the majority of patients ending with visual acuity < 20/200.

There is no EBM for the treatment of RON. Experimental data and small case series suggest that hyperbaric oxygen therapy (30 daily sessions, 100% O2, 2.4ATM for 90 minutes) can be useful to re-establish optic nerve function *(Figure 8)*.

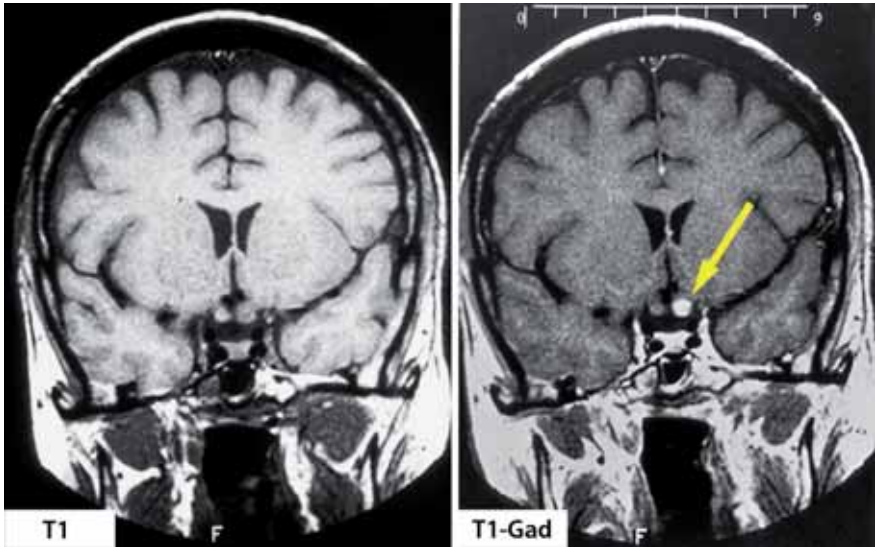

Figure 6

Radiation induced optic neuropathy. MRI, coronal sections, showing swelling of the left intracranial optic nerve, enhancing with gadolinium (arrow).

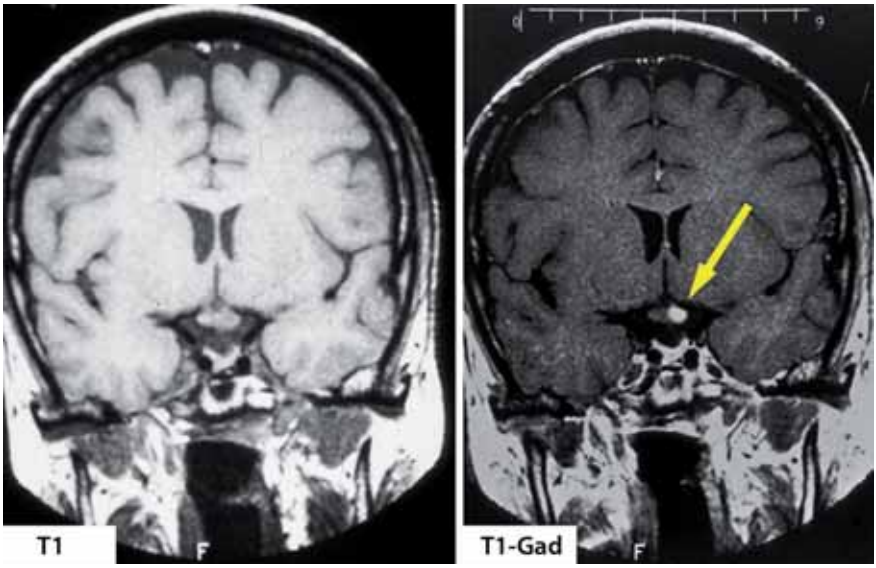

Figure 7

Radiation induced optic neuropathy (same patient as Figure 6). MRI, coronal sections showing swelling of the left hemi-chiasm, enhancing with gadolinium (arrow)

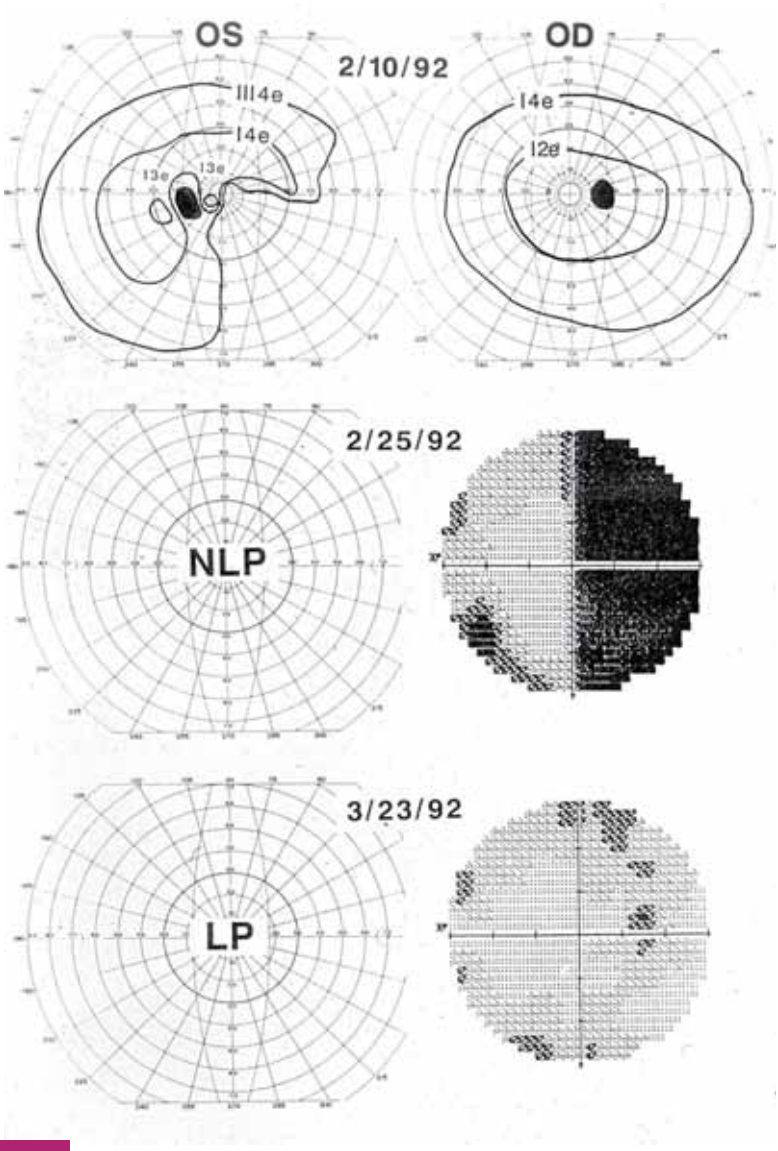

Figure 8

Radiation induced optic neuropathy (same patient as Figure 6). Initial visual field (Top) showed a left arcuate scotoma. Two weeks later (Middle), left visual loss was almost complete and a right temporal hemianopia was present. The patient was started with HBO therapy. After 28 daily sessions of HBO (Bottom), there was almost complete recovery of the right visual field loss.

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6. Toxic optic neuropathies

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Introduction

The optic nerve is susceptible to damage from toxins, including drugs, metals (eg. lead, mercury, thallium), organic solvents (ethylene glycol, toluene, styrene, perchloroethylene), methanol, carbon dioxide, and probably some sort of tobacco. This group of disorders is named as Toxic Optic Neuropathy and is characterized by bilateral visual loss, papillomacular bundle damage, central or cecocentral scotoma, and reduction of color vision.

Toxic Optic Neuropathy (TON) might be triggered or just enhanced by nutritional deficits, including vitamin thiamine (B1), riboflavin (B2), niacin (B3), pyridoxine (B6), cyanocobalamin (B12), folic acid, and proteins with sulfur-containing amino acids.

For example in malnourished and intoxicated patients both factors usually play synergistic role contributing to the TON. Clinical picture of both disorders, nutritional optic neuropathy (NON) and TON is also very similar and they usually cannot be differentiated on the basis of clinical signs and symptoms. Both are rare in economically developed countries. More prevalent in poor countries, because of more often exposition to toxic substances in work and in food, and of coexisting malnutrition. No racial, sexual and age-dependent predilections were shown.

Pathology

In most of TON the primary lesion has not been localized to the optic nerve and may possibly originate in the retina, chiasm, or even the optic tracts. The pathophysiology of TON is unknown and probably different substances affect optic nerve in a different way. It is usually accepted that the common pathway, for at least some of toxins, lead through mitochondrial injury and imbalance of intracellular and extracellular free radical homeostasis. It is argued that they are acquired mitochondrial optic neuropathies.

Examination

History: drug/toxin exposure: in a workplace (eg. heavy metals, fumes, solvents), ingestion of materials/foods, and use of a systemic medication; social history and habits (eg. amount and sort of tobacco and alcohol used), diet (eg. any special diets used).

Some metabolic diseases, including diabetes mellitus, kidney failure and thyroid disease might cause/increase the disease. It might be due to build up of toxic substances within the body.

A family history also should be taken. When alcohol or drug addiction is suspected, the information from family or friends might be more reliable. Review of symptoms should include sensory disturbances in the extremities and gait problems indicating toxic peripheral neuropathy

and/or toxic effect upon the cerebellum. Patients complains include: loss of vision (acute or chronic), a dimness of vision, a blur in the center of their reading vision (continuously and slowly progressing), a faded colors (particularly red) or a general loss of color perception. All of aforementioned symptoms are painless.

Physical examination

Visual acuity loss is usually progressive, painless and bilateral. It starts with the blur at the point of fixation (a relative scotoma), and is followed by a progressive decline. It varies from minimal reduction to no light perception (NLP) in rare cases (eg. methanol ingestion). Majority of patients have 20/200 vision or better.

Relative afferent pupillary defect (RAPD) is usually not present because the optic neuropathy is virtually always bilateral and symmetric. The pupils are often bilaterally sluggish to light, but they present as otherwise normal response to light and near stimulation. **Dyschromatopsia** is a typical feature.

In the early stages most patients have normal-appearing **optic nerves**, but disc edema and hyperemia may occur in some acute poisonings. Disc hemorrhages may also be present. Than papillomacular bundle loss and optic atrophy develops, initially presented as temporal pallor of the optic disc.

Visual field (VF) test is of major importance in any patient suspected of TON. It reveals relatively symmetric central or cecocentral scotoma, initially relative scotoma, with preservation of the peripheral field. Defects are characterized by soft margins, which are easier to plot for colored targets, such as red, than for white stimuli.

Lab Studies include **CBC, blood chemistries, urinalysis, and a serum lead level; identify specific toxin (like methanol) or its metabolites in the patient's tissues or fluids;** screening of the blood and urine for other toxins if exposure to a particular one is not identified on history (eg. heavy metal screening). To exclude NON test serum B-12 (pernicious anemia) and red cell folate levels (marker of general nutritional status) need to be obtained. Other tests revealing nutritional imbalance include direct or indirect vitamin assays, serum protein concentrations, and antioxidant levels. Serologic testing for syphilis is recommended.

Imaging Studies include MRI of the optic nerves and chiasm with and without gadolinium enhancement is recommended, although it is normal in typical TON.

Electrophysiological tests, including the visual evoked potentials (VEP) and the pattern electroretinography (PERG) might be useful. VEP can be useful in patients with early or sub-clinical optic neuropathy, also to differentiate with demyelinating disease. VEP usually reveals normal or near normal latency with significantly reduced amplitude of P100. The P50 and

N95 components of PERG reflect macular and retinal ganglion cell function, respectively. PERG can be useful in a patient with abnormal VEP to identify a macular lesion.

Electrophysiology tests, **contrast sensitivity (CS)** measurements and **retinal nerve fiber layer thickness** by OCT are also proposed to early detect subclinical toxicity of drugs used, like antibiotic, antimetabolite or antituberculosis medicines.

Diagnosis is based on the identification of a toxic factor and exclusion other pathologies giving similar clinical picture. Differential diagnosis include Nutritional Optic Neuropathies, Leber's Hereditary Optic Neuropathy (LHON), dominantly inherited (Kjer) optic neuropathy, compressive or infiltrative lesion of optic chiasm, bilateral inflammatory or demyelinative optic neuropathy, maculopathies/macular dystrophies, syphilitic optic neuritis, Graves disease, radiation optic neuropathy, diabetic papillopathy, and nonphysiologic visual loss (hysteria/malingering).

Treatment includes removing the toxic substance (eg. discontinuation of the drug), stopping smoking or consumption of alcohol.

Check-up examinations should be continued initially every 4-6 weeks and include visual acuity, color vision, visual field, pupil reaction and optic disc examination.

Prognosis depends on the dosage and duration of exposure to toxic substance. Usually, after discontinuation vision improves to normal over several days or weeks.

Drugs and Toxic Optic Neuropathy

It is known that TON is dosage and duration dependent, and occurs more often with anti-tuberculosis drugs (ethambutol, isoniazid), some antimicrobial agents (linezolid, ciprofloxacin, cimetidine, chloramphenicol), anti-epileptic drus (vigabatrin), disulfiram (for chronic alcoholism), halogenated hydroquinolones (amebicidal medications), anti-metabolites (eg. cisplatine, carboplatin, vincristine, cyclosporine), tamoxifen, and sildenafil. In these cases, esp. when drugs used for longer periods or with higher dosage, patients should be informed about possible toxicity and educated to report any visual problems immediately.

Standard methods for monitoring drug ocular adverse effects (eg. ethambutol use) include visual acuity assessment, visual field testing, funduscopy, colour vision testing, contrast sensitivity measurement, OCT and VEP.

Alcohol-Tobacco Amblyopia

It was believed for many years that tobacco and alcohol synergistically lead to visual loss and optic neuropathy. Since most heavy drinkers were also smokers, for many years it was difficult to differentiate these two factors, and the term “tobacco-alcohol amblyopia” was commonly used. It now seems likely that there are **two distinct disorders – tobacco optic neuropathy and**

nutritional optic neuropathy related to alcohol over consumption. Although from the end of the 19th century the role of nutritional deficit in provoking optic neuropathy was proposed, it was in the middle of the 20th century when it was provided what appears to be the conclusive evidence. It was showed that patients with TOAN partially or completely recovered their vision following vitamin B supplementation despite continuing their usual intake of alcohol and tobacco.

Tobacco optic neuropathy presents most often in elderly pipe-smoking men, however it was also reproted in cigar smokers, users of chewing tobacco and users of snuff. It is generally believed that nicotine may not play a role in the pathogenesis of the disorder. It is characterized by a bilateral relative centro-caecal field defect, more marked for a red or green target than white, and a characteristic disturbance of color discrimination on the Farnsworth-Munsell 100 Hue Test. Vision can improve to normal or near normal over a period of 3-12 months if they stop smoking.

It was proposed that smoking, especially in genetically susceptible patients, might affect sulphur metabolism, leading to chronic cyanide intoxication and the deficiency of vitamin B12. There are several reports confirming the co-existence of tobacco toxicity with deficiency of hydroxy-cobalamine. On the other hand, most patients with TON have B12 levels within the normal range. It was proposed that genetic susceptibility overlaps with toxic environmental influences. Since the clinical picture is not definitive, the diagnosis should be made after exclusion of the much more common nutritional optic neuropathy, other toxic optic neuropathies, and congenital optic neuropathies, mainly LHON. Tobacco abstinence, and oral and intramuscular B vitamins, particularly vitamin B1 and B12, were proposed as appropriate therapy.

By the end of the 20th century a paradox had become apparent; despite an increased use of tobacco products in the general population, there was a marked decrease in the incidence of tobacco optic neuropathy. One possibility is that a number of early cases were probably mis-diagnosed. For example, it was shown that some patients diagnosed as tobacco optic neuropathy carried a genetic mutation characteristic for Leber hereditary optic neuropathy. Secondly, the nutritional status of the general population, which may have contributed to the development of optic neuropathy in Victorian times, is at present of minor importance, at least in the developed world. Further, the very low current incidence suggests that the most common current form of tobacco consumption, cigarette smoking, may not precipitate the disorder. It is worth remembering that a test for syphilis would not become available until the turn-of-the century, ischemic optic neuropathy wouldn't be discovered until the mid 20th century and demyelinative optic neuritis was just becoming recognized.

The term “tobacco-alcohol amblyopia” is misleading. There is neither amblyopia nor any proven interaction between alcohol and tobacco in the pathogenesis of the disorder and use of the more accurate term, nutritional optic neuropathy, is recommended.

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7. Optic Neuropathy in Graves Orbitopathy

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Optic Neuropathy in Graves Orbitopathy

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Mechanistic pathogenesis of Graves Orbitopathy

Primary effects of disease process

- Inflammatory changes in soft tissues
- Muscle swelling / fibrosis / fatty change
- Increased orbital fat

Secondary effects of disease process

- Impact of volume increase within tight confines of bony orbit

WHAT and HOW should we evaluate GO

- **SEVERITY**
  - The degree of functional or cosmetic deficit at any time point, regardless of disease phase
- ACTIVITY
  - Determinate the phase (active or inactive) of the disease

Rundle FF. Clinical Science 1945; 5: 177

Clinical Activity score

Mourits et al. (Br J Ophthalmol, 73, 639-644, 1989/ Clin Endocr 1997, 47:9-14)

- Spontaneous orbital pain.
- Gaze evoked orbital pain.
- Eyelid swelling
  that is considered to be due to active (inflammatory phase) GO.
- Eyelid erythema.
- Conjunctival redness
  due to active (inflammatory phase) GO
- Chemosis
- Inflammation of caruncle or plica

Optic Neuropathy Mechanism

- **Optic neuropathy <10% of clinical TAO**
  - Etiology:

    COMPRESSION by enlarged EOM

    High intraorbital pressure >< lack of proptosis

    Stretching of the ON

    Ischemia of ON ?

    (Feldon 1988,Nugent 1990,Dosso Safran1994)

Risk factors for DON

- Male gender
- Older age
- Diabetes (10x risk)

(Niegel 1988, Trobe 1981,Kalmann&Mourits1999)

Symptoms of ONp pts

- graying of vision or/and desaturation of color, things look dimmer..
- aching fullness or pressure sensation behind the eye ball

exacerbate by eye mvts

Ocular Signs in OpNp pts

- **Soft tissue signs (score 0 to 4)**
  - Conjuctival inject
  - Chemosis +/- 2 or less
  - Lid edema
- **Lid Fissure** (mean 11mm), **& Lid Retract.**

NO DIFFERENCE between pat with/ without DON

- **Proptosis**
  - Mean 23mm in DON gp << Palpable lacrymal glde
  - Mean 20.5 mm in control gr

(Niegel 1988, Trobe 1981)

Ocular signs in OpNp pts

- **IOP**
  - Mean 20.9mmHg > 30.2 mmHg UPgaze in DON gp
  - Mean 17.6mmHg>21.5mmHg UPgaze in Contrl gp
- Cornea staining (score 0 to 2)
  - Mean 0 to 1
- **Muscles RESTRICTION +++** symmetric/asymmetric

DON gp	>>	Control gp
• 27% ET		13% ET
• 13% XT		13%XT
• 67.3% VERT dev.		33% VERT dev.

(Niegel 1988, Trobe 1981,McKeag2007)

Ocular signs in OpNp pts

- **Optic Nerve appearance**
  - **Normal +/- 45%**
  - Elevation+Hyperemia ON 25%
  - Pallor of ON 24%

Visual function in OpNp

- ***Bilateral ON involvt > 85%***
  - Visual Acuity: is > 5/10 in 59%
  - Color perception (Farnsworth-Munsell100-hue) : abnormal in 64%, Chromatic discrimination sensitivity: Tritan abnl in ON

    (Tanner 1995)

  - Visual Field: abnl in +/- 75%
    - Central or paracentral scotoma
    - Increased blind spot
    - Generalized constriction

Clinical assessement **of Optic N. Involvement**

- Symptoms: blurring, grey spot, color desaturation,light sensitivity, things look dimmer..

- Visual acuity
- Color discrimination
- Relative afferent pupillary defect(RAPD)
- Visual field (Humphrey perimeter)
- Fundoscopy

- VEP
- Contrast sensitivity

- Imaging (apical crowding)

Visual Acuity

- Tested with Snellen chart (

(standard high contrast)

- Best corrected Distance VA > 12/10
- In +/- 50% VA is = or > 5/10
- (Suttorp-Schulten1993, Trobe 1981)

Color Vision

- Op Np > conduction defect of small caliber myelinated nerve fiber of cones syst.
- Red-green>>Blue-yellow macular cones
- *Hardy-Rand-Rittler plates :acquired dyschromatopsi*

! Intensity of illumin 10-60 foot-candles

– *COMPARISON of Colour BRIGHTNESS : Red top of mydriaticum*

Contrast Sensitivity

- Pelli-Robson Test
  - Highly sensitive to ON
- Computer automated method(wave grating)

Contrast threshold at Low spatial frequency

No pronounced relation with the VA

But, **CS** is ALSO reduced by :

macular diseasese, lens opacity, vitreus and , corneal d.

- Pupil response:
  - RAPD = Op NP
  - RAPD is ABSENT If Op Np is BILATERAL(75%)
- Slit lamp exam:
  - Corneal lesion or staining
- IOP

Visual Field

- *Automated static treshold central perimetry (30°):* **Humphrey 30-2 or 24-2** *Octopus 32*

=GOLD Standard

! «Learning effect» and Individual fluctuation

!VF loss Significant : 3points p<5%+ one of which p<1% confirmed on 2 consecutive tests

- *Kinetic treshold Goldman perimetry*

Visual Field Defects

- Paracentral scotoma 25%
- Increased blind spot 20%
- Nerve bundle defct 20%
- Central/centrocecal s17%
- Generalized const 12.5%
- Vertical step 5%
- **NORMAL 34%**

(Niegel 1988)

Fundoscopy

- Optic disc NORMAL
- Optic disk SWELLING 20 to 50% (Garrity 1993)
- Optic disk pallor

- Choroidal folds = severe eyeball compression

- ***Psychophysical testing***

  Visual Evoked Potential (pattern/flash)

  -58 DON pts, 64% dyschromat., 66% VF abnl
  94% VEP abnormal *(Neigel 1988)*

  -88 TAO pts without clinical signs of Op Np:
  VEP (check size 27') latency P100 in 23.8%, ↑
  (Salvi 1997)

  -16pts with TAO without clinical DON/15 contrls > ABN VEP latency P100 (check size 15') (Acaroglu 2003)

Orbital Imaging: Ct scan or MRI

- ***Apical crowding*** = effacement of perineuronal orbital fat in the posterior orbit

  >50% severe, 25-50% moderate,<25%mild

13% with severe apical crowding> no DON

17% DON+, Apical crowd<25%

(Nugent 1990)

- ***Fat prolaps through the sup orb fissure***

(specif91%, sensit94%) (*Birchall1996)*

- *Muscle index >50%:* sensitivity 100%, specificity47%

(Giaconi2002)=A+B/C

Graves Ophthalmopathy: The Bony Orbit in Optic Neuropathy, Its Apical Angular Capacity, and Impact on Prediction of Risk

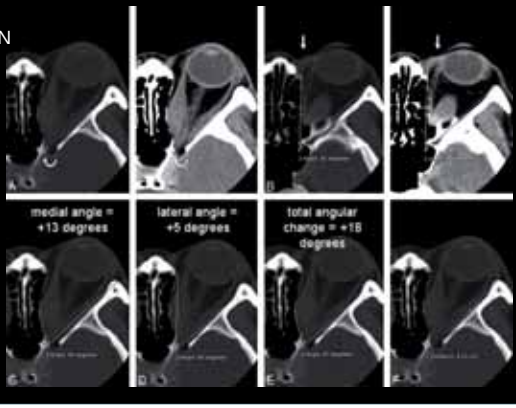
L.-L. Chan

et al AJNR 30:597-602, 2009

41pts GO

19p withON

22p withoutON



When Diagnose a Dysthyroid Optic Neuropathy?

– If optic disc SWELLING+ ↓Color percept.***>DON***

– If optic disc Normal or Near Nl> DON dg if:

- 2 or more abnl parameters: VA, Color dis., RAPD, VF, (VEP).

– *« Apical crowding, Fat prolapse, Muscle index>50%.... « raise the index of suspicion of DON.*

Who should be treated? How should be treated?

- The decision of whether the ophthalmopathy should be treated should rely on the assessment of two different features:
  – severity of GO (Dickinson AJ, 2001)
  – activity of GO (Mourits MP, 1989)

Local supportive measures

Sign/symptom	Action
Photophobia	Sunglasses
Gritty sensation	Artificial tears
Eyelid retraction	[illegible]-blocking drops
Increased IOP	[illegible]-blocking drops
Lagophthalmos	Nocturnal taping
Mild diplopia	Prisms

Eliminate risk factors!SMOKING, THYROID FCt!

Severe disease with Optic Neuropathy

- Active: Medical treatment
  - (immunosuppression, especially glucocorticoids and/or orbital radiotherapy)
  - Inactive: surgical treatment
    - (orbital decompression)

NO EVIDENCE BASED TREATMENT for OptNp in GO!

Severe Optic Np GO TT

- ***The treatment of choice seems to be pulses of iv glucocorticoids (GCs): Methylprednisolone 1gr/d for 3 d***

Consensus on GO management Bartalena et al 2007

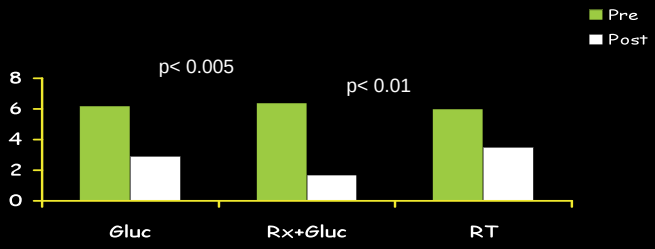
Severe Optic Np GO TT

- ***If clinical response is +:***
  - ***Continu IV Cortisone Weekly to a total cumulative dose of maximum 8 g in one course of therapy***
- These pts should be first screened for liver dysfunction, hypertension, history of peptic ulcer, diabetes, urine infections and glaucoma, and then monitored for side-effects

Consensus on GO management Bartalena et al 2007

Severe Optic Np GO TT

- ***If clinical response is +:***
  - ***Add Radiation Therapy (10-20Gy)***



Consensus on GO management Bartalena et al 2007

Severe Optic Np GO TT

If response to Glc is insufficient:

- **Bone ORBITAL DECOMPRESSION**
  - **Different technics**
  - **Aim is to reduce compression and/or streching of the Optic Nerves > ! Posterior decompression of the medial wall!**

Prognosis of Optic Np in GO

- **Visual function restoration is highly susceptible to:**
  - **Early diagnosis > Early TT!**
  - **Age,**
  - **Associated vascular risk factors**

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8. Congenital optic nerve anomalies

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Congenital optic nerve anomalies

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Congenital optic nerve anomalies

Account for 15% of severe visual impairment in UK, optic nerve hypoplasia alone accounting for 12%.

Congenital optic nerve anomalies

- Understanding
  - ophthalmoscopic features
  - diagnosis
  - neuro-ophthalmologic associations
  - treatment and follow-up

Congenital optic nerve anomalies

- Bilateral optic nerve anomalies ⟹ poor vision, nystagmus
- Unilateral optic nerve anomaly ⟹ strabismus
- Congenital optic nerve anomaly ⟹ color vision relatively preserved ⟺ acquired optic neuropathy

Congenital optic nerve anomalies

Any structural ocular abnormality that reduces visual acuity in infancy may lead to superimposed amblyopia

trial of occlusion therapy may be warranted

Brodsky et al, Pediatric neuro-ophthalmology

Optic nerve hypoplasia: Most common optic disc anomaly

- Dramatic increase in prevalence?
  - Greater recognition by clinicians
  - Parental drug and alcohol abuse

Pathogenesis ONH

- Due to a primary failure of retinal ganglion cell differentiation at the 13-15 mm stage of embryonic life (4-6 weeks of gestation).

- Very hypoplastic discs: early insult
- Subtle hypoplasia: later insult

Optic nerve hypoplasia

Direct ophthalmoscopy:

- Abnormal small optic disc gray or pale, surrounded by a yellowish, mottled peripapillary halo, bordered by a ring of increased or decreased pigmentation
- Major retinal veins often tortuous
- Unusually straight retinal vessels with decreased branching

Optic nerve hypoplasia: wide variation in appearance!

Double ring sign: not pathognomonic for ONH!!

Optic nerve hypoplasia

- Visual acuity: 20/20 to lightperception - correlating with the integrity of the papillomacular bundle and not with the overall size of the optic disc
- Stable visual problem, except if associated with growing suprasellar tumours
- Visual field: localized VF defects, often combined with a generalized constriction of the field
- Refraction! Superimposed amblyopia!

Optic nerve hypoplasia

Diagnosis: : ONH? Difficult!

- Ophthalmoscopy
- Fundus photographs: several techniques

Optic nerve hypoplasia

Diagnosis of ONH is reserved for patients with small optic discs who have reduced vision or visual field loss with corresponding nerve fiber bundle defects.

ONH and noninvasive neuroimaging: MRI

- High contrast resolution and multiplanar imaging capability to visualize anterior visual pathways
- Specific prognostic information regarding neurodevelopmental deficits and pituitary hormone deficiency

ONH: Associations with a wide variety of CNS abnormalities

- Referral to the endocrinologist: Follow-up of growth, and endocrinological investigation in case of posterior pituitary ectopia, neonatal jaundice or hypoglycemia
- Subclinical hypopituitarism can manifest as acute adrenal insufficiency following general anaesthesia

Causes?

- nonspecific abnormality resulting from an insult to any part of the visual system at an early stage of development
- teratogens: quinine, LSD, anticonvulsants, crack cocaine, maternal alcohol and diabetes

Excavated Optic Disc Anomalies

- Morning glory Disc Anomaly
- Optic disc coloboma
- Peripapillary Staphyloma
- Megalopapilla
- Optic Pit
- Papillorenal syndrome

Excavated Optic Disc Anomalies

Three distinct anomalies, with their own specific embryological origin, and not simply clinical variants along a broad spectrum! *(Brodsky)*

- Morning glory Disc Anomaly
- Coloboma
- Peripapillary Staphyloma

Morning glory disc anomaly

- 1929: Handemann - 1970: Named by Kindler
- Congenital funnel- shaped excavation of the posterior fundus that incorporates the optic disc
- Pathogenesis?
  - error in mesenchymal differentiation with abnormal closure of the scleral wall and lamina cribrosa
  - failed closure of fetal fissure, similar to optic nerve coloboma

Morning glory disc anomaly

Enlarged optic disc surrounded by annular zone of pigmentary disturbance. Retinal vessels are increased in number, arising from the periphery of disc, with straight radial configuration.
A white glial tuft overlies the central portion of the optic disc.

