**Decision Trees**
- Abnormal Optic Discs
- Anisocoria
- Bilateral Ophthalmoplegia and Ptosis
- Blepharospasm
- Diplopia
- Horizontal Gaze Palsy
- Nystagmus
- Proptosis
- Ptosis
- Transient Visual Loss
- Unexplained Visual Acuity Loss
- Unexplained Visual Field Loss with Normal Acuity
- Vertical Tropia
- Visual Illusions and Hallucinations

**Management**
- Blepharospasm
- Congenitally Elevated Discs
- Craniopharyngioma
- Graves' Optic Neuropathy
- Graves' Disease Duction Deficits
- Hemifacial Spasm
- Horner's Syndrome

**Ocular Motility**
- Isolated 3rd Nerve Palsies
- Isolated 4th Nerve Palsies
- Isolated Unilateral non-traumatic 6th Nerve Palsies
- Bilateral 6th Nerve Palsies
- Myasthenia Gravis

**Optic Nerve**
- Glioma
- Meningiomas
- Optic Neuritis
- Optic Neuropathy - Ischemic
- Optic Neuropathy - Traumatic
- Painless Bilateral Loss of Central Vision
- Parachiasmal Meningiomas
- Pituitary Tumor Field
- Recommendations
- Pseudotumor Cerebri
- Pseudotumor of Orbit

**Evaluation/Work Up**
- Optic Neuropathy
- Myasthenia Gravis
- Papilledema

**Syndromes/Diseases/Signs**
- Pseudotumor Cerebri
- Pseudotumor of Orbit

Acknowledgements: Information in this document has often been derived directly from:
- Clinical Decisions in Neuro-Ophthalmology - Burde, Savino, & Trobe
- Clinical Pathways in Neuro-ophthalmology –Lee & Brazis
- emedicine.com
- ophthalmic.hyperguide.com
- whonamedit.com

Please email suggestions & corrections to: tcooper@stanford.edu
Abnormal Disc Decision Tree
Urgently determine if papilledema is present.

Papilledema: this term is reserved for disc swelling due to increased intracranial pressure.

Discs not elevated
- Signs of Dysplasia Absent
  - Cupping Present
    - Glaucoma
    - Nonglaucomatous Cupping
    - Dysplasia
  - Cupping Absent
    - Optic Atrophy
- Signs of Dysplasia Present
- Coloboma
- Megalopapilla
- Other Dysplasia Hypoplasia
  - (Hypoplasia Associations)

Discs elevated
No single feature can reliably separate congenital and acquired disc elevation.

All features must be considered together.

Congenital abnormality

Management of Congenitally Elevated Discs
Disc drusen
- Disc photos and VF
- Confirm with ocular ultrasound if uncertain

No clearly identifiable congenital disc abnormality
- Observe if neurologic exam normal and strong suspicion of congenital elevation
- Imaging to rule out mass or hydrocephalus if both aspects of above are not present

Give patient with congenital disc abnormality a disc photo to carry with them to avoid future confusion and recommend a medical alert bracelet to avoid unnecessary neurologic procedures.

Acquired Disc Swelling
Unilateral
- Rule out ocular causes
  - No ocular cause - optic neuropathy workup

Bilateral
- Check blood pressure to rule out malignant hypertension
- Rule out ocular causes
- No ocular cause –
  - Papilledema workup
    - CBC to rule out blood dyscrasia

Please email suggestions & corrections to:
  tcooper@stanford.edu
Neuro-imaging to urgently rule out intracranial acute vascular process, trauma or mass
MRA & MRV if available to rule out arterial disease and venous obstruction
If there is no structural lesion and no hydrocephalus on neuro-imaging get LP with pressure measurement and CSF analysis (cell count & differential, glucose, protein, cytology, VDRL, appropriate studies for microbial agents).

**Causes of Elevated Discs**

<table>
<thead>
<tr>
<th>Features of Congenital Abnormalities &amp; Papilledema</th>
<th>Congenital</th>
<th>Papilledema</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Color</strong></td>
<td>Yellow</td>
<td>Hyperemic (acutely)</td>
</tr>
<tr>
<td><strong>Nerve fiber layer</strong></td>
<td>Clear</td>
<td>Opacified</td>
</tr>
<tr>
<td><strong>Large disc vessels</strong></td>
<td>Anomalous</td>
<td>Normal</td>
</tr>
<tr>
<td><strong>Small disc vessels</strong></td>
<td>Normal</td>
<td>Telangetatic</td>
</tr>
<tr>
<td><strong>Vessels from Central Apex of disc</strong></td>
<td>May be present</td>
<td>No</td>
</tr>
<tr>
<td><strong>Anomalous branching of vessels</strong></td>
<td>May be present</td>
<td>No</td>
</tr>
<tr>
<td><strong>Nerve fiber layer Hemorrhage</strong></td>
<td>Rare</td>
<td>Frequent</td>
</tr>
<tr>
<td><strong>Physiologic cup</strong></td>
<td>Small or Absent</td>
<td>Present</td>
</tr>
<tr>
<td><strong>Spontaneous venous pulsations</strong></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Exudates or cotton wool spots</strong></td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Hyaline Bodies</strong></td>
<td>May be present</td>
<td>No</td>
</tr>
<tr>
<td><strong>Family Occurrence</strong></td>
<td>May be present</td>
<td>No</td>
</tr>
<tr>
<td><strong>Bilateral</strong></td>
<td>May be present</td>
<td>Almost always</td>
</tr>
<tr>
<td><strong>Irregular disc margins with deranged peripapillary RPE</strong></td>
<td>May be present</td>
<td>No</td>
</tr>
</tbody>
</table>

**Causes of Elevated Discs**
- Central retinal vein occlusion/stasis
- Compressive optic neuropathy
- Diabetic papillopathy
- Hypertensive Crisis
- Hypotony
- Infiltrative optic neuropathy

Please email suggestions & corrections to: tcooper@stanford.edu
Clinical Features of Diabetic Papillopathy
May be unilateral or bilateral (simultaneous or sequential)
May have relative afferent pupillary defect if unilateral or bilateral but asymmetric
May be associated with type I or type II diabetes
Disc swelling is mild to moderate and the disc is consistently hyperemic
Disc edema usually resolves within 1 to 10 months
Macular edema and capillary nonperfusion are frequent associated findings
Small cup-to-disc ratio in uninvolved fellow eyes (the “disc at risk”)
Significant (~ 5 seconds) delay in fluorescein filling of all or a portion of the optic disc may occur
Minimal if any visual symptoms
May have enlarged blind spot or arcuate defect
Residual visual loss due to associated macular edema and retinopathy
Occasionally residual mild optic atrophy

Anisocoria Decision Tree
Check for Relative Afferent Pupillary Defect before pharmacologic testing of pupils
  RAPD= optic neuropathy till proven otherwise
Greater in light
  EOM
    Abnormal rule out 3rd cranial nerve palsy
    Normal
      Slit-lamp exam
        Abnormal Iris abnormality, uveitis, angle closure glaucoma, surgical changes
        Normal
        Near reaction
          None
            Pharmacologic dilation (confirm with 1% pilocarpine)
            Acute Adie’s tonic pupil (observe for development of supersensitivity)
            Tonic
              Adie’s tonic pupil (confirm with 0.01% pilocarpine)
Greater in dark
  Ptosis on side with smaller pupil = Horner syndrome
  Cocaine test
    Much less dilation in eye = Horner syndrome
    Hydroxyamphetamine test

Please email suggestions & corrections to:
tcooper@stanford.edu
Dilation = Preganglionic (1\textsuperscript{st} or 2\textsuperscript{nd} order neuron) defect
   Head, neck, brachial plexus and lung lesions – get neuro-imaging
No dilation = Postganglionic (3\textsuperscript{rd} order neuron) defect
   Cavernous sinus, headache syndromes, adjacent inflammation,
   neoplasm, systemic disorders, trauma, carotid artery disease, GCA –
   workup consistent with other signs and symptoms.

Dilation about equal
   Physiologic anisocoria
   Pharmacologic mydriasis

**ICU Pupillary Signs**

Unilateral large poorly reactive pupil
   Third nerve palsy
   Contusion of eye
   Accidental exposure to aerosolized anticholinergics or spilling of atropine droplets during
   preparation of the syringe
   Transient (ipsilateral or contralateral) during focal seizure or as part of an absence seizure Oval
   unilateral nonreactive pupil—transitory appearance in brain death

Bilateral mydriasis with normal reaction to light
   Anxiety, delirium, pain
   During seizure
   Botulism
   Drugs—systemic atropine, aerosolized albuterol, amyl nitrate, magnesium sulfate, norepinephrine,
   dopamine, ammoglycoside, polypeptide, tetracycline overdose

Bilateral midposition and fixed to light—brain death

Unilateral small, reactive—Homer’s syndrome
   Traumatic carotid dissection
   Brachial plexopathy
   Internal jugular vein catheterization
   Extensive thoracic surgery
   Spastic miosis in acute corneal penetration injury

Bilateral miosis (reaction present but may be difficult to see even with magnifying glass)
   Narcotic agents (e.g., morphine)
   Any metabolic encephalopathy
   Respiratory distress with hypercapnea and tachypnea

Bilateral pinpoint, reactive
   Acute pontine lesion, especially hemorrhage
   Nonketonic hyperglycemia

**Spontaneous Eye Movements in Comatose Patients**

<table>
<thead>
<tr>
<th>Movement</th>
<th>Description</th>
<th>Localization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodic alternating gaze</td>
<td>Cyclic horizontal roving</td>
<td>Bilateral cerebral damage, rarely posterior fossa</td>
</tr>
<tr>
<td>(ping-pong gaze)</td>
<td></td>
<td>lesion, hepatic, hypoxic, carbon monoxide, drug</td>
</tr>
</tbody>
</table>

Please email suggestions & corrections to:

`tcooper@stanford.edu`
### Repetitive Divergence
- **In intoxication**
- **Metabolic encephalopathy**

### Monocular Nystagmoid Status Epilepticus
- **Vertical, horizontal, or rotatory movements**
- **Middle or low pontine lesion**
- **Diffuse encephalopathy (hypoxic)**

### Ocular Bobbing
- **Fast down, slow up**
- **Pontine lesion, extraaxial posterior fossa mass, diffuse encephalopathy**

### Inverse Ocular Bobbing (Ocular Dipping)
- **Slow down, fast up**
- **Anoxia, post—status epilepticus (diffuse encephalopathy)**

### Reverse Ocular Bobbing
- **Fast up, slow down**
- **Diffuse encephalopathy, rarely pontine**

### Slow-Upward Ocular Bobbing
- **Slow up, fast down**
- **Diffuse encephalopathy bobbing**

### Pretectal Pseudobobbing
- **“V-pattern”; down and in**
- **Pretectal (hydrocephalus)**

### Vertical Ocular Myoclonus
- **Pendular, vertical isolated**
- **Pontine**

---

### Bilateral Ophthalmoplegia and Ptosis - Differential Diagnosis
- **Abetalipoproteinemia (Bassen-Kornzweig syndrome)**
- **Charcot-Marie-Tooth disease**
- **Congenital myopathies**
- **Friedreich's ataxia**
- **Mitochondrial disease**
  - Chronic Progressive External Ophthalmoplegia (CPEO)
  - Kearns-Sayre
  - Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke (MELAS)
  - Mitochondrial Neuro-gastrointestinal Encephalomyopathy (MNGIE)
- **Myasthenia gravis (congenital or acquired)**
- **Myotonic dystrophy**
- **Oculopharyngeal muscular dystrophy**
- **Spinocerebellar ataxia**
- **Refsum's disease**

### Blepharospasm Decision Tree
- **Trigeminal irritation**
  - **Anterior ocular inflammation**
  - **Meningitis**

Please email suggestions & corrections to: [tcooper@stanford.edu](mailto:tcooper@stanford.edu)
Subarachnoid hemorrhage
No Trigeminal irritation
  Unilateral facial weakness
  Facial nerve abnormalities after Bell's palsy
  Facial nerve abnormalities in pontine disease
  No unilateral facial weakness
Unilateral essential blepharospasm and/or hemifacial spasm
  Bilateral blepharospasm
  Associated conditions
    CNS disorders
    Neuromuscular disorders
    No associated neurologic conditions
    Essential blepharospasm

Diplopia Decision Tree
Monocular diplopia
  1. Recent EOM surgery = abnormal retinal correspondence
  2. Pinhole test
    2.1 No diplopia = refractive error, poorly fit contact lens, corneal abnormalities, lid abnormalities, iris abnormalities, lens abnormalities, retinal abnormalities
    2.2 Diplopia = Palinopsia, cerebral polyopia, psychogenic
Binocular diplopia
  1. Transient Diplopia
  2. No misalignment
    2.1 Similar images = physiologic diplopia, psychogenic diplopia
    2.2 Dissimilar images = metamorphopsia, aniseikonia
    2.3 No diplopia on testing vergences
      Red glass test
      May bring out latent motility problem.
      May help patient interpret symptoms.
  3. Incomitant misalignment
    3.1 Horizontal tropia – adduction and abduction to determine EOMs affected
    3.2 Vertical tropia Park’s 3 step test to determine EOMs affected
    3.3 Forced duction positive = restrictive disease
      Signs of orbital disease
      Inflammation
      Thyroid ophthalmopathy
      Tumors
    3.4 Forced duction negative
      Tensilon test
      Positive = Myasthenia gravis
      Negative
      Cranial neuropathy
      Nuclear (Doll’s head maneuver does not overcome EOM deficit)
      Infranuclear (Doll’s head maneuver does not overcome EOM deficit)
      Supranuclear disorders (Doll’s head maneuver shows EOM intact)

Please email suggestions & corrections to: tcooper@stanford.edu
Skew deviation
Progressive supranuclear palsy
Internuclear ophthalmoplegia
Ocular myopathies

4. Comitant misalignment

4.1 Decompensated phoria
   Especially after drugs with CNS effect, head trauma, refraction change, illness

4.2 Accommodative esotropia

4.3 Cyclic esotropia: rare condition, characterized by regularly recurring ET often with regular 48 hour cycles of 24 hours with ET and 24 hours of normal binocularity. 72 and 96 hour cycles also reported. Etiology is unknown.

