CLINICAL PRACTICE GUIDELINE: Emergency Department

Binocular Diplopia in Adults

Disclaimer: This Clinical Practice Guideline ('CPG') was written for use in The Royal Victorian Eye and Ear Hospital Emergency Department. It should be used under the guidance of an Ophthalmology or ENT registrar. If clinical advice is required, please contact the Eye and Ear Admitting Officer for assistance: EYE: +61 3 9929 8033; ENT: +61 3 9929 8032. Links to internal Eye and Ear documents cannot be accessed from the website CPG.

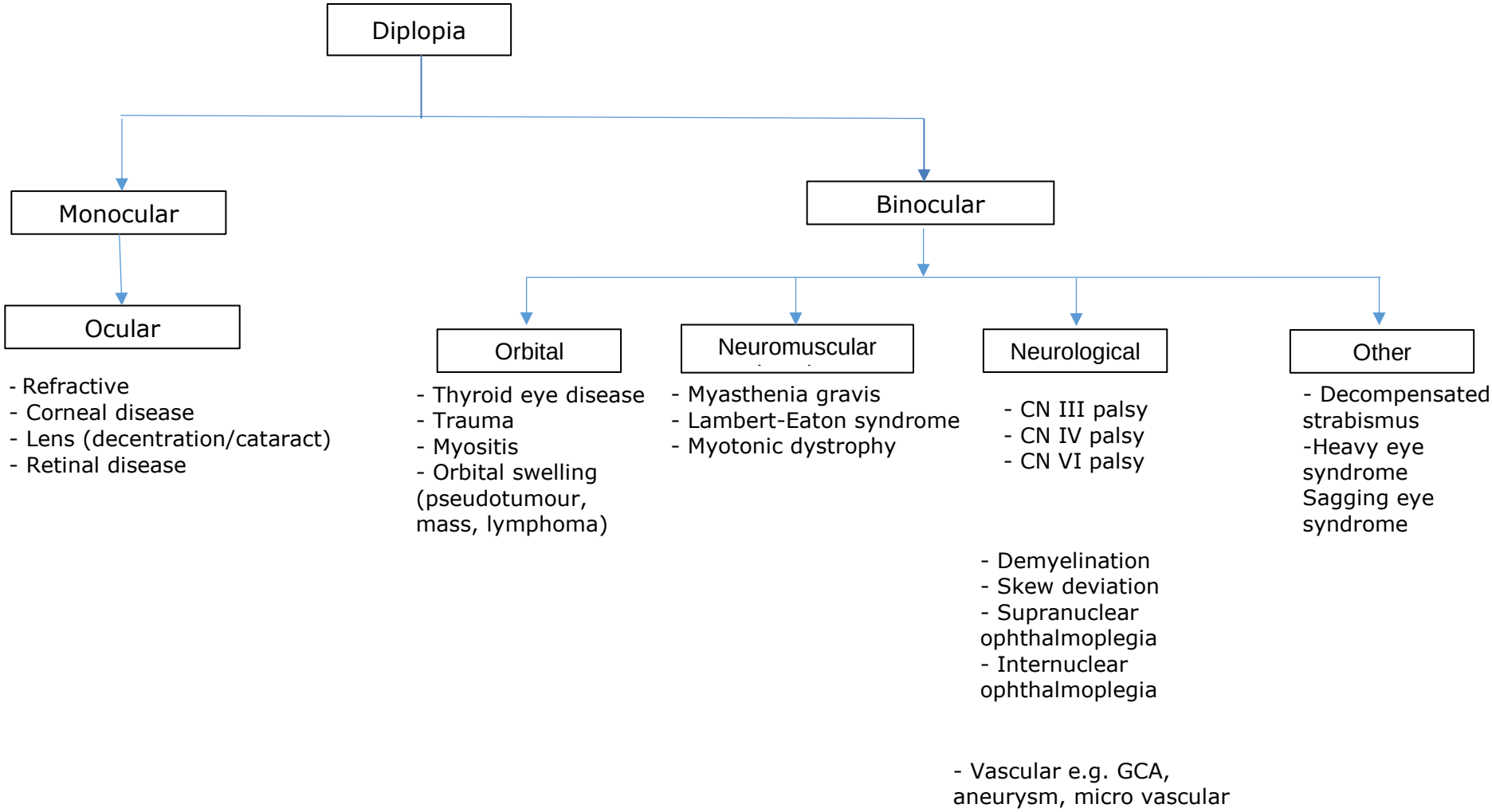
Description:

'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



Differential diagnosis	Symptoms	Signs/distinguishing features	ED investigations & treatment
CNIII	• Diplopia in all positions of gaze • Ptosis	• Ptosis • 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 • Discus with neurology team at St Vincent's regarding posterior circulation imaging

Differential diagnosis	Symptoms	Signs/distinguishing features	ED investigations & treatment
		• Not consistent with an isolated CN palsy • Distinguish from acquired CN IV – which typically has excyclotorsion, and hypertropia worse on opposite gaze (Bielschowsky 3-step test)	
Decompensated strabismus	• Diplopia worse when fatigued	• Strabismus/abnormal head position in old photographs or on examination • Comitant deviation • No pupil involvement	• Non-urgent Ocular Motility opinion
Heavy Eye Syndrome	• Binocular diplopia • Worse at distance • Horizontal, vertical and/or cyclovertical diplopia	• High myopes (>-5 dioptres) • Esotropia (comitant at distance) • Limited abduction • Hypotropia • Limited elevation	• Nil required in ED • Outpatient orbital MRI
Sagging Eye Syndrome	• Binocular diplopia • Worse at distance • Horizontal, vertical and/or cyclovertical diplopia	• Age related / involutional changes in the periorbital skin, fat • Esotropia (comitant at distance) • Limited abduction • Hypotropia • Limited elevation	• Nil required in ED • Outpatient orbital MRI

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:

Neurology	• General neurologic exam:
	  ○ Upper limbs, lower limbs (weakness, numbness, ataxia)
	  ○ Cranial nerves to exclude multiple nerve involvement (e.g., in cavernous sinus lesion)

Scalp	• Temporal artery palpation for GCA – point tenderness over superficial temporal arteries, decreased pulse
External eye	• Ptosis associated with CN III palsy/myasthenia gravis • Proptosis/chemosis suggestive of orbital disease • Upper lid lag, retraction suggestive of TED
Pupils	• Relative afferent pupillary defect • Anisocoria (pupil dilation in CN III palsy): check pupil size in light and dark
Extraocular motility	• Abnormal head position • Cover test – distance and near • Versions and ductions – assess for comitance and deviation in different positions of gaze • Smooth pursuit: with both eyes open, and covering each eye

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:

Palsy	**Neuroimaging**
CN III	CT+CTA brain and cavernous sinus or MRI+MRA brain and cavernous sinus on the same day.
CN IV	MRI Brain and orbits – within 2 weeks as outpatient.
CN VI	MRI brain within 2 weeks. If there are other neurological features, then immediate CTB

*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 antibiotic 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

Author(s)	Title	Source	Level of Evidence (I – VII)
Tiffin P, MacEwen C, Craig E, Clayton G.	Acquired palsy of the oculomotor, trochlear and abducens nerves	Eye. 1996;10(3):377.	VI
Pane A, Burdon M, Miller N.	The Neuro-Ophthalmology Survival Guide	Elsevier Health Sciences; 2006	VII
Tamhankar MA, Biousse V, Ying G-S, Prasad S, Subramanian PS, Lee MS, et al.	Isolated third, fourth, and sixth cranial nerve palsies from presumed microvascular versus other causes: a prospective study	Ophthalmology. 2013;120(11):2264-9.	IV
Jacobson DM.	Relative pupil-sparing third nerve palsy: etiology and clinical variables predictive of a mass	Neurology. 2001;56(6):797-8.	VI
Kissel JT, Burde RM, Klingele TG, Zeiger HE.	Pupil-sparing oculomotor palsies with internal carotid—posterior communicating artery aneurysms	Annals of neurology. 1983;13(2):149-54.	VI
Lustbader JM, Miller NR.	Painless, pupil-sparing but otherwise complete oculomotor nerve paresis caused by basilar artery aneurysm. Case report.	Archives of ophthalmology (Chicago, Ill : 1960). 1988;106(5):583-4.	VI
Trobe JD.	Third nerve palsy and the pupil: footnotes to the rule	Archives of Ophthalmology. 1988;106(5):601-2	VII
Wong AMF.	Understanding skew deviation and a new clinical test to differentiate it from trochlear nerve palsy	Journal of AAPOS : the official publication of the American Association for Pediatric Ophthalmology and Strabismus. 2010;14(1):61-7.	VII
Galtrey CM, Schon F, Nitkunan A.	Microvascular Non-Arteritic Ocular Motor Nerve Palsies—What We Know and How Should We Treat?	Neuro-Ophthalmology. 2015;39(1):1-11.	V
Gerstenblith AT, Rabinowitz MP.	The Wills eye manual: office and emergency room diagnosis and treatment of eye disease.	Lippincott Williams & Wilkins; 2012 May 11.	VII

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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