Morning glory disc anomaly

- Usually unilateral
- Vision 20/200 to finger counting, but case with 20/20 have been described
- Superimposed amblyopia!
- Increased risk for serous retinal detachment (26-38%)
- Does not present as part of a multisystem genetic disorder

Morning glory disc anomaly

- Association with transsphenoidal form of basal encephalecoele is well established!
- Association with NF2
- PHACE syndrome

- MR angiography: association with ipsilateral intracranial vascular dysgenesis, Moya-Moya disease. The coexistence of these intracranial vascular anomalies implicates a primary vascular dysgenesis with mesodermal dysgenesis.

Optic disc coloboma

- Closure of the embryonic fissure starts at the equator and extends anteriorly and posteriorly ➡ defect of any size from the margin of the pupil to the optic disc

- The excavation is typically decentered inferiorly

- In case of inferior extend with involvement of choroid and retina: microphthalmia is present

Optic disc coloboma: a sharply delimited, glistening white bowel-shaped excavation occupies an enlarged optic disc.

Optic disc coloboma

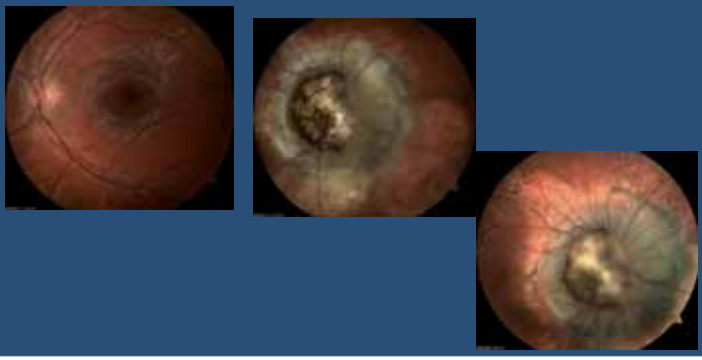
- Uni-or bilateral
- Poor visual acuity in case of macular involvement and microphthalmia
- Isolated optic nerve coloboma: risk of serous macular detachment
- Retinochoroidal coloboma: risk of rhegmatogenous retinal detachment

Optic disc coloboma

- Sporadically or inherited in AD, AR or X-linked fashion
- The subtle phenotypic expressions have the same diagnostic and genetic implications as gross manifestations
- Association with
  - multiple systemic and chromosomal abnormalities
  - PHPV, glial tissue, lens notches, …
- Mutations in a fraction of colobomas have been identified in PAX6, CHX10, MAF, SHH, CHD7, GDF6 and SOX2 genes

Phenotypic profiles can overlap!!!

early embryonic injury involving both the proximal embryonic fissure and the distal optic stalk



Peripapillary staphyloma

- Rare non-hereditary unilateral anomaly, in which a deep fundus excavation surrounds the optic disc
- Normal optic disc and retinal vessels suggest that these structures are complete, prior to the onset of the staphylomatous process
- Diminished peripapillary structural support, resulting from incomplete differentiation of posterior sclera from posterior neural crest cells in the fifth month of gestation

Peripapillary staphyloma


Visual acuity ranges from normal to markedly reduced. Usually unassociated with systemic or intracranial disease.

Megalopapilla

Megalopapilla comprises two phenotypic variants:

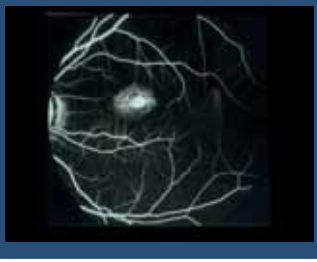
- Usually bilateral abnormal large optic disc (> 2.1 mm in diameter) with an otherwise normal configuration. Associated with a large cup-to-disc ratio dd glaucoma.
- Unilateral megalopapilla in which the normal optic cup is replaced by a grossly anomalous noninferior (dd coloboma) excavation.

Megalopapilla

- Usually normal visual acuity, normal visual field, enlarged blind spot
- Pathogenesis: statistical variant of normal

Optic disc pit

- Round, oval, grey, white or yellowish depression in the optic disc, most often temporally located, typically unilateral
- Usually asymptomatic and diagnosed as incidental finding
- Visual loss when complicated by macular oedema



Optic Disc Pit

- Pathogenesis??
- Histologically: herniation of dysplastic retina into a collagen-lined pocket extending posteriorly, often into the subarachnoid space, through a defect in the lamina cribrosa
- Source of intraretinal fluid in eyes with optic pits: controversial

- Familial cases: autosomal dominant mode of transmission
- In 25-75% of eyes: serous macular elevations, symptomatic around 3rd-4th decade- children

Papillorenal syndrome

- Rieger 1977
- Previous: Renal-coloboma syndrome
- High phenotypic variability: optic disc pit with vascular abnormalities and cilioretinal arteries- optic nerve dysplasia
- 10 different mutations in the developmental gene PAX 2 in 50% (chrom 10q24.3-q25.1)

Papillorenal syndrome

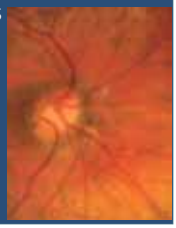
Pathogenesis: primary deficiency in angiogenesis

Papillorenal syndrome

- High phenotypic variability of renal and ophthalmological symptoms
- Ophthalmologist: Finding on fundoscopy of typical disc ⟹ nephrologic investigation
- Nephrologist: renal hypoplasia ⟹ fundus examination

Congenital tilted disc syndrome

- Frequent anomaly on 2% population based surveys
- Secondary to a posterior ectasia of the inferonasal fundus and optic disc
- Nonhereditary bilateral condition
- Optic disc dysversion and/or torsion, astigmatic refractive error, situs inversus of the retinal vessels, peripapillary atrophy, posterior staphyloma, visual field defects

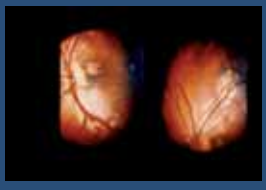


Aicardi Syndrome

- Cerebroretinal disorder of unknown aetiology, X-linked dominant genetic disorder
- Clinical features:
  - infantile spasms, hypsarythmia, severe mental retardation, gastrointestinal dysfunction
  - microcephaly, dysmorphic facies
  - agenesis of the corpus callosum, cortical migration anomalies,..
  - vertebral and costal malformation
  - De novo mutation on X-chromosome, lethal in males.

Aicardi Syndrome

- Pathognomonic: abnormal optic disc (including optic disc coloboma, pigmented optic disc and hypoplasia) with multiple de-pigmented 'chorioretinal lacunae' clustered around the disc.
- Histopathologically they consist of full-thickness defects limited to the RPE and choroid, retina is intact
- Microphthalmia, retinal detachment, cataract, pupillary membrane, iris synechiae and colobomas

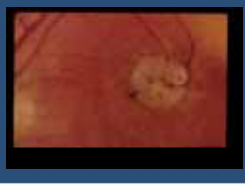


Aicardi Syndrome

Aicardi syndrome should be kept in mind while investigating a female child with seizures and typical fundoscopic findings!

Doubling of the optic disc

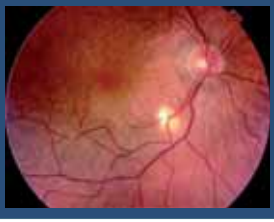
- Rare unilateral anomaly associated with decreased vision in which two discs appear to be in close proximity to one another.
- Results from a duplication or separation of the distal nerve into two fasciculi
- Separation of optic nerve into two or more: common in lower vertebrates, rare in humans



Pseudodoubling of the optic disk

- Pseudodoubling: juxtapapillary retinochoroidal coloboma. Double blind spot, altitudinal defects.
- dd doubling of optic disc:
  - MRI scan depicting one optic nerve
  - fluorescein angiography: unique system of retinal blood vessels

Retina; 2009 May;29(5):715-6.



Optic Nerve Aplasia

- Very rare, mostly unilateral, nonhereditary malformation
- One study reporting an AD type of nonsyndromic ONA *(Meire et al, 2011)*
- Absence of optic disk, optic nerve, retinal ganglion cells and central retinal vessels. Scleral aperture can be present.
- Ophthalmoscopy: mild differences due to the variable involvement of retinal vascular net, optic pathways, and associated eye abnormalities

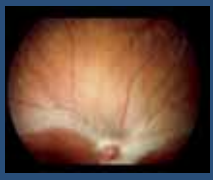
Optic Nerve Aplasia

- Unilateral
- Association with malformation of the eye- microphthalmos, anterior segment dysgenesis and retinal dysplasia
- Visual acuity: no lightperception
- Pathogenesis: unknown
- If bilateral: association with other CNS and cardiac malformations

Myelinated Nerve Fibers

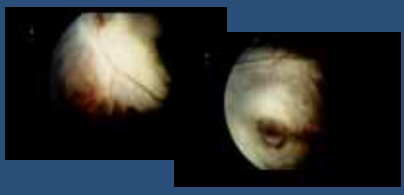
Pathogenesis

Defect in the lamina cribrosa ⟹ oligodendrocytes gain access to the retina



Myelinated Nerve Fibers

- Extensive unilateral myelination of nerve fibers can be associated with high myopia and severe amblyopia
- Many children with this association are refractory to occlusion therapy



Imaging the developing visual system

Foetal and infant brain:

non-invasive ultrasound and MRI

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9. Inherited optic neuropathies

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Summary

Inherited optic neuropathies comprise a group of heterogeneous optic atrophies with variable mode of inheritance: autosomal dominant, recessive, X-linked and mitochondrial (Leber's hereditary optic neuropathy: LHON). Only 3 defective autosomal genes have so far been identified despite seven mapped loci. There are three predominant mutations in the mitochondrial genome which are associated with over 90% of cases of LHON in Europeans.

The severity of the disease varies considerably both within and between families.

The first symptom in autosomal disease is usually variable reduction in visual acuity, with onset being very early or infantile, juvenile or in young adulthood.

- Decline in vision appears to take place slowly with age.
- The visual field is always affected. The field defect is centrocaecal to begin with. The progression of the visual field defect is very variable from case to case even in a same family.
- There are always colour vision deficits, which may be red-green or blue-yellow in axis.
- The disc is characterized by variable grades of temporal or total pallor.
- Electrophysiology reveals that the primary disease is of retinal ganglion cells. The pattern ERG shows a reduction in the P50: N95 ratio, which is specific to ganglion cell dysfunction and loss.
- A syndromic association should be considered, especially in children.
- Genetic testing is available for OPA1, OPA3 and TMEM126A genes.

In mitochondrial LHON the loss of vision is characterisctically sudden, profound, and consecutive in the second eye, typically in three months presenting in early adult life.

- Vision declines rapidly within days/ week to 6/60 or less. Even modest visual recovery is not the norm.
- An initial centrocaeal scotoma may be documented, which rapidly enlarges to occupy a substantial proportion of the visual field.
- The disc may initially show hyperaemia and a microangiopathy, which does not leak on fluorescein angiography. Subsequently the disc becomes pale and atrophic.
- Genetic testing is widely available.

Genetic counseling is mandatory in all forms of inherited optic neuropathy.

Primary mitochondrial mutations associated with Leber Hereditary Optic Neuropathy (LHON).

	LHON mutation		
	3460	**11778**	**14484**
Mitochondrial gene	ND1	ND4	ND6
Amino acid position	52/ A to T	340 R to H	64/ M to V
Prevalence, %	10-15	60-70	15-20
Males affected, %	~70	70-85	70-85
Mean age onset, yrs	~29	~28	25-27
Visual recovery, %	22-29	2-4	36-50
Time to nadir, mths	2-3	2-4	2-4

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10. Oculomotor palsies

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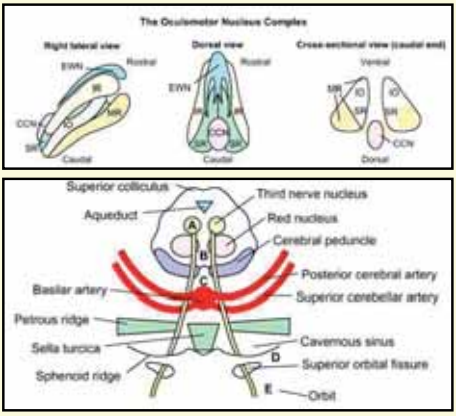
Anatomy: III



regions:

nuclear

fascicular

subarachnoid

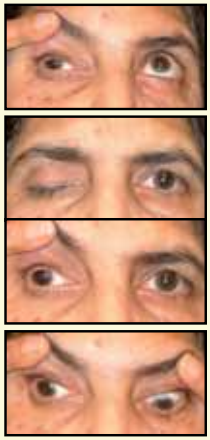
cavernous

SOF

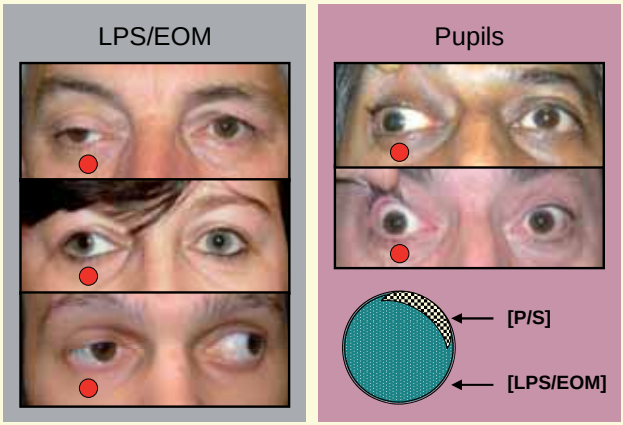
orbital

Clinical Features: III Palsy (Full)

63yo ♀
SAH & ICAD
during attempted
stenting of right
MCA aneurysm



Clinical Features: III Palsy ("Less")



Clinical Features: III Palsy ("More")

Nuclear III: ipsilateral III + contralateral SR/LPS

Benedikt's syndrome = III + contralateral tremor

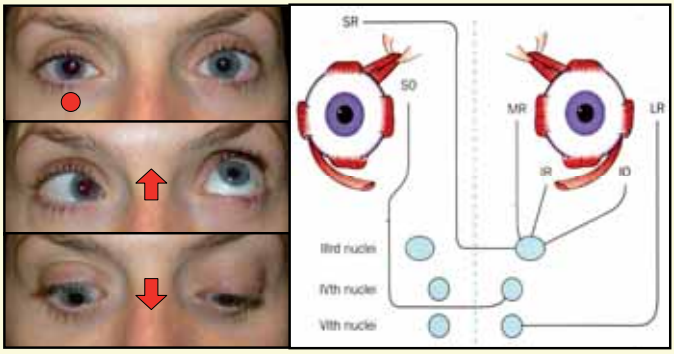
Weber's syndrome = III + contralateral hemiparesis

Cavernous syndrome = III + HS/IV/V/VI

Apex syndrome = III + V + ↓vision

Orbital syndrome = III + proptosis

Clinical Features: III Palsy ("AR")



Causes of III Palsy

nuclear
CVA
(inflammation)
(tumour)

subarachnoid
aneurysm
tumour
uncal herniation
meningeal pathology

orbital
inflammation
tumour
trauma

fascicular
CVA
(inflammation)
(trauma)
(tumour)

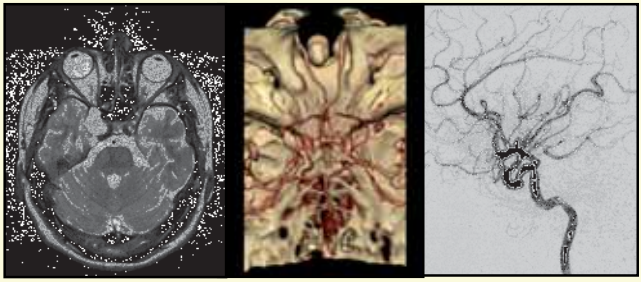
cavernous
aneurysm
CCF
tumour
inflammation

non-localising
microvascular / ischaemic

Mimics of III
MG GCA

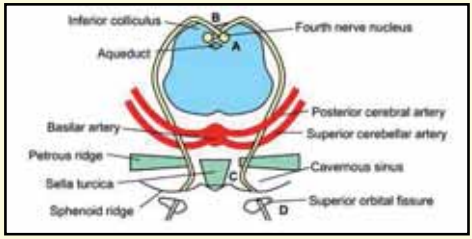
Investigating III Palsy

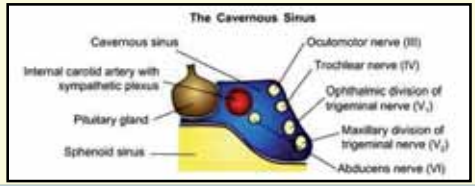
elderly, complete but pupil-sparing painless III: watch



bloods / CSF: inflammatory & infective screens

Anatomy: IV

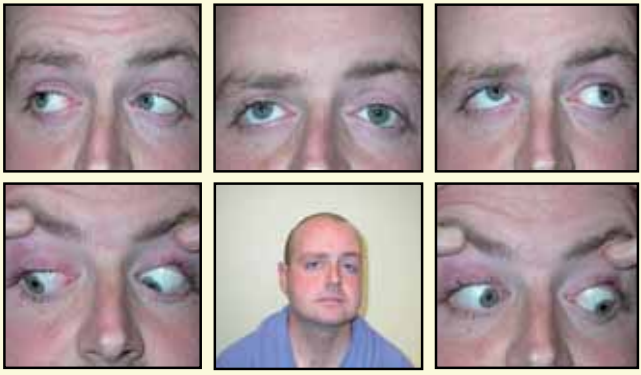




- contralateral
- dorsal
- longest
- thinnest
- <u>regions:</u>
  - nuclear
  - (fascicular)
  - subarachnoid
  - cavernous
  - SOF
  - orbital

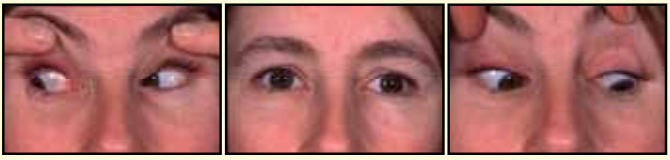
Clinical Features: IV Palsy

c/o: vertical/diagonal/torsional diplopia



Clinical Features: IV Palsy

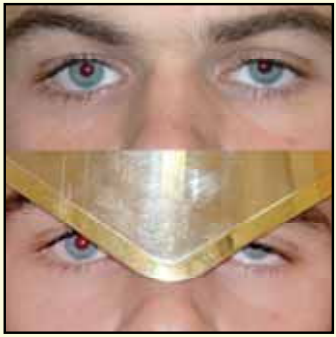
new or old?	UL or BL?	localising?
longstanding if: CHP ↑ vertical fusion range	suspect BL if: HI torsion+++ BHTT+ (BE) V-eso chin depression	nuclear if: contral. HS ipsilat. RAPD other signs if: cavernous SOF/orbital



ΔΔ & Investigation: IV Palsy

<u>aetiology</u>
congenital
trauma
ischaemic
(SOL, inflammation)

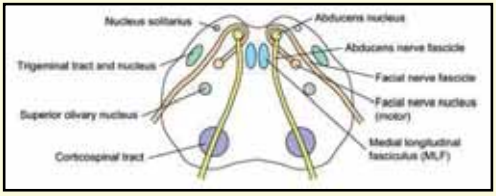
<u>ΔΔ</u>
skew
TED
Brown's
(MG)

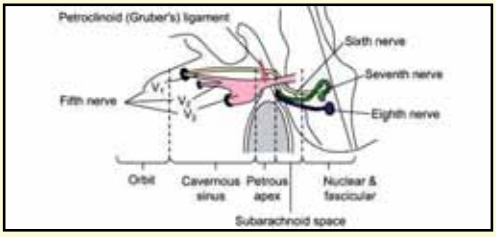


<u>Ix for cause:</u>
MRI
CSF
Bloods

<u>Ix for treatment:</u>
PCT
Hess
synoptophore

Anatomy: VI





<u>regions:</u>

nuclear
- motoneurones
- interneurones

fascicular

subarachnoid

cavernous

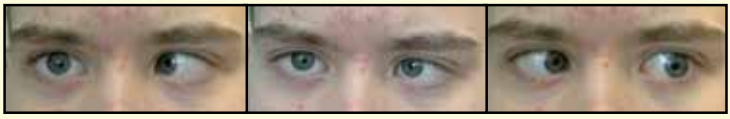
SOF

orbital

Clinical Features: VI Palsy

c/o: horizontal diplopia in R or L gaze

note: may be bilateral



Clinical Features: VI Palsy 'Plus'

horizontal gaze palsy = nuclear VI

one and a half syndrome = nuclear VI & MLF

horizontal gaze palsy & facial paresis = nuclear VI & VII

Foville's syndrome = V, VI, VII, VIII & HS

Raymond-Cestan syndrome = fascicular VI & contralat. hemiplegia

Millard-Gubler syndrome = fascicular VI & VII plus contralat. hemiplegia

petrous apex syndrome = V, VI, VII & VIII

Causes of VI Palsy

nuclear
CVA
inflammation
tumour
trauma

subarachnoid
aneurysm
tumour
trauma
meningeal pathology

cavernous
aneurysm
CCF
tumour
inflammation

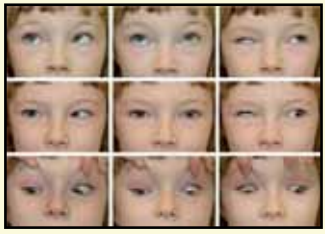
fascicular
CVA
inflammation
infection
tumour

petrous
mastoiditis
ICA aneurysm
tumour
basal skull #

non-localising microvascular / ischaemic
RICP

Mimics of VI Palsy

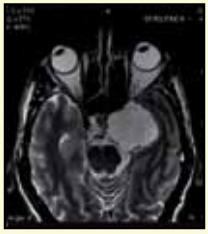
- concomitant ET
- over-correction of XT
- convergence spasm
- Duane's / Mobius
- high myopia
- myaesthenia gravis
- orbital disease



Investigating VI Palsy

1. optic discs:

2. isolated VI in >50yo:
   - BP & routine bloods
   - wait 8 weeks



3. isolated VI in <50yo or VI 'Plus':
   - imaging
   - CSF / bloods

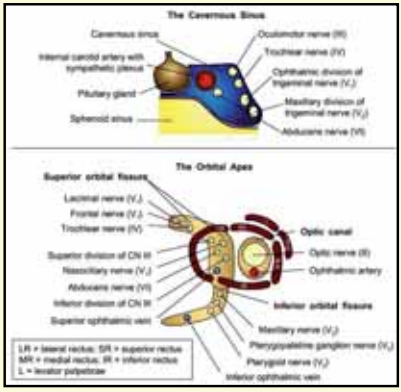
Multiple CN Palsies: 'Focal'

Brainstem:
- CVA, tumour,
- encephalitis, Wernicke's

Subarachnoid:
- meningeal pathology,
- trauma, tumour

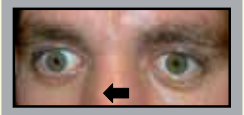
Cavernous:
- tumour, aneurysm,
- CCF, Tolosa-Hunt

Orbital:
- tumour, trauma,
- inflammatory/infectious

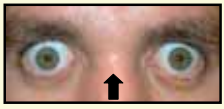


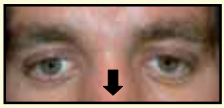
Multiple CN Palsies: 'Diffuse'

Inherited:
- Abetalipoproteinaemia
- Refsum's

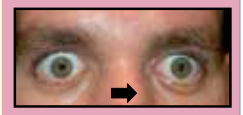


ΔΔ:
- CPEO / KSS
- SANDO / MELAS





Acquired:
- GBS / MFS
- Bickerstaff's



ΔΔ:
- MG / LEMS
- Botulism

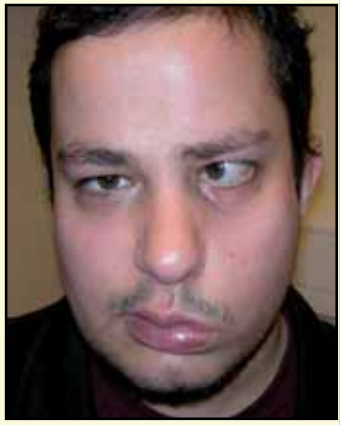
General Tips

- context?
- onset / NH?

- UL or BL?
- isolated?

- Imaging?
- Bloods / CSF?

- always remember MG!



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11. ANISOCORIA

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I. Introduction

The pupil size is determined by the sum of active sympathetic and parasympathetic input to two iris muscles, the radial dilator and the sphincter. Unequal pupil sizes implies an asymmetry in the neuromuscular forces between the two irides. The evaluation of anisocoria begins, like all evaluations, with a careful history. A history of previous ocular trauma, infection or surgery suggests the possibility of a damaged iris which can result in a small pupil that does not dilate well, a large pupil that does not constrict well or simply a non-mobile pupil. a list of all eyedrops should be obtained. Over-the-counter drops for allergies often contain phenylephrine or similar agents which may dilate the pupils. Pilocarpine is a cholinergic agonist used in the treatment of glaucoma and is known to cause small, poorly reactive pupils. Newer eyedrops which lower the intraocular pressure and are based on stimulation of presynaptic alpha -2 receptors may also have secondary effects on pupil size and reactivity.

After the history, examiatnion of the anterior segment is essential as many ocular lesions can result in miosis, mydriasis or poor pupillary response. Acute corneal injury or anterior chamber inflammation may cause ciliary spasm and miosis. Blurred vision, pain,red eye associated with a mid-sized nonreactive pupil suggests angle closure glaucoma Clues that iris damage is the cause of anisocoria include a distorted pupillary shape, iris transillumination defects, synechiae, intraocular inflammation and pigment dispersion (1,2)..

When the ocular history and examination do not, however, reveal any ocular cause of pupillary inequality, then neurologic lesions must be considered. This review will focus on those lesions causing unilateral pupillary dysfunction. Although seemingly a simple task, identifying the abnormal pupil is not always immediately apparent. Two helpful maneuvers are 1. examining the light reflex and 2. measuring the anisocoria in darkness and in bright roomlight.

II. A large and poorly reactive pupil

If the larger pupil reacts poorly to light stimulation compared to the smaller pupil, the larger pupil is the faulty pupil. Such patients will often note that their anisocoria is most evident when they are outdoors or in bright room lighting. Recall that it is the parasympathetic pathway that regulates pupilloconstriction.

The neurons originating the efferent impulse for pupilloconstriction lie in the parasympathetic Edinger-Westphal subnuclei of the oculomotor nuclear complex in the dorsal midbrain and their exiting axons (termed preganglionic fibers) travel with the motor branches of the oculomotor nerve. These parasympathetic fibers eventually synapse at the ciliary ganglion in the posterior orbit. The parasympathetic fibers that exit the ciliary ganglion (termed post-ganglionic fibers)

travel in the short ciliary nerves to reach the iris sphincter which mediates pupilloconstriction and the ciliary muscle which mediates accommodation.

The next step is to determine whether a large, poorly reactive pupil represents an oculomotor nerve palsy (preganglionic lesion), a tonic pupil (postganglionic lesion) or pharmacologic manipulation. The features of these three disorders are summarized in the following paragraphs.

A. An oculomotor nerve palsy

1. The pupil is large and responds poorly to light and near stimulation.
2. The pupil constricts normally to full-strength (1% to 4%) pilocarpine. It may also constrict well to dilute 0.1% pilocarpine due to denervation cholinergic supersensitivity.
3. An ipsilateral ptosis is present. The ptosis may range from a slight, barely noticeable ptosis to complete ptosis.
4. There is a disturbance of ocular motility in the ipsilateral eye. This may not always be an obvious ductional deficit so it is important to perform cross-cover testing in all gaze directions to detect subtle motility defects.
5. A partial oculomotor nerve palsy may manifest as weakness in only 1 or 2 extraocular muscles or levator palpebra. For example, there may be only ptosis (levator weakness) and limited upgaze (superior rectus weakness). Likwise, a partial oculomotor nerve palsy may not demonstrate dysfunction of its parasympathetic function i.e. the pupil may be spared and normal.
6. A dilated and unreactive pupil that occurs in isolation, i.e. no ptosis and no ocular motility, is not an oculomotor nerve palsy.

B. Tonic pupil (7-9)

1. A “freshly denervated” pupil (acute tonic pupil) is very large.
2. The pupil response to light is very poor and may even appear to be completely absent when examined with the naked eye. The slit-lamp, however, will reveal alternating segments of the iris sphincter paralysis and contraction (segmental palsy and segmental contraction).
3. The pupil contraction amplitude to near (accommodative) stimulation is greater than the contraction amplitude to light stimulation. This is called light-near dissociation.
4. The velocity of pupilloconstriction to near stimulation is slow and sustained, i.e. “tonic”. The re-dilation movement after near constriction is also tonic.
5. The tonic pupil constricts better than the normal pupil to dilute 0.1% pilocarpine because of denervation cholinergic supersensitivity.
6. A chronic tonic pupil is often smaller than the normal pupil but shows the characteristic features of a poor light response, segmental palsy, light-near dissociation and tonicity.

Dilute pilocarpine (1.0% or less) is a popular pharmacologic agent for demonstrating cholinergic denervation supersensitivity of the iris sphincter. A dilute 0.1% pilocarpine solution can be pre-

pared in a syringe from 1 part commercially available 1% pilocarpine and 9 parts normal saline. The criterion for diagnosing cholinergic supersensitivity has been proposed as either 1) the affected pupil constricts 0.5mm more than the unaffected pupil under dim ambient lighting or 2) the suspected pupil which is larger than the normal pupil before instillation of pilocarpine then becomes the smaller pupil after instillation of pilocarpine (10,11). About 80% of patients with a tonic pupil will demonstrate cholinergic denercvation supersensitivity. It is important to remember that patients with a dilated pupil from third nerve palsy may also show cholinergic supersensitivity.

Full-strength pilocarpine can be used to differentiate a neurologic pupil from a pharmacologic pupil. An atropinized pupil does not respond (constrict) to either dilute pilocarpine or full strength pilocarpine, such a 1%-4% pilocarpine. A tonic pupil or third nerve palsy may constrict to dilute pilocarpine and both will definitely constrict to full-strength pilocarpine.

C. Pharmacologic mydriasis: the atropinized pupil

1. The pupil is enormously large (8-9mm).
2. The pupil is completely non-reactive to light and near stimulation. There are no areas of segmental contraction visible at the slit-lamp.
3. The pupil does not constrict to full-strength (1%, 2% or 4%) pilocarpine.
4. The patient is typically healthy and there are no other ocular or neurologic examination findings.

Topical mydriatic agents can be divided in to two categories: parasympathetic inhibitors (atropinic-like substances) and sympathomimetics. Remember that it is the atropinized pupil that exhibits all of the aforementioned features. Products containing atropine-like substances include including mydriatic eye drops, scopolamine patches, certain insecticides, plant-based belladonna alkaloids such as Jimson weed and anticholinergic inhalants (12).