4.4 Periodic alternating esotropia: a rare cyclic disorder associated with periodic alternating nystagmus or periodic alternating gaze. While one eye maintains fixation, the other undergoes a phase of waxing then waning inward deviation. Is associated with severe brain dysfunction especially in young children with ataxia or hydrocephalus.

4.5 Acute esotropia of childhood

4.6 Vergence Disorders

4.6.1 Convergence insufficiency and paralysis
   4.6.1.1 Insufficiency is an EXodeviation greater at near.
   Have normal adduction, a remote near point of convergence and decreased fusional convergence at near. It is common in students with an increased visual work load.
   4.6.1.2. Paralysis - diplopia only at near, adduction is normal but patient is unable to converge. Preservation of accommodation or pupillary miosis at near confirms an organic etiology (must see miosis to confirm patient cooperation and effort). Usually lesion in midbrain (trauma, demyelination or infarction within brainstem).

4.6.2 Divergence insufficiency & paralysis is an ET at distance.
   4.6.2.1. Insufficiency (primary divergence insufficiency) is due to divergence impairment in healthy individual – self limited
   4.6.2.2 Paralysis (secondary divergence insufficiency) is usually seen with brainstem disease - mild bilateral 6th cranial nerve palsy, demyelination, trauma, infection or tumor
   4.6.2.3 Skew deviation
   4.6.2.4 Foveal displacement syndrome – due to retinal disease that moves the fovea from its normal location. Symptoms due to rivalry between central and peripheral fusional mechanisms. Prisms due not control symptoms.
   4.6.2.5 Central disruption of fusion

4.6.3 Convergence Spasm: is characterized by sustained maximal convergence associated with accommodative spasm and miosis. Often functional. Rarely associated with organic disease of the central and ocular motor system.

4.6.4. Acquired Motor Fusion Deficiency: a rare condition with loss of both fusional convergence and divergence after head trauma, stroke, brain tumor and neurosurgery. Patients complain of transient or permanent diplopia despite apparent ocular alignment. No effective therapy.

Please email suggestions & corrections to: tcooper@stanford.edu
4.6.5. Hemifield Slide Phenomenon: is seen in complete or nearly bitemporal hemianopias. Fusion is disrupted and a previous phoria decompensates. This is due to lack of cortical representation of corresponding points in VF from each eye.

**Transient Diplopia Causes**
- Transient ischemia
- EOM ischemia e.g. GCA
- Vertebrobasilar artery ischemia
- Decompensated phoria
- Retinal hemifield slide phenomena
- Myasthenia Gravis
- Mechanical
  - Thyroid ophthalmopathy
  - Brown’s syndrome
  - Silent sinus syndrome
- Intermittent phenomena
  - Migraine
  - Neuromyotonia
- Intermittent or paroxysmal skew deviation
- Paroxysmal superior rectus and levator palpebrae spasm
- Increased ICP
- Multiple sclerosis (days- weeks)

**Gaze Palsies**

**Horizontal Gaze Palsies**
- Final common pathway for supranuclear mediated horizontal gaze act through the medial longitudinal fasciculus (MLF) – Internuclear neurons cross 6th cranial nerve and ascend to 3rd cranial nerve in MLF.
- Horizontal gaze inputs: vestibular, optokinetic, smooth pursuit and saccadic systems.
- Unilateral restriction of horizontal conjugate gaze to one side is usually due to contralateral frontal or ipsilateral pontine damage.

**Internuclear Ophthalmoplegia (INO)**

**One-and-a-Half Syndrome**

**Horizontal Gaze Palsy Decision Tree**
- Do oculocephalic maneuver or caloric stimulation
  - Intact extraocular movements = Supranuclear defect
  - Impaired extraocular movements = Pontine defect
- Get MRI
- If negative
  - Get EEG to rule out seizure
  - If negative consider alternative etiologies including Myasthenia Gravis

**Vertical Gaze Palsies**
- Motor neurons of vertical gaze and torsional movements are in the oculomotor and trochlear nuclei. They receive afferent input from the vestibular, smooth pursuit, optokinetic and saccadic systems.

Please email suggestions & corrections to: tcooper@stanford.edu
The constellation of findings seen with pretectal lesions are known as the Parinaud syndrome, sylvian aqueduct syndrome, pretectal syndrome, dorsal midbrain syndrome and Koerber-Salus-Elschning syndrome. May be simulated by myasthenia gravis, Lambert-Eaton myasthenic syndrome, thyroid eye disease, or Miller Fisher variant of Guillain-Barre syndrome.

Workup
Isolated impairment of upward gaze in elderly is commonly physiologic and requires no work up. If vertical gaze paresis fluctuates without signs of neurologic or systemic disease get Tensilon test.
In the presence of evidence of metabolic or degenerative disease evaluate them. If no evidence of metabolic or degenerative disease are present or their work up is negative get MRI with attention to dorsal midbrain. In patients with CSF shunts consider shunt malfunction. If MRI normal consider LP to rule out meningitis, run routine CSF tests including FTA. If MRI and LP normal get B12 and consider, thiamine deficiency, Whipple’s diseases, paraneoplastic process, and Syphilis.

Supranuclear Monocular Elevation Paresis: can be due to primary superior rectus palsy, myasthenia, fascicular third nerve lesion or pretectal supranuclear lesions. Vertical one-in-a-half syndrome: a vertical upgaze palsy with monocular paresis of downgaze. Usually due to lesions in thalamus and/or mesodiencephalon.

Skew Deviation

Acute Esotropia of Childhood
Acute-onset esotropia must be differentiated from accommodative esotropia. May be associated with nystagmus. If motor fusion is not established with appropriate hyperopic spectacles or prisms a MRI and neurologic evaluation is indicated. Rule out tumors of brainstem or cerebellum.

Nystagmus Decision Tree (also see Eye Movements that Mimic Nystagmus)
The slow phase reflects the underlying abnormality causing nystagmus. Oscillations present at birth
Congenital
Latent
Manifest Latent
Oscillations acquired
Monocular or asymmetric binocular
Monocular visual loss
Primary position = Spasmus Nutans, Monocular Visual Deprivation, Superior Oblique Myokymia, Motor Nystagmus of MS
Eccentric gaze = INO, PseudINO, Cranial Nerve Paresis, Restrictive Syndromes, Superior Oblique Myokymia
Binocular
Disconjugate

Please email suggestions & corrections to: tcooper@stanford.edu
**Applied Neuro-Ophthalmology – Web References © 2009**  
An eLearning Resource for Stanford Ophthalmology Residents  
Talmadge (Ted) Cooper, MD

**Vertical** = **Seesaw**  
**Horizontal**  
*Oculomasticatory myorhythmia* rule out Whipple’s disease  
Repetitive Divergence rule out hepatic disease  
Convergence Retraction or Divergence get MRI  
Convergence,  

**Conjugate**  
**Pendular**  
*Normal Afferent* = Motor, *Spasmus Nutans, Oculopalatal Myoclonus*, Pontine or cerebellar lesions, Pelizaeus-Merzbacher disease, mitochondrial cytopathy, Cockyane Syndrome, neonatal adrenoleukodystrophy (a perioxisomal disorder) and toluene addiction.  
*Abnormal Afferent* = Visual Deprivation  

**Jerk**  
*Spontaneous*  
**Primary**  
Vertigo = Vestibular (Central or Peripheral)  
No Vertigo  
Horizontal = Periodic alternating, drug-induced, epileptic  
Vertical = Upbeat, Downbeat  
*Eccentric* = Brainstem/cerebellar disease, Brun’s, Physiologic, Gaze-paretic, Drug-induced, Horizontal Rotatory, Rebound, Downbeat, Upbeat  

**Induced**  
*Optokinetic*  
*Vestibular* = Rotational, Caloric  
**Positional**

**Congenital Nystagmus:** noted at birth or early infancy. Usually is a pendular nystagmus but occasionally is jerk nystagmus. Visual fixation accentuates and active eyelid closure or convergence attenuates it. It may have null position. Associated with many disease processes affecting the visual afferent system including ocular and oculocutaneous albinism, achromatopsia, optic nerve hypoplasia, Leber’s amaurosis, coloboma, aniridia, cone dystrophies, corectopia, congenital stationary night blindness, Chediak-Higashi syndrome, Joubert syndrome, and perioxisomal disorders. Also associated with hypothyroidism.  

**Congenital Nystagmus Workup:**  
Complete ophthalmologic evaluation.  
Check for photophobia and paradoxical pupillary constriction in darkness.  
Order thyroid function tests.  
Order ERG (56% found to have retinal disease).  

**Latent Nystagmus:** common and generally congenital. When one eye is covered both eyes develop conjugate jerk nystagmus, with the viewing eye having a slow phase directed toward the nose. It is a marker for congenital ocular motor disturbance and does not indicate a progressive structural brain disease. Manifest latent nystagmus occurs in a patient with latent nystagmus and one of the eyes has poor vision (the equivalent of covering one eye).

Please email suggestions & corrections to:  
tcooper@stanford.edu
Spasmus Nutans: a benign syndrome characterized by the triad of head nodding, nystagmus and abnormal head position. Typically seen in the first year of life and remits spontaneously within 1 month to 8 years. May be mimicked by tumor of the optic nerve, chiasm, third ventricle, thalamus, arachnoid cyst, Leigh’s subacute necrotizing encephalomyelopathy, congenital stationary night blindness, retinal dystrophy and Bardet-Biedel syndrome. A MRI is indicated in Spasmus Nutans as well as monocular or predominantly monocular oscillations. If the child is myopic electrophysiologic testing to rule out congenital stationary night blindness should be considered.

Seesaw Nystagmus: cyclic movement of the eyes with conjugate torsional and disjunctive vertical components. One eye rises and intorts while the other falls and extorts, these movements are then reversed to complete the cycle.

Types of Nystagmus with Localizing Value
- Vestibular peripheral = labyrinthitis
- Vestibular central = lateral pons
- Upbeat in primary gaze = pontine tegmentum
- Upbeat in upgaze = midbrain, thalamus, cerebellum, toxicities
- Dissociated = Pons
- See-saw = chiasm
- Convergence retraction = dorsal midbrain
- Opsoclonus = brainstem encephalitis or toxicities

Eye Movements that Mimic Nystagmus
- Voluntary
- Lid nystagmus
- Myasthenic (quiver-like) movements
- Dysmetria, flutter, opsoclonus, saccadomania
- Square wave jerks
- Macrosaccadic oscillations
- Ocular bobbing
- Periodic deviations

Proptosis Decision Tree
Lid retraction present = Graves' Disease
No lid retraction
  - CT Scan
    - Orbital Mass
      - Intraconal Mass = Primary or Metastatic Lesion
      - Extraconal Mass = Superior, Inferior, Medial, Lateral Orbit Lesion
    - No Orbital Mass = Thyroid ophthalmopathy, Idiopathic orbital inflammation, cellulitis, carotid-cavernous fistulae, trauma, developmental abnormalities

Thyroid Ophthalmopathy

Please email suggestions & corrections to: tcooper@stanford.edu
May occur in hyperthyroidism, hypothyroidism, Hashimoto’s thyroiditis and in euthyroid individuals.

Thyroid ophthalmopathy is usually self limited with a course of 1-3 years.

**Thyroid Ophthalmopathy Management**

Treatment is aimed at short-term control of the inflammatory component of the disease, acute intervention for vision-threatening proptosis or compressive optic neuropathy and long-term reconstructive management of lid retraction, strabismus and proptosis. Smoking is associated with worsening of thyroid ophthalmopathy.

Local signs: topical artificial tears and lubricating ointments, tinted or wrap-around glasses, elevation of the head of the bed, or taping the eyelids shut during sleep.

Marked inflammatory signs: systemic corticosteroids 2-4 weeks during active phase or radiation therapy.

Lid retraction: lid surgery when inactive and stable and without evidence of optic neuropathy, and for whom strabismus or orbital decompression surgery is planned.

Strabismus: prisms until stable and after decompression surgery.

Compressive optic neuropathy: 1. initial course of oral or IV corticosteroids, orbital radiotherapy and orbital decompression.

RAI with prednisone may prevent worsening of thyroid ophthalmopathy often seen with RAI treatment.

**Ptosis Decision Tree**

Pseudoptosis

- **Blepharospasm**
  - Apraxia of lid opening (motor neuron, hemispheric and extrapyramidal disease)
  - Dermatochalasis
  - Contralateral lid retraction
  - Hypertropia
  - Hyperglobus

True Ptosis

- **Lid deformity** = Tumor, infection, chalazion, lost contact lens, trauma
  - **No lid deformity**

  - Onset at birth = Congenital ptosis, Myopathies, Myasthenia, Jaw-winking phenomenon

  - Acquired

  - **Topical steroid use** = corticosteroid induced ptosis
    - **No Topical steroid use**

    - Pupillary Abnormality
      - 3rd nerve palsy
      - Traumatic iridoplegia
      - Horner's
      - Guillain-Barre (Fisher's variant)
      - Botulism
    - Pupil Normal
      - **Tensilon**
        - **Positive** = Myasthenia gravis
        - **Negative**

Please email suggestions & corrections to:

`tcooper@stanford.edu`
**Associated neurologic signs**
- Hemispheric ptosis (bilateral ptosis due associated with cerebral hemispheric dysfunction)
- Brainstem ptosis (bilateral ptosis due to lesions of the levator subnucleus)

**No associated neurologic signs**
- Idiopathic "senile" ptosis, levator disinsertion
- Myasthenia gravis

**Causes of Ptosis**
- Mechanical
- Neurogenic
- Myogenic
- Neuromuscular junction

**Transient Visual Loss Decision Tree**

**Scintillations Present**
- Features of classic migraine = Migraine
  - 15-20 minutes of scintillating scotoma followed by one sided pounding headache
  - No evidence of neurologic illness
- Features of classic migraine absent = Ocular Migraine
- Symptoms of Migraine are a "reaction pattern" and may occur in many conditions e.g. lupus erythematosus, occipital lobe lesions causing epilepsy, chronic meningitis

**No Scintillations Present**
- *Strongly consider emboli as cause* because of subsequent stroke risk
- Young patients and patients without risk factors for atherosclerotic should be evaluated for nonarteriosclerotic vasculopathy and blood dyscrasias.

