Description:

‘double vision’ with binocular viewing. Aetiologies can include neurological, neuromuscular and orbital conditions. Monocular diplopia is generally due to ocular pathology and is not discussed in this document.

Red Flags:

- Rule out Giant Cell Arteritis (GCA): cranial nerve (CN) palsy or skew deviation in patients with relevant risk factors
- In CN III palsy:
  - Dilated pupil: compressive lesion more likely
  - Cannot rule out compressive lesion with normal pupils, especially if palsy is incomplete.
- Microvascular cause unlikely if age < 50 years old
- Multiple cranial nerve palsies and/or associated neurologic dysfunction will warrant imaging
- Orbital/muscular causes of diplopia (e.g., thyroid eye disease, myasthenia gravis) can be confused with CN III, IV, VI palsy
Approach to diplopia

Diplopia

Monocular

Ocular
- Refractive
- Corneal disease
- Lens (decentration/cataract)
- Retinal disease

Binocular

Orbital
- Thyroid eye disease
- Trauma
- Myositis
- Orbital swelling (pseudotumour, mass, lymphoma)

Neuromuscular
- Myasthenia gravis
- Lambert-Eaton syndrome
- Myotonic dystrophy

Neurological
- CN III palsy
- CN IV palsy
- CN VI palsy

Other
- Decompensated strabismus
- Heavy eye syndrome
- Sagging eye syndrome

- Demyelination
- Skew deviation
- Supranuclear ophthalmoplegia
- Internuclear ophthalmoplegia

- Vascular e.g. GCA, aneurysm, micro vascular
<table>
<thead>
<tr>
<th>Differential diagnosis</th>
<th>Symptoms</th>
<th>Signs/distinguishing features</th>
<th>ED investigations &amp; treatment</th>
</tr>
</thead>
</table>
| **CN III** | • Diplopia in all positions of gaze  
• Ptosis | • Paresis  
• Mydriasis  
• Exotropia, hypotropia (eye is “down and out”) | • If pupil involved refer immediately to St Vincent’s Emergency Department for same day CT angiogram  
• Consider investigations for GCA |
| **CN IV** | • Binocular vertical or torsional diplopia | • Head tilt to contralateral side  
• Positive Bielschowsky 3-step test | • If no vascular risk factors or <50 years old, MRI brain as outpatient.  
• Consider investigations for GCA |
| **CN VI** | • Diplopia worse on looking towards the affected side | • Impaired abduction of eye  
• Binocular horizontal diplopia, worse in direction of paretic muscle  
• Deviation distance >near | • If no vascular risk factors or <50 years old, MRI brain within 1-2 days  
• Consider investigations for GCA |
| **Thyroid eye disease (TED)** | • History of thyroid dysfunction  
• Symptoms of thyrotoxicosis | • Exophthalmos/proptosis  
• Upper lid retraction and lid lag  
• No pupil involvement | • Thyroid function tests: beware thyrotoxicosis  
• If presentation atypical or optic nerve dysfunction CT orbits  
• Perform ECG if thyrotoxic  
• Oculoplastics opinion |
| **Myasthenia gravis** | • Severity of symptoms variable | • Blepharoptosis  
• Orbicularis weakness, Cogan’s lid twitch, fatiguability  
• Positive ice test (improvement of ptosis in primary gaze on application of ice pack for 5 minutes)  
• No pupil involvement | • Acetylcholine receptor antibody (anti-AChR), Antibodies to tyrosine kinase receptor (MuSK)  
• Neurology/neuro-ophthalmology opinion  
• Warn patient to seek immediate medical attention if experiencing difficulty breathing/swallowing |
| **Skew deviation**  
- Central v peripheral skew deviation | • Can produce vertical diplopia | • Comitant or incomitant  
• Torsional abnormalities  
• Signs and symptoms of brain stem and/or cerebellar disease (eg. vertigo, oscillopsia, limb neurology)  
• Alternating skew on lateral gaze (ipsilateral hypertropia on looking to side of hypertropia that switches when gaze directed to opposite side – becomes left hypertropia on left gaze)  
• Peripheral skew hypertropia may improve by 50% on supine posturing (Agnes Wong test) | • MRI brain  
• Discuss with neurology team at St Vincent’s regarding posterior circulation imaging |