Adrenergic-like ubstances that excessively stimulate the dilator muscle can also produce mydriasis but do not paralyze the sphincter muscle. Thus, the pupil is dilated but retains a light reflex that be less extensive compared to the normal pupil. Examples include epinephrine, phenylephrine, ephedrine, hydroxyamphetamine, cocaine, ocular decongestants and adrenergic inhalers. The mydriatic effects of a dilator stimulator can be suspected from the blanching of the conjunctival vessels and mild lid retraction in the eye with the larger pupil.

III. Anisocoria and normal pupil light reflexes

If the pupillary light reflex is normal in both eyes, then it can be assumed that the para-sympathetic system for pupilloconstriction is intact. Often, the anisocoria is apparent only in dim lighting conditions. In such a case, the anisocoria is either due to a sympathetic defect of the smaller pupil or represents a simple physiologic anisocoria. The next step is to examine and compare the rate of pupillary dilation in darkness between the two eyes. If the smaller pupil shows slow and delayed dilation, there is an oculosympathetic defect (Horner syndrome) on that

side. However, only about 50% of patients with Horner syndrome demonstrate an observable dilation lag of the miotic pupil so the absence of dilation lag does not rule out the possibility of a Horner's syndrome. The definitive test to differentiate between physiologic anisocoria and Horner's syndrome remains the cocaine test (discussed in the next section).

Horner syndrome and physiologic anisocoria are summarized in the next paragraphs (13).

A. Horner syndrome

1. The smaller pupil reacts normally to light and near stimulation.
2. The anisocoria in roomlight is small, often 1mm or less, and may be overlooked. The anisocoria becomes more apparent in darkness.
3. The smaller pupil may show dilation lag in darkness.
4. The ipsilateral upper lid ptosis is mild-to-moderate, about 1-2mm, and complete ptosis is never seen. 12-13% of patients with Horner syndrome do not have ptosis. Lower lid ptosis (elevation of the lower lid) may be observed.
5. The distribution of anhidrosis and depends on the location of sympathetic lesion. In lesions of the preganglionic neuron, the entire side of the head, face and neck are usually involved whereas in postganglionic lesions, anhidrosis is limited to a patch on the forehead and the medial side of the nose.
6. The smaller pupil responds (dilates) poorly to cocaine in comparison to the fellow pupil.

Pupillary dilation lag is a very specific clinical finding which, when present, is definitive for an oculosympathetic defect (14). When a light stimulus (roomlight) is abruptly turned off, the dilator muscle in a normal eye is readily activated and promptly dilates the pupil, usually within 5 seconds in darkness. In contrast, the affected pupil of Horner's syndrome, lacking the active sympathetic impulse, is slow to dilate in darkness.

The definitive pharmacologic test for diagnosing a Horner syndrome remains the cocaine test (15). Cocaine inhibits the pre-synaptic reuptake of released norepinephrine at the postganglionic synapse and in doing so, dilates the pupil. When there is a lesion anywhere in the sympathetic pathway to the eye, cocaine fails to dilate the pupil. To perform cocaine testing, place 2 drops of 4% or 10% cocaine HCl solution in each eye and wait 45-60 minutes. A denervated pupil dilates less than the normal pupil, and a post-cocaine anisocoria of 1.0 mm or more is considered diagnostic of a Horner's syndrome.

Apraclonidine (either 0.5% or 1%) is an alternative pharmacologic diagnostic test for Horner syndrome. Apraclonidine has a weak □1-adrenergic agonist action, which produces no significant effect on a normal irisl. In sympathetically denervated eyes, however, the iris dilator is supersensitive to adrenergic substances and the miotic Horner pupil will dilate to topical apraclonidine. In addition, the ptosis of Horner syndrome improves or resolves. Apraclonidine is generally avoided in children younger than 1 year of age, in whom it may cause central nerv-

ous system depression and even acute respiratory arrest. Brimonidine cannot be used as a substitute for apraclonidine for Horner testing.

B. Physiologic anisocoria

1. The anisocoria in roomlight is 0.6 mm or less and may be more notable in darkness.
2. Both pupils constrict normally to light and dilate symmetrically in darkness.
3. Rarely, the anisocoria can change sides. In other words, the smaller pupil appears sometimes on the right side and sometimes on the left side. This has been called "see-saw" aniscoria.
4. After instillation of topical cocaine, both pupils dilate. The anisocoria often disappears after cocaine. The post-cocaine ansicoria is typically less than 1.0 mm.
5. There are no ocular or neurologic abnormalities related to the anisocoria.

Pupillary inequality of size becomes clinically observable at around 0.3 mm. In dim light or darkness, almost 20% of the normal population has an anisocoria of 0.4 mm or more at the moment of examination. In room light, this number drops to about 10%. The degree of inequality in patients with physiologic anisocoria may change from day to day or even from hour to hour (21,22). The pupil response to pharmacologic agents is symmetric between the two eyes.

IV. Bilateral pupillary disorders

Generalized peripheral polyneuropathies cause clinical or subclinical evidence of autonomic dysfunction. When small and unmyelinated fibers are selectively or disproportionately damaged, autonomic dysfunction is the dominant clinical picture. Features associated with an autonomic neuropathy include impairment of cardiovascular, gastrointestinal, urogenital, thermoregulatory and sudomotor function. Pupillomotor dysfunction is also present in many of these autonomic neuropathies. The pupil abnormality takes the form of mixed parasympathetic and sympathetic deficits, and when mild, are easily overlooked due to the bilateral and symmetric nature of the neuropathy. When the neuropathy is bilateral and asymmetric, then an anisocoria may ensue. Considerations for anisocoria due to peripheral neuropathy include diabetic polyneuropathy, infectious neuropathy, connective-tissue disorders (systemic lupus erythematosus, Sjogren's syndrome, scleroderma), Guillain-Barre syndrome or Miller Fisher syndrome.

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12. Nystagmus: a diagnostic guide

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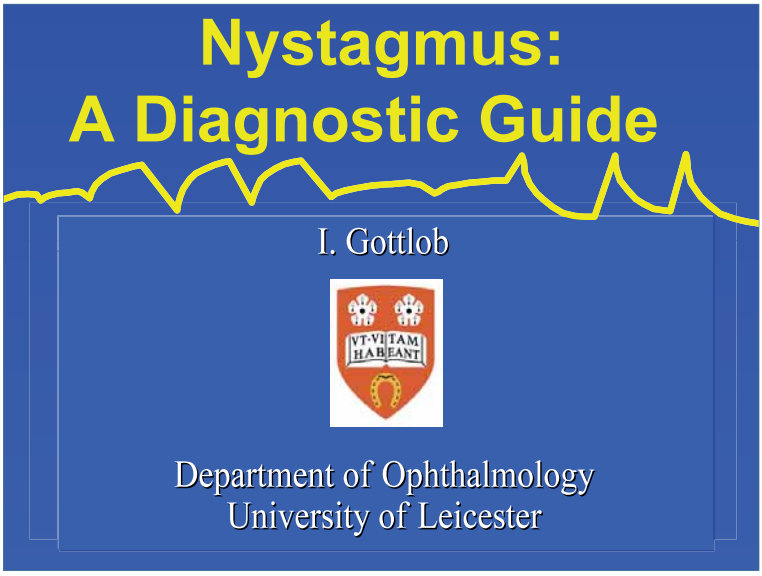
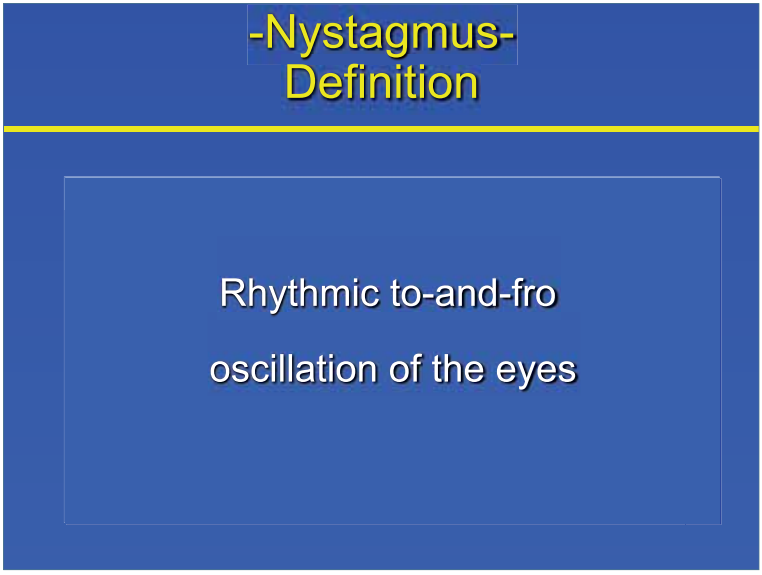




-Nystagmus-
Importance of Classification

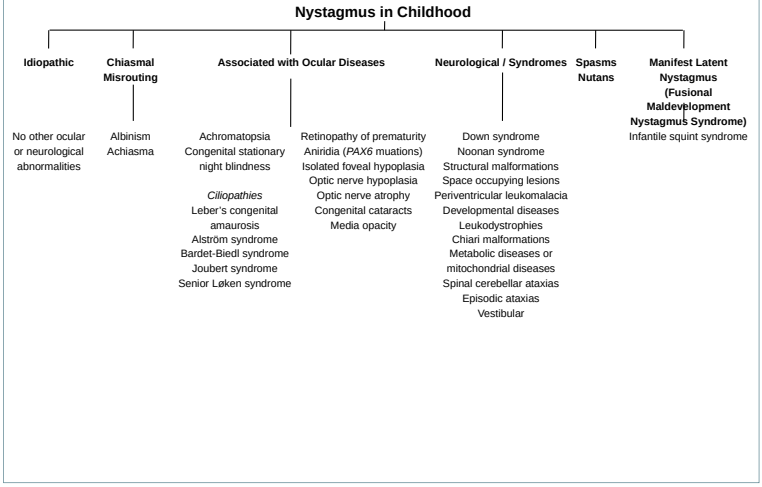
First Sign of:

- Brain disorder
- Congenital squint syndrome
- Idiopathic
- Retinal disease, low vision

Useful Classification

Time of Onset of Nystagmus

- Infancy (stable perception of environment)
- Acquired later in life (illusion of oscillating environment “oscillopsia”)



Investigations

- Visual acuity
- Head position
- Orthoptic/ opthalmological examination
- Electrodiagnostics
- Eye movement recordings
- OCT
- MRI
- Genetics

Investigations Clinical

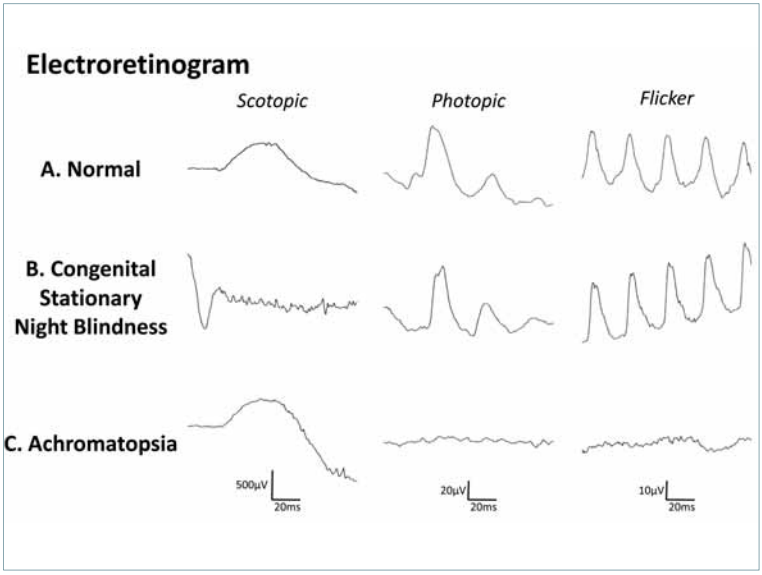
- Visual acuity
  - Both eyes open, RE, LE
  - Head position
  - Both eyes open, RE, LE
  - During visual effort (reading VA chart, near distance, observe changes)

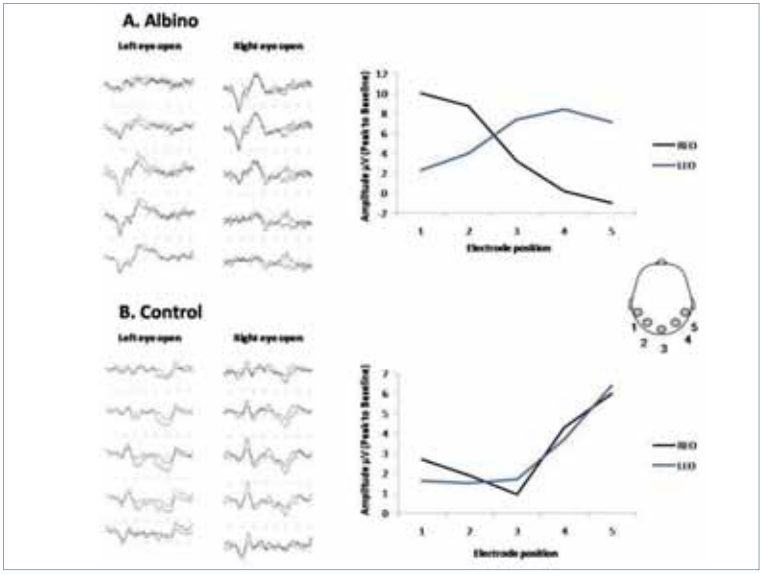
Visual Acuity

- Orthoptics (binocular vision, squint)
- Nystagmus (typical horizontal, other)
- Anterior segment (iris transillumination)
- Posterior Segment (retinal dystrophy, optic nerve, pigmentation)

Electrophysiology

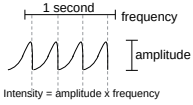
- VEP
  - abnormal crossing (albinism, achiasma)
- ERG
  - Retinal disorders (achromatopsia, congenital stationary night blindness, Lebers congenital amaurosis, etc)



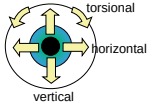


Classification using eye movements: what to look for

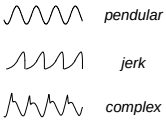
Intensity



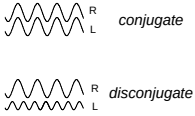
Plane



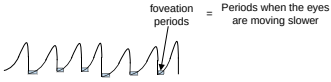
Waveform



Conjugacy



Foveation Dynamics

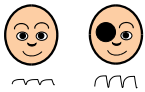


Classification using eye movements: what to look for

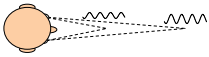
Dependant upon:

Time

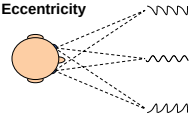
Occlusion



Convergence



Eccentricity

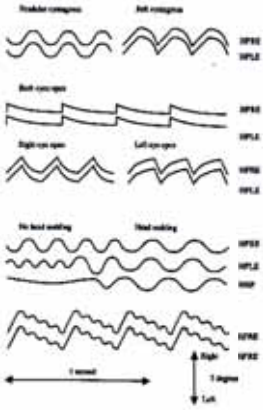


Idiopathic

Latent Nystagmus

Spasmus nutans

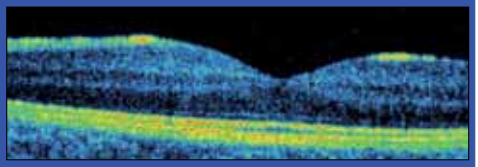
Sensory nystagmus



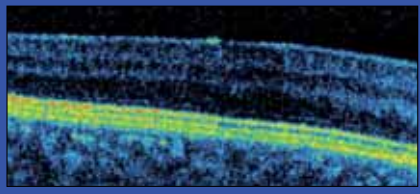
I. Gottlob: Curr Opin Ophthalmol. 12: 378-83, 2001.

Optical Coherence Tomography

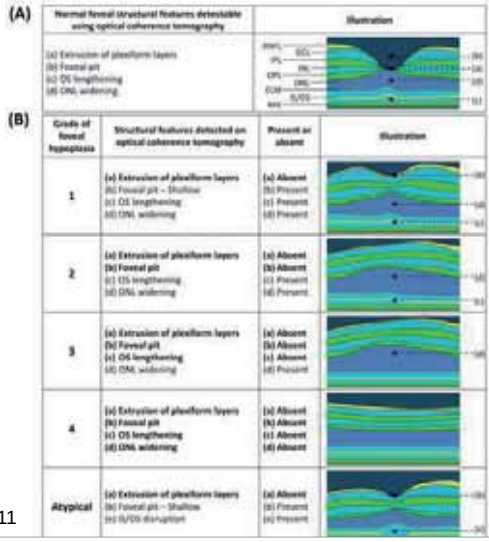
Normal



Foveal hypoplasia

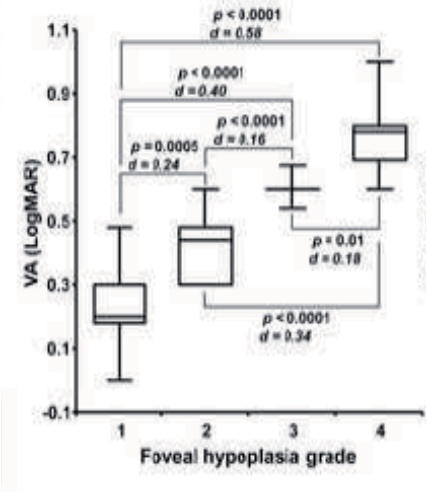


Grading of Foveal Hypoplasia



Thomas et al.
Ophthalmology 2011

Visual Acuity and Foveal Hypoplasia Grade



MRI

- Nystagmus not typical (not horizontal, dysconjugate, onset at unusual age)
- Oscillopsia (acquired)
- Other Neurological problems
- Optic nerve anomalies (hypoplasia, atrophy)
- Not when known ocular anomalies (latent nystagmus, retina…)

Genetics

- Genetics
  - *FRMD7*
  - *PAX6*
  - Achromatopsia
  - Albinism
  - Congenital Stationary Night Blindness
  - …

Nystagmus Forms in Infancy

- Latent / manifest latent
- Idiopathic
- Spasmus nutans
- Retinal diseases / low vision
- Neurological - syndromes

Latent/ Manifest Latent Nystagmus

- Infantile squint syndrome
- Increases in amplitude and changes direction upon covering one eye
- Typical eye moment recordings (jerk, decreasing velocity of slow phases)
- Dampens on adduction and small squint angle

Latent Nystagmus Treatment

- Treatment of amblyopia
- Correction of head turn
- Correction of squint can reduce nystagmus amplitude

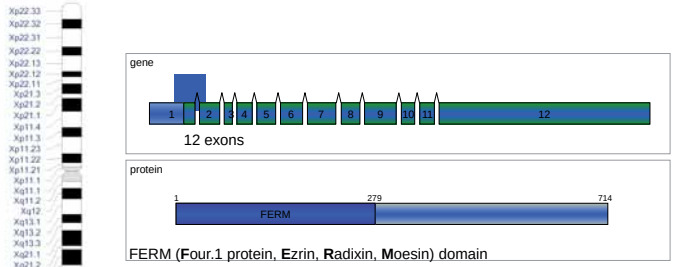
Idiopathic Infantile Nystagmus

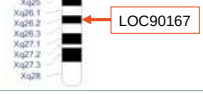
- Diagnosis of exclusion
- Often hereditary (mostly X-linked, *FRMD7* gene)
- Onset in first 3 months of life
- Nystagmus amplitude and form changes with age
- Horizontal
- Direction and size same in both eyes

Idiopathic Infantile Nystagmus

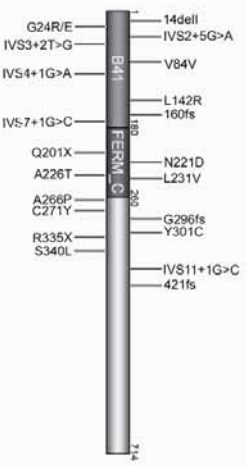
- Null point
- Abnormal head turn
- Often refractive errors
- Head nodding
- Good visual acuity (6/6 to 6/12)

FERMD7
(FRMD7= FERM domain containing 7)



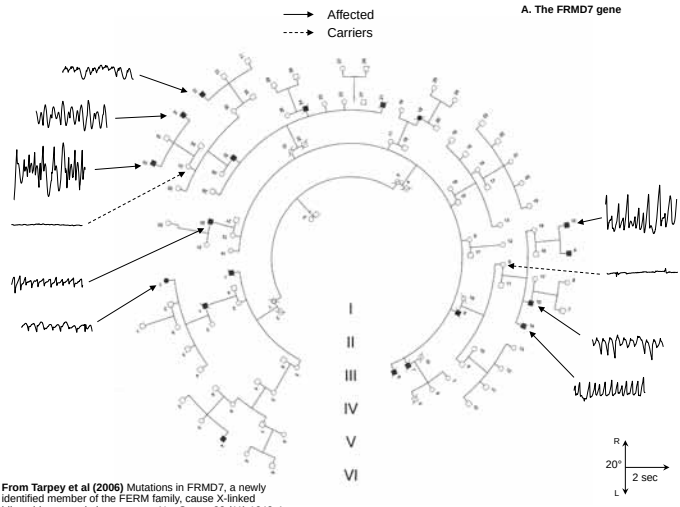


FRMD7



Sample	Class	Mutation	Origin
N15	M	G70A, G24R	Ireland
N7	T	IVS2+5G>A	England
N4	T	IVS3+2 T>G	England
N5	S	G252A, V84V	England
N1, F26	T	IVS4+1G>A	England, England
N16	M	T425G, L142R	Ireland
N13	T	IVS7+1G>C	Madagascar
N2	T	C601T, Q201X	Italy-Germany
N3	M	T691G, L231V	Ireland -Germany
N6, SF21	M	G796C, A266P	England, England
N11	M	G812A, C271Y	Scotland
N14	T	887delG, G296fs	Austria
N12	M	A902G, Y301C	England
N10, F24, SM08	T	C1003T, R335X	England, India, England
N9	T	IVS11+1G>C	Germany
F31	del	41_43delAGA, 14dell	England
F21	M	G71A, G24E	Austria
F28	T	479InsT, 160fs	England
F15	M	A661G, N221D	England
F16	M	G676A, A226T	England
F20	M	C1019T, S340L	Romania
SM10	T	1262delC, 421fs	England

Family tree where inherited nystagmus is caused by mutations of the FRMD7 gene



From Tarpey et al (2006) Mutations in FRMD7, a newly identified member of the FERM family, cause X-linked idiopathic congenital nystagmus. Nat Genet. 38 (11):1242-4.

Phenotype of Patients with Mutations in FRMD7

Median VA 6/9.5

7% squint

Most patients good stereovision

With FRMD7 mutation no sigificant head turn

~50% of carriers affected

Idiopathic Congenital Nystagmus Therapy

- Exact refraction, contact lenses
- Surgery for abnormal head position if patients have eccentric null point
- Artificial divergence surgery
- Pharmacological therapy

Periodic Alternating Nystagmus in IIN

- From 70 patients with IIN investigated for PAN 21had PAN (24%)
- All had mutations in *FRMD7* (missense)

Thomas M et al. Brain 2011

Periodic Alternating Nystagmus in IIN

- PAN only detected on eye movement recordings
- Cycle 90 to 200 s
- Significant sibship clustering although not all affected family members have PAN

Spasmus Nutans

- Triad: Nystagmus, Head nodding, abnormal head position
- Onset 6 months to 1 year of age
- Disappears by 2 to 4 years of age clinically
- Not hereditary

Spasmus Nutans

- Small nystagmus of high frequency
- Disconjugacy in amplitude and frequency of right and left eyes
- Horizontal, vertical, oblique
- Head nodding suppresses nystagmus
- Retinal diseases can mimic spasmus nutans

Spasmus Nutans

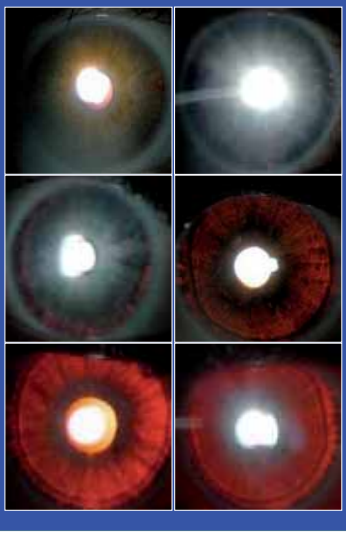
- Associated with brain lesions (Tumors)
- Neurological examination, MRI

Albinism

- Pigment deficiency
- Hereditary
- Nystagmus similar to idiopathic nystagmus

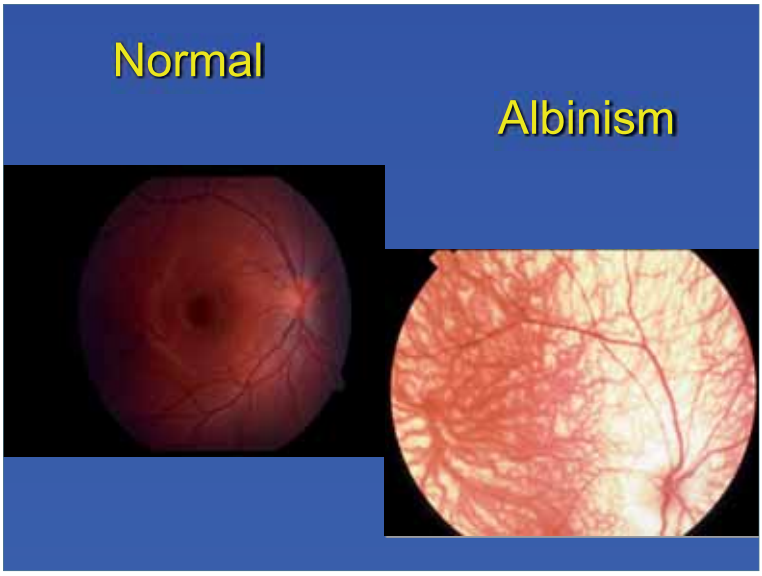
Albinism

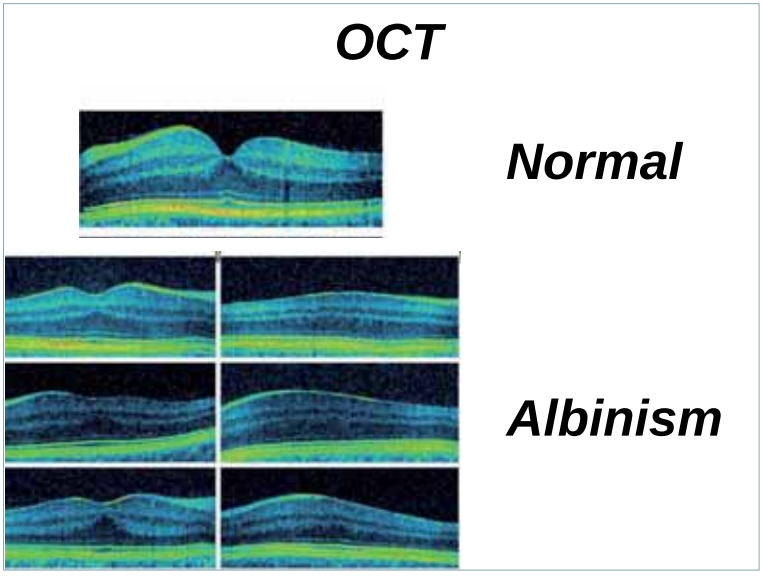
Iris transillumination



Albinism

- Retinal hypopigmentation
- Hypoplasia of central retina
- Small cupless optic disks

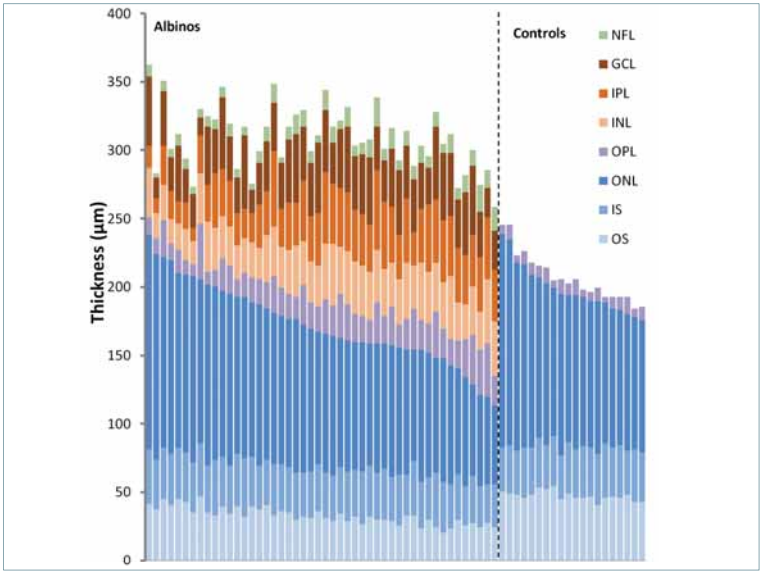

Normal
Albinism


OCT
Normal
Albinism

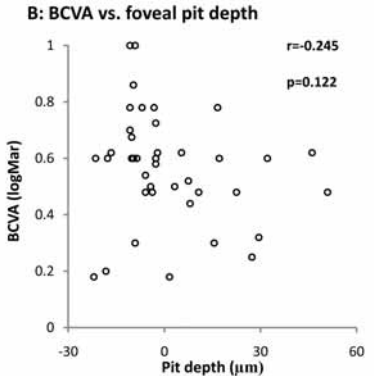
Albinism
Can OCT Predict VA?

Literature

- Weak inverse correlation between foveal thickness and VA (Harvey et al.)
- Foveal pit insignificant for VA (Marmor et al., Mc Alistair et al.)

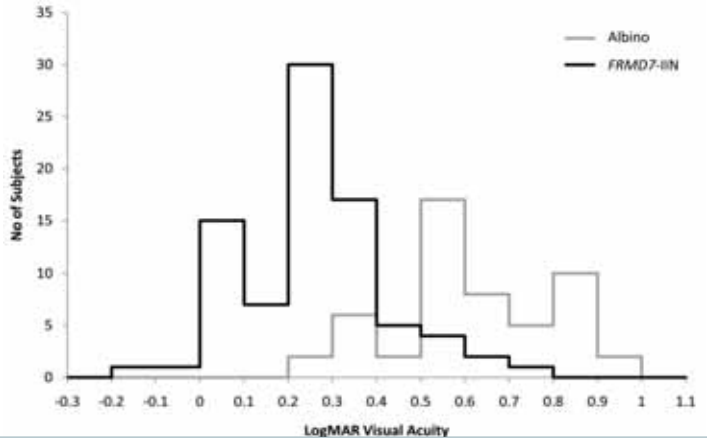


Albinism
What Determines Visual Acuity ?



