SPECIFIC DISORDERS

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OPTIC NEURITIS

Optic neuritis is an autoimmune demyelinating disorder of the optic nerve. It can be idiopathic, post infectious, or a component of multiple sclerosis. (Scheifer et al. Clinical Neuro-ophthalmology 2007).

Optic neuritis encompasses:

- Papillitis
- Retrobulbar neuritis
- Neuroretinitis

20% of optic neuritis is papillitis and 80% is retrobulbar. This shows that retrobulbar neuritis is more common and may show more susceptibility due to the length of the optic nerve.

Any patient with RAPD, decreased colour vision and brightness must have an MRI scan of the brain. A central field defect with papilloedema (swollen disc from raised intracranial pressure) occurs if the swelling is chronic, if the edema spreads to the macula area or if there is associated macular hemorrhage. Otherwise papilloedema presents with a constricted field and an enlarged blind spot.

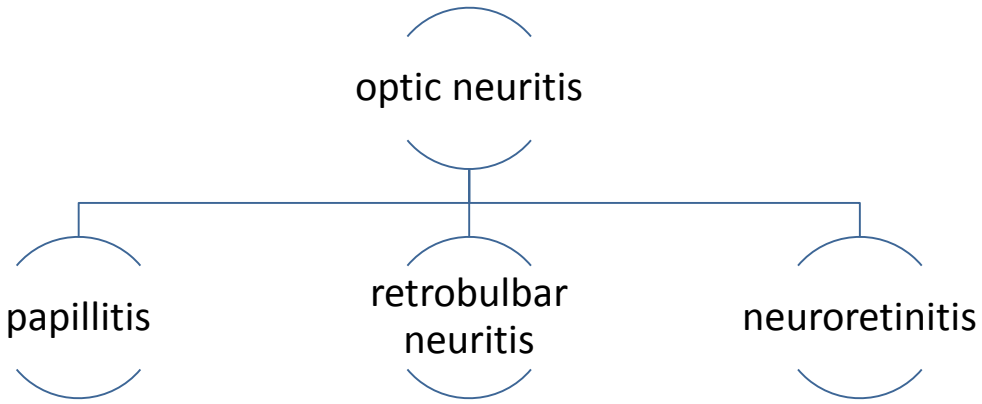

Figure 7.1: *Optic neuritis*

CLINICAL FEATURES OF OPTIC NEURITIS

Optic neuritis has the following characteristics:

- There is an acute or subacute loss of vision.
- Pain is noted on eye movement. Pain is due to inflammation that has spread to the sheath. It is usually unilateral in adults and bilateral in children (measles, mumps).
- Acquired colour vision defect (red cap desaturation)
- Reduced brightness sense (brightness comparison test)
- Uhthoff's symptom is a decrease in vision with increase in body temperature and suggests demyelinating disease. With exercise or hot shower, there is poor vision.
- Almost never present with no light perception (NLP); usually light perception (LP) or counting fingers (CF).
- The Pulfrich phenomenon occurs in unilateral optic neuritis. It has been demonstrated in experiments where the patient sees a pendulum taking a circular path rather than a horizontal movement due to differences in the speed

of conduction of vision between the two eyes. Patients with the Pulfrich phenomenon complain that when driving the straight line on the road appears curved rather than straight. Demyelination decreases the speed of conduction on the abnormal side compared to the normal side.

- LeHermitt's sign: patient flexes neck, tingling sensation down limbs.

PAPILLITIS

Etiology:

- Idiopathic
- Childhood infections
- Measles
- Mumps
- Chicken pox
- Meningitis
- Upper respiratory tract infection (URTI)
- Adults – viruses, juxtapapillary choroiditis, toxoplasmosis, Multiple sclerosis

Signs:

- Sudden unilateral visual loss
- Decreased visual acuity
- RAPD (defect in direct light reflex ipsilaterally to the defect in the afferent pathway)
- Swollen disc, vitreous cells, sheathing of vessels
- Perivascular cuffing
- Decreased colour vision and brightness sense
- Central, centrocaecal, or arcuate visual field defect
- Only ONH is swollen

Treatment:

- Corticosteroids
- Corticosteroid-sparing agents may be used if patient is corticosteroid-intolerant or requires chronic intensive therapy
- Antibiotics for infection, if present

RETROBULBAR NEURITIS

Retrobulbar neuritis has a normal appearing optic disc, acute unilateral visual loss and RAPD.

Etiology:

- Multiple Sclerosis (80% of Optic neuritis due to MS is retrobulbar)
- Collagen vascular disease (e.g. SLE)

- Viral infections (EBV, VZV)
- Granulomatous infection: Tuberculosis, Syphilis, Sarcoidosis, Cryptococcus
- Intraocular inflammations (e.g. uveitis)
- HIV

Signs:

- Decreased Visual acuity
- Normal optic nerve head appearance – no oedema (this is how one can differentiate between neuritis and retrobulbar)
- Optic nerve inflamed behind the eye
- RAPD
- Pain on eye movements

NEURORETINITIS

Neuroretinitis is characterized by optic papillitis and a macula star which is composed of hard exudates.