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<tbody>
<tr>
<td><strong>Decompensated strabismus</strong></td>
<td>• Diplopia worse when fatigued</td>
<td>• Strabismus/abnormal head position in old photographs or on examination</td>
<td>• Non-urgent Ocular Motility opinion</td>
</tr>
<tr>
<td><strong>Heavy Eye Syndrome</strong></td>
<td>• Binocular diplopia</td>
<td>• High myopes (&gt;5 dioptres)</td>
<td>• Nil required in ED</td>
</tr>
<tr>
<td></td>
<td>• Worse at distance</td>
<td>• Esotropia (comitant at distance)</td>
<td>• Outpatient orbital MRI</td>
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<tr>
<td></td>
<td>• Horizontal, vertical and/or cyclovertical diplopia</td>
<td>• Limited abduction</td>
<td></td>
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<td></td>
<td></td>
<td>• Hypotropia</td>
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<td>• Limited elevation</td>
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<tr>
<td><strong>Sagging Eye Syndrome</strong></td>
<td>• Binocular diplopia</td>
<td>• Age related / involutional changes in the periorbital skin, fat</td>
<td>• Nil required in ED</td>
</tr>
<tr>
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<td>• Worse at distance</td>
<td>• Esotropia (comitant at distance)</td>
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How to Assess:

History:

- Diplopia: horizontal/vertical/torsional, onset, duration, constant/intermittent/variable
- Associated
  - Ocular symptoms: ptosis, dilated pupil
  - Systemic symptoms: GCA, TED or thyroid dysfunction, inflammatory disease
  - Neurologic symptoms:
    ▪ STROKE: Upper or lower limb stroke related symptoms,
    ▪ MYASTHENIA: weakness, fatiguability, variability
    ▪ POSTERIOR CIRCULATION: vertigo, dysarthria, dysphagia, ataxia
    ▪ SPINAL SYMPTOMS: urinary/ bowel incontinence
  - Vascular risk factors: hypertension, diabetes, dyslipidaemia, family history, smoking, alcohol consumption, weight gain
- Trauma
- Malignancy
- Radiation: orbital or brain
- Previous eye muscle surgery as a child/ adult
- History of amblyopia, patching, and/or wearing glasses as a child

Examination:

Focus on:

<table>
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<th>Neurology</th>
<th>General neurologic exam:</th>
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<tbody>
<tr>
<td></td>
<td>Upper limbs, lower limbs (weakness, numbness, ataxia)</td>
</tr>
<tr>
<td></td>
<td>Cranial nerves to exclude multiple nerve involvement (e.g., in cavernous sinus lesion)</td>
</tr>
<tr>
<td>Scalp</td>
<td>Temporal artery palpation for GCA – point tenderness over superficial temporal arteries, decreased pulse</td>
</tr>
<tr>
<td>External eye</td>
<td>Ptosis associated with CN III palsy/myasthenia gravis</td>
</tr>
<tr>
<td></td>
<td>Proptosis/chemosis suggestive of orbital disease</td>
</tr>
<tr>
<td></td>
<td>Upper lid lag, retraction suggestive of TED</td>
</tr>
<tr>
<td>Pupils</td>
<td>Relative afferent pupillary defect</td>
</tr>
<tr>
<td></td>
<td>Anisocoria (pupil dilation in CN III palsy): check pupil size in light and dark</td>
</tr>
<tr>
<td>Extraocular motility</td>
<td>Abnormal head position</td>
</tr>
<tr>
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<td>Cover test – distance and near</td>
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<tr>
<td></td>
<td>Versions and ductions – assess for comitance and deviation in different positions of gaze</td>
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<td>Smooth pursuit: with both eyes open, and covering each eye</td>
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</tbody>
</table>
Investigations:

Direct investigations based on clinical findings and may be discussed with Neuro-ophthalmology on call

Isolated CN Palsy (III, IV, VI)

Neuroimaging on presentation is generally not required for isolated CN III, IV, VI palsies in patients with one or more microvascular risk factors and no red flags. It may be required at follow-up if the palsy has not resolved after 3 months. For all other patients:

<table>
<thead>
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<th>Palsy</th>
<th>Neuroimaging</th>
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<tbody>
<tr>
<td>CN III</td>
<td>CT+CTA brain and cavernous sinus or MRI+MRA brain and cavernous sinus on the same day.</td>
</tr>
<tr>
<td>CN IV</td>
<td>MRI Brain and orbits – within 2 weeks as outpatient.</td>
</tr>
<tr>
<td>CN VI</td>
<td>MRI brain within 2 weeks. If there are other neurological features, then immediate CTB</td>
</tr>
</tbody>
</table>

*Paediatric patients need prompt neuroimaging and discussion with the ophthalmology team at The Royal Children’s Hospital

*Pregnant patients: discuss with radiology re: avoiding ionizing radiation in neuroimaging and liaising with foetal maternal physician.