Mohammad et al. (2011) *Ophthalmol 2011*

Visual Acuity in IIN and Albinism

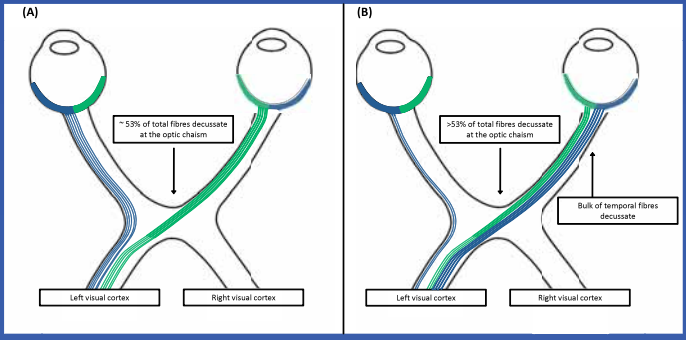


Albinism

Abnormal crossing of axons

Normal

Albinism



Retinal Diseases

- Congenital stationary night blindness
- Achromatopsia
- Blue-cone monochromatism
- Lebers congenital amaurosis

Achiasma

- No crossing of optic nerve fibers in chiasm (VEP)
- See-saw nystagmus
- Sometimes optic nerve hypoplasia

Nystagmus
Retinal Diseases

- Congenital stationary night blindness
- Achromatopsia
- Blue-cone monochromatism
- Lebers congenital amaurosis
- PAX6 mutations (aniridia)

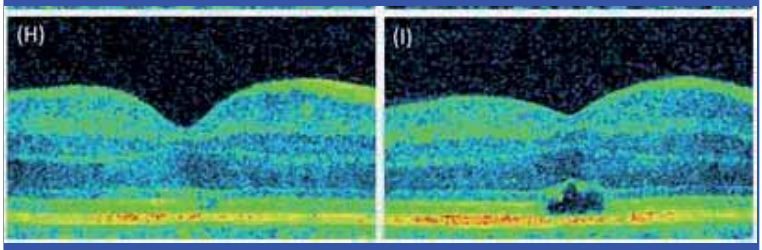
Retinal Diseases Associated with Nystagmus

- Low visual acuity (6/9 to blind)
- Sensitivity to light/night blindness
- Head nodding
- Abnormal head turn

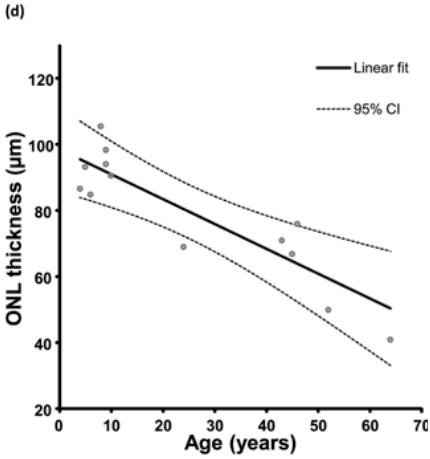
-Retinal Diseases and Low Vision-
Nystagmus

- Vertical and/or horizontal
- Associated and dissociated

Achromatopsia: OCT

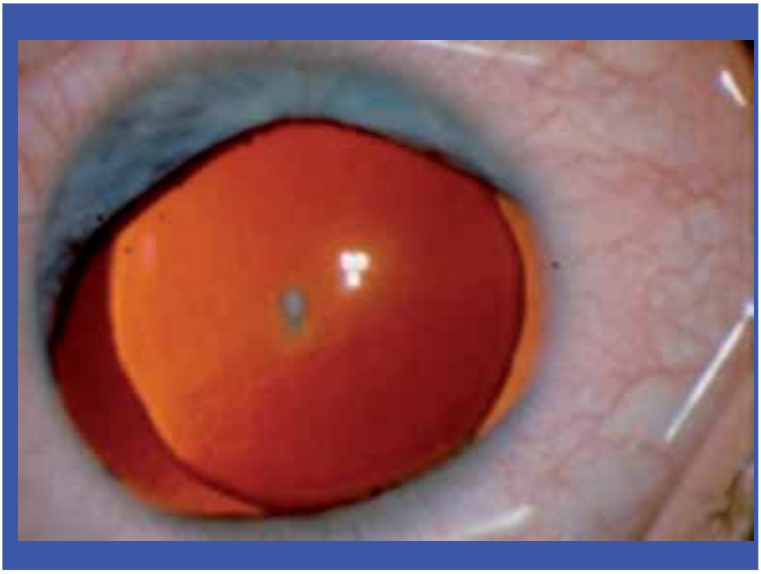


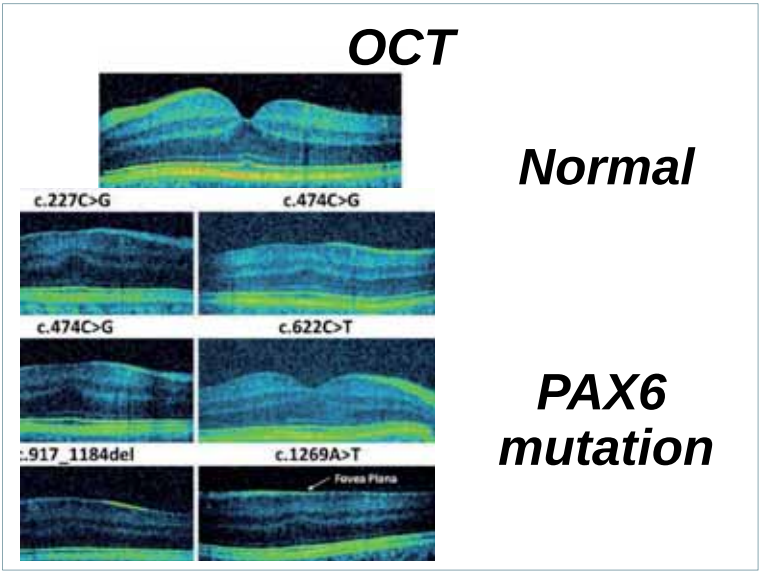
Achromatopsia: OCT



PAX6 Mutation

- Autosomal dominant inheritance (11p13)
- Variable phenotype
- Aniridia
- Early cataract
- Nystagmus
- Foveal hypoplasia




OCT
c.227C>G
c.474C>G
c.474C>G
c.622C>T
.917_1184del
c.1269A>T
Fovea Plana
Normal
PAX6
mutation

Low Vision in Infancy

- Optic nerve hypoplasia
- Congenital cataract
- Retinopathy of prematurity

Neurological disorders Syndromes

- Downs Syndrome
- Brain malformation
- Leigh subacute necrotising encephalopathy
- Pelizaeus-Merzbacher Disease
- Joubert Syndrome

Pelizaeus-Merzbacher Disease

- X-linked leukodystrophy
- Elliptical, pendular and up-beat nystagmus
- Head shaking, athetoid movements, cerebellar signs, pyramidal signs, spasticity, seizures
- On MRI lack of myelination

Joubert Syndrome

- Retinal dystrophy with relative good VA
- Tachypnoea
- Hypoplasia of cerebellar vermis
- Developmental delay
- Torsional, pendular, see-saw nystagmus

-Nystagmus-
When is ERG Indicated?

- Atypical, dissociated, vertical
- Low vision
- Photophobia
- Difference in daylight and night vision
- High myopia

-Nystagmus-
When is MRI Indicated?

- Atypical, dissociated, vertical
- Optic nerve hypoplasia or atrophy
- Other neurological symptoms
- Acquired
- Oscillopsia

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13. Involuntary facial movement disorders: the use of botulinum toxin

• Carl GOBIN, Antwerp, Belgium

Introduction

In 1895 prof. E. Van Ermengen from the University of Ghent (Belgium) discovered the organism Bacillus Clostridium Botulinum.

In 1973 Dr. Alan Scott from the Smith-Kettlewell Eye Research Foundation in San Francisco published his first results of the effect of botulinum toxin type-A to weaken the extraocular muscles of monkeys.

In 1980 Dr. Alan Scott published an article in which he presented " Botulinum toxin injections into extraocular muscles as an alternative to strabismus surgery".

In 1989 botulinum toxin was approved for the treatment of strabismus and numerous disorders of spasticity including blepharospasm, hemifacial spasm, Meige's syndrome, cervical dystonia and spastic torticollis.

Botulinum toxin: What is it & how does it work?

Botulinum toxin is produced by Clostridium botulinum: an anaerobic, gram + bacteria.

There are seven different types identified which all inhibit the release of acetylcholine (ACh) at the myoneural junction. Botulinum toxin type-A is the most powerful to block the neuromuscular junction with the longest time of action. It is commercially available as Botox and Dysport.

Botulinum toxin enzymatically inactivates a specific protein that is required for the docking and fusion of vesicles containing ACh into the neuromuscular junction. It takes approximately 3 to 4 days for its effect to become clinically apparent. The inhibition of ACh release results in localized muscle weakness. After 2 months the axon begins to expand and new nerve terminal sprouts emerge and extend towards the muscle surface.

Indications

ESSENTIAL BLEPHAROSPASM – MEIGE SYNDROME

Essential blepharospasm is a segment dystonia of unknown origin characterized by bilateral, involuntary, uncontrollable closure of the eyelids due to spasms of the orbicularis oculi muscles.

John Elston from Oxford (U.K.) categorized blepharospasm into six "levels":
I: functionally blind; II: no television, no reading; III: cannot leave the house unassisted
IV: mild handicap; V: no driving; VI: drives a car
Meige syndrome is a facial dystonia with blepharospasm extending to the oromandibular area and the platysma.

To analyse the blepharospasm clinically we developed a simple protocol:

- palpebral fissure measurement
- levator muscle function measurement
- resistance to manual opening of the eyelids:
  - 1+: no resistance
  - 2+: moderate resistance
  - 3+: 100% resistance; cannot open the eyes

The resistance measurement gives an qualitative analysis of the effect of the treatment with botulinum toxin.

Treatment: the dose of botulinum toxin injected is invariable
the periorbital place of injection is invariable
the only variable is the frequency of injection (/4 months to /1 month)

There are few complications:
local hematoma due to the injection
not enough effect
ptosis due to paresis of the levator muscle

RARE ETIOLOGIES OF BLEPHAROSPASM

- Blepharospasm associated with lesions of the brainstem & basal ganglia
- Blepharoclonus & reflex blepharospasm (CVA, trauma)
- Ocular blepharospasm: trichiasis, entropion…
- Blepharospasm associated with drug-induced tardive dyskinesis (neuroleptica)
- Facial tics (children)
- Non- organic blepharospasm: post emotionally traumatic event
- Focal seizures: epilepsy

HEMIFACIAL SPASM

Unilateral, involuntary, uncontrollable, painless spasms of the muscles innervated by the facial nerve

This leads to facial asymmetry:

- wrinkles of the forehead due to contraction m. frontalis
- arched brow elevation due to contraction m. frontalis
- spasm orbital orbicularis
- flatter naso-labial fold
- platysma contraction

Etiology: compression of the root of the facial nerve

- Vascular: anterior & posterior inferior cerebellar artery (95 %)
- Aneurysma
- Infra-temporal hemangiomas
- Tumors: epidermoids, acoustic neurinoma, meningioma…

Treatment:

- Surgical: Janetta procedure = posterior microvascular decompression
- Botulinum toxine: controls symptoms, no cure
    - 4 x 5 IU periorbital: orbicularis oculi muscle
    - Contralateral "browlift": change balance orbicularis vs. frontalis muscle
    - Unilateral frontalis muscle weakening to lower the brow
    - Zygomaticus major & minor complex to deal with asymmetrical mouth

SPASTIC ENTROPION

Etiology: lesion of the cornea, trichiasis
lower lid laxity (age related: tarsal plate, lower lid retractors)

Treatment: infiltration tarsal part of the inferior orbicularis muscle with 3 x 5 IU botulinum toxin

PTOSIS INDUCTION

Protect the cornea of corneal ulceration: protective ptosis.

- Neurotrophic keratitis: loss of trigeminal innervation
  CVA, aneurysm, MS, acustic neuroma, neurofibroma

- Exposure keratitis: incomplete lid closure
  Neuroparalytic (VII): otitis, herpes, parotic gland, iatrogenic

Treatment: inject 5-10 IU botulinum toxin in the levator muscle; 1-5 months effective
excellent substitute for tarsorraphy

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14. Examination of the strabismic patient

• Daisy GODTS, Antwerp, Belgium

EUPO course 2012

Neuro-ophthalmology and Strabismus

Examination of the strabismic patient

Daisy Godts, orthoptist

Antwerp University Hospital

Universiteit Antwerpen

UZA

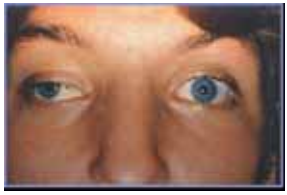
Examination of the strabismic patient

1. **Family, systemic and ocular history**
2. External examination
3. Light reflex
4. Ocular alignment
5. Ocular motility
6. Binocular functions
7. Assessment of visual acuity and fixation pattern
8. Cycloplegic refraction

1. History taken

- Family history
  - Strabismus, “lazy eye”, glasses
- Medical history
  - History of the mother’s pregnancy and birth history
  - General development
  - Past and current illnesses
  - Current medication
  - Any trauma, especially to the head or face
  - Hereditary factors

1. History taken



- Ophthalmic history
  - **Strabismus**
    - Constant / intermittent
    - Unilateral / alternating
    - Horizontal / vertical
    - Near and/or distance

1. History taken

- Ophthalmic history
  - **Diplopia**
    - Horizontal / vertical / oblique / tilted
    - Near and/or distance / primary position / horizontal and/or vertical gaze
    - Permanent / intermittent
    - Onset (sudden-intermittent) / progression
  - **Previous treatment**
    - Spectacles / occlusion / orthoptics / drops / operations

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2. External examination

While taking history, observe the patient

- Eyelids, eyelashes and orbit
- Anatomy of the face and the orbital rim
- Presence of oculofacial anomalies
- Position of the head and face

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Examination of the strabismic patient

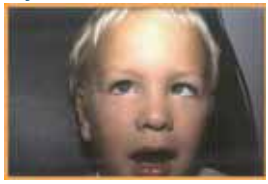
- **Light reflex ± straight**
  - **Brückner test**
  - **15Δ Prism test**
  - **Gracis biprism test**
  - Cover test
  - Ocular motility
  - …..

Age 13 months: Intermittent esotropia

Examination of the strabismic patient

- **Light reflex: strabismus**
  - **Cover test**
  - **Angle of deviation**
  - **Ocular motility**
  - **….**

Age 5 years: Manifest strabismus

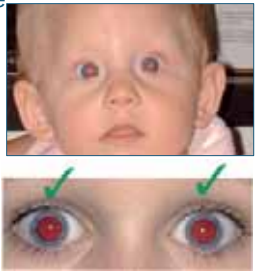


Age 30 years: Manifest strabismus

Brückner test

To determine whether both eyes can focus sharply or not, irrespective of the presence of an ametropia

- **Two deep red symmetric reflexes:** equal brightness and color → **normal**
- *No amblyopia, **no strabismus**, no ametropia > 0.5 D and no astigmatism > 1 D is present*



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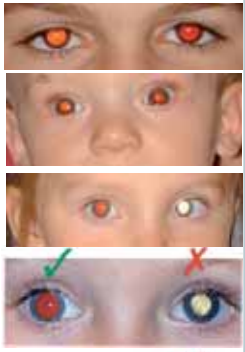
Brückner test

To determine whether both eyes can focus sharply or not, irrespective of the presence of an ametropia

- **Two asymmetric refexes**: one brighter and lighter reflex → **abnormal**
- ***Strabismus**, amblyopia, refractive errors and hypo-accommodation may be present*



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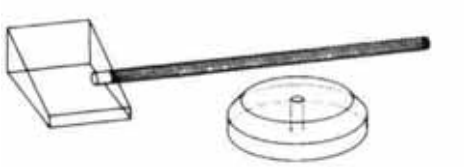
15Δ prism test

The 15Δ prism test is used in all patients with apparently straight eyes or with a microstrabismus and is used to demonstrate **peripheral motor fusion**



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15Δ prism test

- First the prism test **base-out** is performed to demonstrate **convergent motor fusion**

- Then the test is repeated with the prism **base-in** to demonstrate **divergent motor fusion or eye dominance**

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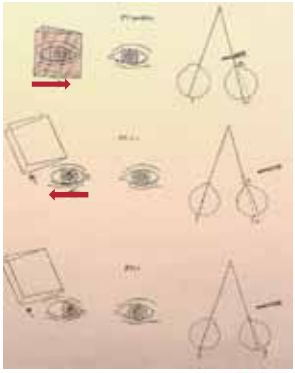
15Δ prism test: Prism base OUT

Monocular movement of the eye behind the prism:

- ***PT positive***: good convergent motor fusion

➡ Recovery movement after removing the prism: ***PT ++***

Motor fusion can induce a recovery movement to maintain bifoveal fixation



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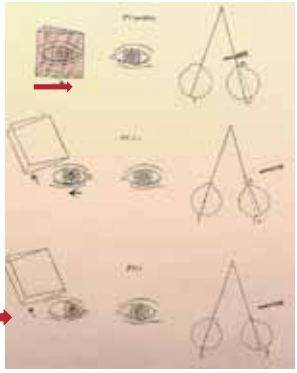
15Δ prism test: Prism base OUT

Monocular movement of the eye behind the prism:

- ***PT positive***: good convergent motor fusion

➡ No recovery movement: ***PT +***

The motor fusion is not strong enough to induce a recovery movement, indicating an **intermittent esodeviation**



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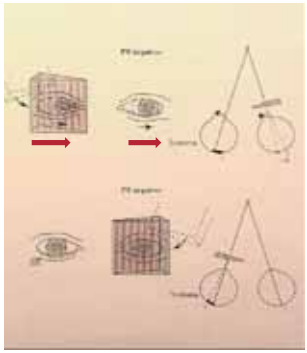
15Δ prism test: Prism base OUT

Conjugate movement of the eyes:

- ***PT negative***

  No convergent motor fusion

  The prism is held in front of the **dominant eye**



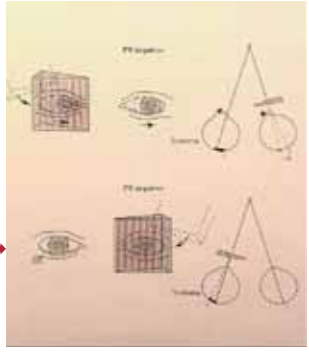
15Δ prism test: Prism base OUT

No movement of the eyes:

- ***PT negative***

  No convergent motor fusion

  The prism is held in front of the **NON-dominant eye**



15Δ prism test: Prism base IN

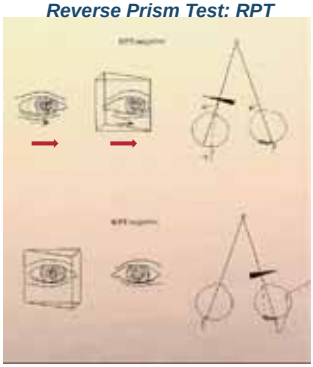
Conjugate movement of the eyes:

- ***RPT negative***

  No divergent motor fusion

  The prism is held in front of the **dominant eye**

Reverse Prism Test: RPT



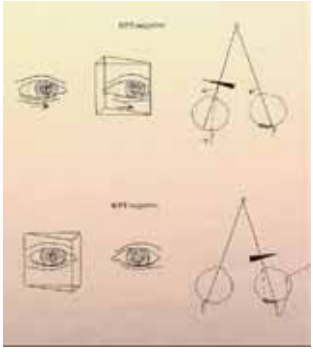
15Δ prism test: Prism base IN

No movement of the eyes:

- ***RPT negative***

  No divergent motor fusion

  The prism is held in front of the **non-dominant eye**



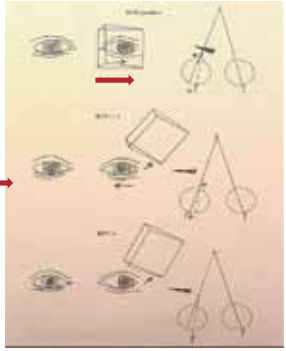
15Δ prism test: Prism base IN

Monocular movement of the eye behind the prism:

- ***RPT positive***: good divergent motor fusion

  Recovery movement after removing the prism: *RPT* ++

  Motor fusion can induce a recovery movement to maintain bifoveal fixation



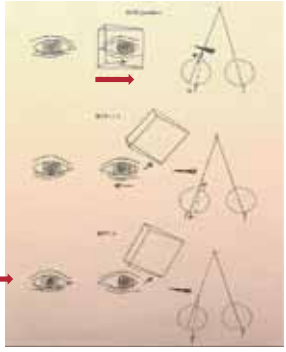
15Δ prism test: Prism base IN

Monocular movement of the eye behind the prism:

- ***RPT positive***: good divergent motor fusion

  NO recovery movement: *RPT* +

  The motor fusion is not strong enough to induce a recovery movement, indicating an **intermittent exodeviation**



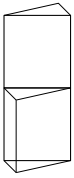
15Δ prism test

A double positive prism test is normal because the motor fusion is strong enough to overcome 15Δ and to maintain bifoveal fixation

A negative reverse prism test with an alternate dominance is normal

Gracis biprism test

- Double prism base-out , base-in of 4, 6 or 8 prism diopters
- To demonstrate: - Foveal fusion or foveal suppression
  - Eye dominance
  - Amblyopia

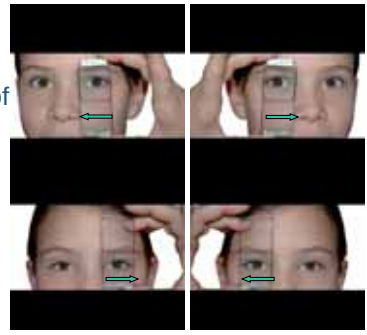


Gracis biprism test

Prism base-IN
base-OUT

- Monocular movement of each eye behind the prism:

Bifoveal fixation

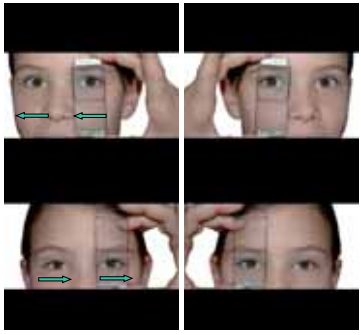


Gracis biprism test

Prism base-IN
base-OUT

- Conjugate movement of both eyes when prisms before LE
- No movement when prism before RE

LE dominant

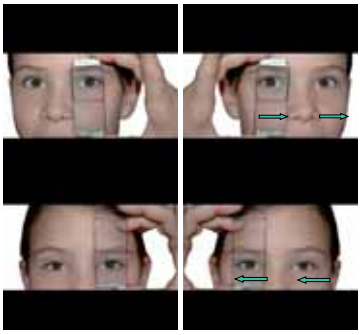


Gracis biprism test

Prism base-IN
base-OUT

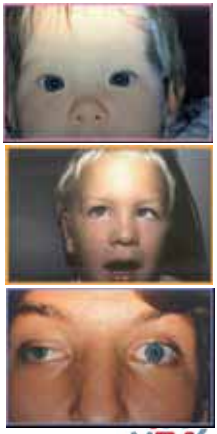
- No movement when prism before LE
- Conjugate movement of both eyes when prisms before RE

RE dominant



Examination of the strabismic patient

- **Light reflex ± straight**
  - Brückner test
  - Prism test
  - Gracis biprism test
  - **Cover test**
- **Light reflex strabismus**
  - **Cover test**
  - Angle of deviation
  - Ocular motility



4. Ocular alignment - Cover test

The cover test for near and distance fixation is the most important part of any examination for strabismus or amblyopia

It can be done with patients of all ages and requires only the minimum of cooperation from a patient

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4. Ocular alignment - Cover test

The term **"*cover test*"** refers to the whole test

The cover test has been subdivided into the ***cover-uncover test*** to detect the presence of a **manifest deviation**, and the ***alternate cover test*** to detect a **latent deviation** by dissociation of the eyes

4. Ocular alignment - Cover-uncover test

- No movement of the uncovered eye:

  No manifest deviation →

- Any movement of the uncovered eye:

  Manifest deviation

4. Ocular alignment - Cover-uncover test

- No movement of the uncovered eye:

  No manifest deviation

- Any movement of the uncovered eye: →

  Manifest deviation

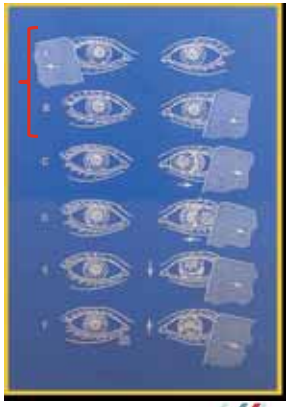
4. Ocular alignment - *Alternate cover test*

- No movement of the covered eye: →

  No latent deviation

- Any movement of the covered eye:

  Latent deviation



4. Ocular alignment - *Alternate cover test*

- No movement of the covered eye:

  No latent deviation

- Any movement of the covered eye: →

  Latent deviation

4. Ocular alignment - *Alternate cover test*

Evaluate recovery movement

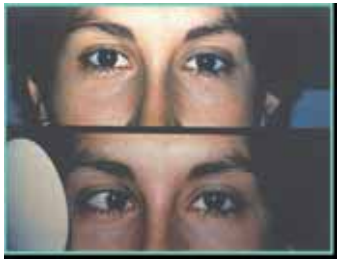
Latent deviation

esoforia

Bad recovery

↓

Esotropia RE



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4. Ocular alignment - *Alternate cover test*

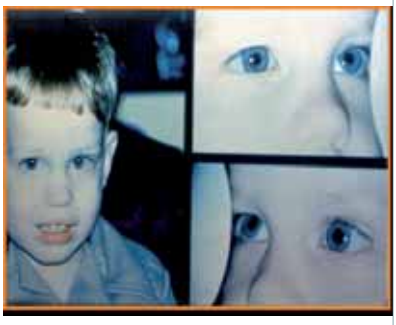
Evaluate vertical movement behind the cover

RE fixing: LE up

LE fixing: RE up

↓

Dissociated Vertical Deviation (DVD)



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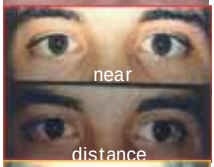
Cover test: *Information provided by the cover test*

- The direction of the deviation

- The difference in angle for near and distance fixation



- The effect of accommodation and of the patient's refractive error

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Cover test: *Information provided by the cover test*

- Constant or intermittent strabismus

- Unilateral or alternating strabismus

- The difference in primary and secondary deviation

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Cover test: *Information provided by the cover test*

- Estimation of the visual acuity in a constantly squinting eye by a study of fixation

Cover test

Measure:

- At distance and near
- With and without glasses
- With and without torticollis
- On light and object fixation

4. Ocular alignment - *Angle of deviation*

The angle of deviation can be measured objectively or subjectively or can be estimated by the observer from the position of the corneal reflection in the squinting eye

- Hirschberg's test
- Prism reflection test
- Prism cover test
- Maddox Rod
- Synoptophore

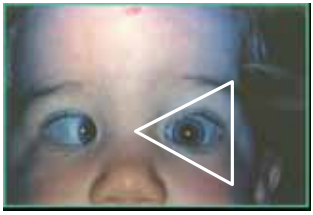
4. Ocular alignment - Hirschberg's test

1mm displacement = 7° deviation

- In the middle of the pupil: 0°
- On the margin of the pupil: 12° - 15°
- Between pupil and limbus: 25° - 30°
- Over the limbus: 45°

4. Ocular alignment - Prism reflection test

- Place prism in front of the fixing eye with the apex of the prism in the direction of the deviation
  - **Base-out: esotropia**
  - Base-in: exotropia
  - Base-down: hypotropia
  - Base-up: hypertropia



4. Ocular alignment - Prism reflection test

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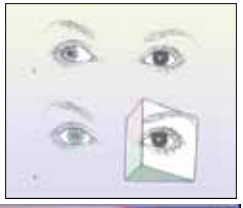
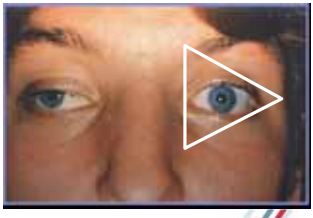
  - Base-down: hypotropia
  - Base-up: hypertropia





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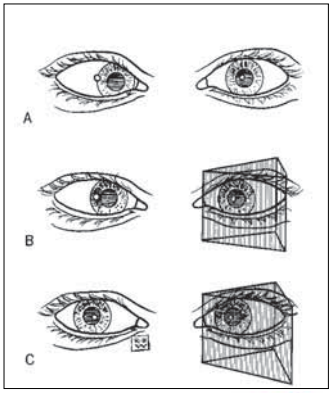
  - Base-in: exotropia
  - **Base-down: hypotropia**
  - Base-up: hypertropia

4. Ocular alignment - Prism reflection test

- Place prism in front of the fixing eye with the apex of the prism in the direction of the deviation
  - Base-out: esotropia
  - Base-in: exotropia
  - Base-down: hypotropia
  - **Base-up: hypertropia**

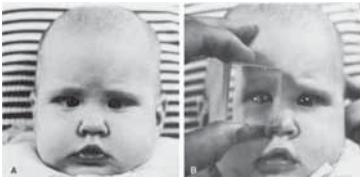
4. Ocular alignment - Prism reflection test

- The prism strength is increased until the reflection matches that previously noted in the fixing eye



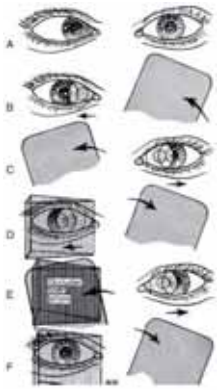
4. Ocular alignment - Prism reflection test

- Use in patients with:
  - Poor vision
  - Nystagmus
  - Poor cooperation



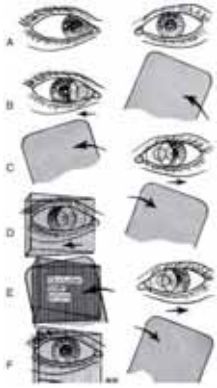
4. Ocular alignment - Alternate Prism Cover Test - APCT

- The APCT is the method of choice to measure the **objective** angle of deviation
- In patients with:
  - Good cooperation
  - Good fixation



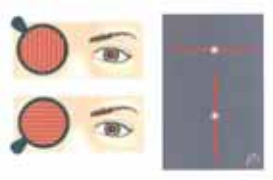
4. Ocular alignment - Alternate Prism Cover Test - APCT

- The patient fixes a light and a prism or prism bar is placed in front of the eye
- The prism strength is adjusted until there is no movement when the eyes are covered



4. Ocular alignment - Prism and Maddox rod

- A **subjective** method of measuring small horizontal, vertical and torsional deviations
- Dissociations of the eyes is achieved by presenting a spotlight to one eye and a line image to the other eye



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4. Ocular alignment - Prism and Maddox rod

The grooves of the Maddox rod are placed horizontally to measure a horizontal deviation, the patient sees a vertical line