Etiology:

- Viral infections
- Cat-scratch fever
- Syphilis
- Lyme disease

Signs:

- Decreased visual acuity
- Decreased colour vision
- Swollen optic disc
- Macular star
- ODEMS: Optic disc edema and macular star
- Self-limiting disorder that resolves in 6 – 12 months

Table 7.1: *Summary of clinical features of optic neuritis*

	Retrobulbar neuritis	**Neuroretinitis**	**Papillitis**
ONH	normal	swollen	swollen
VA	decreased	decreased	decreased
Pupils	RAPD	normal	RAPD

TREATMENT OF OPTIC NEURITIS

Prior to commencing treatment, exclusion of infective or immunosuppressive diseases must be conducted. Oral steroids are not recommended in typical cases. Intra-venous (IV) methylprednisolone 250mg/ 6 hourly x 3 days, followed by Prednisone 1mg/kg for 11 days. Recommendation by ONTT (Optic Neuritis Treatment Trial). If treated early and aggressively, recovery of vision is very good.

TYPICAL VS ATYPICAL OPTIC NEURITIS

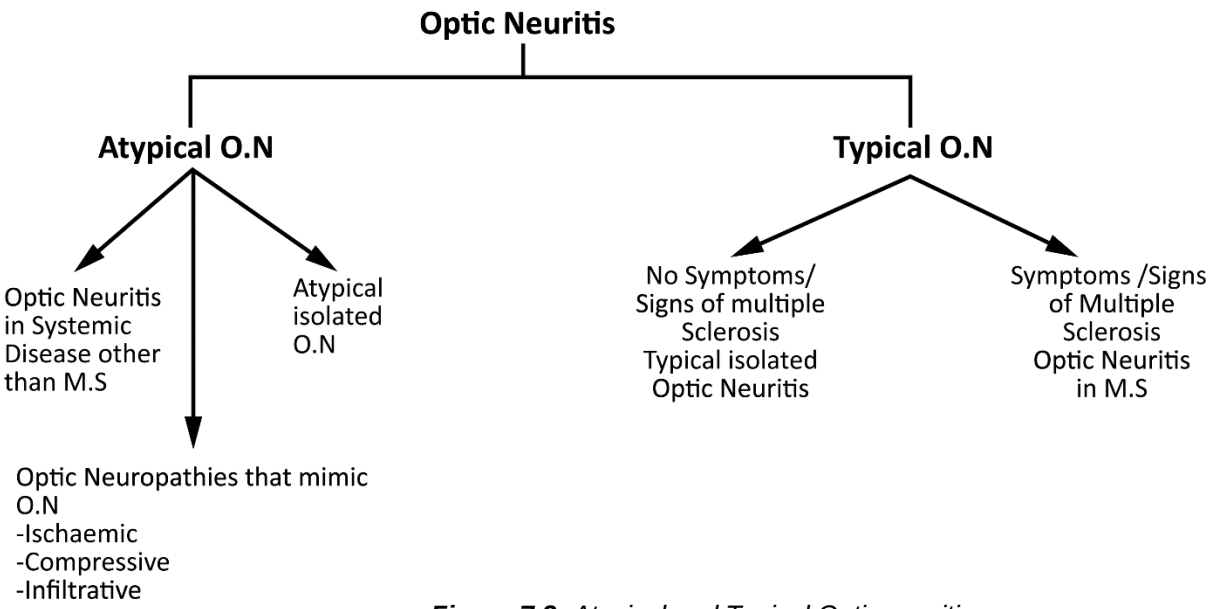

Figure 7.2: *Atypical and Typical Optic neuritis*

Optic neuritis can be divided into

- Typical optic neuritis
- Atypical optic neuritis

Typical optic neuritis

Typical optic neuritis is characterized by acute or sub-acute monocular visual loss caused by primary demyelination of the optic nerve. It is accompanied by ipsilateral periocular pain intensified by eye movement. There is an afferent pupillary defect, reduced visual acuity and visual field defects of the affected eye. The optic disc appears normal in the majority of the cases. Typical optic neuritis can be an isolated idiopathic condition or part of multiple sclerosis (MS). There is spontaneous near total recovery of visual function within 6 months in approximately 85% of cases.