Laboratory investigations

- GCA suspected: full blood examination (FBE), C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR).
- Myasthenia gravis: anti-AChR (Acetyl Choline Receptor) Antibody, Anti-MuSK (Muscle Specific Kinase) Antibody
  - Note: 50% of patients with ocular myasthenia will be anti-AChR antibody negative.
  - 10-15% of generalised myasthenia will be anti-AChR antibody negative
  - Anti-MuSK antibodies are detected in a variable percentage of generalised myasthenia who are anti-AChR antibody negative
  - False positives for anti-AChR antibody can occur in patients with immune liver disease, thymoma without myasthenia gravis, Lambert-Eaton syndrome (associated with small cell lung cancer)
- Orbital disease
  - Thyroid eye disease: thyroid function tests
  - Orbital infection/inflammation: FBE, inflammatory markers
Acute Management: based on clinical diagnosis

- If neuroimaging reveals cerebrovascular malformation/aneurysm, urgent consultation and transfer to St Vincent’s Hospital neurosurgery is required.
- Isolated CN III, IV, VI
  - Microvascular cause suspected: symptoms are usually self-resolving within 3 months but can take up to 12 months to completely resolve. Management should be aimed at managing underlying microvascular risk factors. Follow up Neuro-ophthalmology Clinic in 8 – 12 weeks. For CN IV palsies patients should be asked to bring old photographs as this may be a clue to decompensated fourth nerve palsy.
- Consider:
  - Consult Neuro-ophthalmology for:
    - GCA: see GCA CPG
    - Myasthenia gravis
      - Refer to St Vincent’s Hospital Emergency Department if any swallowing difficulties
    - Skew deviation: immediate symptomatic management of diplopia with occlusion of affected eye (patching, tape over spectacle lens on affected eye. Stick on Fresnel prisms may be helpful for small stable deviations (contact orthoptics)
  - Consult Oculoplastics for:
    - TED
    - Orbital inflammatory disease
  - Consult oculomotility clinic if: MRI is negative and there is an isolated microvascular cranial nerve palsy, sagging eyes, heavy eyes or decompensated phorias

Follow up:

Interval and location based on diagnosis and severity of pathology.

Discharge instructions:

- Attend ED if symptoms worsen or if experiencing any new symptoms.
- No driving until review or diplopia resolved.
- See GP/physician to assess and treat vascular risk factors if indicated
Evidence Table

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Title</th>
<th>Source</th>
<th>Level of Evidence (I – VII)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trobe JD.</td>
<td>Third nerve palsy and the pupil: footnotes to the rule</td>
<td>Archives of Ophthalmology. 1988;106(5):601-2</td>
<td>VII</td>
</tr>
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</table>

The Hierarchy of Evidence

The Hierarchy of evidence is based on summaries from the National Health and Medical Research Council (2009), the Oxford Centre for Evidence-based Medicine Levels of Evidence (2011) and Melynk and Fineout-Overholt (2011).

I) Evidence obtained from a systematic review of all relevant randomised control trials.
II) Evidence obtained from at least one well designed randomised control trial.
III) Evidence obtained from well-designed controlled trials without randomisation.
IV) Evidence obtained from well-designed cohort studies, case control studies, interrupted time series with a control group, historically controlled studies, interrupted time series without a control group or with case series.
V) Evidence obtained from systematic reviews of descriptive and qualitative studies.
VI) Evidence obtained from single descriptive and qualitative studies.
VII) Expert opinion from clinician, authorities and/or reports of expert committees or based on physiology.
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<td>Director, Emergency Department</td>
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<tr>
<td><strong>Contributor(s):</strong></td>
<td>Clinical Practice Guideline Working Group Head of Neuro-ophthalmology Unit</td>
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