- No horizontal deviation
- Exodeviation
- Esodeviation

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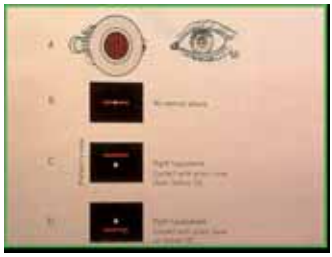
4. Ocular alignment - Prism and Maddox rod

The grooves of the Maddox rod are placed vertically to measure a vertical deviation, the patient sees a horizontal line

- No vertical deviation
- Right hypodeviation
- Right hyperdeviation

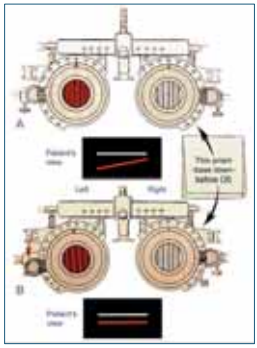


4. Ocular alignment - Prism and Maddox rod

When the patient doesn't see the line through the light, measure the deviation by using a horizontal or vertical prisms until the line is in the middle of the light

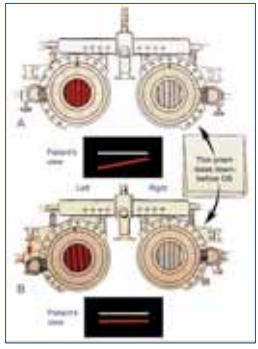
4. Ocular alignment - Maddox double rod

- To measure a cyclodeviation, two Maddox rods are placed vertically in a trial frame, one before each eye
- A vertical prism can be used to separate the lines when no vertical deviation is present



4. Ocular alignment - Maddox double rod

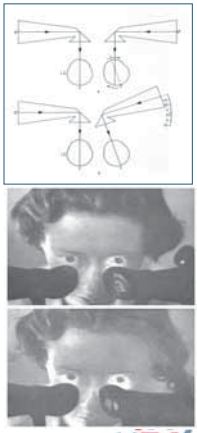
- The patient adjusts the position of the lines by rotating the rods in the trial frame until both lines are parallel and straight
- The amount of cyclodeviation is measured in degrees from the scale of the trial frame
- Can be measured at near/distance and in different gaze positions



4. Ocular alignment - Synoptophore

Horizontal, vertical and torsional deviations can be measured

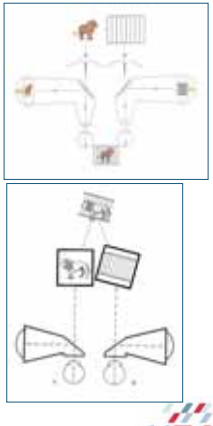
- **Objective angle of deviation**
  - **Adjust the arms until no eye movement is seen**
    - **Horizontal**
    - **Vertical**
- Subjective angle of deviation



4. Ocular alignment - Synoptophore

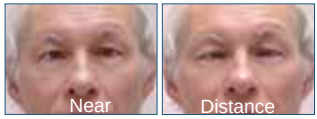
Horizontal, vertical and torsional deviations can be measured

- Objective angle of deviation
- **Subjective angle of deviation**
  - **The patients puts the two images together**
    - **Horizontal**
    - **Vertical**
    - **Torsional**



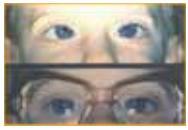
Measure angle of deviation

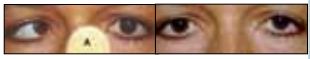
- At near and distance
  - N VI
    - Esodeviation at distance > at near
  - Accommodative esotropia
    - Esodeviation at near > at distance
  - Intermittent exotropia
    - Exodeviation at distance > at near
  - Exotropia with convergence insufficiency
    - Exodeviation at near > at distance

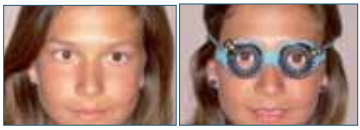


Measure angle of deviation

- With and without glasses
  - Effect of optical correction
- Fixating light and an accommodative object
  - Effect of accommodation
- With +3.00 glasses: Relax accommodation
  - Eso <<
  - Exo >>





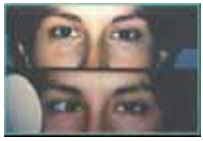


Measure angle of deviation

- With and without torticollis

- Left and right eye fixating
  - Paralytic strabismus
  - Difference in accommodation

- After occlusion: Interruption of fusion
  - Intermittent exotropia
  - Intermittent esotropia
  - DVD

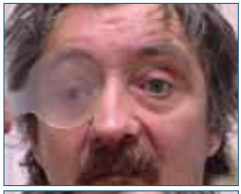


Measure angle of deviation

- After prism adaptation
  - Measure maximum deviation of strabismus by APCT
  - Let the patient wear the total amount of prism during 60'
  - Measure deviation again and add prisms if necessary

Especially in exotropia

*Before strabismus operation***s**



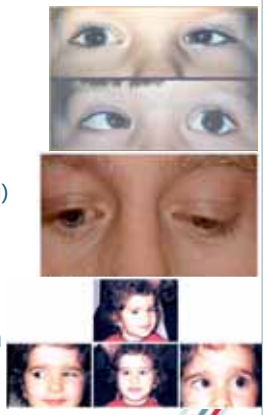
5. Ocular motility

- Look for incommitancies in all gaze positions
  - Horizontal gaze
  - Vertical gaze
  - Oblique gaze
  - Head tilt to right and left shoulder

- Compare ductions and versions
- Evaluate limitations in one or both eyes

5. Ocular motility

- Evaluate narrowing or widening of palpebral fissures
- Evaluate abnormal eyelid movements (ptosis–retraction–lid lag)
- Evaluate the difference in pupil size during eye movements
- Evaluate retraction or protrusion of the globe

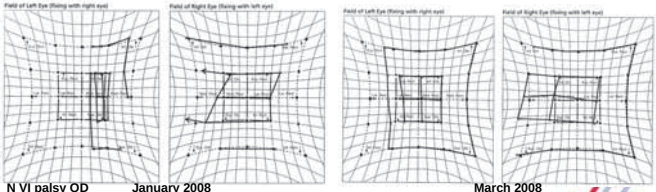


5. Ocular motility

- Evaluate smooth pursuit movements in horizontal and vertical directions
- Evaluate saccades in horizontal and vertical directions
- Evaluate the presence or change in nystagmus
- Measure ductions in the synoptophore
  - By moving each tube in horizontal and vertical direction until the eye stops following

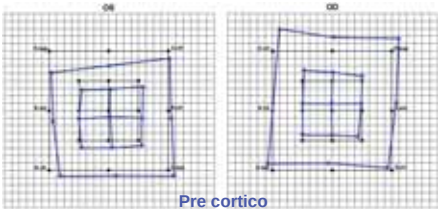
5. Ocular motility

- Record movements on Hess or Lancaster screen
  - Evolution of paralytic strabismus
  - Follow-up after medication, radiotherapy, …
  - Before and after operations

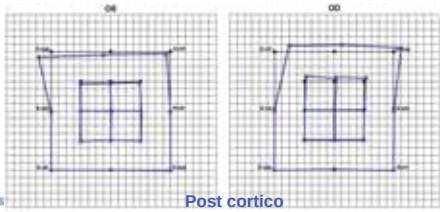


N VI palsy OD January 2008 March 2008

Evolution of the deviation after medication

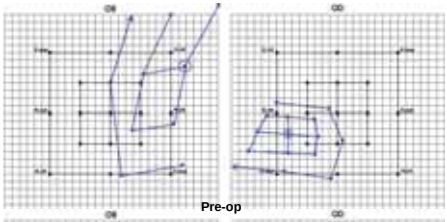


Pre cortico

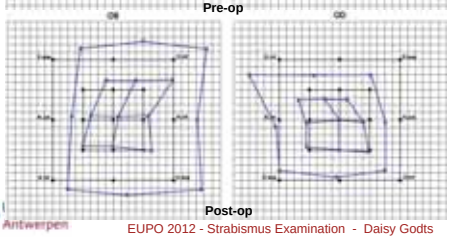


Post cortico

Evolution of the deviation before and after surgery (aberrant regeneration of N III)



Pre-op



Post-op

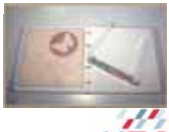
6. Binocular functions

- **Check binocularity or suppression**
  - 15^ prism test
  - Gracis biprism test
  - **Measure fusion/suppression prism bars**
    - Distance and near
    - Horizontal (Base-IN and Base-OUT)
    - Vertical (Base-UP and Base-Down)

Increase prism strength until diplopia appears

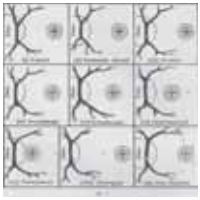
6. Binocular functions

- **Check binocularity or suppression**
  - **Measure fusion/suppression in synoptophore**
    - On subjective angle of deviation
    - Horizontal
    - Vertical
  - **Stereoacuity**



7. Assessment of visual acuity and fixation pattern

- Examine visual acuity according to the age of the patient
  - For distance and near
  - After binocular examination in case of straight eyes to avoid decompensation
- Evaluate fixation pattern
  - Central fixation (good VA)
  - Eccentric fixation (low VA)



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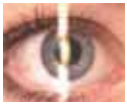
8. Cycloplegic refraction



- Should always be done
  - In young children
  - Cyclopentolate
  - Add tropicamide in dark eyes
  - Wait at least 45 minutes

- Retinoscopy or automatic refractometry

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15. Concomitant strabismus: esodeviations

• Vincent PARIS, Marche-en-Famenne, Belgium

1. Introduction

In this course we will describe all forms of esodeviations, macro or micro, accommodative or not, acquired or not. Our topic will be limited to concomitant strabismus, that is all forms of esotropia considered to be functional with complete motility. These types of strabismus are opposed to paralytic (acquired or congenital) associated with restrictive movements. Many classifications exist based on the variation of deviations from near to distance, with or without accommodative factors. A relationship exists between accommodation and convergence: the convergence response of an individual to a unit stimulus of accommodation may be expressed by his or her AC/A ratio. The most important is to make the crucial difference between early onset and acquired strabismus (fundamental differences in clinical presentation and binocular prognosis), to be aware of clinical clues of underlying lesion or malformation in the central nervous system and to evaluate the fusion potential disregarding the importance of the deviation. We don't want to confuse the reader by all the different theories trying to explain the different clinical presentations keeping in mind that accommodative factor can be present in every case. Strabismus is still in constant evolution. All the descriptions that you will find in this presentation are strictly based on clinical reproducible observations in 25 years experience of clinical practice. Some are classical, some are less. We hope that this practical approach of the different types of functional esodeviations will help you to make a better idea about this topic.

2. Early Onset Strabismus

2.1. Deviations on the fixing eye

Deviation concerning a fixing eye could be considered as an unusual terminology. Deviation is supposed to be measured in the non fixing eye. Nevertheless the key of comprehension for the specific visual comportment of early onset strabismus includes the fact that these patients have a specific pathology of their fixation mechanism. The main specificity of this strabismus is the presence of the so-called Latent or Manifest-Latent Nystagmus (MLN). This kind of Nystagmus is never met outside this type of strabismus. It is characterized by a slow nasally directed drift, followed by a fast corrective saccade in the temporal direction. Nasal drift is the primary phenomenon followed by a rapid movement mandatory to restore foveal fixation. Therefore,its direction is depending on the fixing eye, beating to the right when the right eye is fixing, beating to the left when the left eye is fixing. It has two main characteristics: it decreases in adduction and when both eyes are open. The incidence of MLN has been debated. In our experience, it is present in every case but can be very latent and only observed at the fundus with the visuscope in abduction when the other eye is occluded. A rotary component is very often associated when torsional deviation is present.

MLN has the same presentation in esotropia and in exotropia. From a practical point of view, it seems to represent a form of strabismic deviation in a fixing eye.This can explain why these patients adopt systematically an abnormal head position to displace the fixing eye in adduction.

In this position the amplitude of LN is lower and they simply have a better quality of vision. When torsional component appears (after 6 months) the abnormal head posture transformed into an associated tilted position mostly tilted on the ipsilateral shoulder. This attitude can be considered as a monocular intorsional process of compensation. When we have these data in mind we can have a better analysis of what happen when a patient is fixing unusually in abduction and /or in excycloposition. In case of abducting position we have to consider the presence of associated classical congenital Nystagmus and its classical process of blockage. In case of extorsional position of fixation we have to think about the presence of additional cause of extorsion (IV nerve palsy, plagiocephaly, anatomical predisposition..). (MLN means that the amplitude and the frequency are depending on the position of gaze (worst in abduction) and binocular inputs (worst when one eye is covered) but also on other factors such are fatigue, uncorrected refraction… When MLN is manifest, very early surgery (< 1 year) can be indicated.

2.2. Deviations on the non fixing eye

The vast majority of the cases are in esodeviation. Most of them develop shortly after birth (within 4 months) an usually large deviation. The age of apparent onset is not the main point. Some patients can decompensate later. Conversely, some acquired esotropia could appear very early (before the age of 1 y) but never develop any MLN. Approximately half part of these patients has a small hyperopia < 2D, few (10%) are myopic.

The second particularity of early onset strabismus is the presence of dissociated deviation which do not obey to Hering's law. Beside horizontal deviations the most difficult deviation to define is DVD which is a slow movement leading the non fixing eye to rise and extort. When the deviating eye comes down, the other eye stays at the same position. These curious movements violate the Hering's law and are only encountered in early onset strabismus. Nevertheless, this dynamic aspect may transform with the time due to a progressive superior rectus contracture. The lack of elasticity of this muscle can lead to an hypotropia effect on the other eye, respecting the Hering's law again. This situation can be present very early but mostly in cases with long term asymmetric DVD when the most hypertropic eye is dominant. One of the most difficult aspect in treating DVD is indeed its frequent asymmetry. Therefore, strong dominance or alternate fixation is a very significant factor to fix a surgical plan. This deviation is difficult to measure and has only to be considered as an estimate. The best result that we can achieve with surgery is a residual small, symmetric and well compensated vertical deviation.

In some cases the vertical deviation is only present in adduction, it is rare, usually symmetric and due to pure inferior oblique muscles overaction (IOOA). Many authors pay attention to differentiate DVD and IOOA. Considering that to extort and rise both superior rectus (SR) and inferior oblique (IO) are involved we don't see the interest to make any difference between the role of these two muscles. Horizontal deviation is always present at first, vertical and torsional deviation are very frequently associated but not present systematically. When present,they appear from the age of 7 months to 13-14 months. The association between horizontal, vertical and torsional in variable and individual proportion, symmetric or not has been called Dissociated Strabismus Complex in the strabismological literature.

DVD can be long term compensated especially when horizontal deviation has been controlled by surgery / botulinum toxin or optical correction or both. It can be elicited by decreasing cortical attention such are dreaming, drugs, fatigue, stress..It rarely decreases with age and is closely associated with the torsional component of the fixation torticollis. In our experience decompensate DVD is the main cause of multiple reoperations in Strabismology.

2.3. Alphabetic pattern

Torsional deviation can also lead to alphabetic pattern. In some cases dynamic alternation of excyclo and incyclo movements can introduce a basic excycloposition associated with V pattern or a basic incycloposition linked to A pattern. It is not systematic but it represents an additional cause of complexity in the clinical analysis and the surgical treatment.

2.4. Visual / Binocular Outcome

The best surgical outcome in such cases is therefore a stable microtropia with small compensated vertical deviation and non significant alphabetic pattern. Surgery is needed in the vast majority of cases. Prevention of amblyopia and optical correction of moderate hyperopia is often required to maintain a good long term result in these types of complex cases (be aware that accommodative factors may be present in every case, at every state in strabismic patients). Because this form of strabismus is mainly associated with abnormal fixation I'm convinced that the efficacy of the treatment is not only related to cosmetic reasons but mainly to visual and binocular (even limited) advantages. That's why we advocate to operate before the age of 2 years in order to give this sensorial gain as soon as possible at the beginning of psychomotor development.

2.5. Microtropic Form

Congenital microtropia are almost in esoposition. This form of early onset strabismus is less complex but very often associated with a strong dominance and a high incidence of amblyopia. It can decompensate spontaneously or during the treatment with occlusion.

2.6. "Acquired" Early Onset Strabismus

When an obstacle in the development of vision (cataract, corneal scar,..) occurs unilaterally very early in the life (< 6 months), it impairs the maturation of binocular vision and, in one third of the cases, lead to the same presentation as it is encountered in early onset strabismus. This has been called Monophtalmic Syndrome. So, in the majority of these cases, unilateral visual loss is not a sufficient condition to elicit a specific form of early onset strabismus.

3. Acquired Strabismus

3.1. Accommodative Esodeviation

As a rule, the onset of accommodative esotropia is between the age of 2 and 3 years. As we said before, some rare case can occur earlier even before the age of 1 y. (range: 6 months to 7 years). This is the age when children start to look for details and look with better attention at

near objects. This call into play their accommodation and accommodative reflexes and may precipitate an esotropia, particularly if there is a hypermetropic refractive error and a family history of strabismus. The evolution of accommodative esotropia is usually gradual, and most patients pass through a stage of intermittent strabismus. If normal fusion and stereopsis were present prior the onset of esotropia and the child is still visually immature, active inhibition of the deviating eye at the cortical level will occur. This may cause a deterioration in visual acuity, fusion and stereopsis within a few days. Therefore these children has to be seen and treated without delay.

3.1.1 Accommodative Esotropia Associated with Hypermetropia

Total hypermetropic correction is the treatment but we have to make sure that the glasses will straighten the eyes completely and emphasize to parents the importance of full time wear of spectacle. The efficacy of optical correction is not proportional to the importance of hypermetropia, so do not hesitate to prescribe +0.75 D. The classical question asked by the parents: "how long glasses will be worn"? Longitudinal studies all shown that there was no significant change in hypermetropia in this pathology except in cases with familial myopia. So, the only promise that we can make is to deliver contact lenses (from the age of 8 years in good conditions). The failure of emmetropization in children with accommodative esotropia was supposed to have two origins: an intrinsic defect and the effect of wearing full correction. Recent studies didn't support the fact that undercorrecting hypermetropia speeds its resolution. Some authors proposed to prescribe one or two diopters less than the full plus to maintain a small esophoria and stimulate the maintenance of the fusional divergence mechanism. This method could then allow the patient to remove his glasses for brief periods without developing esotropia. Nevertheless we have to be aware that in human being the amplitude of divergence (8-10 PD) is much lower than the convergence amplitude (150-180 PD), so we think that it is not mandatory to stimulate what we are congenitally not able to perform. Therefore there is actually no more argument justifying nothing but the full (and full time) correction in these cases.

3.1.2 Accommodative Esotropia Associated with Esophoric Myopic Patients

These patients have an uncomfortable position. Without glasses at near they less accommodate. Wearing their glasses at near provokes an accommodation stimulus and increases the esophoria. They use remove their glasses at near but it is not always possible. They suffer from frequent asthenopic complaints associated with headache and unstable vision. When undercorrected, the less effort to accommodate can help for better fusion. When appropriate correction is delivered it can lead to esophoria decompensation or esotropia When trial contact lenses (CL) esophoria increases also for another accommodative reason: with CL the size of the images is no more reduced and appears to be relatively larger, provoking an additional accommodation stimulus. Nevertheless, some esophoria can remain relatively latent and only weakly attested by the cover test. Maddox Wing for near and streaky red glass for distance are more specific means to assess the real deviation and understand why these patients see badly despite appropriate optical correction. For the same reasons, in rare cases, successful refractive surgery can precipitate

an esotropia in esophoric myopic patients. It has to be considered has an acute form of acquired normosensorial strabismus responding very well to surgery.

3.1.3 Accommodative Microtropia

Microtropia has been considered as a form of strabismus with small angle (< 10 PD) and always from congenital origin. In our experience a significant proportion of microtropic patients (25 %) could regain normal or subnormal binocular vision after treatment. The vast majority of these patients are hypermetropic. After treatment of amblyopia and refraction error the mean deviation transforms from 6 PD to 0.5 PD. This acquired form has specificities, different from the congenital form: angle is always reduced by the treatment (amblyopia, hypermetropic correction), amblyopia is never deep and easy to treat, occlusion never lead to esotropia decompensation (as it occurs approximately in 20% in congenital microtropia) and some of them complain of asthenopia(indirect sign of subnormal binocular vision).

3.1.4 Non Refractive Accommodation Esotropia

In these cases, esotropia is more important at near than at distance. The etiology is unrelated to the underlying refractive error (which is anyway most frequently hypermetropia). Here the effort to accommodate elicits an abnormal high accommodative convergence. Depending on the motor fusion, the patient have a latent (esophoria) or a manisfest (esotropia) esodeviation.

3.1.5 Hypoaccommodative Esotropia

This category has also an esodeviation greater at near but the unique treatment is based on the prescription of bifocal or multifocal lenses (better multifocal from the age of 5y). In fact these patient are totally or partially unable to accommodate. Without glasses their accommodative effort is associated with a convergence excess. This pathology is rare. The cause is usually unknown and seems to be acquired at varying ages.
It can be due to head trauma and may then be reversible. It must be recognized in order to avoid any inappropriate surgery

3.1.6 Convergence Spasm

This has to be differentiate from Esotropia induced by stress. This form is associated with accommodative spasm (associated with miosis). This usually occurs in patients with hysteric tendencies

3.1.7. Partially Accommodative Esotropia

Accommodative factors contribute to but do not account for the entire deviation. Only the non accommodative component of the strabismus should be corrected surgically. Cycloplegia must be repeated anyway to make sure that full correction of hypermetropia has been given. Special care must be taken to explain in great details to the parents, who otherwise may expect that glasses will not be required after the operation.

4. Non Accommodative Esodeviation

4.1 Stress Induced Esotropia

This refers to esodeviation that is precipitated by stress, such as debilitating illness, emotional trauma, physical injury or aging. It is thought to be due to the breakdown of previously adequate fusional divergence. Surgery is usually required and is very efficient.

4.2 Esotropia of Elderly People

Patients of the fourth age are in a raising proportion in our populations. They frequently complain of diplopia at distance due to progressive esophoria. It is probably associated with a progressive laxity of the lateral recti. Esodeviation is usually not important (3-10 PD) but these patients have often very small capacities of fusional divergence. This pathology has to be recognized because it responds very well to treatment (prisms, surgery or both)

4.3. Cyclic Esotropia

Very rare and curious phenomenon. Most of the cases are acquired. Esotropia is present intermittently, usually every other day (one day squinting, the day after not). Some have described twins squinting successively (cortical influence is never far away from any strabismus process). Surgery is often necessary.

4.4 Esotropia Following Recovered VI Nerve Palsy

After partial recovery of VI nerve palsy, the residual esotropia may became concomitant, showing the same measurement in side gaze to right and left and fixing either eye.

4.5 Acute Esotropia

Careful motility analysis is always necessary to rule out a paretic deviation. As we mentioned this deviation may quickly become concomitant, in which case it will be difficult to recognize the paretic element. The presence of Nystagmus, alphabetic pattern or persistence of abnormal fusion after successful surgery should be sufficient cause to proceed with a neurological evaluation. This form can occur in the course of treatment of amblyopia in patients without strabismus or even when one eye had been bandaged for several days (after corneal trauma, lid surgery …). It can occur also spontaneously in children with good potential for binocular cooperation. The refraction, as a rule, is insignificant and the accommodative element is minimal. Surgery is often necessary. In children under the age of 5 years, this procedure should not be delayed to avoid the development of suppression and amblyopia. The prognosis for restoration of normal binocular vision is excellent.

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16. Exodeviations

• Rosario GOMEZ DE LIANO, Madrid, Spain

They can be latent (phoria) or manifest (tropia)

1. **Exophoria:** exodeviation controlled by fusion. The deviation appears when binocular vision is interrupted (cover test, fatigue, alcohol intake, sedation, unilateral diminution of VA example a patient developing an asymmetric cataract…). The patient may have good estereopsis although he may have asthenopsia while reading. Convergence should be checked. Treatment include refraction, some patients need prism or orthoptic exercises and eventually surgery for the most decompensate situations.

2. **Infantile Exotropia:** Exodeviation that develops within the first 6 months of age. It may be associated to ocular or neurological pathology (hydrocephalus, periventricular leukomalacia, craniofacial syndromes, cerebral palsy…) Usually the deviation is large, they alternate fixation (amblyopia occurs < 25% of the cases). They may have, DVD, Oblique muscle dysfunction, mild nystagmus latent and X, V or A patterns. It is important to rule out any ocular and systemic pathology. Surgery is indicated if deviation is large and after any refractive errors and amblyopia have been treated. Early surgery may be beneficial but it is controversial. Reoperations are required up to 50% of the cases.

3. **Intermittent Exotropia:** Outward drifting of an eye with periods of orthotropia. It is the most frequent type of XT in children.
   Etiology: combination of mechanical and innervational factors (imbalance between fusional convergence and divergence. It may begin before 12 months of age but as often is quite compensate and many times the family detects it much later. The periods of decompensation may be variable upon the cases and over the years (degree of decompensation).
   Classification:
   a. Divergence excess pattern: Deviation larger at distance
   b. Convergence Insufficiency pattern: Larger at near distance
   c. Basic Type: The distance deviation is approximately equal to the near deviation.
   d. Simulated Divergence Excess pattern: Apparently the deviation at primary position of gaze is larger that at near distance but after a prolonged monocular occlusion and evaluating them with + 3.00 add lenses at near the deviations we may find the cause (tenacious proximal fusion and high AC/A or normal AC/A cases).

   The ***natural evolution*** of this type of strabismus is controversial: some patient's progresses from compensated situations to more decompensate ones and even from divergence excess to a basic type. Distance measurements should be made at least at 6 mt. (better 20 mt. through a window) Intermittent exotropia may be associated to oblique

muscle dysfunctions and V and A patterns. The evaluation of the retinal correspondence reveals NRC when the patient is aligned, while ARC when the exotropia is present. Most patients have good stereopsis with different degrees of suppression at distance fixation. Amblyopia if present usually is mild. Patients frequently close one eye when they are exposed to bright light but exceptionally have asthenopia. It is important to ***assess the control of the deviation***

1. Excellent: Parents refers XT < 10% waking hours, at distance only.
2. Good: < 5 times a day, at distance. In our examination deviation appears only with a cover test. Realignment occurs spontaneously.
3. Fair > 5 times a day, at distance. The patient needs more time to realign the eyes, to refixate or blinking them.
4. Poor: frequent XT both at distance and near assessed by the parents. We see the patient XT at the examination without any cover test.
5. ***Treatment:*** Nonsurgical management is indicated in patients with good control. Accommodation and fusional mechanism may improve the degree of control of the exodeviation. Myopia, astigmatism and any anisometropic correction should be prescribed. Even "over-minus lenses" -1,5 to -4 dp lenses may help to control the deviation (better in younger children and smaller deviations). Treatment of amblyopia reduces suppression and helps to control the deviation. Some doctors use unilateral patching some hours per day over the dominant eye to control the deviation. Orthoptic exercises and prisms are also used to control smaller deviations although. Most of the times the patients have a temporary benefit. Surgery is indicated when the deviation becomes more manifest. Most surgeons prefer to delay surgery if possible until the child is 4-6 years old. The most frequent type of surgery is the bilateral lateral rectus recession although an alternative is a unilateral medial rectus resection and a lateral rectus recession.

4. **DHD (Dissociated Horizontal Deviation):** It is the horizontal component of the dissociated complex syndrome. It may be confused with intermittent XT and may be also associated to Consecutive XT. Horizontal deviation is different while fixating with either eye; usually it is associated to DVD and nystagmus latent.

5. **Consecutive XT:** ET that converts to an XT, most of the cases appear after ET surgery (immediate or long term cases) but there are spontaneous cases. Etiology: surgical dosage, slippage of the MR, stretched scars; change in muscle tonus and fusion over the years. Taking the glasses of in cases of anisometropia and severe amblyopia are associated to consecutive XT. It is important to evaluate the patient as a new case taking care if there are any muscle limitations.

6. **Sensorial XT:** Exotropia associated to severe reduction of VA of one eye or to chronic poor vision.

7. **Other forms of XT**
   a. Exotropia associated to III nerve palsy
   b. XT associated to Duane Syndrome or other congenital fibrosis of the extraocular muscles
   c. XT with hemianopic visual defects

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17. Secondary and Iatrogenic strabismus

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INTRODUCTION

1. Visual impairment can secondarily lead to **"Sensory strabismus"**

2. Age- related orbital changes can secondarily lead to vertical strabismus, **"Sagging eye"**, and/or horizontal strabismus, "Distance esotropia".

3. Ocular surgery (strabismus surgery or other procedures) can lead to **"Iatrogenic strabismus"**

SENSORY STRABISMUS

Reduced vision is an obstacle to sensory and motor fusion and can in this way lead to sensory strabismus.

If the onset of the visual impairment is before the age of five, the subsequent sensory strabismus can be eso- or exotropia. With advancing age there is an increased incidence of sensory exotropia. However, any eso-or exotropia, at any age, may be sensory and can be the first clinical sign of severe pathology leading to loss of vision. With this in mind, a complete examination of the eyes is absolutely necessary and the first thing to do in every new strabismic patient.

A longstanding visual impairment demands, where possible, an investigation of the sensory status to determine the aim of treatment: either restoration of binocular single vision or just improvement of the cosmetical appearance. From the nature of the case sensory strabismus very often precludes restoration of binocular functions.

Important questions are:

1. Is fusion possible? based on NRC, or ARC?
2. Can we find suppression? with underlying NRC, or ARC?
3. Is there a risk of diplopia?

Important to know:

1. Low visual acuity is not a safeguard against diplopia
2. Blurred and remote images are easier to bear than closer images.
3. The presence of ARC and/or suppression has to be respected.

Naturally, when the visual acuity is low, the sensory status can be difficult to unveil.

If fusion is present, surgery can lead to a functional result with a good prognosis for long-term alignment. In these cases a resulting small exophoria is preferable over a small esophoria. However, when fusion is absent the aim of surgery is only esthetical, in these cases a resulting small esotropia has a better prognosis on the long term.

We prefer surgery on the deviating eye, which means recession and resection of opposite recti, after a peroperative forced duction test.

The surgical results in sensory strabismus may not be stable in the long term, late recurrence or evolution towards consecutive strabismus is always possible. We have to inform our patients about this.

STRABISMUS SECONDARY TO AGE- RELATED ORBITAL CHANGES

With age, orbital connective tissue can degenerate; especially the connective band between the superior and lateral rectus muscle is susceptible to degeneration. Moreover, the horizontal pulleys can sag. This can happen symmetrically on both eyes, or asymmetrical or unilateral.

All this can cause slow progressive horizontal and/or vertical strabismus:

- Lateral recti frequently slip downwards, thus their abductive action decreases!
  In case of pre-existing esophoria or when fusional divergence is weak, this can lead to **“age related distance esotropia”**.
  In these cases, surgery is not a good solution; the only safe treatment is correction by prisms.