Atypical optic neuritis

Atypical optic neuritis is characterized by visual loss from secondary demyelination of optic nerve. The common causes include:

- Sarcoidosis
- Non–multiple sclerosis (MS) autoimmune disorders
- Uveitis
- Infectious retinitis and meningitis
- Idiopathic disorders

Clinical findings of atypical optic neuritis:

- Visual loss
- Nerve fiber bundle visual field defects
- Afferent pupil defect
- Optic disc swelling
- Signs of posterior uveitis which include: choroidal infiltrates, vitreous cells
- Retinopathy which may include infiltrates, serous detachment and macular star exudates
- Anterior uveitis may be present

The underlying condition should be treated. Vision improves corticosteroid treatment (corticosteroid-responsive) and worsens when corticosteroids are tapered or withdrawn (corticosteroid-dependent).

NEUROMYELITIS OPTICA (DEVIC'S SYNDROME)

NMO is characterized by unilateral or bilateral optic neuritis followed by transverse myelitis and ascending paralysis. Differentiating features from typical optic neuritis include:

- Slightly older age at initial presentation (late thirties)
- Bilateral and severe vision loss with limited recovery of vision.
- Frequently normal MRI of brain.
- Multiple and contiguous segments of spinal cord lesions.
- Positive NMO IgG titer.

IDIOPATHIC INTRACRANIAL HYPERTENSION (IIH)

IIH – SYNONYMS

- **Pseudotumour Cerebri**: because patients present as though they have a tumor in the brain
- **Benign intracranial hypertension**: not benign anymore since it can produce a decrease in vision/blindness therefore cannot be considered to be benign
- **Otitic Hydrocephalu**s: patients present with noises in the head, buzzing, whooshing sound

IIH – DEFINITION

Idiopathic intracranial hypertension is a syndrome characterized by raised intracranial pressure with no evidence of any mass lesion or hydrocephalus or venous sinus thrombosis (normal brain scan). Raised intracranial pressure can result in transient visual obscurations. It is caused by impaired drainage of cerebrospinal fluid (CSF) at arachnoid granulations.

ETIOLOGY

- Unknown
- Various associations

- Obesity (or recent increase in weight). There is restriction to blood draining into the thorax from the brain and abdomen and therefore pressure in upper extremities and the head goes up.
- Hyper/hypovitaminosis A
- Endocrine – pregnancy, menstrual irregularities (2 days, or sometimes increase in duration 8-10 days), Addison's Disease (Adrenal gland is under-functioning), polycystic ovarian dx
- Haematological – Iron deficiency anaemia, Polycythaemia
- Drugs – oral contraceptives, steroid withdrawal, tetracycline, nalidixic acid, acne preparations

MECHANISMS

- There is brain swelling and elevated CSF pressure
- This can be due to decreased cerebro-spinal fluid (CSF) absorption. The CSF is absorbed by the arachnoid granulations and obscuration causes elevation of CSF pressure.
- An increase in intracranial pressure can also be due to an increase in CSF production.
- Venous sinus stenosis
- There are various studies which support these different mechanisms. (most popular: decreased CSF absorption)

CLINICAL FEATURES

Idiopathic intracranial hypertension can affect patients of any age but is usually prevalent in the 3rd and 4th decades of life. It occurs more often in females than males with a ratio of 8:1, especially in the idiopathic group.

SYMPTOMS

Patients with idiopathic intracranial hypertension present with:

- Headaches
- Transient visual obscurations
- Impaired vision
- Tinnitus (usually a whooshing sound in the head)
- Diplopia

The headache is characterized by a headache that wakes the patient up in the early hours of the morning, more severe when bending forward, worse when coughing or straining, associated vomiting and headache worse when lying down.

The visual obscurations may last for a few seconds. The tinnitus and diplopia are due to elevated CSF pressure. A false-localizing 6th nerve palsy may occur. In women, IIH is suspected if there is recent weight gain, fluid retention, and menstrual dysfunction. It may also occur during the first trimester of pregnancy or postpartum period. Transient visual obscurations which lasts for seconds → whenever they move their head, vision is lost.

SIGNS

The major signs of idiopathic intracranial hypertension include:

- Obesity
- Papilloedema
- 6th nerve palsy

INVESTIGATIONS

- Brain imaging – Ventricles usually small. An empty sella may be present
- Visual Fields – Enlarged blind spot: monitor for peripheral field constriction
- Lumbar puncture – measure pressure: > 25cm CSF (normal is 10-20cm of water)
- Intracranial Pressure monitoring- if diagnostic doubt persists
- MR Venogram – will identify a sinus thrombosis due to CSF absorption obstruction.

TREATMENT

- Treat the underlying cause if known e.g. if it is due to drugs or oral contraceptives - stop them.
- Weight reduction is indicated if obesity is the underlying cause.
- Drugs - Acetazolamide (Diamox), Topiramate (reduce CSF production). Topiramate also causes weight loss
  - thiazide diuretics
- If above fails - lumboperitoneal shunt
  - Ventriculoperitoneal shunt
- Optic nerve sheath fenestration

PROGNOSIS

Most patients respond rapidly to short-term treatment, but up to one third develop recurrent attacks. In 10% of cases visual impairment persists.