**Bilateral**
- Papilledema
- Vertebrobassilar Insufficiency
- Migraine

**Monocular**
- Evidence of non-embolic disease
  - TLV only in eccentric positions of gaze or change of posture
    - Intraorbital mass
    - Idiopathic Intracranial Hypertension
    - Valsalva maneuver
  - TLV with reading
    - Intraorbital mass
    - Intermittent angle closure glaucoma
  - TLV lasting only seconds
    - Papilledema
    - Optic nerve sheath meningioma
  - TLV lasting minutes (2-30 minutes)
    - Very strongly suggests thromboembolic disease

Please email suggestions & corrections to: tcooper@stanford.edu
Ocular ischemia syndrome is associated with bright light exposure induced TVL. Carotid artery dissection - 28% have TLV usually painful and often with Horner syndrome. Venous stasis retinopathy Giant cell arteritis Blood dyscrasia Hypercoagulable conditions Recurrent hyphema (UGH syndrome, postop cataract, AC IOL, iris fixated IOL, vascular malformations and tumors of iris, iritis, pupillary membranes, histiocytosis X, etc. Recurrent angle closure glaucoma Pigmentary glaucoma Compressive optic nerve lesion Other optic neuropathy

**Transient Visual Loss Workup**

TLV with scintillation symptoms present
- Classic migraine symptoms
  - Eye and neuro exam normal
    - If visual aura is always in same hemianopic VF, obtain MRI to rule out tumor.
  - Eye exam abnormal – appropriate evaluation
  - Neuro exam abnormal – appropriate evaluation
- Classic migraine symptoms absent
  - Eye and neuro exam
  - Symptoms consistent with SLE or chronic meningitis do appropriate lab tests

TLV without scintillations
- Unilateral
  - Eye exam with gonioscopy and neuro exam
    - Unilateral disc swelling – [AION workup](#)
  - If no ocular cause found:
    - Neuro-imaging rule out brain and orbital tumors
    - Doppler-ultrasound to rule out carotid artery disease
    - CBC with differential, ESR, CRP – rule out GCA
    - Medical consultation to rule out sources of thromboembolism and hypercoagulable conditions.
- Bilateral
  - Eye and neuro exam with formal visual fields
  - On bright light exposure – rule out bilateral carotid artery disease
  - Associated with vertebrobasilar transient ischemia symptoms
    - MRI & MRA
    - Medical consultation to rule out sources of thromboembolism and hypercoagulable conditions
  - Significant risk of embolism
    - Medical consultation to rule out sources of thromboembolism and hypercoagulable conditions

Please email suggestions & corrections to: tcooper@stanford.edu
Disc swelling - Papilledema workup
VF abnormal – Abnormal VF workup

Visual Field Defect (VFD) Interpretation

Unilateral VFD
- Retinal lesion matches VF defect = retina lesion
- No RAPD unless massive retinal lesion
- RAPD present = evidence of optic neuropathy
- Monocular temporal crescent defect in isolation = contralateral occipital cortex lesion
- Monocular peripheral VFD most often is from a retinal or optic nerve disease, but a lesion of the peripheral nasal fibers in the anterior occipital lobe may also produce a unilateral temporal crescent-shaped VFD from 60 to-90 degrees (half-moon syndrome). If this VFD is present or it is spared in a homonymous VF neuroimaging should be directed at the contralateral calcarine cortex.

Junctional Scotomas:
- are VFDs due to lesions at the junction of the intracranial optic nerve and chiasm. These VFDs may be localizing because within the intracranial optic nerve at the junction of the optic nerve and chiasm, the crossed (nasal retina) and uncrossed (temporal retina) fibers are anatomically separated and the inferior nasal crossing fibers may loop anteriorly for a short distance into the contralateral optic nerve (Wilbrand’s knee). 4 types of Junctional VFDs are possible.
- For a lesion on the right at the junction of the optic nerve and chiasm both monocular and binocular VFDs may result.
- 1. Unilateral temporal hemianopic VFD from ipsilateral compression of the crossing nasal fibers.
   - The “junctional scotoma of Traquair”.
- 2. Unilateral nasal hemianopic VFD from ipsilateral compression of the temporal fibers.
- 3. Unilateral superotemporal VFD from lesion affecting fibers from contralateral inferonasal retina that loops forward from the chiasm into the optic nerve (Wilbrand’s knee). VFD is contralateral to the lesion.

Please email suggestions & corrections to: tcooper@stanford.edu
4. Bilateral VFD due to a lesion affecting ipsilateral nasal and temporal retinal nerve fibers and fibers crossing from contralateral nasal retina.

This VFD is known as “the junctional scotoma”

Bilateral VFD

Bilateral VFDs = chiasm or retrochiasmal disease

Unless there are bilateral retinal lesions matching the bilateral VFD or bilateral optic nerve disease or a junctional scotoma (4. above) is present.

Bilateral superior of inferior altitudinal defects

Usually due to bilateral optic nerve or retinal disease.

Rarely large prechiasmal lesion

1. causes bilateral superior hemianopia directly compressing inferior aspect of both optic nerves
2. causes bilateral inferior hemianopia from pushing both optic nerves on to the dural shelves that extend from superior aspect of the intracranial end of optic canals

Bilateral symmetric damage to postchiasmal pathways

Bilateral occipital lesions

Bilateral “checker board” (superior VFD in one VF and inferior VFD in the other)

Bilateral cecocentral or central scotomas

Bilateral macular disease

Bilateral optic neuropathy including bilateral optic neuritis

Toxic or nutritional causes

Syphilis

Leber’s hereditary optic neuropathy

Bilateral occipital lesions involving macular projections

Bitemporal hemianopsia – May peripheral, paracentral or central and may split or spare fixation.

Pseudochiasmal VFDs are seen with tilted discs, colobomas, bilateral nasal retinal disease (schisis), glaucoma and bilateral optic neuropathies.

Should be considered topographical localizing to chiasmal lesion till proven otherwise.

Binasal hemianopsia

Usually due to bilateral intraocular disease in the retina or optic nerve

Chronic papilledema, ischemic optic neuropathy, glaucoma, optic disc drusen, retinal edema, sector retinitis pigmentosa or retinoschisis

Rarely compression of lateral chiasm, hydrocephalus with 3rd ventricle enlargement displacing optic nerves against the suprachinoid internal carotid arteries, empty sella syndrome and suprasellar lesions.

Homonymous Hemianopia

Optic tract

Complete unilateral optic tract lesion splits macular fixation

Please email suggestions & corrections to:
tcooper@stanford.edu
Often associated with RAPD in the eye with temporal field loss (contralateral to the lesion)
Incomplete lesions cause incongruous homonymous hemianopia

Optic radiations
Temporal lobe: Pie-in-the-sky FVDs = superior homonymous quadrantic defects caused by a lesion in the temporal loop (Meyer’s loop) of the optic radiations. VFDs are incongruous in topography and depth. Fibers from ipsilateral eye travel more anteriorly and laterally in Meyer’s loop.
Parietal lobe: lesions congruous homonymous hemianopia denser below than above ("pie-in-the-floor").
Occipital lobe: congruous homonymous quadrantanopia or hemianopia.

Macular sparing of the central 5 degrees of vision is common probably due to a combination of a large macular representation and dual blood supply.
Lesions of the anterior tip of the occipital lobe affect the monocular temporal crescent of the contra lateral VF (temporal crescent or half-moon syndrome). Conversely this area may be spared by more posterior lesions such that the temporal crescent is preserved with a homonymous hemianopia. Bilateral occipital lesions may spare both maculae causing tunnel or key-hole VFs.

Homonymous Hemianopia with normal neuro-imaging:
1. Heidenain variant of Jakob-Creuzfeld disease
2. Alzheimer’s disease
3. Carbon monoxide poisoning, organophosphate intoxication
4. Nonketotic hyperglycemia
5. Functional

Unexplained VFD
Carefully examine retina and optic nerve
VFDs that respect the vertical midline should undergo neuroimaging
Repeated VFs

Unexplained Visual Field Loss with Normal Acuity Remember!
Retinal diseases that cause visual field defects may not produce obvious fundus abnormalities.
(Dystrophies - skilled & careful examination required)
Optic neuropathy may cause visual field defects without degrading visual acuity
  Glaucoma
  Ischemic Optic Neuropathy
  Pseudotumor Cerebri
  Optic Nerve Drusen
Optic chiasm lesions may spare visual acuity
Retrochiasmal lesions always spare acuity unless they are bilateral or impinge on one or both optic nerves
Artifacts are a common cause of unexplained visual field defects (especially automated visual field testing).

Please email suggestions & corrections to: tcooper@stanford.edu
Unexplained Best Corrected Visual Acuity Loss - Decision Tree

Improved with potential visual acuity tests
Due to refractive error or media opacity
Unimproved with potential acuity test-look for:
  - Signs of optic nerve or tract lesion
  - Signs of compression of optic nerve or tract
  - Signs of retrobulbar optic nerve lesion
  - Evidence for amblyopia
  - Evidence of macular or other retinal lesion
  - No evidence of macular or other retinal lesions
  - Commonly overlooked retinal diagnoses

Signs of Optic Nerve or Tract Lesion
  - Afferent Pupillary Defect
  - Afferent Sensory Deficits

Best Correction:
A concept used in ophthalmology and optometry to designate the subjective refraction that enables a patient to see their best on a visual acuity chart.
A subjective refraction is determined by a structured process involving the patient comparing their vision through two sets of lenses and choosing the set that provides clearer vision. After a series of such comparisons the set of lenses that enables the patient to see the distant visual acuity chart is determined.

Potential Visual Acuity Tests:
  - Visual acuity through a pinhole
  - Potential acuity meter
  - Near visual acuity
  - Visual evoked potentials
  - Fovea electoretinogram

If visual acuity is improved with a potential acuity test it is likely that the decreased visual acuity is explained by:
  - most likely an uncorrected refractive error,
  - possibly a corneal surface abnormality, or
  - an abnormality of the lens.

The Swinging Flashlight Test: Afferent Pupillary Defect
The swinging flashlight test is done with exam room with lights adjusted to provide the least amount of back-ground illumination that permits observation of the pupils
  - patient fixates a distance target
  - use a bright light without inducing photophobia
  - briskly and rhythmically move light from eye to eye (1-2 seconds for each eye)
  - a pupil that dilates as it is illuminated has an afferent defect
The presence of an afferent pupillary defect usually indicates unilateral or asymmetric optic nerve disease (macula, retinal, and optic tract lesion may also produce an APD)
Reference: Levatin, P., Pupillary escape in disease of the retina or optic nerve

Please email suggestions & corrections to: tcooper@stanford.edu
Afferent Sensory Defects: subjective tests of optic nerve function
   Visual Acuity
   Color saturation comparison
   Brightness comparison
   Contrast sensitivity
   These tests are useful in confirming a positive swinging flashlight test.

Signs of Compression of Optic Nerve or Tract:
The presence of an afferent pupillary defect and:
a non-hemianopic visual field defect indicates a lesion in the optic nerve
a bitemporal hemianopia indicates a lesion at the optic chiasm
a homonymous hemianopia indicates a lesion at the optic tract (this is very rare)

Signs of Retrobulbar Optic Nerve Lesion: Optic Neuropathy
The presence of an afferent pupillary defect, no obvious fundus defect and a non-
hemianopic defect of the visual field indicates the presence of a retrobulbar optic nerve
lesion.
Non-hemianopic visual field defects:
Generalized depression of the visual field
Central scotoma
Centrocecal scotoma
Arcuate scotoma
Wedge-shaped scotoma

Evidence of Amblyopia:
History:
   Lazy eye
   Poor vision from early child hood
   Strabismus surgery
Examination:
   Better acuity with single letters than groups
   No decrease in acuity with 2-log unit neutral density filter
   4-diopter prism introduced before eye does not result in a refixation movement
   (also positive in cases of central scotoma)
   Anisometropia
   Strabismus
   Scars in proximity of ocular muscle insertions
   Media opacities consistent with early childhood
   Afferent pupillary defects have been reported in amblyopia.
   (rarely is the APD in amblyopia clinically noticeable)

Evidence of Macular Lesion:
Subjective:
   Distortion of images, especially print
   Please email suggestions & corrections to:
   tcooper@stanford.edu
Objective:
- Photostress test
  - Highly magnified examination of macula
  - Fluorescein angiography

Photostress Test
The time required for the patient to read the line above their best corrected visual acuity after shining a direct ophthalmoscope at the patient’s macula should be less than a minute if macular function is normal. It is used to differentiate optic nerve from macular disease. Optic nerve disease should give a normal photostress test recovery time. In macular disease the recovery time is usually 1.5 to 3 minutes.

No Evidence of Macular or Other Retinal Lesions - Decision Tree
Visual field
- Normal
  - ERG normal
  - subtle bilaterally symmetric optic neuropathy
  - psychogenic
  - ERG abnormal = cone-rod dystrophy
- Constricted
  - media opacities / refractive errors / miotic pupils
  - outer retinal degeneration
  - optic neuropathy
  - bilateral visual cortex lesions
  - psychogenic

Bilateral nerve fiber bundle defects
- bilateral optic neuropathy
- old central retinal artery occlusion
- bitemporal hemianopia = chiasmal lesion
- bilateral homonymous hemianopia = bilateral retrogeniculate lesions

Commonly Overlooked Retinal Diagnoses:
- serous detachment
- macular edema
- premacular fibrosis
- retinal inflammation
- multiple evanescent white dot syndrome (MEWDS)
- acute macular neuroretinopathy (AMN)
- acute retinal pigment epitheliitis (ARPE)
- acute multifocal placoid pigment epitheliopathy (AMPPE)

Multiple Evanescent White Dot Syndrome (MEWDS)
Usually women age 20-40
Symptoms
- reduced acuity
- scotoma (often flickering) in one eye

Please email suggestions & corrections to:
tcooper@stanford.edu
Examination
grayish white dots at the level of the retinal pigment epithelium in macula and peripapillary region

**Acute Macular Neuroretinopathy (AMN)**
Examination - reddish-orange lesions in macula

**Acute Retinal Pigment Epitheliitis (ARPE)**
Examination - dark spot in macula surrounded by a halo of depigmentation
Rule-out systemic involvement, especially neurologic

**Acute Mutifocal Placoid Pigment Epitheliopathy (AMPPE)**
History - viral illness
Examination - cream-colored, mostly extra macular large lesions
Rule-out systemic involvement, especially neurologic

**Unexplained Visual Loss with Normal Visual Acuity and Visual Fields Decision Tree**
Patients that complain that their vision is not normal but their visual acuity and visual field testing appear normal fall into two groups:
- Subclinical optic neuropathy or maculopathy - evaluate intensively if their history is convincing or if there is measurable interocular difference in swinging flashlight test, color vision/perception or contrast sensitivity.
- Visual acuity and visual field tests are truly normal; the complaint relates to some other aspect of vision (color deficits; floaters; glare; photophobia; metamorphopsia; micropsia; hallucinations; scintillations; reading, attention, perceptual, or visuospatial difficulties; poor stereopsis; double vision; or oscillopsia).