- At the same time, when the lateral recti slip downwards, their action as a depressor increases! If this happens unilaterally or asymmetrically, one eye sags in relation to the fellow eye and if the vertical fusion is insufficient, a vertical tropia will result. Hence we see “acute” vertical diplopias after cataract surgery, **the ”sagging eye”** mimicking a superior oblique palsy.
  (Retrobulbar anaesthesia can also cause restrictive strabismus after cataract surgery. Nowadays, however, topical anaesthesia being the standard procedure, this has become a rare condition).

- When a unilateral cataract is longstanding, disruption of fusion is possible. Cataract surgery can be followed by a sensory strabismus, and as suppression will not normally occur, diplopia is the result. Therefore in cases of unilateral cataract, it is advised not to delay cataract surgery too long.

- In case of a longstanding pre-existing strabismus, suppression can be present. Cataract surgery on the strabismic eye can lead to fixation switch with disturbing diplopia. In these cases it is better to perform the cataract surgery on the dominant eye only.

- High myopic eyes are more susceptible for these changes, and we all know a "myopic sagging eye" as **a heavy eye**. And there is more: degeneration of the SR-LR band creates space for protrusion of the posterior pole of the high myopic eye between these both recti. This leads to what we call **"mape"** (Myopia acquired progressive esotropia).

- Muscle binding surgery is our treatment of choice.

IATROGENIC STRABISMUS (IS)

IS after strabismus surgery.

Iatrogenic strabismus is strabismus caused by a medical act, including strabismus surgery. When over – or undercorrections or important new incomitancies are caused by inadequate diagnosis or careless strabismus surgery, we call the resulting strabismus " iatrogenic". Of course, over- and undercorrections after strabismus surgery can occur without obvious cause, in these cases we speak of "secondary strabismus", consecutive or residual.

When a strabismus reintervention is required we have to take a few key points into consideration.

1. *What was the nature of the previous strabismus?*
   Be aware of this, it helps us to fix the purpose of our reintervention: only esthetical or also functional
2. *Which surgical procedures have already been performed?*
   More specifically: which rectus muscles have been operated?
   Surgery on too many rectus muscles can lead to anterior segment ischemia!
3. *We have to evaluate the spontaneous evolution.*
   An urgent reintervention is only required:
   - in case of a lost muscle,
   - in caseof a large overcorrection after resection or tuck
   - in case of a large postoperative deviation after a muscle transposition procedure.
4. *An extensive orthoptic examination is necessary,*
   Ocular motility? alphabetical patterns? ductions? sensory status?
5. *Because of esthetical reasons, we have to pay attention to the palpebral fissures*
6. *What are the preoperative findings?*
   We check:
   - the eye position under anesthesia
   - the forced duction test, comparing the results with the orthoptic examination
   - the location and integrity of the previously operated muscles
   - the muscle elasticity
   - the conjunctival status

In conclusion, the procedure to determine the final surgical plan can be summarized as follows:

1. Orthoptic investigation
2. Preliminary plan
3. Peroperative examination
4. Final peroperative decision
5. Surgery!

IS post orbital decompression

Orbital decompression techniques cause some degree of destabilisation of the orbital structures, leading to horizontal, vertical and especially cyclodeviations.

Any cyclodeviation can occur, so a double Maddox rod test is indispensable before surgery can be envisaged.
Furthermore, if we operate for the vertical or horizontal deviation, the effect of the planned surgery upon the existing cyclodeviation must be taken into account.

Treatment of torsional diplopia after decompression surgery remains an important challenge for the strabismologist.

IS post Functional Endoscopic Sinus Surgery

FESS can be complicated by damage to the midportion of the medial rectus muscle. The exact diagnosis can be made by (dynamic) MRI.

In case of section of the muscle, surgery is difficult because repair of the transsected muscle is usually impossible. The only remaining possibility: recession of the lateral rectus combined with Botox injection, followed by (partial?) nasal transpositioning of the vertical recti.

When the muscle is only superficially damaged or paralysed, spontaneous recovery may occur, so surgery should not be carried out too quickly. However, in some cases a Botox injection in the lateral rectus can provide more visual comfort during this stage. If recovery remains incomplete we perform a recess- resect procedure.

IS after refractive procedures

Refractive surgery can be followed by diplopia.

Risk factors are: pre-existing strabismus, prisms in spectacle correction, latent or under-corrected hyperopia, overcorrected myopia, longstanding monovision, masked IVth Nerve palsy, thyroid eye disease and myasthenia.

Refractive surgeons have to identify patients at increased risk for diplopia. It is important that the dominant eye remains dominant at all times, especially in case of suppression and risk of fixation switch.

IS after external retinal detachment repair

Scleral buckling procedures may cause motility disorders by adhesions, direct muscle trauma, muscle ischemia, muscle slippage and/or muscle disinsertion with (incorrect) repositioning. Most of these problems are transient and resolve within 6 months, observation during this period is important.

In case of remaining diplopia we have to perform muscle surgery because removal of the explants and/or of the encircling element diminishes the diplopia in only 10 % of the cases.

IS after Macular Translocation

Macular translocation can improve central visual acuity in some cases of ARMD, but causes torsional diplopia and disturbing tilted images. The amount of macular translocation extends to up to 65°.
When the macula is rotated downwards, a retinal excyclodeviation is created and an incyclo-counterrotation of the globe is required. This can be done by disinserting the Inferior Oblique Muscle (IOM) and tucking the Superior Oblique Muscle (SOM).
When the macula is rotated upwards, the retinal incyclodeviation demands an excyclo-counterrotation of the globe, which can be obtained by strengthening of the IOM and a recession of the SOM.

However, oblique muscle surgery corrects only 10°of cyclodeviation which in most cases will be insufficient.

In combination with a full -tendon transposition of two opposite rectus muscles, a larger degree of counterrotation can be achieved (+/-30°), but this is still insufficient to counterrotate the majority of macular translocations.

A half tendon transposition procedure of the four rectus muscles in combination with the oblique muscle surgery can correct this amount of rotation:

- a crossed half tendon TP of the 4 RM's ("split and cross" procedure) corrects 45° of cyclodeviation
- an uncrossed half tendon TP of the 4 RM's ("split and neighbour cross" procedure) rotates the eye up to 65°.

These interventions can be complicated by Anterior Segment Ischemia, especially in these older, vascular compromised patients. Careful splitting of the four recti is obligatory and demands experience in muscle surgery.

Possible residual horizontal and vertical deviations can subsequently be corrected by prisms.

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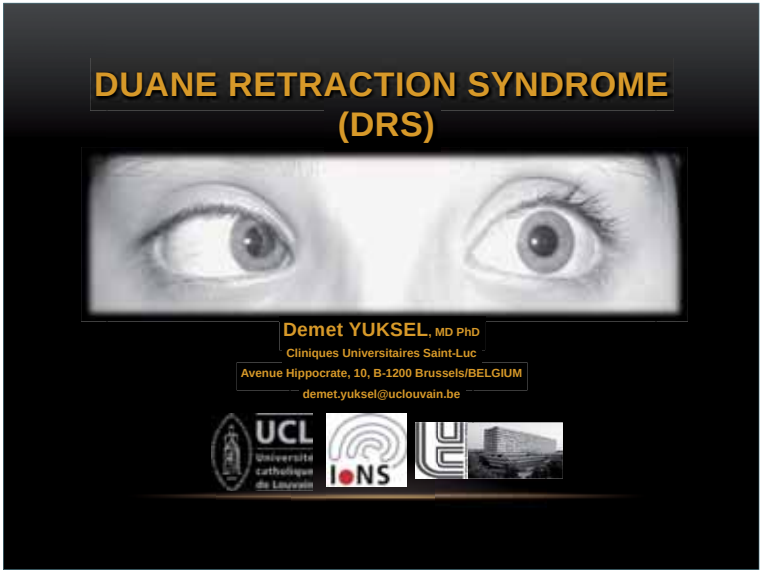
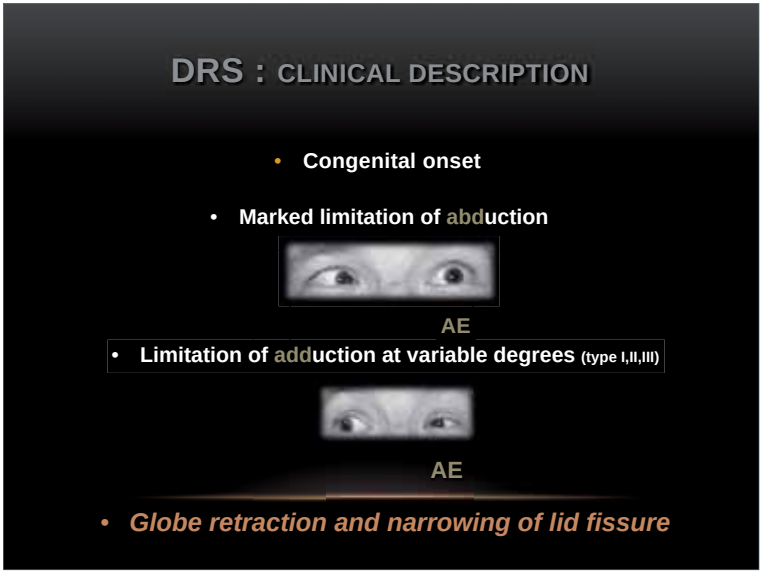
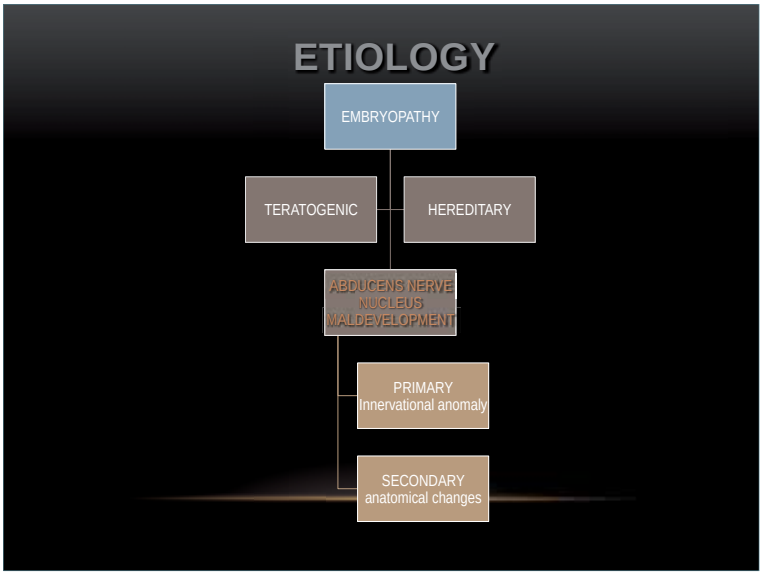
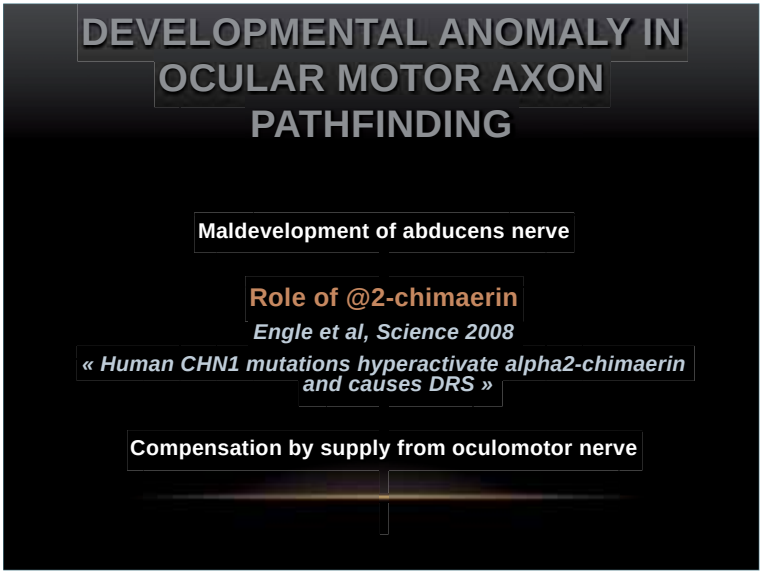
18. Duane retraction syndrome / Brown syndrome

- Demet YUKSEL, Brussels, Belgium

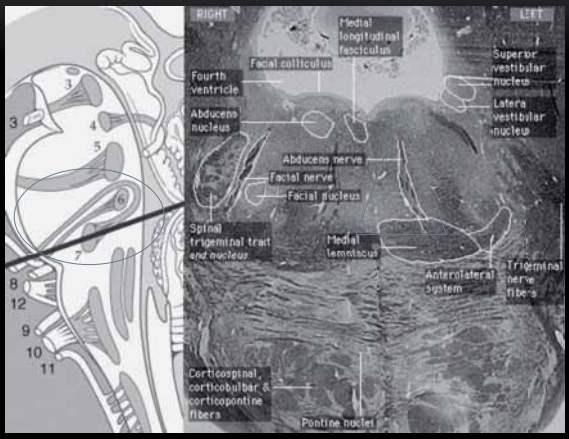


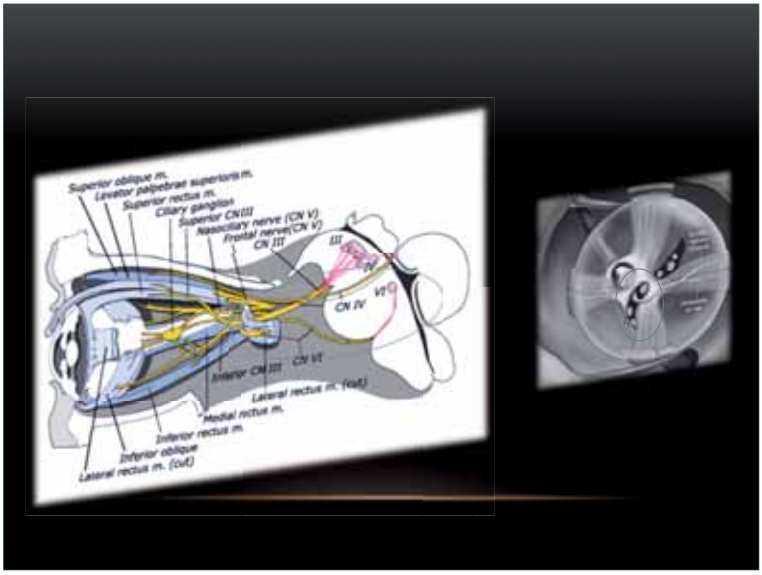


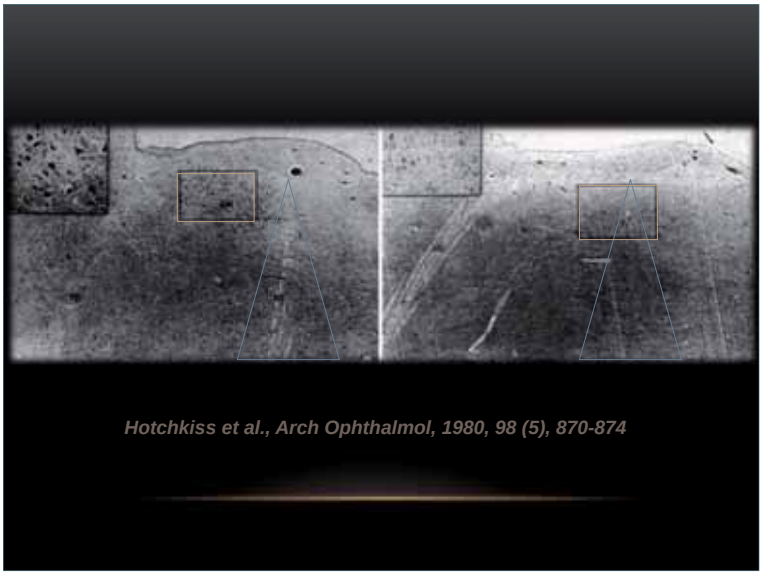

ETIOLOGY
EMBRYOPATHY
TERATOGENIC
HEREDITARY
ABDUCENS NERVE NUCLEUS MALDEVELOPMENT
PRIMARY
Innervational anomaly
SECONDARY
anatomical changes


DEVELOPMENTAL ANOMALY IN OCULAR MOTOR AXON PATHFINDING
Maldevelopment of abducens nerve
Role of @2-chimaerin
Engle et al, Science 2008
« Human CHN1 mutations hyperactivate alpha2-chimaerin and causes DRS »
Compensation by supply from oculomotor nerve

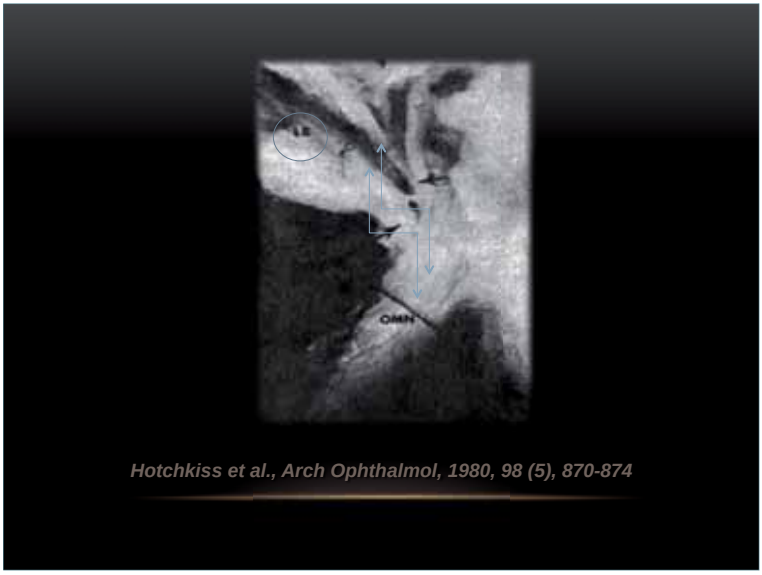
ANATOMY


RIGHT
LEFT
Medial longitudinal fasciculus
Facial colliculus
Superior vestibular nucleus
Fourth ventricle
Abducens nucleus
Latera vestibular nucleus
Abducens nerve
Facial nerve
Facial nucleus
Spinal trigeminal tract and nucleus
Medial lemniscus
Anterolateral system
Trigeminal nerve fibers
Corticospinal, corticobulbar & corticopontine fibers
Pontine nuclei


Superior oblique m.
Levator palpebrae superioris m.
Superior rectus m.
Ciliary ganglion
Superior CN III
Nasociliary nerve (CN V)
Frontal nerve (CN V)
CN III
CN IV
CN VI
Inferior CN III
Lateral rectus m. (cut)
Medial rectus m.
Inferior rectus m.
Inferior oblique
Lateral rectus m. (cut)



Hotchkiss et al., Arch Ophthalmol, 1980, 98 (5), 870-874



Hotchkiss et al., Arch Ophthalmol, 1980, 98 (5), 870-874

Electromyography

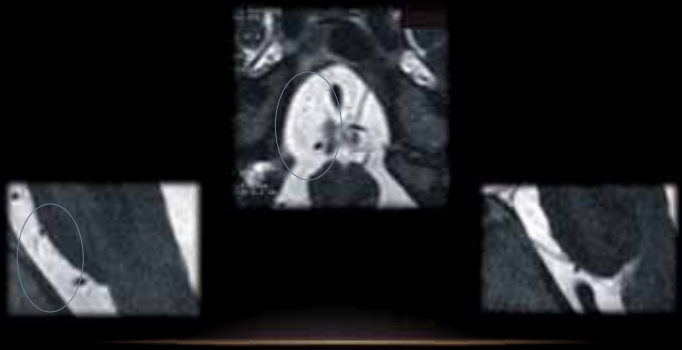
Electrical activity measured in the affected lateral rectus (LR) LE
depending on the movement of the eye

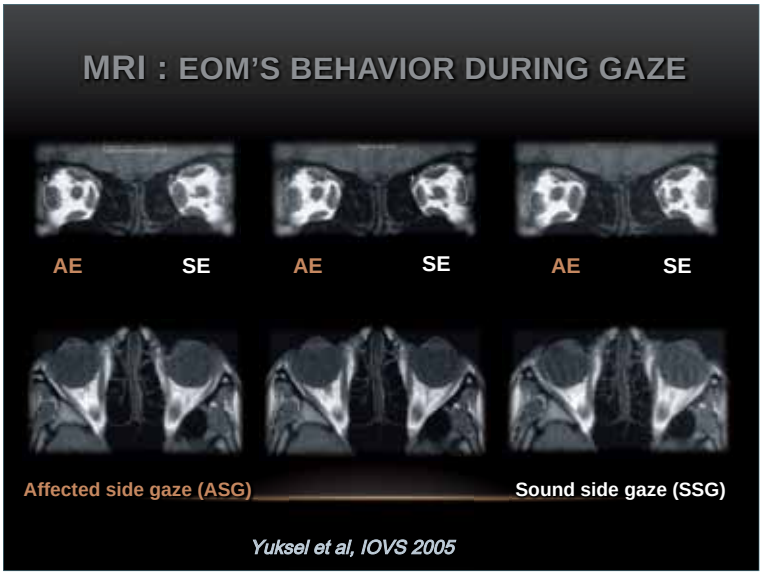
NO NORMAL LR RECRUITMENT IN THE FIELD OF ACTION

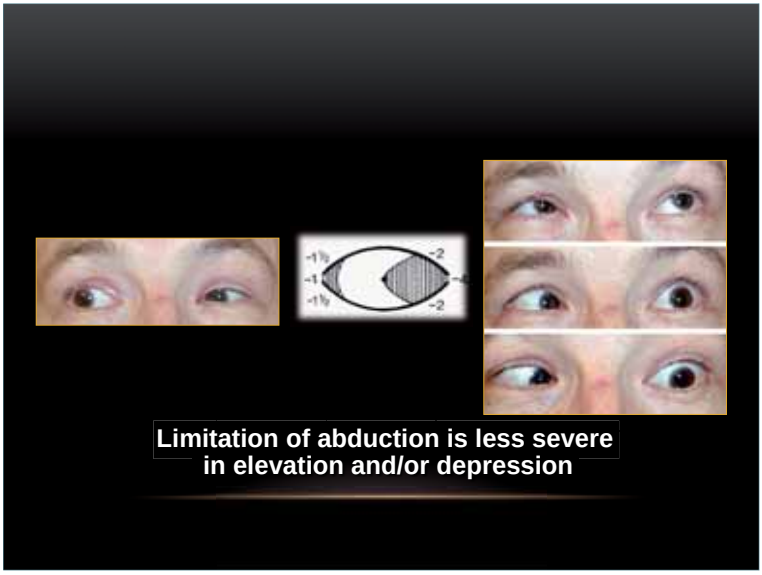
Anomalous LR Recruitment in Right/Up/Down Gaze

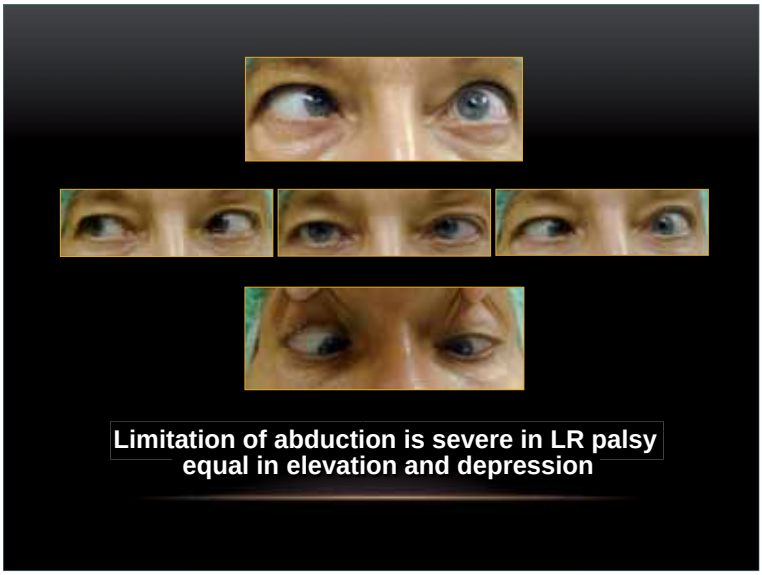
Rosenbaum, Santiago
« Clinical strabismus management »

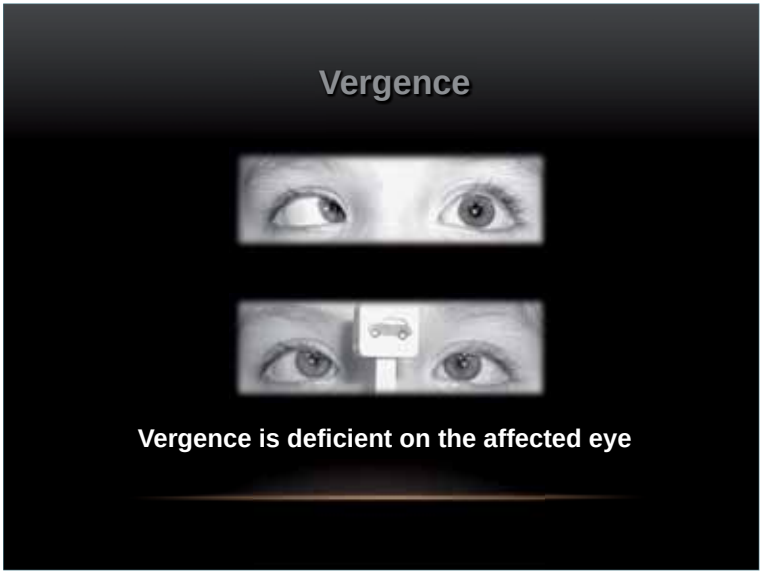
MRI FINDINGS

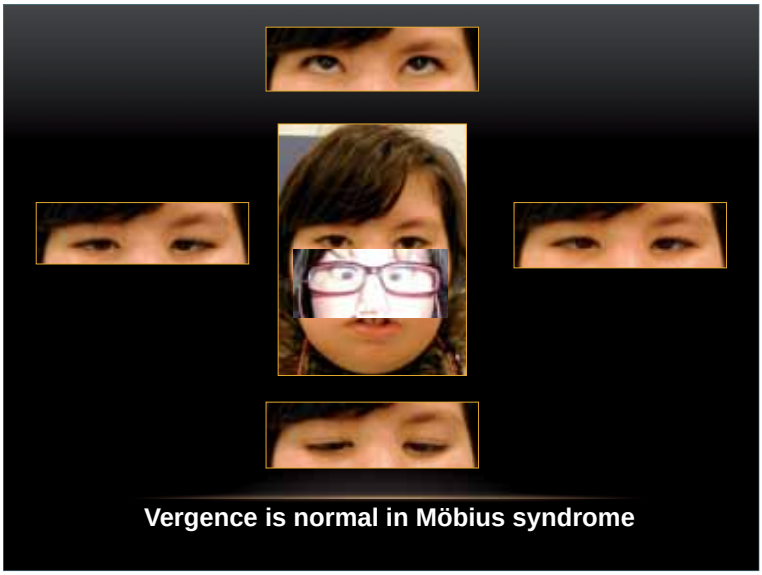


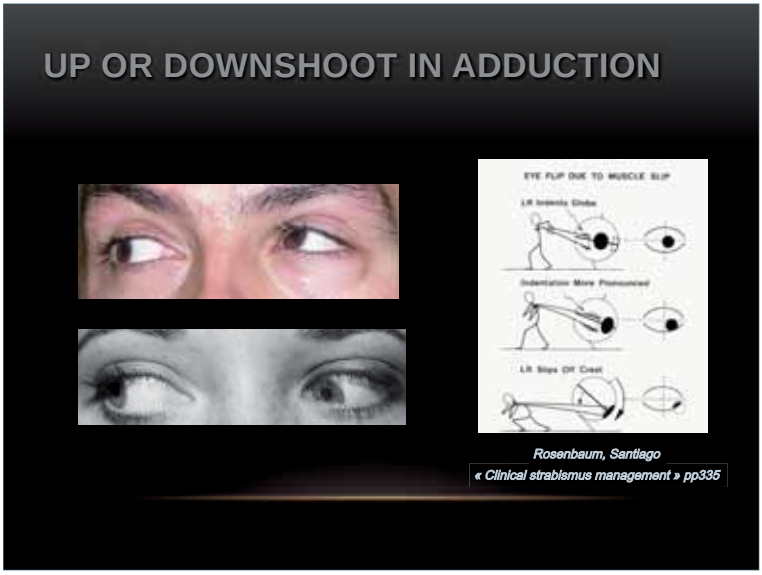

MRI : EOM'S BEHAVIOR DURING GAZE
AE
SE
AE
SE
AE
SE
Affected side gaze (ASG)
Sound side gaze (SSG)
Yuksel et al, IOVS 2005


Limitation of abduction is less severe
in elevation and/or depression


Limitation of abduction is severe in LR palsy
equal in elevation and depression


Vergence
Vergence is deficient on the affected eye

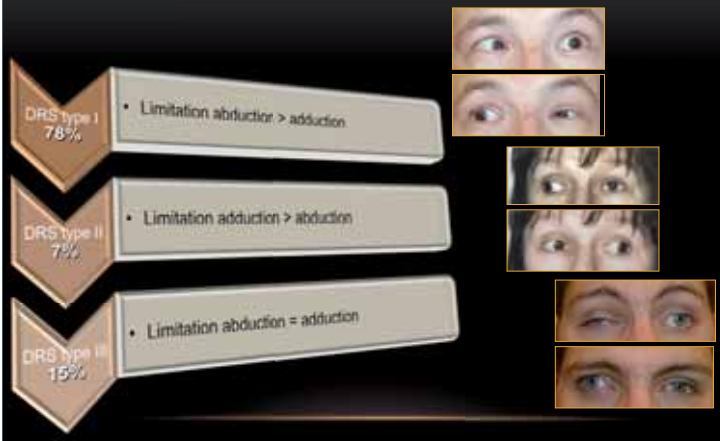

Vergence is normal in Möbius syndrome


UP OR DOWNSHOOT IN ADDUCTION
EYE FLIP DUE TO MUSCLE SLIP
Rosenbaum, Santiago
« Clinical strabismus management » pp335

FACIAL ASYMMETRY

Hemiface on the side of torticollis is less developped

Clinical classification



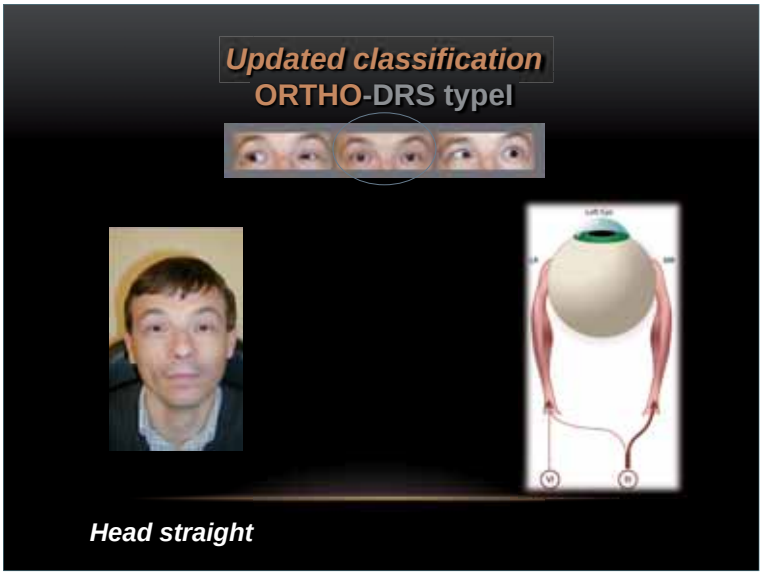
DRS type I 78%

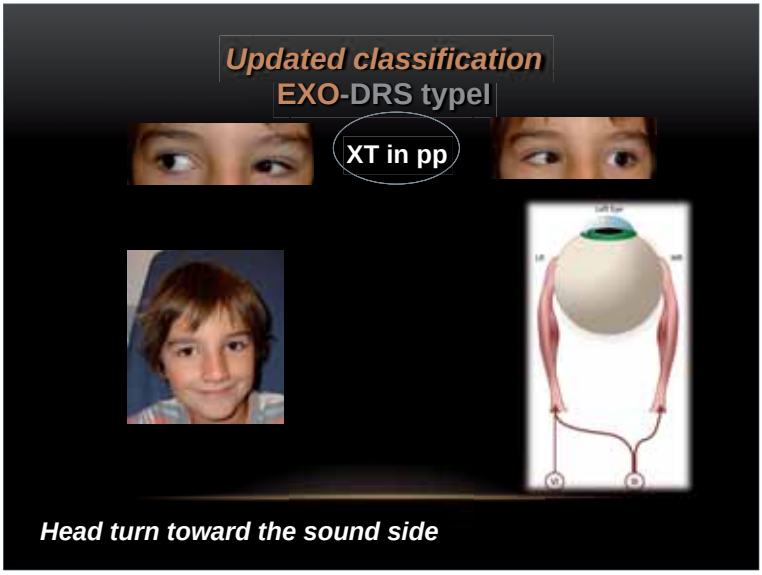
Limitation abduction > adduction

Updated classification

ESO-DRS typeI

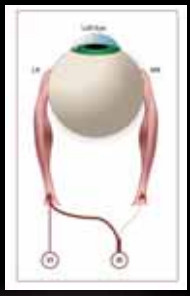
Head turn toward the affected side


Updated classification
ORTHO-DRS typeI
Head straight


Updated classification
EXO-DRS typeI
XT in pp
Head turn toward the sound side

DRS type II 7%

Limitation adduction > abduction



SYNERGISTIC DIVERGENCE

DRS type III 15%

Limitation abduction = adduction

SURGICAL MANAGEMENT

Torticollis

Disfiguring up or downshoot in adduction

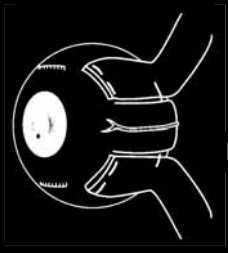
Variable outcome of vertical muscle transposition

Be aware of the amount of IIIrd nerve supply!