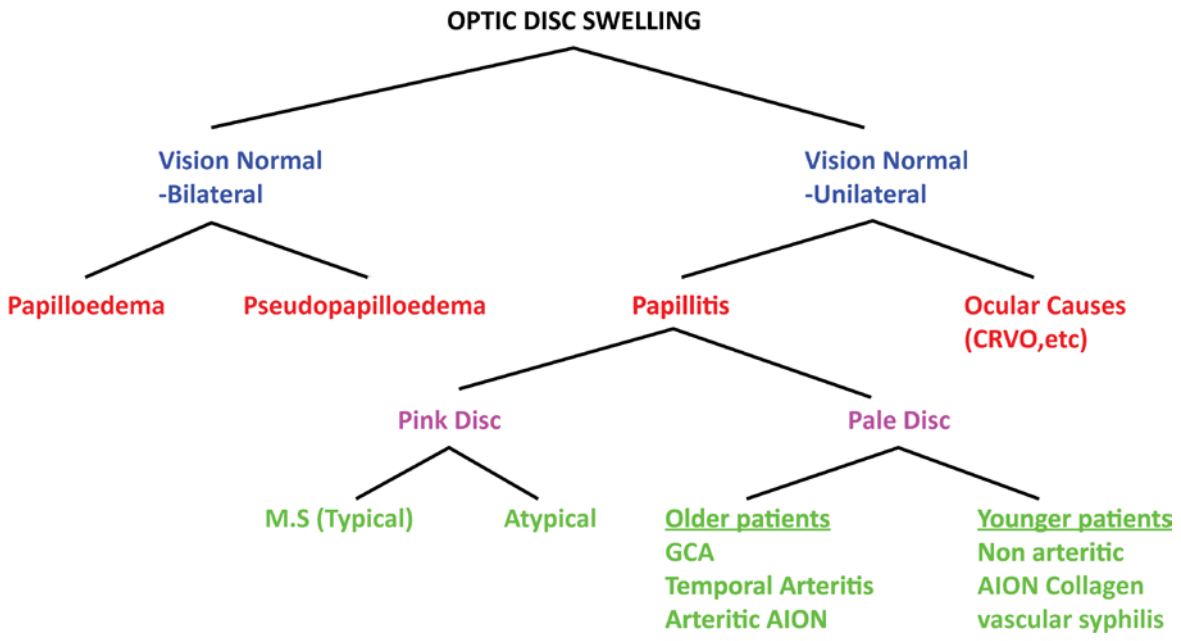

Figure 7.3: *Optic disc swelling*

MYASTHENIA GRAVIS

Myasthenia gravis is an autoimmune disorder characterized by muscle fatigue and weakness of voluntary muscles. It is a disease of the neuromuscular junction (Figure 7.4). Eye muscles are the most active skeletal muscles in the body (usually 1 axon to 200 muscle fibers, but in the eye, the ratio is almost 1 to 1, therefore presenting much more activity).

Weakness is caused by the destruction of post-synaptic membranes at the neuromuscular junction inhibiting the stimulative effect of the neurotransmitter acetylcholine.

- Myasthenia gravis is prevalent in young females aged 15-20 and older men aged 50-60.
- 90% of patients have ocular involvement, including ptosis and diplopia.
- 60% of patients report ocular signs as the initial MG presentation.
- 80% with ocular signs develop other muscle group involvement within 2 years.
- Alternating or transient ptosis and diplopia is reported with signs being worse at the end of the day.
- Fluctuating ocular signs occur with fatigue.