Proper diagnosis depends less on procedures and decision trees than on skilled interviewing.
Consider Alzheimer's disease - Symptom of things popping into vision. Perform testing with color confusion plates that depend on intact visuospatial function, paragraph reading, picture interpretation and puzzle assembly are often poorly performed in Alzheimer's disease. Visual rehabilitation is unrewarding.
Vertical Tropia Decision Tree

The Park’s 3 step test
Determine which eye has Hypertropia (the eye that sees the lower image)
Determine gaze where Hypertropia is worse (Rt. or Lt. Gaze)
Determine head tilt where Hypertropia is worse (Rt. or Lt. Head Tilt)
Right Hypertropia
  Rt. Gaze
    Rt. Tilt = LIO
    Lt. Tilt = RIO
  Lt. Gaze
    Rt. Tilt = RSO
    Lt. Tilt = LSR
Left Hypertropia
  Rt. Gaze
    Rt. Tilt = RSR
    Lt. Tilt = LSO
  Lt. Gaze
    Rt. Tilt = RIR
    Lt. Tilt = RIO

Illusions & Hallucinations Decision Tree
Psychoactive Agent Present
  Pharmacologically induced illusions or hallucinations
Psychoactive Agent Absent
  Abnormal mental or visual state present
    Dementia
    Altered sensorium
    Psychosis
    Trance-like state
    Impaired vision
  Abnormal mental or visual state absent
    Illusions
    Monocular
    Binocular
    Hemianopic
    Nonhemianopic
Hallucinations
    Monocular
    Binocular
Management of Blepharospasm
Rule out any underlying neurologic or myopathic condition such as Parkinson's disease or progressive supranuclear palsy.

Blepharospasm - Associated Conditions
Try anxiolytic agent if stress is a factor and the patient is willing.
If the anxiolytic agent fails, inject botulinum toxin.
If botulinum toxin injections fail and that patient is sufficiently symptomatic, perform orbicularis myectomy

Management of Craniopharyngioma
Surgical - remove as much as possible sparing visual structures
When removal is complete, observe with visual fields and imaging without radiation
Subtotal resections should be radiated if over age 5
If cyst formation is prominent feature of a recurrence, consider intracavitary instillation therapy (radiation, and bleomycin)

Management of Graves' Optic Neuropathy
Give systemic corticosteroids (prednisone 80 to 120 mg/day or high-dose pulse steroids) for 2-3 days, followed by transorbital decompressive surgery (maxillary and ethmoid sinuses).
If surgery is to be delayed for several days, continue systemic corticosteroids.
Radiation of orbits is an alternative to surgery if optic nerve dysfunction is mild.

Management of Graves' Disease Duction Deficits
Administer oral prednisone, 80-100 mg/day; D/C if no clinical improvement in 2 weeks
If steroids relieve symptoms, taper slowly 10 mg/day/week
Steroid therapy should last no longer than 3 months
If orbitopathy worsens during the period of steroid reduction, increase dose
No definitive tapering schedule exists; titrate dose against symptoms
Radiotherapy may also be used.

Management of Hemifacial Spasm
Perform brain imaging (posterior fossa) to rule out mass
If imaging negative, inject botulinum toxin
If botulinum fails and patient is severely symptomatic and understands the risks, perform suboccipital craniectomy

Management of Horner's Syndrome
Horner's Syndrome: Unilateral ptosis and miosis
Children without evidence of birth trauma
- Perform imaging studies to rule out cervical and mediastinal tumors
Adults (When accompanying signs are present they dictate the evaluation steps.)
  Confirm diagnosis by cocaine test
  Localize lesion by hydroxyamphetamine test

Please email suggestions & corrections to: tcooper@stanford.edu
If 1st or 2nd order neuron is involved perform imaging studies of midthorax to angle of jaw.

Arm pain in Horner's Syndrome suggests Pancoast's tumor in (84% of cases involving the 1st or 2nd order neurons).

If 3rd order neuron is involved in isolation, no studies are indicated. Otherwise think of cavernous sinus, headache syndromes, adjacent inflammation, neoplasm, systemic disorders, trauma, carotid artery disease, GCA and do workup consistent with other signs and symptoms present.

**Cocaine Pupillary Test**

Measure each pupil in mm
Instill 4-10% cocaine one drop each eye, repeat in 5 minutes.
Measure each pupil in 30 min
If neither pupil has dilated instill one more drop in each eye.
Observe for 1-2 hours
The involved pupil will not dilate as much as the uninvolved pupil
If anisocoria exceeds 0.8 mm the mean odds ratio having Horner's Syndrome is 1054:1; at 0.5 mm 74:1
Inform patient that urine will test positive for cocaine derivatives for at least 36 hours

**Hydroxyamphetamine Pupillary Test**

Wait 24 hours after Cocaine test.
1% Hydroxyamphetamine one drop OU
Measure pupils in 45 minutes
If the suspect pupil fails to dilate or only partially dilates then a sympathetic postganglionic third order neuronal lesion is present
If the suspect pupil dilates to the same extend or more than the normal one then a sympathetic preganglionic first or second order neuronal lesion is present

**Management of Isolated Third Nerve Paresis**

i.e. a 3rd nerve paresis with no other neurologic signs or symptoms.
Non-isolated 3rd cranial nerve palsy requires neuro-imaging and other work up appropriate to other signs or symptoms.
Urgent concerns for isolated 3rd cranial nerve palsy are aneurysm.& CGA.
Under age 10 years - do MRI in all regardless of pupil.
Over age 10 years - do MRI/MRA in patients if pupil involved - rule out aneurysm.
  Expect 10-20% of such studies to be negative because 10-20% of patients with ischemic third nerve palsies have pupillary dysfunction.
10-40 - do MR with MRA or CTA with pupil sparing palsies
  If negative MRI evaluate medically, follow closely.
  If pupil becomes involved or signs of subarachnoid hemorrhage develop get angiogram.
Over age 40 with pupil sparing and isolated complete third nerve palsy
  BP measurement and screening for diabetes
Observe daily for 5-7 days for signs of pupillary involvement
If not improved at 12 weeks get MRI.

Please email suggestions & corrections to:
[ tcooper@stanford.edu ]
Over age 50 with pupil sparring and isolated complete third nerve palsy
Stat ESR & CPR to rule out GCA
BP measurement and screening for diabetes
Observe daily for 5-7 days for signs of pupillary involvement
If not improved at 12 weeks get MRI.
If aberrant regeneration is present without head trauma get MRI with gadolinium to rule out mass.
If third nerve palsy occurs after minor head trauma get MRI (findings out of proportion to extent of injury).
Isolated complete or partial pupil dysfunction (dilated) with completely normal external function of the 3rd nerve and no ptosis do not require neuro-imaging.
Do not subject patients with isolated ptosis or dilated fixed pupil to invasive studies unless other signs or symptoms of greater somatic nerve or brain stem involvement become evident.

Aneurysm Risk Table

<table>
<thead>
<tr>
<th>Complete external dysfunction</th>
<th>Partial external dysfunction</th>
<th>No external dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete internal dysfunction (pupil involved)</td>
<td>Highest risk MRI with MRA OR CTA Angiography</td>
<td>Highest risk MRI with MRA OR CTA Angiography</td>
</tr>
<tr>
<td>Partial internal dysfunction (relative pupil sparing)</td>
<td>Uncertain, but probably low risk MRI with MRA OR CTA Consider angiography*</td>
<td>Uncertain, but probably low risk MRI with MRA OR CTA Consider angiography*</td>
</tr>
<tr>
<td>No internal dysfunction (normal pupil)</td>
<td>Low risk of aneurysm in vasculopathic patient, observe. MRI with MRA OR CTA if nonvasculopathic or unresolved.</td>
<td>Uncertain risk MRI with MRA OR CTA Consider angiography*</td>
</tr>
</tbody>
</table>

* If the clinician is confident in the capability, availability, and reliability of the neuroradiologist and of the imaging technology at the institution (e.g., MRI, MRA, CTA) and if the pre-test likelihood of aneurysm is low or if the risk of angiography is unreasonably high (e.g., elderly, high risk of renal
Management of Isolated Fourth Nerve Palsies
The evaluation of isolated fourth nerve palsies is determined by the clinical setting. Traumatic and congenital palsies do not require additional neuroimaging or further evaluation. Fourth nerve palsies caused by ischemia to the subarachnoid segment (vasculopathic) do not require any initial neuroimaging studies. They may be observed for improvement over the following 6 to 8 weeks. Spontaneous recovery occurs within 12 weeks in more than 95% of patients. Patients with progressive or unresolved palsies, or those with new neurologic signs or symptoms, should undergo neuroimaging. Elderly patients with diplopia and headache, scalp tenderness, jaw claudication, or visual loss should undergo an appropriate evaluation for giant cell arteritis (e.g., erythrocyte sedimentation rate and a temporal artery biopsy). Variability or fatigable diplopia or ptosis should be evaluated for myasthenia gravis (e.g., Tensilon test, anti-acetylcholine receptor antibodies). Patients without vasculopathic risk factors (e.g., hypertension, diabetes, smoking, elevated cholesterol) may require initial neuroimaging, but observation for spontaneous improvement is also reasonable. Coppeto and Lessell reported 12 idiopathic cases that resolved by 4 months. Nemet and colleagues reported 13 patients who resolved by 10 weeks. Isolated fourth nerve palsies rarely have an underlying intracranial etiology although pituitary adenoma or other compressive lesions have been reported. Patients who do not improve within 2 months should be considered for neuroimaging. Unlike the isolated third nerve palsy, cerebral angiography is not recommended for evaluation for fourth nerve palsy unless an aneurysm is suggested by other neuroimaging studies.

Management of Isolated Unilateral Nontraumatic Sixth Nerve Palsies
Under age 14 do not require imaging
  Follow every 2 weeks for 6 weeks
  If recovery is incomplete in 6 months do MRI
  EOM surgery after 6-9 months
Age 15-40 do MRI though most negative
  Rule out hypertension, collagen vascular disease, MS, Lyme disease and syphilis
  Follow in 6 weeks
  Repeat work-up in 6 months if no improvement has occurred
Over age 40
  Medical evaluation including diabetes test
  MRI if not recovered in 6 months
Over age 55 Stat Set Rate and CRP to rule out GCA

Please email suggestions & corrections to:
tcooper@stanford.edu
Management of Bilateral Sixth Nerve Palsies
Suspect children and adults with bilateral sixth nerve palsies in the absence of severe head trauma of having increased intracranial pressure or meningeal-based disease and obtain LP even if MRI is negative.
Suspect battered child syndrome in any infant or child with an ocular motor paresis. Look for other stigmata.

Management of Optic Gliomas - (No good evidence for recommendations)
MRI with gadolinium to define tumor extent
No biopsy if imaging features are typical, the tumor is intra-axial, or the patient has neurofibromatosis
If the tumor is confined to the optic nerve, no treatment is indicated regardless of visual signs. Surgery may be considered for unsightly proptosis or exposure keratitis
Radiation therapy for chiasmal/hypothalamic tumor in children over 5 with clinical or MRI signs of progression. If vision cannot be adequately assessed, Burde, Savino and Trobe favor treating the patient
Chemotherapy in lieu of radiation for children under 5 years of age
Surgery for any chiasmal lesion with an exophytic component
Shunting procedures for obstructive hydrocephalus

Management of Optic Nerve Sheath Meningiomas
Clinically reevaluate every 6 months, including visual fields.
Repeat MRI with gadolinium-DTPA every 6 months for 2 years then yearly.
If visual function deteriorates administer 5000 cGy of radiation.
Surgical intervention is considered only if intracranial extension through the optic canal occurs.
Biopsy of these lesions is unnecessary unless atypical clinical behavior or imaging findings occur.

Management of Optic Neuritis
Typical Optic Neuritis
Monocular visual loss between 20-50 years of age
Visual symptoms (blurring, diplopia, nystagmus) with increased core body temperature (as little as 0.1 degree C). Hot baths or exercise may exacerbate these symptoms (Uhthoff’s phenomenon). Walking upstairs or across the street may be enough to bring on symptoms.

Atypical Optic Neuritis
Outside age range 20-50
Both eyes simultaneously
Continues to worsen after 14 days
Does not recover in 3 months
Features of history that cannot be attributed to MS Atypical
Get MRI, if normal consider repeat at 2-3 months if findings persist or are increasing.

Please email suggestions & corrections to:
tcooper@stanford.edu
The Optic Neuritis Treatment Trial (ONTT) Recommendations: 1. Chest x-ray, blood tests and lumbar puncture are not necessary in evaluating patients with typical clinical features of ON. 2. Treatment with oral prednisone in standard doses should be avoided. Brain MRI should be considered to assess the risk of future neurologic events of MS. 3. Treatment with IV methylprednisolone should be considered, particularly if brain MRI demonstrates multiple signal abnormalities consistent with MS, or if a patient has a need to recover vision rapidly. Methylprednisolone 250 mg IV q6h for 3 days, followed by prednisone 1 mg/kg/d in a single dose for 11 days, 20 mg day 15 and 10 mg days 16 and 18.