ABSENCE OF VITH & VIITH NERVE AFTER SURGICAL EXCISION

R/ AUGMENTED FULL TENDON VM TRANSPOSITION

Superior rectus



LR

Inferior rectus

EARLY ONSET AND RESTRICTIVE STRABISMUS = incomitant

Congenital cranial dysinnervation disorders « CCDD »

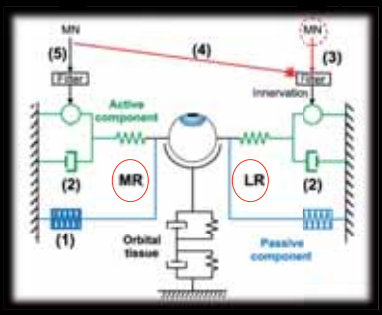
clinical, genetic, and molecular biologic approaches

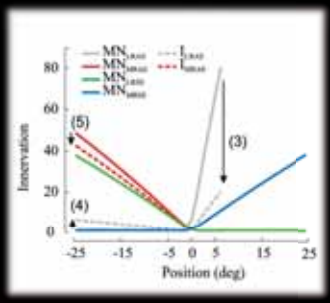
In the last decade, we have focused our research studies on understanding the genetic etiology of a series of complex strabismus syndromes in which eye movement in at least one direction is limited or paralyzed

We are discovering that these disorders result from mutations in genes necessary for the normal development and connectivity of brainstem ocular motoneurons, including *PHOX2A, SALL4, KIF21A, ROBO3,* and *HOXA1*

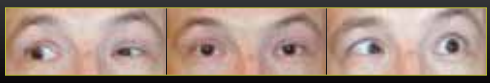
Engle et al, Science 2008

Model of the eye plant

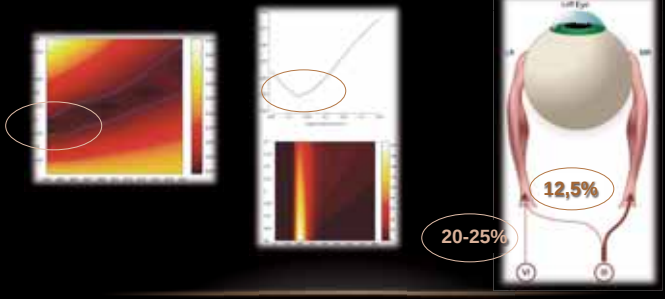




Orban de Xivry J, Yüksel D, Lefèvre P
Neuroscience meeting, Washington DC, November 2008



Ortho-DRS type I



Yuksel et al, Vis Res 2010 (review)

BROWN SYNDROME

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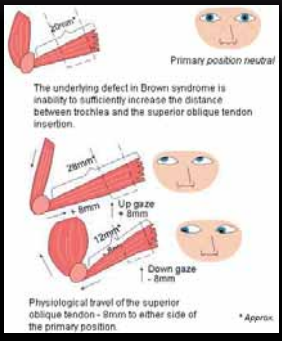
demet.yuksel@uclouvain.be



HELVESTON Cyber-sight, Orbis, Telemedecine

Clinical Characteristics of Brown Syndrome

1. Vision and stereo acuity usually normal
2. Chin up face points to opposite side
3. Deficient elevation in adduction
4. Usually some elevation limitation in straight upgaze and in abduction
5. Widened palpebral fissure on adduction
6. May or may not have downshoot of involved eye in adduction
7. May be acquired
8. May be intermittent with or without pain

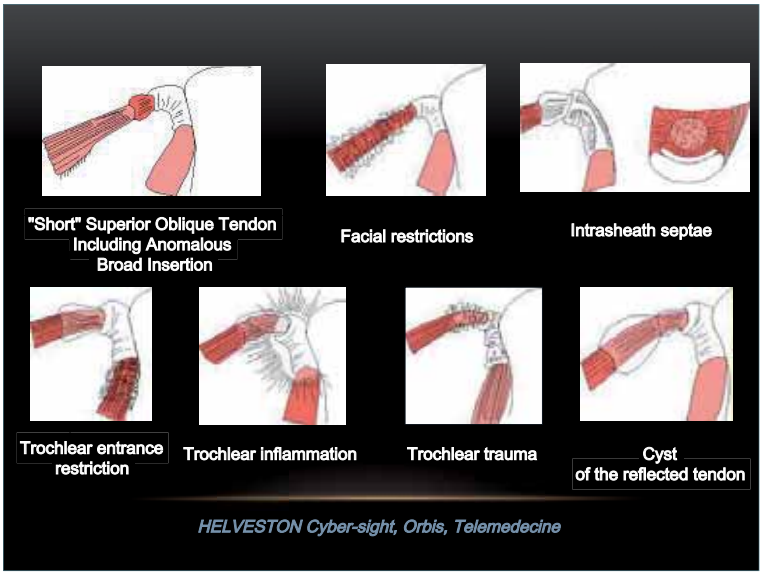
Theories of tight or inelastic SO tendon-muscle complex

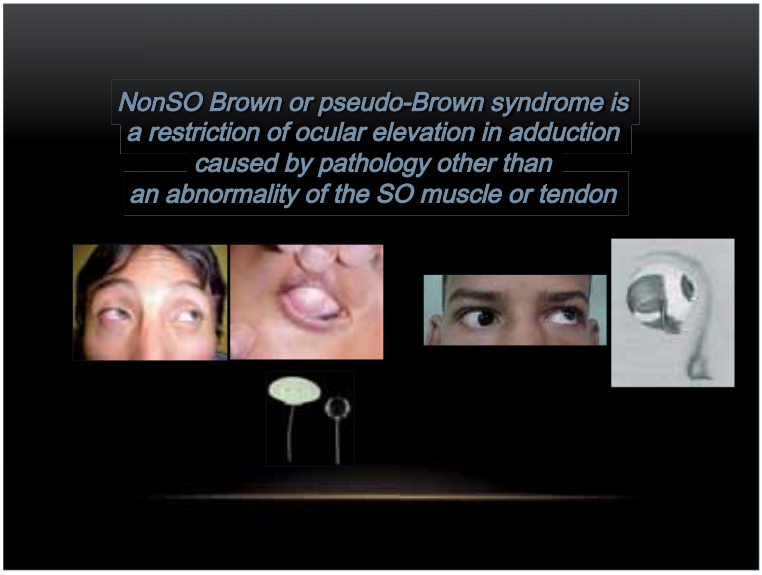
HELVESTON

Theory of abnormal telescoping mechanism

WRIGHT

Hypothesis of congenital inelastic SO muscle-tendon complex


"Short" Superior Oblique Tendon Including Anomalous Broad Insertion
Facial restrictions
Intrasheath septae
Trochlear entrance restriction
Trochlear inflammation
Trochlear trauma
Cyst of the reflected tendon
HELVESTON Cyber-sight, Orbis, Telemedecine

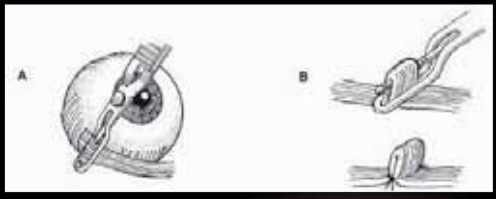

NonSO Brown or pseudo-Brown syndrome is a restriction of ocular elevation in adduction caused by pathology other than an abnormality of the SO muscle or tendon

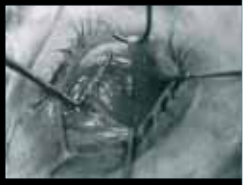
Acquired Brown syndrome

Peritrochlear scarring and adhesions
Chronic sinusitis
Trauma (superior temporal orbit)
Blepharoplasty and fat removal
Lichen sclerosus et atrophicus and morphea

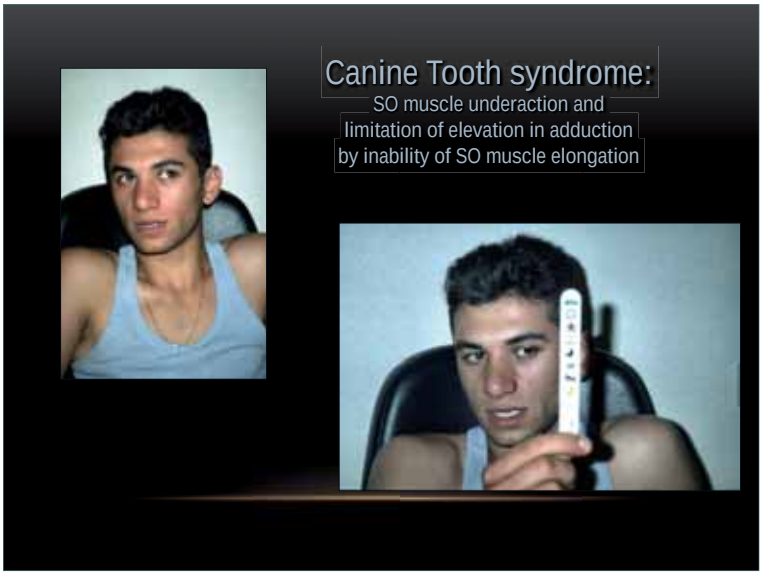
Tendon-trochlear inflammation and edema
Idiopathic inflammatory (pain and click)
Trochleitis with SO myositis
Acute sinusitis
Adult/Juvenile rheumatoid arthritis
Systemic lupus erythematosus
Possibly distant trauma (cardiopulmonary resuscitation and long bone fractures)
Postpartum hormonal changes

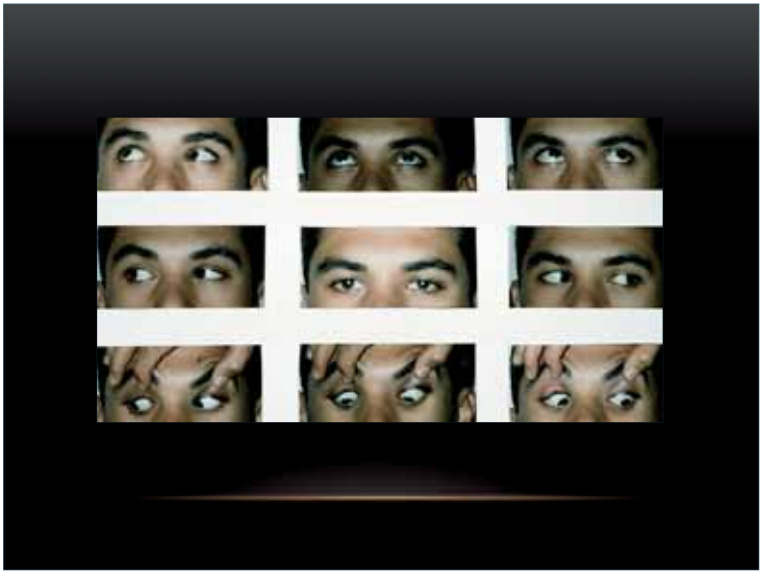
Iatrogenic Brown syndrome : « SO tuck »





"Never tuck the superior oblique"
if not enough laxity


Canine Tooth syndrome:
SO muscle underaction and
limitation of elevation in adduction
by inability of SO muscle elongation



Treatment

Spontaneous recovery exists !!!

Etiologic management

Anti-inflammatory drugs

Surgical approach
only if risk for BV and / or uncomfortable torticollis

**SO tenotomy*
**SO silicone expander or lengthening procedure*

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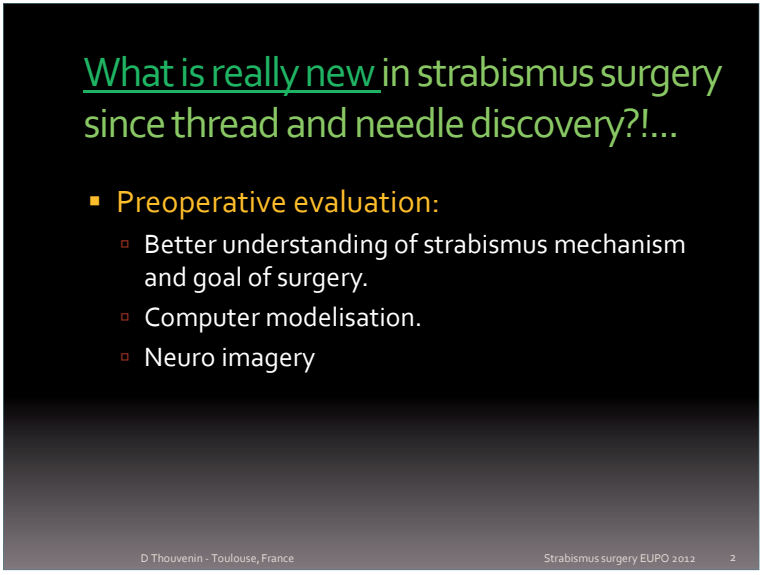
19. Strabismus surgery techniques: strengthening, weakening…

• Dominique THOUVENIN, Toulouse, France



What is really new in strabismus surgery since thread and needle discovery?!...

- During surgery
  - Use of operative microscope ++++
  - Evaluation of strabismus under sedation
  - « New » techniques (Posterior fixation, adjustable sutures, botulinum toxin)
  - and improvement of old one...

What do you need before surgery?

- Type of strabismus
- Angle of squint at distance and near fixation measured with adequate optical correction of any ametropia.
- Sensory state
  - Monocular : amblyopia, fixating eye
  - Binocular : Retinal correspondance, neutralisation, diplopia, fusion amplitude...
- Description of motility disorders
- And a lot more if possible

Preop explanations to patient

- Goal of surgery in each case (rarely perfection)
- Technical aspects
- Type of anaesthesia
- Risks of surgery
- Post operative recovery

How surgery works?

- Tension/length
  - Active and passive force of EOM
- Arc of contact
- Plane of action
- Innervationnal effect
- Role of orbital pulleys of muscles

General rules of EOM surgery

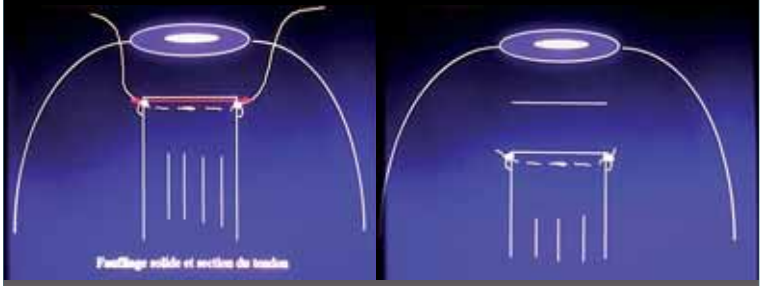
- Learn it with the use of operative microscope and get used to it
- Respect orbital and perimuscular tissues
- Respect muscle anatomy when repositionning
- Stay simple in first intention
- No more than 2 recti at the same time

Weakening a rectus muscle

- Recession
  - Reposition behind its physiological insertion
  - On its action line
  - Reduces active & passive force and arc of contact
  - Innervationnal effect
  - Indication =
    - The most used and known technique
    - Treatment of « anatomic » part of strabismus

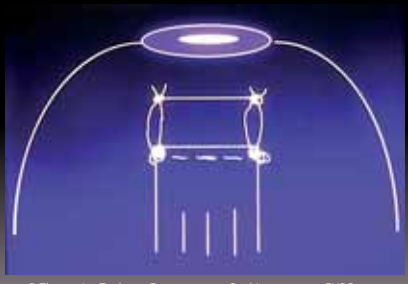
Weakening a rectus muscle

- Recession



Weakening a rectus muscle

- Recession with loop
  - Same effect, except for arc of contact
  - Used in adjustable sutures



Weakening a rectus muscle

- Posterior fixation
  - ie :
    - Cüppers Fadenoperation
    - Retroequatorial myopexy
    - Posterior strapping
  - Major technique but
  - Not much popular because surgeons keep in mind difficulties that occured with the primarily described technique

Weakening a rectus muscle

- Posterior fixation
  - Effect :
    - Supresses arc of contact
    - Innervationnal effect on yoke muscle ++
  - Treats variable or « spastic » deviations
  - Without effect in primary position
  - Combination possible with recession, frequently used.

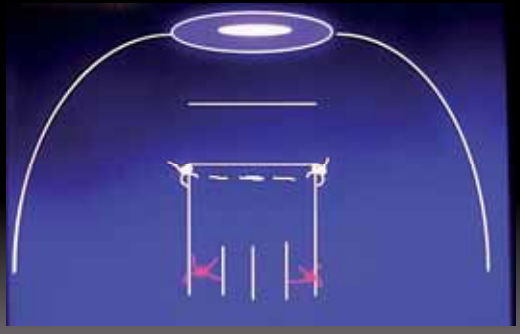
Weakening a rectus muscle

- Posterior fixation : Cüppers original procedure
  - Without microscope
  - With multifiber thread
  - Anchoring lateral part of muscle to sclera on each side

- Difficult, risky
- Frequently unefficient because too anterior
- Major difficulties in second surgery (fibrosis of anterior part of the muscle)

Weakening a rectus muscle

- Posterior fixation : Cüppers original procedure

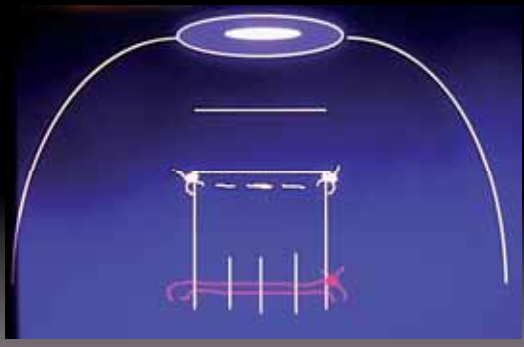


Weakening a rectus muscle

- Posterior fixation = Posterior strapping :
  - Under microscope
  - With nylon thread, spatulated needle
  - No bite in the muscle = anchored to sclera laterally and passed over the muscle's belly
- As easy, or difficult, as any scleral suture = learning curve.
- 2nd surgery possible, few fibrosis
- Few complications

Weakening a rectus muscle

- Posterior fixation : Posterior strapping

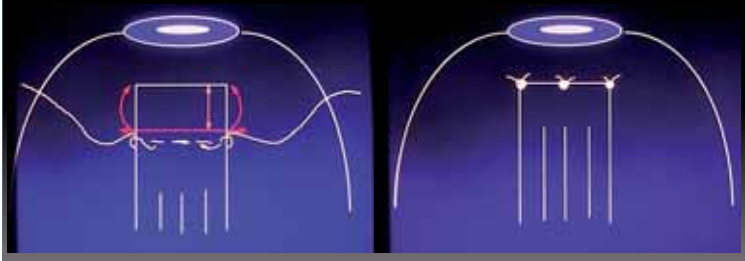


Weakening a rectus muscle

- Posterior fixation : Radius of action
  - Tonic part of strabismus
    - Variable angle
    - Attraction toward adduction in infantile esotropia
  - Oculomotor palsies (paresy against paresy (Cüppers))
  - Helps to stabilize ML Nystagmus and slow phase of patent nystagmus.
  - Vast majority on Medial recti (esotropias, 6th nerve palsies, nystagmus), and Superior recti (DVD).

Strengthening a rectus muscle

- Resection :
  - Elimination of a measured part of the anterior portion of the muscle.
  - Refixation at the physiological scleral location



Strengthening a rectus muscle

- Tucking of a rectus muscle :
  - Same procedure, without section
- Anteriorisation of a rectus muscle
  - Used for previously recessed muscle

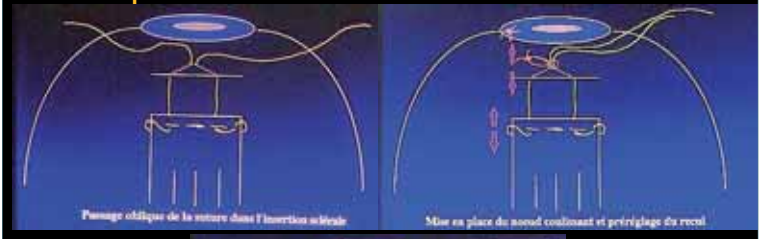
Strengthening a rectus muscle

- Resection : action
  - None on arc of contact
  - None on active force
  - Strengthen passive force
  - To be adapted to peroperative passive duction test+++ to avoid over or under correction
    - In strabismus = hyper elastic muscle
    - In palsies = paretic muscle

Adjustable suture

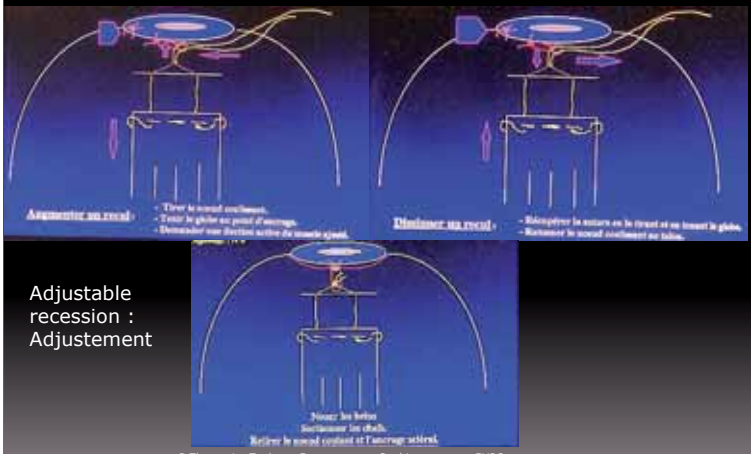
- Allows adjustment of recession or resection of a muscle after surgery :
  - Awaken patient
  - « Normal » motility recovered (distance from local or general anesthesia)
- Allows to dare what you wouldn't have without it…
  - Very useful in adult surgery, difficult cases, fibrosis
  - With some limits

Adjustable suture



Adjustable recession : Surgical technique

Adjustable suture



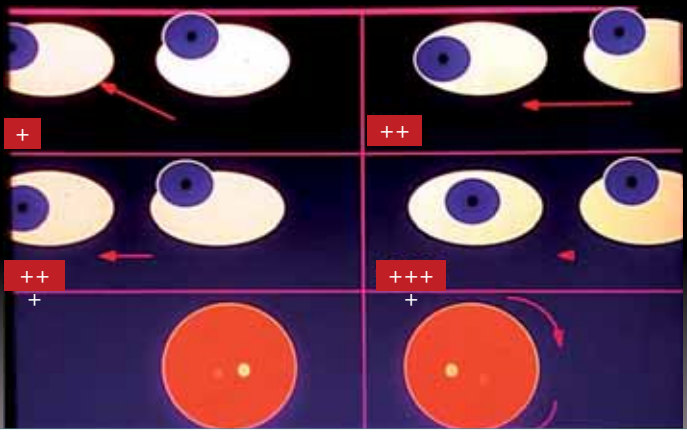
Adjustable recession : Adjustement

Oblique muscle surgery

- More difficult
  - Posterior position, cross recti muscles
  - Difficult access
  - Complex physiology
- Learning curve
- Micro surgery
- Respect its physiology as for recti
- Very efficient and satisfying

Inferior oblique muscle surgery

- EXTORSION, elevation (add), abduction



25

Inferior oblique muscle surgery

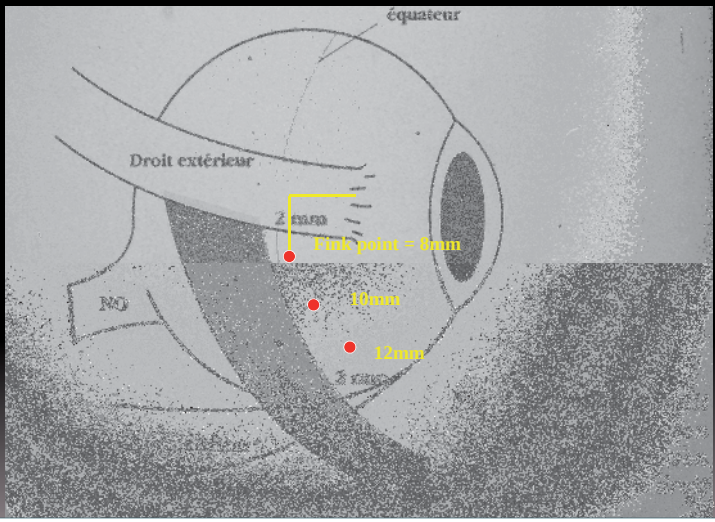
- Weakening <u>without</u> scleral refixation:
  - Myectomy
  - Myotomy

  - Non graduable techniques
  - Non predictible effect
  - Interest= no touch of scleral (and far…) insertion

Inferior oblique muscle surgery

- Weakening with scleral refixation:
  - More physiological and graduable
  - Separate reinsertion of anterior (torsion) and posterior (elevation) fibers
  - Graded recession
  - Antero transposition
  - Anterotransposition with nasal refixation

Graded Recession

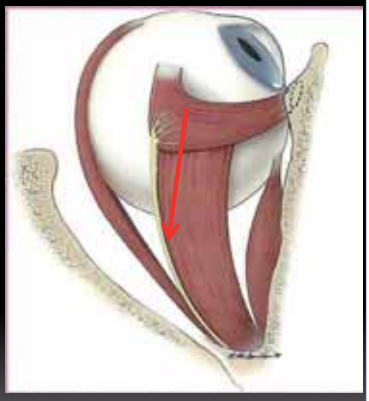


Anterotransposition

- Very efficient on torsion and elevation

Side effects :

- Y sd (exo in elevation)
- Anti elevation Sd with limitation of elevation in ADD & ABD, clinical aspect of contralateral IO hyperaction

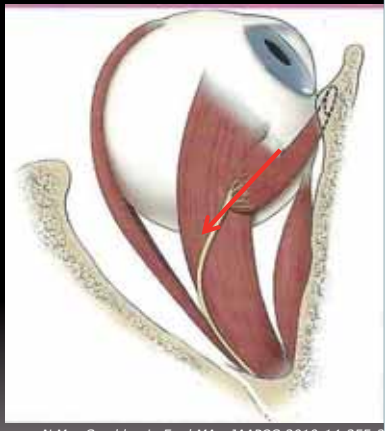


N Mac Spadden in Fard MA : JAAPOS 2010;14:355-3

Nasal transposition

- Even more efficient on elevation and torsion:

Reverses the effects of IO



N Mac Spadden in Fard MA : JAAPOS 2010;14:355-3

Inferior oblique muscle surgery

- Weakening with scleral refixation:
  - IOOA + = no surgery or 8mm recession
  - IOOA ++ = no surgery or 10mm recession
  - IOOA +++ = 12mm recession
  - IOOA++++ or residual IOOA after graded recession = anterior or nasal transposition
  - Extirpation denervation for extreme cases

Inferior oblique muscle surgery

- Strengthening:
  - Very rarely used
  - Resection and re insertion
  - Pulled under LR and reinsertion in supero temporal quadrant.