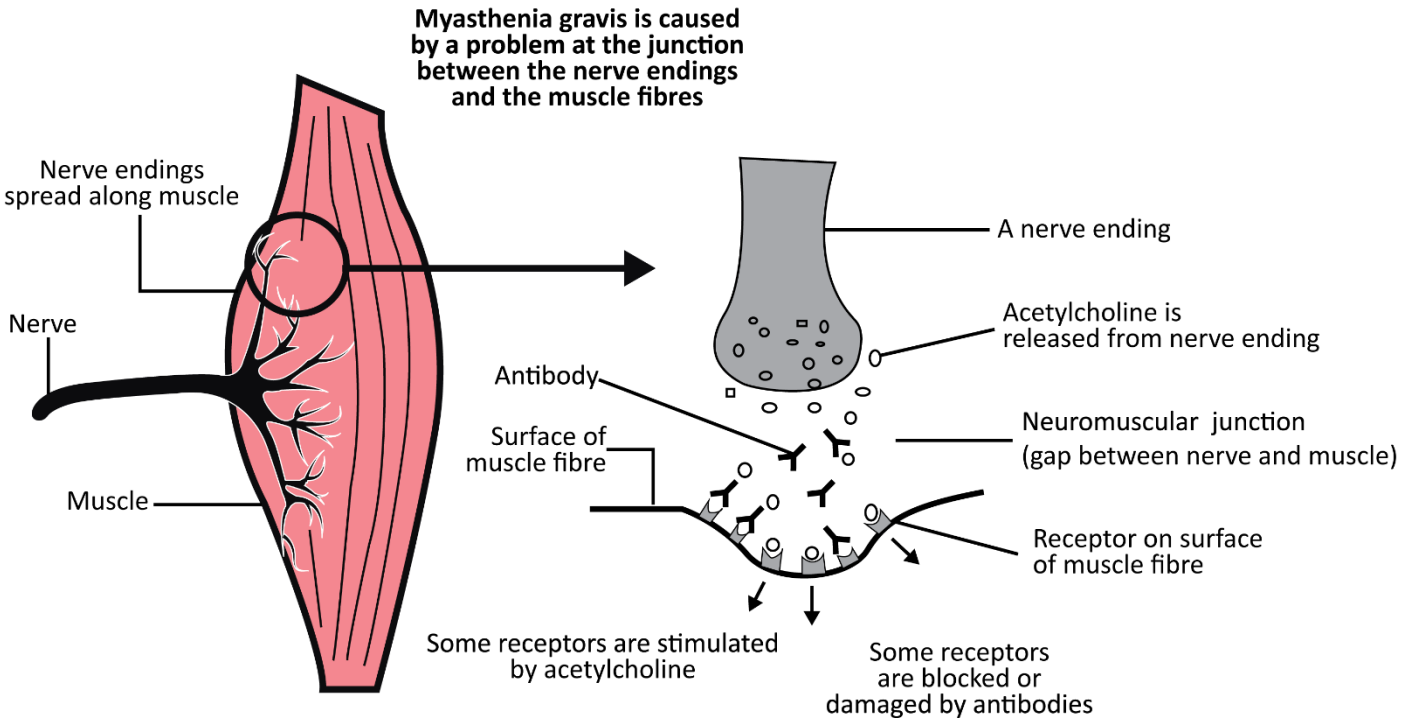

Figure 7.4: *Myasthenia gravis*

INVESTIGATION

Ptosis is one of the ocular signs of myasthenia gravis. During sustained upgaze the patient will experience fatigue. The ice pack test is conducted where a 2mm improvement is noted after 2 minutes of exposure. Cogan's lid twitch sign is noted if there is an overshoot of the lid on upgaze. Cold inhibits the action of acetylcholinesterase, thereby increasing the synaptic concentration of acetylcholine. Therefore an ice pack for 2min with a greater than 2mm change in ptosis indicates myasthenia gravis. It is a very sensitive test.

The tensilon test (Edrophonium) involves the intravenous injection of 10mg of Edrophonium and an evaluation of improvement of ptosis or eye movements within minutes. The Neostigmine test is similarly performed but the response is measured after 15 minutes due to its slower action. The Tensilon and Neostigmine tests both require atropine to reduce the muscarinic side effects.

Vertical diplopia is frequently reported, however any or all of the extraocular muscles may be affected.

Lab tests to be conducted include ACh receptor antibodies which are positive in 85% of patients (50% of patients with pure ocular involvement), thyroid function tests and antinuclear factor due to the association with other auto-immune disorders.

Other tests include a chest X-ray, CT chest to investigate for Thymoma and Single fiber EMG

TREATMENT

- Pyridostigmine
- Steroids
- Thymectomy
- Immunomodulatory treatment

PROGNOSIS

- Ptosis and diplopia can usually be adequately palliated with low-dose prednisone with or without pyridostigmine or a corticosteroid-sparing agent
- Spontaneous remissions occur in 20% of patients

GRAVES OPHTHALMOPATHY

Graves ophthalmopathy is an ocular manifestation of thyroid disease.

It may present in patients who are:

- Euthyroid (5%),
- Hyperthyroid (90%)
- Hypothyroid (5%).

Hyperthyroidism is an auto-immune disorder in which IgG antibodies bind to thyroid stimulating hormone (TSH) receptors in the thyroid gland and stimulate secretion of thyroid hormones (Clinical Ophthalmology, 2003).

Graves ophthalmopathy is characterized by:

- Exophthalmos and ophthalmoplegia
- Orbital oedema
- Infiltration by inflammatory cells lead to orbital fullness
- Conjunctival oedema
- Hyperaemia
- Proptosis
- Some limitation of ocular movements
- Eyelid retraction
- Optic neuropathy

In 1969, the American Thyroid Association adopted the formal classification of Ocular Graves' disease, represented by the pneumonic NOSPECS. The disease process passes through 6 stages. However, because the disease is recognized as variable, the formal classification was revised in 1974 to range from no manifestations to mild, moderate or severe manifestations.