The ONTT, Controlled High-Risk Subjects Avonex Multiple Sclerosis Prevention Study (CHAMPS), and Early Treatment of Multiple Sclerosis Study Group (ETMSS) studies provide useful guidelines in the management of first attack optic neuritis in patients who have had no prior clinical diagnosis of multiple sclerosis. 1. There are still no guidelines as to how to manage first-attack optic neuritis in patients with normal brain MRI scans. 2. If such patients are found to have 2 or more "demyelinative" MRI signal abnormalities measuring 3 mm or more in diameter, they stand to develop fewer clinical relapses and accumulate fewer MRI signal abnormalities within the next 3 years if they are treated prophylactically with beta interferon 1a. 3. Acute treatment with intravenous corticosteroid may speed resolution of the visual deficit but probably provides little or no benefit over interferon treatment alone on the frequency of relapses or MRI changes. 4. In deciding to recommend prophylactic interferon, the physician must contend with several drawbacks: a) the drug is expensive; b) it causes unpleasant side-effects in some patients; c) antibodies develop with 2 years in up to 25% of patients, rendering the drug useless; d) the drug only reduces the relapse rate by about 30%; and e) studies have yet to demonstrate any benefit on visual or other neurologic disability.

Management of Ischemic Optic Neuropathy
Two types: Arteritic and Non-arteritic
Always do erythrocyte sedimentation rate and CPR STAT on all cases of ION

Management of Traumatic Optic Neuropathy
Usually from closed head trauma. Imaging evidence of structural abnormalities adjacent to the intracanalicular optic nerve (fractures, hematomas) is common but not constant. No ophthalmoscopic abnormalities occur in the acute phase. Autopsy examinations have confirmed the site of injury is usually the intracanalicular optic nerve, which shows infarction. Visual loss usually remains static from the initial to subsequent examinations, but a substantial minority of patients show a decline. Traumatic optic neuropathy usually from closed head trauma. Imaging evidence of structural abnormalities adjacent to the intracanalicular optic nerve (fractures, hematomas) is common but not constant. Often there are often no ophthalmoscopic abnormalities occur in the acute phase. Autopsy examinations have confirmed the site of injury is usually the intracanalicular optic nerve, which shows infarction.

Please email suggestions & corrections to:
tcooper@stanford.edu
Visual loss usually remains static from the initial examination, but a substantial minority of patients show a decline of visual acuity over time.

**Care path**

1. Confirm clinical diagnosis
2. Treat vision or threatening injuries
   - If vision down or RAPD present with proptosis (tight orbit), perform lateral canthotomy.
   - Consider IV corticosteroids even when vision is NLP. Spectacular results without controlled studies have been reported.
   - Methylprednisolone 30 mg/kg IV over 30 minutes.
3. Perform high-resolution CT of optic canal and orbit
4. Consider optic nerve decompression of bony fragments impinge on optic nerve
5. If vision improves on IV corticosteroids after 48 hrs, start rapid oral taper of prednisone
6. If no improvement in 48 hrs or vision deteriorates during steroid taper offer surgical decompression especially for patients with severe visual loss (worse than 20/800).


**Management of Bilateral Painless Loss of Central Vision**

Get CT/MRI in all cases despite low yield
Screen all patients for pernicious anemia with CBC & indices and serum B-12 level
If no history of familial vision loss or sever alcoholism exists, perform a thorough work-up of non-compressive cases (LP, 24-hour urine for lead or thallium intoxication)
When evidence of smoking and alcohol abuse is present and other causes have been reasonably excluded, assume toxic and nutritional factors are pathogenic. Smoking and alcohol, eat balanced diet and take multivitamins and thiamin, 25 mg three times a day

**Management of Parachiasmal Meningiomas**

Perform total resection sparing visual structures
Follow with neuro-ophthalmic evaluation to detect progression
Radiation for residual tumor or with progresses

**Pituitary Tumors Visual Field Frequency Recommendation**

Immediately postop
At the end of radiation therapy
   - Then every 3 months till stable
   - Then every 6 months for 2 years
   - Yearly for 5 years
Medical therapy - (bromocriptine) monthly till stable
   - then every 6 months for 1 year
then yearly unless dose of bromocriptine is changed

Management of Pituitary or Sphenoid Sinus Infection
Mucoceles from ethmoid and sphenoid sinuses may simulate pituitary apoplexy
Sinus surgery and excision of mucocele
Pituitary Abscesses - rare but curable
Chiasmal syndrome or meningitis presentation
Often preexisting tumor present
Trans-sphenoidal drainage and antibiotics
Prognosis is guarded - 28% mortality, 45% with meningitis

Management of Pseudotumor Cerebri: Idiopathic Intracranial Hypertension (IIH)
IHH Features
Usually seen in women of childbearing age
Obesity very frequent
Headache 94%, pulsatile tinnitus 58%, transient obscuration of vision 68% often with change of posture, photopsia 54%, retrobulbar pain 44%, diplopia 38%, sustained vision loss 26%
Papilledema usually bilateral
6th cranial nerve palsy

IIH Workup
Rule out drugs associated with IIH
Hypervitaminosis A, steroid withdrawal, anabolic steroids, lithium, nalidixic acid, chordecone (Kepone) insecticide, isoretinoin, ketoprofen, indomethacin in Bartter syndrome, thyroid replacement in hypothyroid children, danazol, all-trans-retinoic acid (ATRA) tretinoin, cyclosporine, exogenous growth hormone, tetracycline and minocycline
Rule out systemic conditions associated with IHH
Beeches syndrome, renal failure, Addison’s disease, hypoparathyroidism, systemic lupus erythematous and sarcoidosis – probably secondary from venous obstruction
Neurologic exam: normal except for papilledema and possibly a 6th cranial nerve palsy
MRI and MRV if available not reveal a secondary cause of IIH and be normal except for:
Flattening of posterior sclera 80%
Distention of perioptic subarachnoid space 50%
Enhancement of prelaminar optic nerve 54%
Empty sella 70%
Intraocular protrusion of prelaminar optic nerve 30%
Vertical tortuosity of orbital optic nerve 40%
Visual fields – Humphrey 30-2

IIH Treatment & Follow-up
Papilledema, no symptoms and otherwise normal ophthalmologic exam
Please email suggestions & corrections to: tcooper@stanford.edu
urge weight loss for obese patients
follow monthly for 3 months, if still normal follow every 3 months
Papilledema, headache, and transient visual obscurations or signs of optic nerve dysfunction
acetazolamide 1-4 gram/day, follow every 2-4 weeks for signs of progressive optic nerve dysfunction
Progression of visual field defects on acetazolamide
nerve sheath decompression or
lumboperitoneal shunt - primary procedure if headache is present

Management of Pseudotumor of Orbit
Treat with corticosteroids (prednisone 80-100 mg/day for 2 days)
No response = biopsy
Dramatic response
Taper response
Recurrence of symptoms increase corticosteroids
No response = biopsy
Symptoms abate = taper corticosteroids
Additional Recurrence = biopsy
No recurrence = continue to taper
Cyclophosphamide has been effective for bilateral pseudotumor resistant to 100 mg of prednisone daily. These cases had inflammation centered within the walls of small blood vessels, no systemic vasculitis was identified
Syndromes-Diseases-Conditions

*Acute Esotropia of Childhood*

*Adie's Syndrome*

*Acute macular Neuroretinopathy (AMN)*

*Acute Multifocal Placid Pigment Epitheliopathy (AMPPE)*

*Anton's Syndrome*

*Acute Retinal Pigment Epitheliitis (ARPE)*

*Balint Syndrome*

*Bardet-Biedel Syndrome*

*Benedikt Syndrome*

*Bielschowsky's Test*

*Brown's Superior Oblique Tendon Sheath Syndrome*

*Claude Syndrome*

*Claude Bernard*

*Charles Bonnet*

*Chronic External Ophthalmoplegia*

*Churg-Strauss Disease*

*Cogan's lid-twitch sign*

*Complicated Hereditary Optic Atrophy*

*de Morsier Syndrome*

*Devic's Disease*

*Divergence Nystagmus*

*Dominant Optic Neuropathy*

*Duane's Retraction Syndrome*

*Foville's Syndrome*

*Fetal Alcohol Syndrome*

*Foster-Kennedy Syndrome*

*Gaze Deficits*

*Gradenigo's Syndrome*

*Guillian-Barre-Strohl Syndrome*

*Horner's Syndrome*

*Huntington's Disease*

*Internuclear Ophthalmoplegia*

*Kearns-Sayre Syndrome*

*Leber's Optic Neuropathy*

*Macular Star Pattern with Optic Neuropathy*

*Millard-Gubler Syndrome*

*Miller Fisher Syndrome*

*Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke*

*Multiple Evanescent White Dot Syndrome*

*Moebius Syndrome*

*Neuromyelitis Optica*

*Nothnagel's Syndrome*

*Ocular Bobbing*

*Oculogyric Crises*

Please email suggestions & corrections to:  
tcooper@stanford.edu
Ocular Myoclonus
Ocular Neuromyotonia
Oculomasticatory myorhythmia
Oculoparyngeal muscular dystrophy
One and One Half Syndrome
Opsoclonus and Saccadomania
Optic Disc Hypoplasia - Associated Conditions
Parinaud Syndrome
Parkinson's Disease
POEMS Syndrome
Progressive Supranuclear Palsy
Pulfrich stereo-illusion
Pseudo-Foster-Kennedy
Recessive Optic Neuropathy
Restrictive Diplopia - Causes
Retinal Diagnoses - Commonly Missed
Superior Oblique Myokymia
Tolosa-Hunt Syndrome
Tip of the basilar artery
Upper Eyelid Retraction - Causes
Wallenberg Syndrome
Weber Syndrome

Acute Esotropia of Childhood: An acute-onset esotropia. May be associated with nystagmus. If motor fusion is not established with appropriate hyperopic spectacles or prisms MRI and neurologic evaluation is indicated. Rule out tumors of brainstem or cerebellum.

Adie's Syndrome: Areas of paresis of the iris sphincter are interposed with sections of actively constricting muscle (called vermiform movements). Sector paresis produces a shifting of the iris stroma toward the areas of active constriction ("iris streaming"). Extraordinarily slow constriction to either light or near stimuli. Very slow redilation ("tonic reaction"). 90% are unilateral, and 80% develop cholinergic super sensitivity. Most common in women aged 10 to 30 years. Aberrant re innervation from axons of the damaged ciliary ganglion to the iris sphincter is given as the explanation for pupillary and ciliary muscle tonicity. Regional corneal hyperthesia due to interruption of fibers of the ophthalmic division of the trigeminal nerve as they pass through the ciliary ganglion. Symptoms of glare from slowly reacting pupil. Accommodative difficulties from segmental ciliary muscle paresis causing lenticular astigmatism.

Anton Syndrome: A condition characterized by denial of blindness with resort to confabulation by blind person. It is a peculiar delusion of reality of the blind in which the blind person lacks conscience of his own condition. Despite the presence of complete

Please email suggestions & corrections to: tcooper@stanford.edu
blindness, there is persistent confabulation and denial by the patient that there is any loss of visual perception. Occurs mostly after apoplexy.

**Balint Syndrome:** A syndrome combining paralysis of visual fixation, optic ataxia, and impairment of visual fixation. It is marked by inability to execute voluntary movement in response to visual stimuli. Despite normal field of view and normal acuity the patients perceives only one object, from which he can hardly move his eyes, while all other objects are not recognized. A rare disorder of oculomotor function due to bilateral lesions of the parietal and occipital lobes.

**Bardet-Biedl Syndrome:** polydactyly, obesity, cognitive delay and retinal degeneration. May have asymmetric nystagmus which resembles Spasmus Nutans.

**Bielschowsky's Test:** used to evaluate 4th cranial nerve function in patients with hypertropia. With 4th cranial nerve palsy the hypertropia increases head tilt toward the paralyzed side. This is the 3rd step in the 3 step test for hypertropia.

**Brown's Superior Oblique Tendon Sheath Syndrome:** Fibrosis and shortening of the superior oblique tendon and attachment of the tendon sheath to the trochlea, resulting in restriction of eye movements. Palpebral fissure may widen when attempting upward gaze. Adduction and abduction restriction or abolished. Also associated with bilateral blepharoptosis, backward head tilt, and choroidal coloboma. Etiology unknown. Both sexes affected; present from birth.

**Causes of Light-near Dissociation:** Lesions of anterior afferent visual system, diabetes mellitus, prectetal lesions (compressive and syphilis).

**Causes of Mechanical (Restrictive) Diplopia**
- Graves' ophthalmopathy
- Brown's superior oblique tendon sheath syndrome
- Orbital pseudotumor
- Ocular myositis
- Orbital mass
- Trauma
- Fracture
- Intrinsic muscle damage

**Causes of Retraction of Upper Eyelids**
- Graves' ophthalmopathy
- Non-Graves' cicatricial lid retraction
- Midbrain lid retraction (Collier's Sign)
- Sympathetic chain irritation (Claude Bernard Syndrome)
- Volitional lid retraction

**Cerebral Polyopia:** Some patients with signs and symptoms of posterior hemispheric dysfunction complain of seeing multiple images either monocularly or binocularly.

Please email suggestions & corrections to: tcooper@stanford.edu
Charles Bonnet Syndrome: Visual hallucinations in psychologically normal elderly people. Charles Bonnet in 1760 described vivid, complex visual hallucinations in his psychologically normal 87 year old grandfather, who had cataract operations on both eyes and was practically blind. His grandfather saw pictures of men, women, birds, carriages, buildings, tapestries and scaffolding patterns. Most affected persons are elderly and psychologically normal, but visually impaired. However, the phenomenon is not exclusively restricted to people with visual impairment.

Chronic Progressive External Ophthalmoplegia: Consists of weak extraocular muscles and thin, atrophic extraocular muscles. It is slowly progressive. Diplopia is unusual. Most patients have bilateral ptosis which is the usual presenting symptom and may proceed ophthalmoplegia by months or years. Proximal extremity muscle weakness is often present. Other ophthalmologic abnormalities include corneal opacities, cataracts, and pigmentary retinopathy. Hearing loss and peripheral neuropathy may also occasionally be present. Onset is usually in the 20s or 30s but may have an onset late in life. It is usually associated with a sporadic genetic defect with large-scale deletions in the mitochondrial DNA, but maternal mitochondrial inheritance, autosomal dominant and recessive inheritance of nuclear DNA have been reported. Three specific gene mutations associated with autosomal dominant nuclear DNA: ANT1 (chromosome 4q), TWINKLE (chromosome 10q), and POLG (chromosome 15q).

Churg-Strauss Disease: is a noninfectious leukocytoclastic (ie, fibrinoid, necrotizing, inflammatory) systemic vasculitis that invariably involves the lungs and may, in addition, affect a wide variety of other tissues and organs of the body, including the nervous system.