Superior oblique muscle surgery

- INTORSION, depression, abduction
- « Noli me tangere » (Von Graefe)…
- Difficult surgery
  - With microscope
  - Thin sclera

Superior oblique muscle surgery

- Weakening of SO
  - Graded recession
    - Passing under SR muscle
    - Differenciate anterior (torsion) and posterior (depression) fibers+++
    - Cautious when scleral repositioning because very thin sclera
  - Silicone expander or Z chicane on nasal tendon
  - Indication = SO Overaction, A pattern, Brown

Superior oblique muscle surgery

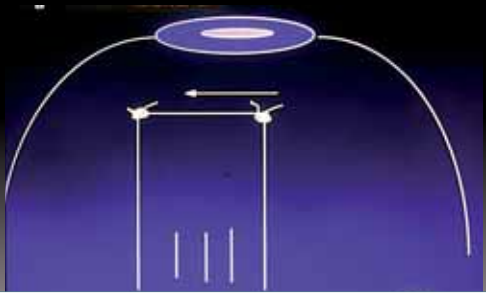
- Strengthening:
  - Resection or « tuck » at the scleral insertion (supero temporal access)
    - Frequent postop Brown Sd that may vanish with time
      - Adapt tuck to muscle elasticity, pre and post tuck passive duction test +++
    - Indication in SOUA, V Pattern, IVth NP

Superior oblique muscle surgery

- Strengthening:
  - Selective strengthening
    - Posterior tuck = vertical action (increases depression in ADD)
    - Anterior tuck (De Decker, Cüppers) or anteriorisation of anterior fibers (Harada Ito, Fells, Souza Dias) = Torsionnal action (increases intorsion)

Special procedures on recti muscles

- Transposition of recti muscles
  - Useful in incomitant patterns
  - And for diverse types of vertical deviations



37

Special procedures on recti muscles

- Transposition of horizontal recti muscles
  - Lowering = decreases action in downgaze
  - Upward = decreases action in upgaze
  - Provoque adverse torsionnal effects++

V patterns :

- Decrease add in downgaze = lower MR
- Strengthen abd in upgaze = raise LR

Opposite in A patterns

D Thouvenin - Toulouse, France - Strabismus surgery EUPO 2012 38

Special procedures on recti muscles

- Transposition of Vertical recti muscles
  - Nasal transposition: strengthen their ADD effect
  - Temporal transposition strengthen their ABD effect

In V pattern

- Nasal transpo of SR, Temporal transpo of IR
- Helps to decrease excyclotorsion

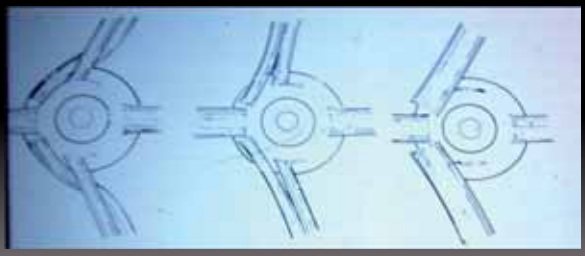
Opposite in A pattern

Special procedures on recti muscles

- Transposition for EOM palsies
  - Proposed in first or second intention
  - Only in cases of
    - Definitive palsies
    - Total palsies
    - Without major mechanical restriction of movement (duction test)

Transposition for EOM palsies

- Partial
  - Hummelsheim (1907) (b)
  - Modified by Kaufmann (1985), add of posterior fixation
  - O'Connors (a) (1935)
- Total = O'Connors (1921) (c)
- Myopexy = Jensen (1964)



Special procedures on recti muscles

- Transposition of both Horizontal recti for vertical deviations (Knapp)
  - Upward transposition of MR and LR helps to treat hypotropia
  - Downward transposition of both MR & LR helps to treat hypertropia
  - In case where there are no other motility disorders, such as oblique dysfunction or restrictive syndromes.

Special procedures on recti muscles

- Transposition for strabismus in High Myopia
  - Supero temporal part of the myopic globe pushes aside :
    - SR nasally => it becomes adductor, and less elevator
    - LR inferiorely => it becomes depressor, and less abductor
  - Explains the very large deviations in add and hypotropia found in high myopia
  - Surgery tries to reposition LR and SR, by suturing them together at the equator by a loop myopexy, without scleral bite, like a fan (Kaumann, Krzizok, Yokoyama…)

Special procedures on recti muscles

- Desinsertion
- Traction suture
- Periosteum suture
- Surgery with botulinum
- …

How much surgery in each case…

- Many options to determine
  - Timing of surgery : very early, early, late surgery.
  - Distribution between classical (resect/resect) and innervationnal surgery (posterior fixation).
  - Uni or bilateral surgery.
  - …
- Learning, training, examining and personnal experience are important.

How much surgery in each case…

No general solution because too many factors are involved

- Age = Tonic part of strabismus decrease with age, as anatomic part increases
- Type of strabismus
- Strabismus measured under anesthesia gives indications :
  - on the « anatomic » part of strabismus, that persists under anesthesia
  - And on « tonic » part, that vanishes under anesthesia,
- Duction test on operated EOM and its antagonist helps to adapt the amount of recession and resections
- The way to perform surgery
  - Use of microscope or binoculars?
- Which muscle
- Biometry of the eye (axial length; refraction)
- Binocular function *(ARC or NRC)*
- …

How much surgery in each case…

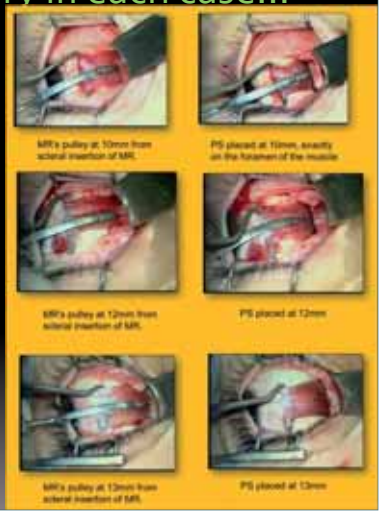
- General rules
  - Tables are to be used with caution. They may be optimized by each surgeon.
  - MR, SR, IR : recess 1mm = 3 PD
  - LR : recess 1mm = 2 PD
  - Resections to be adapted to duction test +++
  - Combining resection to a resection on a same eye majors its efficiency of 20%
  - If posterior fixation is added to rescession, it does not modify its efficiency on « anatomic deviation ».

How much surgery in each case…

Posterior fixation

- Too anterior = unefficient
- Too posterior = palsy…
- MR and SR = between 10 à 14mm, function of pulley position

- We don't recommend pulley fixation (fibrosis)



3 Steps to determine surgery :

- Clinical
  - Preoperative examination
  - Which eye, which muscle. Indication on tonic/anatomic repartition
  - Explanations to patient (goals, limits)
- Under anesthesia
  - Compare « sleeping to « awaken » strabismus!
  - Which eye is the more deviated
- Duction tests
  - Helps dosage of recess/resect surgery
  - Prefer surgery on muscles with abnormal duction tests.
- Position of eyes at the end of surgery
  - Avoid the biggest mistakes… that's all

Conclusion

- Strabismus surgery may seem easy at first glance
- In fact many factors influence the final choice of procedure
- Learning, watching, training are fundamental

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20. (Non-surgical) management of strabismus

• Tjeerd DE FABER, Rotterdam, The Netherlands

(Non-Surgical) Management of Strabismus

Jan-Tjeerd de Faber MD

EUPO 2012

Why should we manage Strabismus?

- Diplopia
- Binocular single vision
- Stereopsis
- Psycho-social aspects
  - Selfesteem
  - Radiance
  - Social eye contact

WOULD YOU PREFER A PRESENTATION BY

The animal world

Primates need social eye contact

- Primates who live in social groups have interaction and hierarchy.
- Eye contact is an important tool for social behaviour to show:
  - Admiration
  - Submission
  - Hierarchy power (alpha male eg Silverback)
  - Nonverbal communication
- Primates have a highly specialized brain area to recognize facial expressions (Prosoposagnosia)

Social Eye Contact

- Social eye contact is extremely important for non-verbal communication, to show and read emotions and human expression
- Eye contact should be mutual

Eye contact mistakes

- When talking to people in a group they look aside:

" Are you talking to me or my neighbour ??"

Employment

- Coats D, Paysee E, Towler A, et al. Impact of large angle horizontal strabismus on ability to obtain employment. Ophthalmology 2000:402-405.
- Conclusion: Strait eyes give the best , esotropia second best and exotropia the poorest chance of getting a job.

Job chances

- Opinion of headhunters about the ability of strabismic subjects to obtain employment. Mojon-Azzi & Mojon DS. Ophthalmologica. 2007;221(6):430-3
Conclusion:.....?

Asked about six facial disfigurements, strabismus was found to have the second largest negative impact on employment directly after acne.

Mojon-Azzi SM,MojonDS Ophthalmologica.2007;221(6):430-3

CONCLUSIONS:

Visible strabismus influences negatively the ability to obtain a job. Because of its impact on the employability of a person, we believe that strabismus surgery in adults cannot be considered to be only a beautifying procedure.

Less job opportunity

- The first impression
- Getting an interview
- Radiance
- Self esteem
- You are not the only one for the position:“Get in line!”
- Get aligned !!

Field expansion

- Kushner B. Binocular field expansion in adults after surgery for esotropia. Arch Ophthalmol 1994;112:639.
- Conclusion: Significant expansion of binocular visual field after correction of esotropia.
  - “After XT surgery the field shrinks, however one might not need a shrink anymore”

Economics

- “Strabismus surgery is a more economical solution for a patient with poor self esteem due to strabismus than psycho therapy.....”

Twins with poor self esteem and heavy eye syndrome




Dating problems

Opinions of dating agents about strabismic subjects' ability to find a partner.

Mojon-Azzi,Potnik, Mojon
BJO 2008;92:765-769

Conclusion:Less chance of being successful in finding a matching partner

Negative self esteem

- Not comfortable to speak in public
- "Wall flower" in the disco and at parties
- Under estimating own capacities
- Avoiding social eye contact

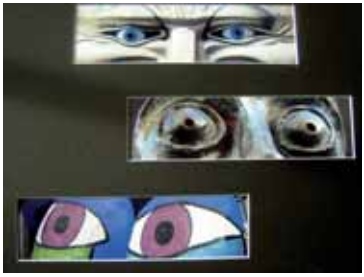
Diplopia in adults

- Dangerous in traffic
- Past pointing
- Lack of stereopsis
- Closing one eye to avoid double vision
- Pirate patch to avoid diplopia

Cultural differences

- In most cultures strabismus has a negative impact:
  - The bad eye
  - The evil eye
  - Witchery
  - Unreliable....

  However...

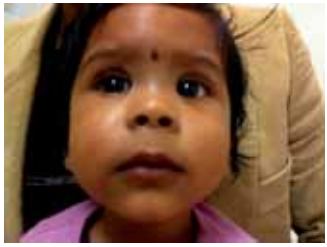


Small angle ET

- By the end of the 1800's a small ET in women was considered one of the 7 beauties.
- It stimulated male protective feelings toward a seemingly helpless harmless "virgin".

India

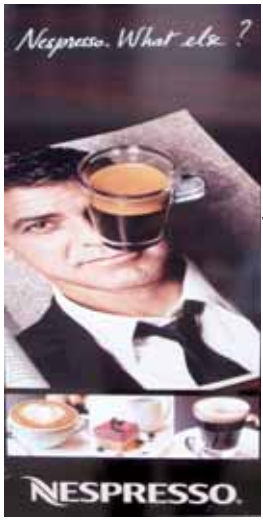
- If a girl with ET is born in a family in Southern India, It is considered a touch of luck. It will bring wealth into the family.



One of the 7 beauties?

However not in every culture..

- In Maya culture strabismus was induced in children by a convergence stimulating object
- Strabismus was a prerequisite to become a priest resembling the “squinting Sun God”



Why is his left eye covered?

Exotropia... What else...

Some make strabismus to their image and selling point

Royal Danish ET + DVD “Queeny Eyes”

Political (under)cover test?

WHO “Health” definition

- Health: “...is not mere the absence of disease, but the human condition in which there is a physical, mental and social well-being....

World Health Organization

So.....

- It is our job as ophthalmologists to guide patients with strabismus to either cope with it or help them to get better functional eye alignment, improved self esteem and augmented social capacities.

Non-Surgical options

- Optical
- Medical
- Orthoptic exercises

Optical Treatment for Strabismus

- Plus or minus glasses
- Prism glasses
- Bifocals
- Bangerter foils or occlusion
- Excentric Iris-print scleral contactlens

Plus glasses

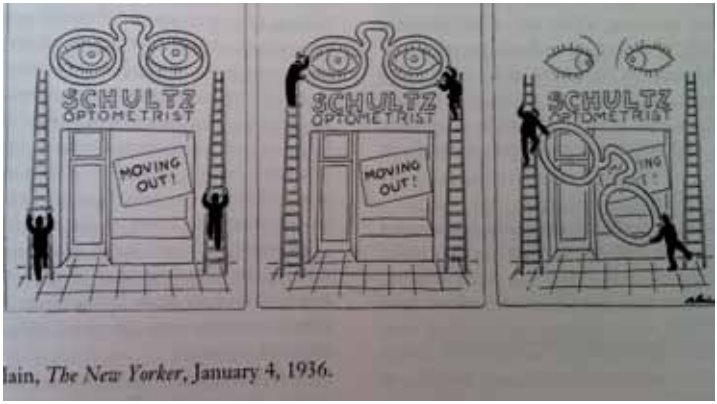
Treatment of choice

- Full accommodative esotropia:
  - Full + correction will straigthen the eyes!!

- Partial accommodative esotropia:
  - With plus glasses part of esotropia corrected rest ET needs surgery

"Swimming pool esotropia "

Glasses correct ET



lain, *The New Yorker*, January 4, 1936.

Twins with ET

- Twins with mirrored ET and S+8.75 OU
- Twin A full acc.ET
- Twin B partial acc ET needed surgery

Minus Glasses

- Minus glasses can correct intermittent Exotropia because the effort to accommodate will keep fusion intact and alignment

Prism Glasses

- Small angle strabismus with diplopia:
  - Thyroid
  - IV nerve palsy
  - VI nerve palsy
  - Post traumatic strabismus
  - Myasthenia ??

Prism Glasses

- Fresnel stick-on prism
- Ground in prism (max 5 prism dpt)

Bifocals

Treatment of high AC/A refractive accommodative esotropia

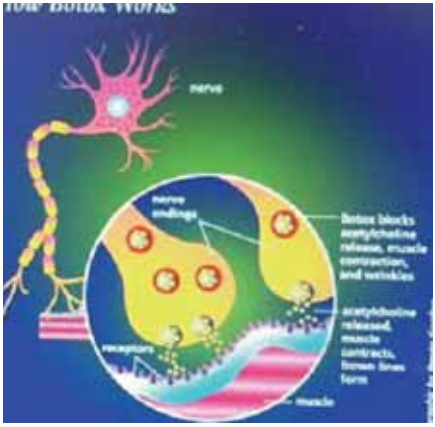
Bangerter foils or occlusion

- Occlusion to prevent diplopia
- Bangerter foils can filter image from 0.8-LP
- Scotch tape can do the same

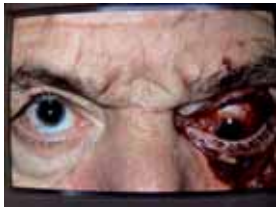
Medical treatment for strabismus

- Botox
- Steroids
- Anticholinesterase agents
- Mestinon (Myasthenia)
- Membrane stabilizers (myokemia,nystagmus)
- Antihelmenthics

Botox



Botox



- VI nerve palsy
- III nerve palsy
- Congenital ET
- Trauma

Steroids

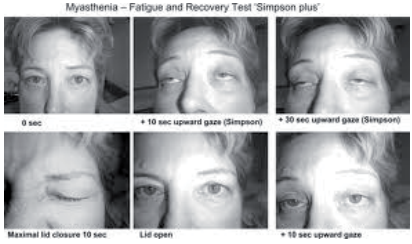
- Thyroid myopathy
  - Systemic
  - Peribulbar
  - Acquired Brown Syndrome
  - Myositis

Anticholinesterase agents

- Eserine
- Echotiophate iodine (Phospholine iodine)
- In residual ET

Mestinon

- Myasthenia



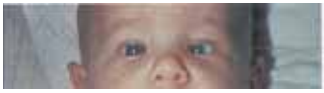
Orthoptic exercises

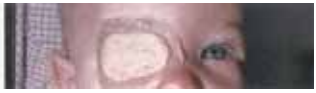
- Pencil push-up's work for convergence insufficiency
- In older day's fusional exercises were tried and have a revival with computer programs

Propranolol systemic

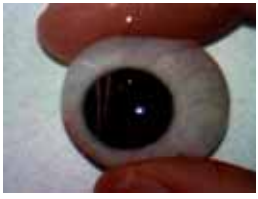
Amblyopia Treatment

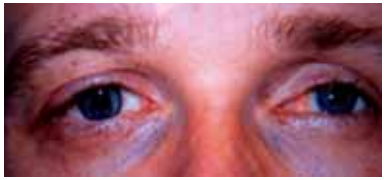
- Occlusion
- Penalization
  - Optical
  - Atropine
  - Combination





Strabismus camouflage handpainted contactlens





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21. Management of paralytic strabismus

• Seyhan ÖZKAN, Aydin, Turkey

Paralytic strabismus is one of the most challenging areas in strabismus practice. In this presentation the general principles of surgical treatment will be reviewed and then the treatment strategies in third, fourth and sixth cranial nerves will be evaluated. The major aims of treatment are enlargement of diplopia free field, restoration of ocular alignment and restoration of the appearance of the patient, to correct abnormal head posture, and to improve ductions.

In all types of paralytic strabismus the stability of the deviation must be observed before considering any surgical intervention. The time period that the spontaneous recovery occurs is usually accepted as 6 months, however this period may last longer especially in third nerve palsies. A waiting period of 12 months is recommended for third nerve palsies and spontaneous recovery may occur even in a longer period of time in some cases. As a general rule one must consider that if the deviation is still unstable following consecutive examinations after 6 months, surgical treatment must be postponed till the deviation becomes stable.

Preoperative assessment: For a correct surgical planning the following questions need to be answered preoperatively in cases with paralytic strabismus:

1. Is the problem a partial (paresis) or total (paralysis)?
2. Are there any restrictive factors?
3. Is the problem congenital or acquired?
4. Is there “acquired loss of fusion” or in other words “central fusion disruption”

Is the paralytic problem partial or total? Are there any restrictive factors? If there are no restrictive forces it is not difficult to assess whether the paralytic condition is partial or total. These factors may be primary as it is the case in blow out fracture or secondary as the contracture of the antagonist muscle(s) in long standing paralytic problems. For a correct evaluation of the role of accompanying restrictive factors and the residual function of the paretic extraocular muscle the following tests may be used:

- Measurement of the deviation in 9 positions of gaze
- Assessment of the ocular rotations
- Traction test
- Active forced generation test
- Electromyography (EMG)
- Increase of intraocular pressure with positions of gaze
- Measurement of saccadic eye movements
- Botulinum toxin A (BTXA) injection into the antagonist extraocular muscle

The secondary unopposed contracture of the antagonist extraocular muscle may not allow the eye to move towards the direction of the affected muscle despite some spontaneous recovery. In such cases an improvement of the movement towards the functional area of the paretic muscle following BTXA injection into the antagonist muscle, indicates that there is some residual function of the paretic muscle.

Despite the numerous methods for preoperative assessment of the restrictive forces the surgeon may have to change the surgical plan depending upon the traction test results under general anaesthesia. In long standing paralytic strabismus the contracture and fibrosis may not only affect the extraocular muscles but also the fascial structures and extraocular muscle pulleys and an orbital fibrosis develops.

Is the problem congenital or acquired? In congenital paralytic disorders there may be some developmental abnormalities like the tendon abnormalities in congenital superior oblique palsy, extra-ocular muscle fibrosis or orbital fibrosis. Most of the congenital cases do not complain of diplopia. The exception of this is decompensated congenital fourth nerve palsy presenting with vertical diplopia.

Is there "acquired loss of fusion (central fusion disruption)"? Acquired loss of fusion or central fusion disruption may occur in paralytic strabismus cases especially the posttraumatic ones. In these cases because of the involvement of the fusional areas which is supposed to be located at the midbrain, the previously healthy fusional ability is lost causing intractable diplopia. If the patient has an acquired loss of fusion and intractable diplopia, the deviation should better be corrected temporarily by prisms or BTXA in order to allow the assessment of the tolerance of diplopia. In some cases during this period the fusional ability may be regained and in those ones surgery may be performed safely. Our preferred method is BTXA injection in such cases to provide a temporary period of orthophoria under real life conditions.

Methods of Surgical Treatment:

- Decreasing the strength of the antagonist: Recession or disinsertion of the antagonist are the preferred methods. Fixation of the extraocular muscle into the orbital wall is a recently described method in order to totally inactivate the overacting muscle. If a recession will be combined with full tendon transposition BTXA injection instead of surgical recession should be preferred for the risk of anterior segment ischemia.
- Strengthening the paretic extraocular muscle: Resection or tendon tuck could be performed. For strengthening procedures the paretic muscle is preferred to have some residual function. The exception of this is superior oblique palsy. Because of the tendon length and the anatomical characteristics, superior oblique tendon tuck may be performed in a superior oblique muscle with no residual function.
- Weakening the yoke muscle in the sound eye: Recession or faden operation of the yoke muscle in the unaffected eye are the preferred methods to increase the field of binocular diplopia free field.

Third nerve palsy

Third nerve palsy may present with a total or partial involvement and it represents a wide range of ocular motility problems. The involvement of the inferior branch of the third nerve affects medial rectus, inferior rectus and inferior oblique muscles, whereas the superior branch affects the superior rectus and levator palpebrae superioris muscle.

In complete third nerve palsy the major problem is the unopposed contracture of the antagonist lateral rectus muscle. There is a small hypotropia with a large angle exodeviation and ptosis due to the involvement of levator palpebrae superioris muscle. If the pupillary fibers are affected a mydriatic pupilla will be observed. In congenital and long standing cases fibrosis of the intra-orbital structures develops. The aims of treatment in a complete third nerve palsy are to obtain an improvement of the appearance of the patient, orthophoria in primary position and a field of binocular single vision in a very limited area. The surgical treatment modalities in complete third nerve palsy may be summarized as follows:

- Weakening of the lateral rectus muscle by recession or orbital wall fixation
- Resection of the medial rectus muscle
- Superior oblique tendon transposition
- The procedures that keep the eye in passive adduction
- Medial transposition of lateral rectus muscle

Orbital fibrosis is the bad prognostic sign for any type of surgery. A temporary pulling by traction sutures is very effective that allows the development of the scar tissue while the globe was fixated on adduction.

In incomplete third nerve palsy with a superior or inferior branch or isolated extraocular muscle involvement, the treatment should be planned depending upon the affected extraocular muscle(s). Recess-resect or transposition with a recession or BTXA injection may be considered. As the goal is to enlarge the diplopia free field the sound eye may be operated where necessary. In that case faden operation or recession of the yoke muscle in the sound eye may be used.

Fourth nerve palsy

In fourth nerve palsy hypertropia, inferior oblique overaction and superior oblique underaction is observed in the affected eye. In long standing unilateral cases a secondary contracture of the superior rectus develops and a pseudo overaction of the superior oblique muscle in the sound eye is observed. Abnormal head posture and a positive Bielschowsky head tilt test are the other findings of fourth nerve palsy. In bilateral cases the abnormal head posture may be as unilateral cases if there is marked asymmetry. If the bilaterality is symmetrical then the abnormal head posture aims to compensate the “V” pattern. In acquired cases vertical and/or torsional diplopia is the main complain of the patients. Congenital cases do not usually complain about diplopia, however in decompensated congenital fourth nerve palsy the patient has vertical diplopia. Some patients may benefit from prisms but most of the patients require surgical treatment.

For a correct surgical plan one needs to have the correct answers for the following questions:

- What is the amount of the deviation in primary position?
- What is the position of gaze with the largest deviation?
- Is it congenital or acquired?
- Is there any superior oblique tendon laxity?
- Is there any superior rectus contracture?
- Is it unilateral or bilateral?
- Is there any torsional diplopia?

What is the amount of the deviation in primary position? If the vertical deviation in primary position is exceeding 15 prism diopters two muscle surgery needs to be considered.

What is the position of gaze with the largest deviation? The surgical treatment should be planned on the extraocular muscles functioning in the field of gaze with the largest deviation. In order to obtain a reliable data, the measurement of the deviation should be done in 9 diagnostic positions of gaze.

Is it congenital or acquired? Congenital cases may present with superior oblique tendon abnormalities; such as abnormal tendon laxity, tendon insertion abnormalities and sometimes even agenesis of the tendon. The differential diagnosis in congenital and acquired cases is not only important for the etiological investigation but also for surgical planning. The clinical clues suggesting that the patient has a congenital superior oblique palsy may be summarized as follows:

- History, old photos
- Absence of a preceding event
- Prominent abnormal head posture
- Facial asymmetry
- Coexistence of amblyopia
- Significant superior oblique underaction
- Large vertical fusional amplitude
- Coexisting horizontal deviation
- Absence of subjective torsion

Is there any superior oblique tendon laxity? Superior oblique tendon laxity can be assessed prior to surgery with traction test. The globe is fixated by two forceps at inferior nasal and superior temporal areas and with retropulsion the globe is elevated on adduction.

Is there any superior rectus contracture? Superior rectus contracture may develop in long standing fourth nerve palsy. In these cases traction test is positive in depression on adduction. Recession of superior rectus muscle is advised in those cases with superior rectus contracture.

Is it unilateral or bilateral? All of the cases with fourth nerve palsy should be carefully evaluated for the clues of bilateral involvement. The clinical clues suggesting bilateral involvement are as follows:

- Bilateral inferior oblique overaction.
- Bilateral superior oblique underaction.
- Positive Bielschowsky head tilt test with the head tilted on both sides. In case of a marked asymmetry Bielschowsky head tilt test may be positive on the side with marked involvement.
- "V" pattern deviation.
- Abnormal head posture to compensate the "V" pattern.
- Objective torsion exceeding 10°.

Is there any torsional diplopia? Torsional diplopia is a symptom that occurs in acquired fourth nerve palsy. The patients with a decompensated congenital fourth nerve palsy has vertical diplopia without a torsional element although an excyclotorsion is observed in fundus examination and this is one of the clues for differential diagnosis of a congenital and acquired fourth nerve palsy.

Surgical methods of treatment may be summarized as follows:

- Inferior oblique weakening procedures
- Superior oblique strengthening procedures
- Superior rectus recession in the affected eye
- Inferior rectus recession in the contralateral eye

Bilateral surgery should be considered in masked bilaterality despite the absence of apparent inferior oblique overaction and superior oblique underaction. Inferior weakening alone provides satisfactory outcome in most of the cases if the vertical deviation does not exceed 15 prism diopters. Ipsilateral superior rectus and contralateral inferior rectus weakening procedures should always be considered in combination with inferior oblique weakening. Superior oblique tuck surgery should not be considered in acquired ones as the risk for symptomatic iatrogenic Brown syndrome is very high. Superior oblique tendon tuck should be reserved for congenital cases with abnormal tendon laxity and a large vertical deviation. Fells modified Harada-Ito procedure is a surgery for acquired bilateral cases with marked torsional component.

Sixth nerve palsy

Lateral rectus underaction, esotropia and a horizontal diplopia which is more prominent at distance, abnormal head posture in unilateral cases keeping the affected eye in adduction are the clinical features of sixth nerve palsy. Botulinum toxin has a major role in treatment of sixth nerve palsy both for diagnostic and therapeutic purposes. During acute stage, injection of BTXA into the medial rectus muscle of the affected eye provides a symptomatic relief. Although it was previously proposed that BTXA increased the possibility of spontaneous recovery, randomized clinical trials demonstrated that BTXA injection does not alter the chance of spontaneous

recovery, but provides a rapid symptomatic relief of diplopia In chronic stage in mild partial cases BTXA injection alone may provide a satisfactory improvement.

For a correct surgical plan one needs to have the correct answers for the following questions:

- What is the amount of the measurement of the deviation in primary position?
- Is the paralysis total or partial?
- Are there any medial rectus contracture?

Surgical methods of treatment may be summarized as follows:

- Medial rectus recession and lateral rectus resection
- Medial rectus weakening of the sound eye
- BTXA injection into the medial rectus muscle + vertical rectus muscle transposition
- Medial rectus recession + vertical rectus muscle transposition: This method carries a risk of anterior segment ischemia. That risk may be reduced by ciliary artery preserved full tendon transposition, performing the surgery in two divided sessions leaving at least 3 months between two operations, or by performing a partial vertical rectus transposition.
- If there is bilateral involvement surgery should be performed in both eyes.

The major pitfall is the misinterpretation of the lateral muscle function because of the secondary medial rectus restriction in long standing cases. Recess-resect procedure works only in ones with good residual function of the lateral rectus muscle. Consider vertical rectus transposition without augmentation sutures in ones with very limited evidence of lateral rectus muscle function.

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22. Amblyopia: pathophysiology and therapy

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Introduction

Amblyopia is a public health problem in all countries although the foundations of its management have been known from many years and its pathophysiology is known since the works of Hebb (1949) and of Hubel and Wiesel (Nobel, 1981).

Pathophysiology

The functional amblyopia is the result either of a bilateral poor quality visual information arriving in the cortex (organic or ametropic) either of a conflict between the visual information from each eye because a different quality of image (organic pathologies, unilateral strabismus (diplopia) and anisometropias).

During the period of brain plasticity, the cells of the visual cortex does not implement satisfactorily either because of insufficient stimulation (hypothesis one) either to resolve this conflict (hypothesis two). This possibility can only exist during this period plasticity (birth to 8 -10 years) that is genetically programmed.

Screening

As the period of brain plasticity has a limited duration, it is essential that the diagnosis is made early enough to implement an effective treatment. Screening is therefore a key focus in the therapeutic efficacy.

Definition of amblyopia

There are two types of amblyopia:

- Relative amblyopia
  This is a difference in visual acuity between the two eyes, more than 0.1 logMAR.

- Absolute amblyopia
  It's a visual acuity of both eyes, greater than or equal to 0.3 logMAR.

Consequences of amblyopia

Amblyopia has important consequences in the personal and professional life. Amblyopia also achieved self-esteem. In support of AMD, subjects with amblyopia are earlier and longer with a legally blind.

Treatment

Currently, among experts, there is disagreement about treatment goals. For some, an improvement of visual acuity sufficient to consider that the treatment is effective (PEDIG). For others, obtaining an isoacuity is the goal of treatment (personal view). All treatments are based on a simple rule: the time spent in each eye.

Initial phase

For our part, the treatment of amblyopia in the initial phase following rules:

- Port of total optical correction determined by refractometer automatically after using a strong cycloplegic (cyclopentolate and / or atropine);
- Total occlusion and prolonged occlusion of the good eye then symmetrical or asymmetrical alternating until a difference of less than 0.3 logMAR between the eyes.

This treatment appears to be substantially identical in the different European countries.

Consolidation phase

It is based on a set of ways: intermittent occlusion, Bangerter filters, optical penalties, penalties pharmacological, etc.. The following practices seem different schools and countries. Some rules must be followed:

- Requirement rules. The goal is isoacuity.
- Rules of duration. If treatment is stopped too early the risk of recurrence is important. In our team, duration of treatment is five years.

Conclusion

The functional amblyopia is a condition that can be cured if we make the diagnosis early enough and if there is an effective treatment and prolonged. The goal is to obtain an isoacuity. This objective is achieved by current therapeutic means in the vast majority of patients (80-90%).

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