MNEMONIC: NO SPECS

(0) **N**o signs or symptoms present,
(I) **O**nly symptoms of ocular irritation (dryness, tearing, foreign body sensation),
(II) **S**oft tissue involvement (periorbital oedema),
(III) **P**roptosis,
(IV) **E**xtraocular muscle involvement (ophthalmoplegia),
(V) **C**orneal involvement (dense punctate epitheliopathy, infiltration and ulceration),
(VI) **S**ight loss with or without visual field compromise secondary to compressive optic neuropathy.

TREATMENT

- Corticosteroids
- Radiation therapy (though controversial)
- Orbital decompression.

ANTERIOR ISCHAEMIC OPTIC NEUROPATHY (AION)

Anterior ischaemic optic neuropathy presents with unilateral, acute visual loss and optic disc oedema. In 25% of cases, AION affects the two eyes consecutively.

If it occurs after 60 years of age, then Giant cell Arteritis must be considered which results in **Arteritic AION**. Symptoms in arteric AION often include jaw claudication, scalp tenderness and weight loss. Vision loss is severe in this case, and vision loss in the fellow eye often follows.

If AION occurs in patients younger than 60 years, it is usually due to atherosclerosis affecting the microcirculation of the optic nerve head which indicates **Non-Arteritic AION** (more common than Arteritic AION).

SYMPTOMS ASSOCIATED WITH ARTERIC AION

- Headaches
- Jaw claudication
- Scalp tenderness
- Muscle and joint pains
- Weight loss
- Fever

SIGNS

- APD
- Decreased VA's
- Disc Pallor (pale swollen disc)
- Oedema
- Haemorrhages
- Altitudinal field defect
- Tender temporal artery
- High erythrocyte sedimentation rate (GCA).

TREATMENT

Arteritic AION requires urgent and critical intervention – early diagnosis is crucial. It is usually treated using a high dose of systemic steroids which needs to be confirmed by a temporal artery biopsy and high ESR.

Non-arteritic AION has a normal ESR and does not require steroids. Risk factors for NAION include age, hypertension, diabetes mellitus, hypercholesterolaemia and smoking.

IDIOPATHIC ORBITAL INFLAMMATORY DISEASE

This is an immune mediated disorder of the orbit caused by a diffuse granulomatous infiltrate comprising lymphocytes and plasma cells in the orbital fat and external ocular muscles. It usually occurs in middle age and is rarely bilateral.

FEATURES

- Sudden onset of orbital pain with lid oedema
- Proptosis
- Chemosis
- Ophthalmoplegia
- CT reveals a diffuse orbital lesion which may be confirmed by biopsy

TREATMENT

Idiopathic orbital inflammatory disease is initially treated using steroids e.g. Prednisolone. If this is unsuccessful, immunomodulatory drugs or radiation therapy may be considered.

AN APPROACH TO DIPLOPIA

Diplopia may develop from diseases in any of the following structures

- Cerebral cortex
- Deep White Matter
- Thalamus
- Brainstem
- Vestibular apparatus
- Cerebellum
- 3rd, 4th and 6th cranial nerves
- Neuro-muscular junction
- Extra-ocular muscles
- Eye

DIPLOPIA

It is important to consider the following aspects when a patient presents with diplopia:

- History
- Examination

- Investigation
- Treatment

HISTORY

The following should be questioned when enquiring about the history of the diplopia:

- Monocular or Binocular
- Alignment of images
- Direction of greatest separation
- Onset and progression of symptoms
- Exacerbating and relieving symptoms
- Associated symptoms
- Medical History and Family History

CAUSES OF MONOCULAR DIPLOPIA

Monocular diplopia may be due to one of the following factors:

- Refractive error
- Corneal disease (irregular astigmatism)
- Iris injury
- Cataract
- Media opacity
- Macular Disease
- Primary or secondary visual cortex disorder (monocular polyopia)

CAUSES OF BINOCULAR DIPLOPIA

Binocular diplopia resolves when one eye is covered and results from a misalignment of images due to the various causes listed below:

A. COMITANT STRABISMUS

Concomitant strabismus is a condition that could have resulted from a long-standing disease condition and is characterized by a deviation in which the angle of the deviation is the same in all directions of gaze. This usually occurs when the deviation manifests in early life (childhood) or is acquired (vergence paresis: Skew deviation (eyes move upwards and in opposite directions)

B. NON-COMITANT STRABISMUS

Non-concomitant strabismus is a condition that could have resulted from a recent disease condition and is characterized by a deviation in which the angle of the deviation is different in the various directions of gaze. The angle of deviation also varies depending on which eye is fixating. These deviations may be due to:

- Cranial neuropathy

- Supranuclear disorder
- Ocular myopathies
- Neuromuscular junction disorder

C. NO MISALIGNMENT

This is when no movement is noted on cover test and binocular diplopia still occurs. The images may be similar or dissimilar. Diplopia with similar images on both eyes may be due to macular disease or marked refractive asymmetry. When the images are different on each eye, it can either be:

- Intermittent
- Constant

Intermittent diplopia may be due to:

- Multiple sclerosis
- Myasthenia Gravis
- Decompensating heterophoria

Constant diplopia may occur due to:

- Physiological
- Non-organic conditions

ALIGNMENT OF IMAGES

Diplopia may occur where there is misalignment of images along the horizontal, vertical or oblique planes.