Claude Bernard Syndrome: The opposite of Horner's Syndrome. It consists of ipsilateral mydriasis, lid retraction, and hyperhidrosis. May be seen following neck trauma. Thought to be due to irritative lesion involving partial sympathetic denervation in neck after the fibers had emerged from the T1 segment. It is very rare.

CNS Disorders Associated with Bilateral Blepharospasm
Bihemispheric damage
Huntington’s
MS
Parkinson’s
Progressive supranuclear palsy
Rostral brainstem stroke
Tourette syndrome
Tardive dyskinesia

Combined Upgaze and Downgaze Deficits: Progressive supranuclear palsy, Parkinson’s disease, strokes causing "tip of the basilar artery” syndrome and certain myopathies and mitochondrial encephalomyopathies cause vertical gaze deficits.

Please email suggestions & corrections to: tcooper@stanford.edu
Complicated Hereditary Optic Atrophy: Optic atrophy with central or centrocecal scotomas in wide variety of neurodegenerative states. Familial, eponymic spinocerebellar degenerations - Friedreich's, Marie's, Behr's, Charcot-Marie-Tooth, & inborn errors of metabolism.

de Morsier Syndrome: or septo-optic-pituitary dysplasia: Triad of dwarfism, nystagmus, and micropupil. A birth defect characterized by a malformed optic disk and nerve, pituitary deficiencies and often the absence of the septum pellucidum which separates the ventricles of the brain and/or corpus callosum. As a consequence of these abnormalities, visual impairment and inadequate growth hormones may occur. Other features include growth retardation and sometimes mental retardation or learning disabilities.

Divergence Nystagmus and Repetitive Divergence Nystagmus: Divergence nystagmus is a rare form of jerk nystagmus characterized by fast -phase movements away from the nose. It is postulated to be due to cerebellar dysfunction. Repetitive Divergence Nystagmus consists of slow divergent movements followed by a rapid return to primary position at regular intervals. It has been seen in patients with hepatic encephalopathy.

Dominant Optic Neuropathy: Optic atrophy with onset in ages 4-8, acuity 20/40-20/200, no nystagmus, moderate disc pallor, centrocecal scotomas, tritanopic color defect. Autosomal dominant optic atrophy (DOA), Kjer type, is the most common form of hereditary optic neuropathy with an estimated disease prevalence of 1:50,000 in most populations. Histopathological and electrophysiological studies suggest that the underlying defect is a retinal ganglion cell degeneration. There are two known loci mapping to 3q28–q29 and 18q12.2–12.3 for OPA1 (the most common) and OPA4, respectively.

Downgaze Deficits: Patients with downgaze deficits appear to have a ptosis in down gaze (the lids move down but the eye movements are limited). It is due to bilateral lesions of the medial ventral part of the rostral interstitial nucleus of the MLF.

Duane's Retraction Syndrome: characterized by narrowing of the palpebral fissure and globe retraction on adduction. 3 Types: type I – abduction is limited but adduction is normal, type II adduction is impaired but abduction is normal, type III both adduction and abduction are impaired. When bilateral, may see retraction on vertical gaze as well. Rarely complain of diplopia, may have XT, ET and head turn. It is caused by agenesis of the abducens nerve and nucleus. Aberrant innervation of the lateral rectus muscle from various branches of the third nerve accounts for the variations of findings.

Fetal Alcohol Syndrome: Individuals with FAS have a distinct pattern of facial abnormalities, growth deficiency and evidence of central nervous system dysfunction. In addition to mental retardation, individuals with FAS, Alcohol-Related Neuro-developmental Disorder (ARND) and Alcohol-Related Birth Defects (ARBD) may have other neurological deficits such as poor motor skills and hand-eye coordination. They

Please email suggestions & corrections to: tcooper@stanford.edu
may also have a complex pattern of behavioral and learning problems, including difficulties with memory, attention and judgment.
- Growth deficiencies: small body size and weight, slower than normal development and failure to catch up.
- Skeletal deformities: deformed ribs and sternum; curved spine; hip dislocations; bent, fused, webbed, or missing fingers or toes; limited movement of joints; small head.
- Facial abnormalities: small eye openings; skin webbing between eyes and base of nose; drooping eyelids; nearsightedness; failure of eyes to move in same - direction; short upturned nose; sunken nasal bridge; flat or absent groove between nose and upper lip; thin upper lip; opening in roof of mouth; small jaw; low-set or poorly formed ears.
- Organ deformities: heart defects; heart murmurs; genital malformations; kidney and urinary defects.
- Central nervous system handicaps: small brain; faulty arrangement of brain cells and connective tissue; mental retardation -- usually mild to moderate but occasionally severe; learning disabilities; short attention span; irritability in infancy; hyperactivity in childhood; poor body, hand, and finger coordination.

Foster-Kennedy Syndrome: Optic pallor of one disc, papilledema of the other disc, anosmia and dementia caused by a meningioma of the optic foramen or sphenoid-wing. The disc atrophy is caused by compressive optic neuropathy and the papilledema is due to hydrocephalus with increased intracranial pressure.

Foville Syndrome: Ipsilateral paralysis of gaze, facial palsy, loss of taste form the anterior two thirds of the tongue, Horner’s syndrome, facial analgesia and deafness (anterior inferior cerebellar artery syndrome affecting the pons).

Gaze Disturbances
Disorders of Fast Eye Movements
  Unilateral Saccadic Paresis
  Bilateral Saccadic Paresis
  Congenital Ocular Motor Apraxia
  Acquired Ocular Motor Apraxia
  Huntington's Disease
Miscellaneous Saccadic paralysis is reported in:
  Multiple sclerosis
  Ataxia telangetactasia
  Pelizaneus-Merzbacher disease
  Wilson's disease
  Some patients have striking inability to maintain fixation for more than a few seconds, at which time they appear to be distracted and make a saccadic movement to a peripheral target.
Whipple's disease
Disorders of the Slow Eye Movement Systems
Disorders of the Vergence System Disorders of Both the Fast and Slow Eye Movement Systems

Please email suggestions & corrections to: tcooper@stanford.edu
Myopathic Gaze Disorders

**Gradenigo Syndrome:** In children a sixth nerve paresis associated with ipsilateral facial pain and hearing loss due to osteitis of the tip of the petrous pyramid secondary to chronic mastoiditis or middle ear infection.

**Guillian-Barre-Strohl Syndrome:** Acute, infectious, demyelinating polyradiculoneuropathy which ascends from legs to arms. Bulbar variety described by Fisher with facial diplegia and unilateral or bilateral ocular motor palsies. Elevated CSF protein in the absence of pleocytosis is found. Presumed to be a viral lymphocyte mediated demyelination of nerve roots. Also seen after immunizations.

**Huntington’s Disease:**
- Autosomal dominant trait
- Insidious onset, usually beginning in the late thirties
- Random intrusions of saccadic movements during fixation
- Impaired initiation of saccades (increased reaction time)
- Inability to produce saccadic movement without head movement or blink
- All fast movements become progressively slowed until lost
- Smooth pursuit is abnormal in majority
- Vergences are abnormal in one third
- Vestibulo-ocular reflexes and the ability to hold eccentric fixation are preserved even late in the disease.
- Mental deterioration begins a few years after the onset of the involuntary movements.
- Other findings include intermittent, nonstereotypical spasm of facial muscles with periods of lid closure and periods of widely open lids.

**Hypoplasia of Optic Disc Associated Conditions:**
- Superior Segmental Optic Hypoplasia - children of diabetic mothers
- Macular Colobomas
- Chiasmal Malformations-De Morsier syndrome
- Occipital Porencephaly
- Septo-optic Dysplasia-agenesis of septum pellucidum and hypothalamus

**Internuclear Ophthalmoplegia (INO):**
- Lag of ipsilateral medial rectus muscle in conjugate gaze movement (adduction lag) associated with monocular horizontal nystagmus in opposite abducting eye.
- Lesion of MLF between abducens and oculomotor nuclei.
- Patients usually have no symptoms may complain of diplopia or oscillopsia.
- Multiple sclerosis is most likely cause of bilateral INO.
- If the patient is over 50, vertebrobasilar disease must be considered (brainstem infarction).
- Often accompanied of vertical upbeat nystagmus in upgaze and a skew deviation.
- Anterior INO is due to a mesencephalic lesion, usually bilateral, with the eyes aligned in primary position and convergence is maintained.

Please email suggestions & corrections to: tcooper@stanford.edu
Wall-eyed bilateral INO (WEBINO) = exotropic with no convergence with abducting nystagmus in right and left gaze.

**Kearns-Sayre Syndrome:** A rare neuromuscular disorder with onset usually before the age of 20. It is characterized by progressive external ophthalmoplegia (paralysis of the eye muscles) and mild skeletal muscle weakness. It may also be associated with other manifestations such as retinal pigmentation (abnormal accumulation of pigmented material on the membrane lining the eyes), cardiac conduction defects, short stature, hearing loss, increased cerebrospinal fluid protein, inability to coordinate voluntary movements (ataxia), impaired cognitive dysfunction, diabetes, and other endocrine disorders.

**Leber's Optic Neuropathy:** Symptoms start in one eye first, followed by the other within weeks. Almost all are men from 10-30 years old. It is painless. It rarely may improve. VF defect is central or cecocentral scotoma acutely. There are dilated retinal surface vessels on and around the nerve head and a glistening opaque peripapillary nerve fiber layer. F-angio shows shunting around disc without leakage. After a few weeks there is attenuation of retinal arterioles and nerve fiber layer and pallor of nerve head. Cardiac conduction defects and dystonia have been reported. Matrilineal inheritance. Most often missed diagnosis in young males suspected of optic neuritis examine at risks family members. There is no treatment.

**Macular Star Pattern with Optic Neuropathy:** Consider Leber's optic neuropathy

**Millard-Gubler Syndrome:** A lesion of pons producing ipsilateral sixth nerve paralysis with a contralateral hemiplegia.

**Miller Fisher Syndrome:** Total external ophthalmoplegia, ataxia, and loss of tendon reflexes, thought to be a variant of the Guillain-Barré syndrome. 90% have circulating IgG antibodies recognizing the ganglioside GQ1b.

**Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke (MELAS)** A mitochondrial myopathy that involves the central nervous system, skeletal muscle, eye, cardiac muscle, and more rarely the gastrointestinal system. About 80% of patients with MELAS have a heteroplasmic A-to-G point mutation in the dihydrouridine loop of the transfer RNA gene at base pair 3243 (A3243G mutation).

**Moebius Syndrome:** Facial diplegia and horizontal gaze paralysis. Patients may use the mechanism of accommodative convergence to increase their ability to look eccentrically by producing an esotropia and cross-fixating. May have a developmental anomaly affecting motor neurons and interneurons in the abducens nuclei.

**Monocular Elevation Paresis:** Rare acquired disorder with diplopia in upgaze. Lid positions are normal. Lesion interrupts supranuclear input from the vertical gaze center in the pretectum to the oculomotor complex.

Please email suggestions & corrections to: tcooper@stanford.edu
Myasthenia Gravis: An acquired disorder with autoimmunity to motor end plates with antibodies to acetylcholine receptors clinically characterized by varying degrees of weakness and fatigue of voluntary muscles. The weakness increases with repeated or sustained exertion over the course of the day, is improved by rest and may be worsened by elevation of body temperature and improved by cold. Commonly affects the levator and extraocular muscles. 50% of cases present with only Ocular Myasthenia symptoms and signs. 50-78% progress to generalized Myasthenia Gravis within 2-3 years. Patients with onset after age 50 have worse prognosis. Antiacetylcholine receptor antibodies are present in MG: generalized 80-100%, in remission 24%, ocular 50%. The Tensilon test is most easily evaluated with ptosis but may be confusing in ocular misalignments when ptosis is absent. Thymoma is present in ocular myasthenia gravis 4% and generalized 12%. 10-20% of patients with ocular myasthenia gravis undergo spontaneous remission. Cogan's lid-twitch sign: A sign of myasthenia. During refixation from down to primary position, the upper lid may either slowly begin to droop or twitch several times before settling in a stable position.
Myasthenia Gravis Workup
   No test is specific
   Tensilon
   Tensilon positive with only unilateral signs get MRI
   Tensilon negative get serum antiacetylcholine receptor antibodies (most specific)
   Serum antiacetylcholine receptor antibody negative order repetitive nerve stimulation and /or
   single-fiber electromyography (most sensitive).
   With diagnosis of Myasthenia Gravis get CT or MRI of mediastinum to rule out thymoma.

Myasthenia Gravis Management
   Warn patients with ocular myasthenia gravis of likely hood of developing generalized disease.
   Good diet (potassium, adequate rest and avoid precipitants (medicine that worsen MG).
   Thymectomy for thymoma, not without.
   Diplopia: observation, patch, anticholinesterase agents e.g. pyridostigmine bromide (Mestinon)
   often not effective, low-dose alternate corticosteroids, azathioprine.
   Ptosis: observe, crutch, medication as above, sling

Neuromuscular Disorders Associated With Bilateral Blepharospasm
Tetany
Tetanus
Myotonic dystrophy
Hyperkalemic periodic paralysis
Chondrodystrophic myotonia

Nothnagel Syndrome: Cerebellar ataxia with either unilateral or bilateral involvement of
the oculomotor nerve due to midline lesions.

Ocular Bobbing: Repeated brisk downward movements from the primary position,
remain eccentric for a few seconds, and then slowly drift back to the primary position.
May be asymmetric. Indicates severe brainstem dysfunction and is not precisely
localizable. Convergence Nystagmus Pendular nystagmus induced by convergence,
congenital or acquired is rare.

Ocular Myoclonus: A continuous, rhythmic, to-and-fro pendular oscillation, usually
vertical. Often it occurs with similar synchronous movements of the face and palate
(Oculopalatal Myoclonus) and indicates damage in the “myoclonic triangle” formed by
the red, inferior olivary and contralateral dentate nuclei of the cerebellum and their
interconnecting fiber tracts (usually MS or infarction). These movements are present
during sleep and usually persist forever.

Oculomasticatory Myorhythmia: The presence of convergence nystagmus
accompanied by contraction of the muscles of mastication or in synchrony with palatal
and mandibular muscular activity is thought to be pathognomonic of Whipple’s disease.
This finding is often accompanied by supranuclear ophthalmoparesis.

Please email suggestions & corrections to:
tcooper@stanford.edu
Ocular Neuromyotonia: Intermittent diplopia in patients with history of intracranial mass lesion treated by radiation. Presumed cause is radiation-induced cranial neuropathy manifesting a spontaneous discharge from axons with unstable cell membranes. Carbamazepine is often effective in controlling the spasms.

Oculoparyngeal muscular dystrophy: An autosomal dominant or recessive inherited disease causing weakness of the extraocular muscles and pharynx. Ptosis and difficulty swallowing are early symptoms. Later facial and limb weakness occurs. Caused by an abnormal gene for poly(A)-binding protein 1 (PABPN1). French Canadian background is common.

One-and-one-half Syndrome: A conjugate gaze palsy to one side (“one”) and impaired adduction on looking to the other side (“and-a-half”). As a result, the only horizontal movement remaining is abduction of one eye, which may exhibit nystagmus in abduction. The eye on the side of the lesion is immobile during all conjugate horizontal gaze movements. The contralateral eye abducts appropriately but floats back toward the midline in response to a conjugate gaze command ipsilateral to the lesion. It results from lesions of the ipsilateral abducens nucleus and the ipsilateral MLF. This condition may be simulated by myasthenia gravis. If over age 50 ESR and CRP to rule out GCA related infarct. All need MRI of posterior fossa. If MRI negative consider drug intoxication, B12 deficiency, syphilis, consider LP.

Opsoclonus and Saccadomania
Rapid, involuntary, continuous, repetitive, conjugate saccadic eye movements in all directions (persists with sleep). Occurs when cerebellar input to the paramedial pontine reticular formation is entirely disrupted. When seen in children, occult neuroblastoma should be ruled out by imaging studies of the abdomen and thorax. Can be due to carcinoma in adults (usually oat cell carcinoma of the lung) and may be responsive to thiamine. May be part of post infectious syndrome with ataxia, extremity myoclonus and tremulousness in which case it may respond to corticosteroid therapy. Associated with hyperosmotic nonketotic coma, drug toxicity, mesencephalic glioma, ischemic and hemorrhagic stroke, hydrocephalus and trauma.

Palinopsia: The persistence or recurrence of visual images after the stimulus has been removed. Most often associated with unilateral, acute, enlarging, or recovering temporal-parietal-occipital junction lesions. They may be a part of a focal seizure.

Parinaud Syndrome or Dorsal Midbrain Syndrome (also known as the sylvian aqueduct syndrome, pretectal syndrome, and Koerber-Salus-Elschning syndrome)
Common
- Loss of saccadic upgaze (Bells’ phenomenon may be spared)
- Downward gaze preference or tonic downward deviation ("setting sun sign")
- Primary position downbeat nystagmus
- Pupillary mydriasis (4-5 mm) with light-near dissociation

Please email suggestions & corrections to: tcooper@stanford.edu
- Convergence-retraction nystagmus (use OKN tape downward)
- Papilledema
Less Common
- Skew Deviation
- Fourth cranial nerve palsy
- Lid retraction (neurologic lid retraction is Collier's Sign)
- Loss of upgaze pursuit
- Spontaneous convergence-retraction movements elicited by upgaze movements
- Loss of downward saccades
  Infrequent
- Pendular hallucinosis & Precocious puberty

**Parkinson's Disease**: early conjugate saccadic movements become hypometric smooth pursuit movements become saccadic apraxia of lid opening masked facies involuntary laughing drooling difficulty swallowing degeneration of the extrapiramidal system

**Pendular Hallucinosis**: Vivid-colored imagery that the patient does not perceive as being threatening

**POEMS Syndrome**: Polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (POEMS) syndrome is a rare multisystemic disease that occurs in the setting of a plasma cell dyscrasia. The pathophysiologic link between the constellation of symptoms and the underlying disease is not well understood, but the link may be related to changes in the levels of a cytokine or a growth factor

**Progressive Supranuclear Palsy**: A degenerative disease of the CNS characterized by: initially affecting voluntary downgaze & axial rigidity, later affecting upgaze, horizontal gaze; then loss of pursuit. inability to voluntary open lids (apraxia of lid opening), misalignment of eyes with diplopia, loss of facial expression, dementia, insomnia; late loss of caloric EOM response; usually in sixth and seventh decade; downhill course 8-10 years to death.

**Pseudo-Foster-Kennedy Syndrome**: Disc pallor in one eye and disc swelling (not papilledema) in the other eye, due to consecutive ischemic optic neuropathy.

**Pulfrich Stereo Illusion**: In unilateral or markedly asymmetric optic nerve lesions a pendulum oscillating in a plane is incorrectly perceived as describing an ellipse (counterclockwise rotation with right optic nerve lesions; clockwise with left optic nerve lesions).

**Recessive Optic Neuropathy**: congenital, stable vision from 20/200 to HM, nystagmus, achromatopsia, disc pallor, normal arterioles, and normal ERG.

Please email suggestions & corrections to: tcooper@stanford.edu
Skew Deviation: a vertical misalignment resulting from supranuclear derangements. It occurs whenever peripheral or central lesions cause an imbalance of graviceptive brainstem pathways. The lesion can be in the brainstem or cerebellum.

Superior Oblique Myokymia: A monocular tremor caused by spontaneous firing of superior oblique muscle fibers. Symptoms include: tilting of image (episodic intorsion), oscillopsia, shimmering, awareness of eye movement. Episode duration is seconds. Rarely may be caused by intracranial tumor (midbrain) and be the presenting and only symptom (get MRI if atypical or any additional signs or symptoms of neurologic conditions). Natural history - spontaneous remissions and relapses. Treatment: Carbamazepine (variable results), intra-sheath SO tenotomy or IO weakening procedures (may result in diplopia).

Tip of the basilar Syndrome: is caused by a disturbance in circulation at the top of the basilar artery, most often an embolus. Lesions may be widespread in the temporal and occipital lobes, thalamus, midbrain, pons and cerebellum, all supplied by arteries originating around the top of the basilar artery. Infarction of rostral brainstem and cerebral hemispheric regions fed by the distal basilar artery causes a clinically recognizable syndrome characterized by visual, oculomotor, and behavioral abnormalities, often without significant motor dysfunction. Rostral brainstem infarction produces oculomotor and pupillary signs that are identical to those in thalamic hemorrhage. Somnolence, vivid hallucinations and dreamlike behavior may also accompany rostral brainstem infarction. Temporal and occipital infarctions are frequently accompanied by hemianopia with distinctive characteristics, fragments of the Balint syndrome, amnestic dysfunction, and agitated behavior.

Tolosa-Hunt Syndrome: Painful ophthalmoplegia from inflammation of the cavernous sinus or superior orbital fissures.

Ungaze Deficits: Isolated upgaze paralysis is associated with lesions of the dorsolateral region of the rostral inferior MLF and the contiguous posterior commissure.

Uhthoff's Phenomenon: Temporary worsening of visual symptoms (blurring, diplopia, nystagmus) in patients with MS with exercise. It is due to increased core body temperature (as little as 0.1 degree C). Hot baths may also exacerbate these symptoms. Walking upstairs or across the street may be enough to bring on symptoms.

Vertical Gaze Spasms: Oculogyric crises consists of spasmodic involuntary upward deviation of the eyes and lids associated with neck hyperextenseion. It may last from minutes to hours and is seen in phenothiazine therapy, postinfectious Parkinson's disease, trauma or neurosyphilis.

Wallenberg Syndrome: is a neurological disorder characterized by swallowing difficulties and hoarseness which results from paralysis of a portion of the vocal cord. The disorder is generally caused by a blockage in a vertebral or cerebellar artery. Symptoms may include dizziness, a loss of pain or temperature sensitivity, some paralysis of the facial muscles, and a loss of taste. Individuals with the disorder frequently report an unsettling tilt of their environment, which affects their balance.

Please email suggestions & corrections to: tcooper@stanford.edu
Weber Syndrome: A lesion of the pyramidal tract producing ipsilateral oculomotor paresis and contralateral hemiplegia.

Emergency Room Consultations

Common neuro-ophthalmology emergency consultation reasons

- Anisocoria
- Diplopia
- Loss of vision or field
- Swollen or elevated discs
- Ptosis
- Traumatic optic neuropathy

Remember to **urgently** rule-out

- Decreased Vision
  - Central Retinal Artery Occlusion
  - Giant Cell Arteritis
  - Giant Aneurysm
  - Pituitary apoplexy
- Diplopia, or Ptosis, or Anisocoria
- Aneurysm
- Stroke
- Swollen/Elevated Discs
  - Congenital anomaly of discs
  - Increased intracranial pressure
- Homonymous Hemianopia
- Stroke
- Headache &/or neck pain
  - Scalp tenderness
  - Giant Cell Arteritis
  - Ipsilateral ptosis
  - Carotid dissection
  - 3rd cranial nerve palsy
  - Aneurysm

Optic Neuropathy

Clinical Features

- Decreased VA
- Decreased color vision
- VF Defect
- Ipsilateral RAPD in unilateral or asymmetric bilateral
- Light-near dissociation of pupils in bilateral and symmetric
- Optic disc normal in Optic Neuritis
  - edema or atrophy in others

Differential Diagnosis

Common

- Typical Optic Neuritis (under age 40)

Please email suggestions & corrections to:

```
tcooper@stanford.edu
```
Anterior Ischemic Optic Neuropathy (over age 50)
Uncommon
Optic Disc Edema with Macular Star
Compressive Optic Neuropathy
Infiltrative Optic Neuropathy
Inflammatory Optic Neuropathy
Traumatic Optic Neuropathy
Toxic Optic Neuropathy
Nutritional Optic Neuropathy
Radiation Optic Neuropathy
Hereditary Optic Neuropathy
Atypical or Unexplained Optic Neuropathy

Anterior Ischemic Optic Neuropathy Vs Optic Neuritis (ON)
While there tend to be differences in the appearance of the optic discs in AION and ON, the appearance of the optic disc is not specific and does not reliably differentiate reliably among the causes of optic neuropathy. Only 11% of cases with known history of papillitis or ION had sufficient clues to identify previous disc swelling. Trobe JD, Glaser JS, Cassady JC. Optic atrophy. Differential diagnosis by fundus observation alone. Arch Ophthalmol. 1980 Jun;98(6):1040-5.

<table>
<thead>
<tr>
<th>Comparison of Cases of AION &amp; ON</th>
<th>Altitudinal disc swelling</th>
<th>Hemorrhages</th>
<th>Color</th>
<th>Arterial Attenuation</th>
<th>Altitudinal Edema</th>
<th>Disc Hemorrhage</th>
<th>Pale disc plus hemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>AION</td>
<td>3 times more common</td>
<td>Most have</td>
<td>35% pale swelling</td>
<td>90%</td>
<td>82%</td>
<td>81%</td>
<td>100%</td>
</tr>
<tr>
<td>Optic neuritis</td>
<td>Most do not have</td>
<td>Normal or Hyperemic</td>
<td>10%</td>
<td>18%</td>
<td>19%</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>


Band or “bow tie” atrophy occurs in the eye contralateral to involved optic tract and is associated with lesions of the chiasm (unilateral or bilateral).

The degree of vision loss or type of unilateral visual field defect does not differentiate among causes of optic neuropathy.

Critical issues in evaluating a new case of Optic Neuropathy: **Rule-out at once**
1. Giant Cell Arteritis

Please email suggestions & corrections to: 
tcooper@stanford.edu
Optic Neuropathy Workup

Age 40 or less
- Typical Optic Neuritis Findings - ON workup

Age over 40
- Typical AION Findings - AION workup

Atypical Findings – consider the following diagnoses
- Disc edema with macular star – workup
- Atypical Optic Neuritis – workup
- Inflammatory or Infiltrative Optic Neuropathy workup
- Traumatic Optic Neuropathy workup
- Toxic or Nutritional Optic Neuropathy workup
- Radiation Optic Neuropathy - workup
- Hereditary Optic Neuropathy workup
- Atypical or Unexplained Optic Neuropathy workup

Typical Optic Neuritis (ON) Features - ONTT
- Acute usually unilateral vision loss
  - 20/20 to NLP
  - Variable VF defects
    - diffuse 48%
    - altitudinal or arcuate 20%
    - central/ceccocentral 8%
  - RAPD (unilateral or asymmetric bilateral cases)
  - Periocular pain especially with eye movement 92%
  - Disc normal 65%, swollen 35%
  - Less than age 40 (occurs at all ages)
  - Vision improves
    - 90% within weeks
    - May improve for 1 year
  - Residual defects common – contrast, color, stereo, brightness, acuity, fields

Typical ON Workup
- Rule out atypical features
  - If present Atypical ON Workup
- MRI - ONTT
  - Brain - MS evaluation protocol
  - Optic nerves – with fat suppression
- No Lumbar Puncture - ONTT
- Serology
  - Lyme disease – if endemic area exposure

Atypical ON Features
- Bilateral simultaneous onset in adult
- Lack of pain
- Severe headache

Please email suggestions & corrections to: tcooper@stanford.edu
Ocular findings
  Anterior uveitis
  Lipid maculopathy
  Disc
    Severe edema with marked hemorrhages
    Pale edema
  Cotton wool spots
  Retinal arteriolar narrowing
  Retinopathy
  Vitreous cells
Lack of visual improvement after 30 days
Age greater than 50
Preexisting systemic conditions
  Inflammatory
  Infectious
  Hypertension
  Diabetes
  Systemic vasculopathy
Exquisitely steroid sensitive or dependent optic neuropathy

Atypical ON Workup
MRI
LP
Syphilis serology
Bartonella henselae serology
HIV serology
Antinuclear antibody
Rheumatoid arthritis serology
Lyme disease serology
Galium scan for Sarcoidosis

Childhood ON Features
  Bilateral more often
  Papillitis more often
  VA Worse
  MS less often associated
Infectious etiology more common

Devic's Disease Features  Neuromyelitis Optica
  Optic neuritis and transverse myelitis in children
  Prodrome common – fever, headache, sore throat
Vision loss
  May proceed or follow paraplegia
  Usually bilateral and severe
  Central scotoma most common VF Defect

Please email suggestions & corrections to:
  tcooper@stanford.edu
Disc swelling common – mild
Occasional severe swelling, dilated veins and exudates
May have slightly narrowed blood vessels
Myelitis and optic neuritis may be separated in time and recurrent.
The presence of NMO-IgG predicts relapse in patients with longitudinally extensive idiopathic transverse myelitis.