HORIZONTAL DIPLOPIA

Horizontal diplopia may occur if there is impaired neural control or impaired function of the medial or lateral recti muscles or in some cases the involvement of both muscles.

VERTICAL DIPLOPIA

Vertical diplopia may occur if there is:

- Weakness of elevators of the eye, i.e. IO / SR
- Weakness of depressors of the eye, i.e. SO / IR

OBLIQUE DIPLOPIA

Oblique diplopia may exist when one image is tilted and this may occur when there is SO or IO weakness.

EXAMINATION

Upon examination, the following should be evaluated:

- Identify the paretic muscle

- Is the diplopia caused by mechanical restriction or neurogenic paresis
- Is the diplopia caused by a peripheral or a central neurogenic paresis

IDENTIFY THE PARETIC MUSCLE

Performing the unilateral and alternating cover test can identify the paretic muscle. It can be established if the patient has an exotropia, esotropia, hypertropia, hypotropia or a combination of these. The comitancy of the deviation can be evaluated performing the cover test in the nine directions of gaze. The pursuit movement can also be assessed to evaluate the range of movement of the eyes and localize the point of restriction. If vertical diplopia is present, the Parks 3-step test can be used to detect the paretic muscle. Some patients adopt a head turn or tilt to eliminate the diplopia.

Additional areas to be evaluated:

- Evidence of exophthalmos
- Visual field testing
- Eyelid function
    - Ptosis
    - Lid lag
    - Lid retraction
- Pupil examination
- Fatigability of EOM

MECHANICAL RESTRICTION VS NEUROGENIC PARESIS

Diplopia may occur due to mechanical restriction or neurogenic paresis. Mechanical restriction can occur due to:

- Weakness of agonist muscle or restriction of antagonist muscle
- Brown´s syndrome where there is involvement of the superior oblique tendon sheath

This causes restriction in the movement of the eyes.

Neurogenic causes include lesions of the nervous system. It may be supra-nuclear, inter-nuclear, infra-nuclear; depending on the site of the lesion.

Forced duction testing can be performed to assess whether the restriction is due to mechanical restriction or neurogenic paresis. Topical anaesthetic is administered and forceps are used to move the eyeball. The eyeball is moved passively in the direction of the restriction and in the opposite direction. Restrictive movement will be noted if there is mechanical restriction. There is a full range of eye movements if a neurogenic paresis is present.

PERIPHERAL VS CENTRAL NEUROGENIC PARESIS

Neurogenic paresis can occur either centrally or peripherally.

Central paresis includes:

- Brainstem lesions
- Supranuclear gaze disorders

These can be identified by examining the following:

- Fixation

- Saccades
  - Voluntary Saccades
  - Reflexive Saccades
- Smooth pursuit
- Vergence
- Optokinetic nystagmus
- Vestibulo-ocular reflex

Peripheral paresis includes:

- 3rd nerve palsy
- 4th nerve palsy
- 6th nerve palsy
- Combined ocular motor nerve palsy

These can be identified by the incomitancy of the strabismus and characteristic motor deficits. The Hess screen is used to evaluate the incomitancy. There is also an absence of orbital disease, myopathy, myasthenia and mechanical restriction.

INTERNUCLEAR OPHTHALMOPLEGIA

Internuclear ophthalmoplegia (INO) occurs due to a lesion in the medial longitudinal fasciculus (MLF). It is characterized by the inability of the eyes to converge when changing direction of gaze. There is, however, adduction of the eyes during accommodative convergence. INO can be divided into anterior and posterior internuclear ophthalmoplegia.

Anterior INO results due to a rostral lesion. It has the following characteristics:

- Inability of the eyes to converge
- Paralysis of both medial recti

Posterior INO results due to a lesion located caudally. It has the following characteristics:

- Classic variety
- Medial longitudinal fasciculus damage (between 3rd and 6th N)
- Failure of adduction – ipsilaterally
- There is nystagmus of abducting eye – contralaterally
- Causes include MS, Strokes, Tumours, Phenytoin, Tegretol toxicity

INVESTIGATION

- CT Brain and Orbits
- MRI Brain and Orbits
- Nerve conduction studies / EMG
- Tensilon Test / Neostigmine test/ice on eyes test
- Blood Tests: TFT, ACh receptor antibodies

TREATMENT

The underlying cause of the diplopia should be treated. Symptomatic treatment for disabling diplopia can include:

- Unilateral eye occlusion therapy
- Eye patch
- Opaque tape over the lens of glasses
- Fresnel prisms

Surgical treatment is indicated if complete recovery is not achieved in 6-12 months. Botulinum toxin can be injected into the antagonist of a paretic muscle.