At disease onset, the combination of a brain MRI that is either normal or does not meet radiologic criteria for MS (ie, nonspecific white matter lesions) together with the extensive spinal cord lesion is the most powerful diagnostic combination, with sensitivity of 91% and specificity of 97%. The presence of T2-weighted brain MRI lesions that meet imaging criteria for MS occurs in less than 10% of patients with neuromyelitis optica. Therefore, brain MRI results are best evaluated in the context of other criteria. NMO-IgG is specific for neuromyelitis optica and related conditions but is consistently negative in patients with clinically confirmed MS.


Devic’s Disease Features Vs MS
Younger patients
More common in African Americans & Asians
No gender difference
Rare familial history
MRI of brain normal in 90% NMO.
IgG positive in patients with optic neuritis and transverse myelitis NMO about 40% of the time.
Pathology different than MS
  Cerebellum spared
  Tissue affected has cavity formation
  Gliosis is minimal
  Cerebral subcortex arcuate fibers relatively spared

Visual Evoked Potentials in ON: VEPs do not alter the diagnostic or treatment plan of clinically diagnosed ON. They can be useful in identifying a second site when evaluating a patient for MS who does not have clear history or findings of ON. They often remain abnormal after an episode of ON, even when visual symptoms have returned to normal.

Optic Neuritis Treatment Trial (ONTT) Findings
1. Corticosteroids improve vision at 3 weeks
2. Oral prednisone did not improve visual outcome and was associated with increased rate of new ON attacks.
3. IV followed by oral corticosteroids reduced the rate of development of clinical definite MS during first 2 years but not at 3 years.
4. MR findings were of prognostic significance for MS.
5. Treatment was well tolerated.
6. VA at 5 years 20/25 or better = 87%, 202/25-20/40 = 7%, 20/200 or worse = 3%
7. Risk of CDMS at 5 years = 30%
8. Risk of CDMS at 5 years with MRI brain lesions – 0 lesions = 16%, 3 or more lesions = 51%

Please email suggestions & corrections to: tcooper@stanford.edu
Risk of MS with ON as Initial Episode
Increases with
  Number of MRI lesions
  Prior nonspecific neurologic symptoms
  Increased CPF oligoclonal bands
  Increased CSF IgG
  HLA-DR2 & HLA-B7

CHAMPS Findings
1. Interferon-beta-1a had a relative reduction in volume of brain lesions, fewer new lesions or enlarging lesions and fewer gadolinium-enhancing lesions at 18 months.
2. Recommended Interferon-beta-1a at the time of first demyelinating event in patients with MRI brain lesions that indicate a high risk of CDMS.

Optic Disc Edema with Macular Star (ODEMS) Features
  Bilateral 3-35%
  Often painless
  May have retrobulbar pain or pain on eye movement
  Headache
  50% follow nonspecific viral illness
  Acute loss of vision 20/20 to LP
  Dyschromatopsia
  VF shows any type of defect
  RAPD if unilateral
  Disc edema may be severe
  Macular star takes 1 to 2 weeks to develop
  90% Vitreous cells

ODEMS Workup
Focus on exposure history and findings.
Exposure history
  Syphilis
  Lyme disease
  TB
  Cat-scratch fever
Systemic findings
  Typhus
  Viral illness
  Fungi
  TB
  Leptospira
Eye findings
  Toxoplasmosis scar

Nonarteritic Anterior Ischemic Optic Neuropathy
Typical Nonarteritic-AION Features
  Acute unilateral visual acuity loss

Please email suggestions & corrections to: tcooper@stanford.edu
May be static, improve or worsen slightly
Rare to be preceded by amaurosis fugax
VF defects of optic neuropathy
Pain 10%
Greater than age 50
RAPD
Small cup in fellow eye <0.2
Disc edema with or without hemorrhage
Followed by disc pallor
Often associated with vasculopathic factors
(hypertension, diabetes, smoking ischemic heart disease, hypercholesterolemia)

Atypical Nonarteritic-AION
Under age 40
Think of: diabetes, migraine, severe hypertension, hypercoagulopathy, preeclampsia, oral birth control meds,.
Bilateral
VF defect non consistent with optic neuropathy (bitemporal or homonymous hemianopia)
Lack of disc edema
Lack of RAPD
Large C/D
End-stage disc appearance of cupped disc (2% in nonarteritic-AION Vs 92% in arteritic-AION)
Lack of vasculopathic features
Premonitory transient vision loss
Progression after 4 weeks
Recurrent episodes in same eye
Anterior or posterior segment inflammation

Typical Nonarteritic-AION Workup
Emergently rule-out Giant Cell Arteritis
Sed Rate & CRP
Neuro-imaging is not required unless ipsilateral head or neck pain is present.
If present, do MRA to rule out carotid artery dissection.
Carotid doppler/ultrasound is not required unless other signs (ocular ischemia, retinal emboli, TIA or persistent neurologic deficits)
Evaluation for hypercoagulopathy is not required unless other indications are present.

Atypical Nonarteritic-AION Workup
Follow optic neuropathy workup
Evaluation of hypercoagulable risk factors

Typical Nonarteritic-AION Treatment
Medical management of vasculopathic conditions
Offer aspirin to prevent other cardiovascular events; it may help prevent second NAION attacks.

Please email suggestions & corrections to:
tcooper@stanford.edu
The Optic Neuropathy Decompression Trial found that optic nerve sheath fenestration was not effective and may be harmful in nonarteritic-AION.

**Arteritic-Anterior Ischemic Optic Neuropathy - Giant Cell Arteritis (GCA)**

**Typical Features of Arteritic-AION**
- Age greater than 50 (median 69-75 years, 90%>60 years)
- Race: common in Caucasians, rare in Asians and Blacks
- Acute, often severe, vision loss (7-60%), often preceded amaurosis fugax
- More often bilateral than Nonarteritic-AION
- Disc - Initial pale swelling, followed by optic atrophy in 6-8 weeks
  - End stage pallor, cupping and loss of neuroretinal rim

**Other Ocular Manifestations of GCA**
- Eye pain
- Amaurosis fugax
- Diplopia (ocular motor ischemia)
- Visual hallucinations
- Irreversible visual loss (anterior ischemic optic neuropathy, central retinal artery occlusion, ischemic choroidopathy)

**Constitutional signs & symptoms**
- Headache (4-100%)
- Scalp or temporal artery tenderness (28-91%)
- Nodular or nonpulsating temporal arteries
- Weight loss (16-76%)
- Jaw claudication (4-67%)
- Anorexia (14-69%)
- Fever, and night sweats
- Proximal muscle aches or weakness (28-86%) or joint pain
- Morning stiffness of > 30 min.
- Polymyalgia rheumatica
- Fatigue and malaise (12-97%)
- Leg claudication (2-43%)
- Depression
- Elevated ESR and CRP

**Temporal Artery Biopsy – GCA positive**

**American College of Rheumatology**

1990 Criteria for the Classification of Giant Cell (Temporal) Arteritis

*For purposes of classification, a patient shall be said to have giant cell (temporal) arteritis if at least 3 of these 5 criteria are present. The presence of any 3 or more criteria yields a sensitivity of 93.5% and a specificity of 91.2%.*


1. Age at disease onset >=50 years

Please email suggestions & corrections to: tcooper@stanford.edu
Development of symptoms or findings beginning at age 50 or older

2. New headache
   New onset of or new type of localized pain in the head

3. Temporal artery abnormality
   Temporal artery tenderness to palpation or decreased pulsation, unrelated to arteriosclerosis of cervical arteries

4. Elevated erythrocyte sedimentation rate
   Erythrocyte sedimentation rate >=50 mm/hour by the Westergren method

5. Abnormal artery biopsy
   Biopsy specimen with artery showing vasculitis characterized by a predominance of mononuclear cell infiltration or granulomatous inflammation, usually with multinucleated giant cells

This set of criteria were established to sort out patients with known vasculitis in research settings and has limitations for use in clinical practice, but is widely used. Limitations of the 1990 American College of Rheumatology classification criteria in the diagnosis of vasculitis. Rao JK, Allen NB, Pincus T, Ann Intern Med. 1998;129(5):345-52: “Conclusion: The 1990 ACR classification criteria function poorly in the diagnosis of specific vasculitides.”

ESR and CPR

RESULTS: In this study (biopsy proven GCA), the ESR had a sensitivity of 76% to 86%, depending on which of 2 formulas were used, whereas an elevated CRP had a sensitivity of 97.5%. The sensitivity of the ESR and CRP together was 99%. Only 1 of the 119 patients (0.8%) presented with a normal ESR and normal CRP (double false negative); 2 patients (1.7%) had a normal CRP despite an elevated ESR according to both formulas.

Findings that increase the likelihood of a positive biopsy of the superficial temporal artery are vision loss, diplopia, jaw claudication, constitutional symptoms, and beading, prominence and tenderness of the artery.

Associated findings in GCA: 27% aortic aneurysm/dissection, 15% cervical or subclavian stenosis.


Treatment for GCA
Start treatment STAT
Do biopsy within 1 week of starting steroids
   Because long term corticosteroids are needed definitive diagnosis is needed.
   Otherwise there may be a temptation to reduce or stop corticosteroids too soon.
ESR normal values - men divide age by 2, women divide age + 10 by 2

Please email suggestions & corrections to: tcooper@stanford.edu
In initial 48 hours of symptoms IV Methylprednisolone 250 mg q6h for 3-5 days
Followed by prednisone 1.5mg/kg for 2 weeks QD (not QOD)
Taper dose 10%/week if ESR and symptoms normalize
Control ESR and symptoms for 6 months with prednisone
Biopsy (2 cm of temporal artery) if ESR or CPR is elevated or symptoms of polymyalgia or giant cell arteritis are present
   Positive biopsy = Giant Cell Arteritis
   Negative biopsy = biopsy other side (5% of GCA involve only one temporal artery)
   Consider using frozen sections of first biopsy so that if negative, biopsy of other side can proceed at same sitting
   Second negative biopsy = abandon diagnosis of GCA unless clinical features are persuasive (biopsy negative GCA-ION), look for other causes of elevated ESR

**Inflammatory or Infiltrative Optic Neuropathy workup**
High resolution MRI
Rule-out
   Neoplastic disease
      Leukemia, lymphoma, neoplasm, infiltrative orbitopathy in POEMS syndrome, reactive lymphocytosis with pseudolymphoma from phenytoin
   Paraneoplastic disease
   Idiopathic hypertrophic cranial pachymeningitis
Infections
   Cryptococcal meningitis, aspergillus, mucormycosis, cysticercosis, Lyme disease, TB, toxplasmosis, syphilis, cat-scratch disease, HIV/AIDS
Inflammations
   Churg-Strauss, contiguous sinus disease, Bechet’s disease, sarcoidosis, Wegner’s granulomatosis, SLE, Sjogren’s syndrome, relapsing polychondritis, polyarteritis nodosa, inflammatory bowel disease, granulomatous hypophysitis, orbital pseudotumor, sclerosing orbital inflammation

**Traumatic Optic Neuropathy workup**
High resolution MRI

**Toxic and or Nutritional Optic Neuropathy workup**
Confirm that a bilateral painless progressive bilateral optic neuropathy is present.
Confirm that patient has a reasonable diet.
Rule out high intake of alcohol and heavy smoking.
Rule out iatrogenic malabsorption (post gastro-intestinal bypass or major intestinal procedures even 30 years ago)
Carefully question patient, family and coworkers about exposure to toxins and medicines.
Review all medicines patient is taking on PubMed and MedIndex for visual side effects especially optic neuropathy.
High resolution MRI

Please email suggestions & corrections to:
tcooper@stanford.edu
CBC with differential
Serum Vitamin B12, Folate
  B1 (Thiamine), B6, Niacin, and Riboflavin deficiencies have been reported to cause nutritional optic neuropathy.
Erythrocyte Folate
Syphilis serology (RPR, FTA)
Urine heavy metal screen (mercury, lead, arsenic)
Leber’s hereditary optic neuropathy mutational analysis

Radiation Optic Neuropathy
Features
  75% have exposure of at least 5000 cGy.
  Latency period 1-144 months, median 13 months
  VF defects of optic nerve and chiasmal locations.
  There is no proven therapy, prognosis is poor, NLP 45%, 20/200 or worse 85%

Workup
  Rule out radiation exposure to optic nerves.
  High resolution MRI may show enhancement of optic nerves and chiasm that resolves in several months.
  Rule out recurrence of tumor and complications of primary tumor and its treatment, ischemic optic neuropathy, increased intracranial pressure, venous sinus thrombosis, secondary new tumors and metastases.

Hereditary Optic Neuropathy workup
  Seek hereditary history – may be isolated, dominant, recessive or mitochondrial.
    Leber’s hereditary optic neuropathy – mitochondrial
    Kjer Optic neuropathy – dominant
  There are numerous neurologic conditions associated with optic neuropathies.

Atypical or Unexplained Optic Neuropathy workup
First Line testing
  MRI of optic nerves
  ESR
  CBC with differential
  Serum RPR, VDRL, ANA, ACE, ANCA
  Chest X-ray
  LP with opening pressure and CSF analysis

Second line testing (Consult with rheumatology)
  Gallium scan - if Sarcoidosis is suspected
  PPD
  Anti-double stranded DNA, complement levels if SLE or collagen vascular disease suspected.
  Seek hereditary history – may be isolated, dominant, recessive or mitochondrial.
    Leber’s hereditary optic neuropathy – mitochondrial
    Kjer Optic neuropathy – dominant
  There are numerous neurologic conditions associated with optic neuropathies.

Please email suggestions & corrections to:
  tcooper@stanford.edu
Leber’s hereditary optic neuropathy mutational analysis
Heavy metal screen
Serum vitamin B12 and Folate levels
Lyme disease titer if exposure to endemic area
Paraneoplastic antibody profile e.g. autoantibodies for collapsing response mediated protein CRMP-5 (lung cancer especially small-cell type or thymoma associated optic neuropathy)
Consider more specific serologic tests for bartonella, toxoplasmosis, toxocara, etc.