DIPLOPIA SUMMARY

- History
- Monocular vs Binocular Diplopia
- Vertical vs Horizontal vs Oblique
- Associated Symptoms
- Examination
- Identify the paretic muscle
- Mechanical restriction vs Neurogenic paresis
- Central vs Peripheral neurogenic paresis
- 3rd, 4th , 6th nerve palsies
- Saccade, pursuit, vergence
- Associated signs

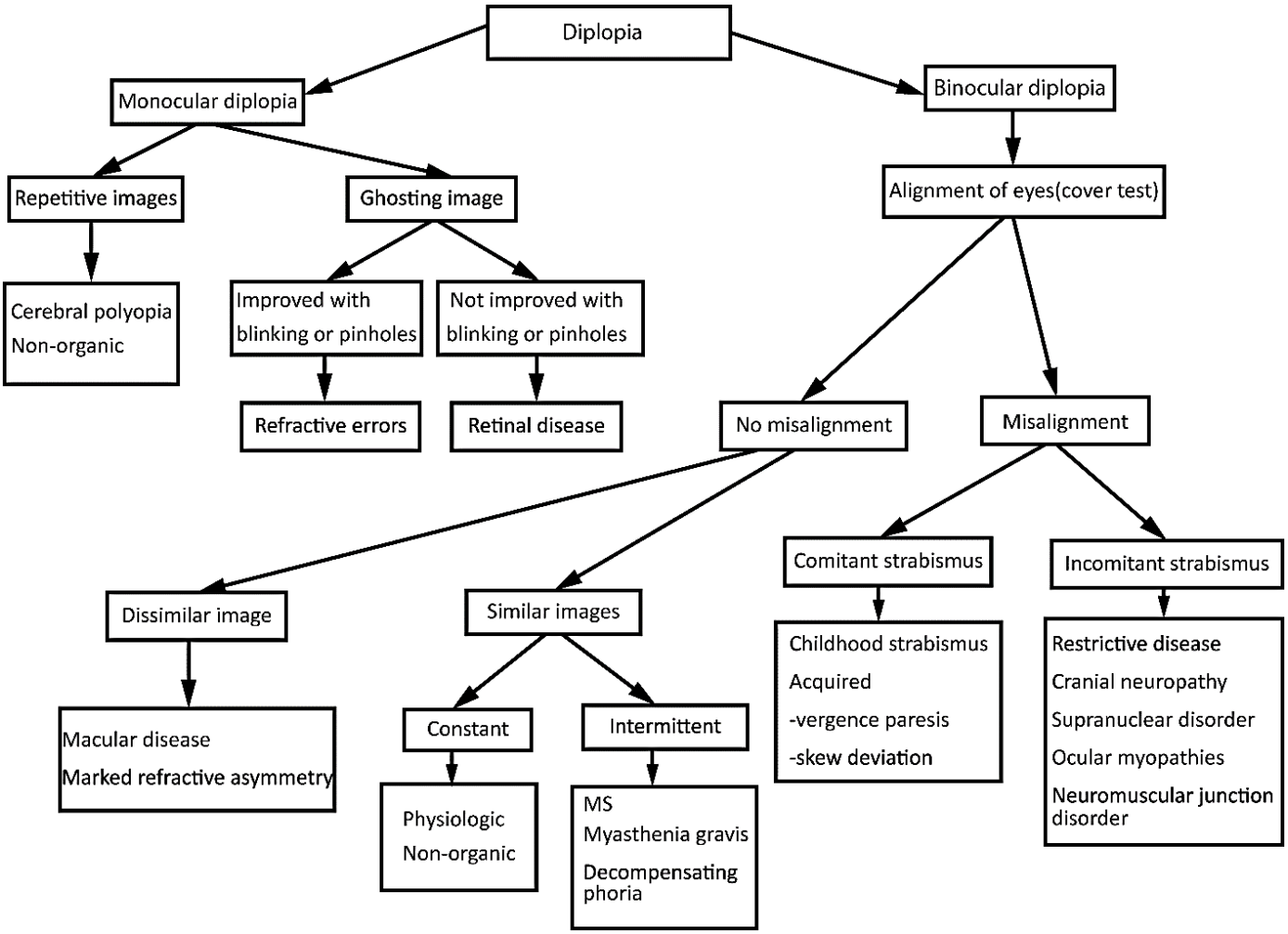

***Figure 7.5**: Flow chart of diplopia*

Adapted from:J Neurol Neurosurg Psychiatry 2004;75:iv24-iv31