Chapter 18 – Diplopia

NOTE: CONTENT CONTAINED IN THIS DOCUMENT IS TAKEN FROM ROSEN'S EMERGENCY MEDICINE 9th Ed.

Italicized text is quoted directly from Rosen's.

Key Concepts:

1. *Monocular diplopia persists in one affected eye, even when the other one is closed. It is an ophthalmologic problem related to refractory distortions in the light path or from buckling of the retina.*
2. *Binocular diplopia resolves when either eye is closed and is the result of misalignment in the visual axes.*
3. *Four lines of questioning that help formulate the differential diagnosis of binocular diplopia are as follows: (1) cadence of onset of symptoms (a sudden onset suggests an ischemic event; a fluctuation of symptoms suggests transient ischemic attacks, impending stroke, or neuromuscular disease); (2) directionality and orientation of diplopia (horizontal, vertical, torsional); (3) presence of pain, which suggests an inflammatory or infectious process, and (4) the presence of other associated symptoms, which suggest a larger disease process (eg, infection, CNS ischemia, neuromuscular disease)*
4. *The diagnostic approach to diplopia entails a methodical consideration of (1) a monocular (refractive) problem, which, when excluded, leads to consideration of (2) a simple restrictive, mechanical orbitopathy, which, when excluded, leads to consideration of (3) a palsy of one or more of the oculomotor cranial nerves, then (4) a more proximal neuraxial process involving the brainstem and related cranial nerves; if all else is excluded, then (5) a systemic neuromuscular process.*
5. *An isolated CN III palsy is associated with diplopia in all directions of gaze, except on lateral gaze to the affected side, and an eye that is deviated down and out, with a dilated pupil, and ptosis. Microvascular ischemia (typically seen in patients with diabetes), classically spares the pupil. A CN IV palsy results in a rotational diplopia that worsens on looking down and toward the nose. A CN VI palsy results in diplopia that worsens on lateral gaze toward the problematic side.*
6. *Simultaneous ipsilateral involvement of more than one of CN III, IV, or VI from a mass, inflammation, or infection in the posterior orbit or cavernous sinus (orbital complex syndrome) may cause a combination of palsies and is associated with retro-orbital pain or blurred vision due to venous congestion and possibly ipsilateral numbness or dysesthesia from involvement of the ophthalmic (V1) and maxillary (V2) trigeminal branches that travel through the orbital complex.*
7. *Diplopia from a neuraxial process involving the brainstem and related cranial nerves may present as (1) a focal lesion in the brainstem (eg. multiple sclerosis), (2) a more diffuse but still localized brainstem process (eg. brainstem tumor, lacunar stroke,*

impending basilar artery thrombosis, vertebral artery dissection, or an ophthalmoplegic migraine), or (3) as part of a more diffuse neurologic syndrome involving the brainstem and oculomotor nerves (eg. infectious, autoimmune, neurotoxic, or metabolic process).

8. *The diplopia in myasthenia gravis is associated with ptosis, gets worse as the patient fatigues, and improves with rest or on placing ice over the eye.*
9. *The empirical treatment of conditions causing diplopia, instituted even before testing for specific entities is begun, is directed toward imminent threats to airway and ventilation (eg. botulism and myasthenia gravis), immediate threats to CNS tissue viability (eg, with basilar artery thrombosis or stroke), and rapidly evolving threats to CNS tissue viability (eg. with meningoencephalitis or Wernicke's encephalopathy).*

Rosen's in Perspective

Welcome back to another episode of CRACKCast. Today, we will spare you the typical introductory case as the content presented below is pretty dense. We will be reviewing a fairly common problem in today's podcast - diplopia. Interestingly, diplopia can have a myriad of causes, and, when present, can be an indicator that something pretty serious is occurring in that patient. We will go about giving you a good way to conceptualize diplopia and teach you what you need to know to best interview, examine, and work up the next patient seeing double. So, sit back, take a sip of your coffee, and enjoy the ride!

Core Questions:

1. What is diplopia and how is it classified?
2. What four questions help clinicians delineate the potential cause of a patient's diplopia?
3. What are the cardinal directions of gaze and how are they tested?
4. Outline the physical exam for the patient with monocular and binocular diplopia.
5. Outline the DDx for monocular diplopia?
6. Outline the DDx for binocular diplopia? [Table 18.1]
7. Detail the different oculomotor palsies. [Figure 18.3]
8. Detail the various lacunar stroke syndromes. [Box 18.1]
9. Define internuclear ophthalmoplegia.
10. What ancillary tests are required for the patient presenting with diplopia? [Figure 18.4]

Wisecracks:

1. What are the most common oculomotor palsies and what causes them?
2. What is orbital apex syndrome?
3. What is the "rule of the pupil" and how reliable is it?
4. Detail the physical exam maneuvers used to identify patients with myasthenia gravis.

Core Questions:

[1] What is diplopia and how is it classified?

Diplopia, the perception of double vision, is classified in many ways. However, Rosen's breaks it down into two simple categories that will help you formulate your initial differential. It's simple:

Monocular Diplopia

- Double vision that exists from dysfunction in one eye. Monocular diplopia persists even when the unaffected eye is closed.
- Monocular diplopia is an ophthalmologic issue, resulting from distortions in the path of light through the eye or buckling of the retina itself.

Binocular Diplopia

- Double vision secondary to misalignment of the visual axes. Binocular diplopia abates when either eye is closed
- Binocular diplopia can arise from several problems:
    - Mechanical orbitopathy
    - Cranial Nerve palsy
    - Proximal Neuraxial Process
    - Systemic neuromuscular process

[2] What four questions help clinicians delineate the potential cause of a patient's diplopia?

The history in a patient with diplopia is profoundly important, and in some cases, will be all you need to make your diagnosis. During your next clinical interaction with a patient complaining of double vision, ask yourself and the patient the following:

1. **What was the cadence of onset of symptoms?**
    a. Rapid onset, often with maximal symptoms immediately, often points to an ischemic cause of the patient's symptoms
    b. Fluctuating diplopia may point to transient ischemia or neuromuscular pathologies causing the patient's symptoms
2. **What is the directionality and orientation of diplopia and what aggravates it?**
    a. Defined as either vertical, horizontal, or torsional
3. **Is there any associated pain with diplopia?**
    a. Points to potential inflammatory or infectious causes of the patient's symptoms
4. **Are there any systemic symptoms other than diplopia that are present?**
    a. May lead you to a diagnosis of a systemic illness causing diplopia

[3] What are the cardinal directions of gaze and how are they tested?

We are going to take you back in time to the clinical examination course in medical school for this question.

There are six cardinal movements of gaze. Each cardinal direction marks the point at which the extraocular muscle and the nerve supplying it have their maximal effect. When visualizing it, think of a six-spoke asterisk or an "H" pattern. Each corner of the asterisk or "H" denotes one of the cardinal directions of gaze. The following table should help you think about it a bit better:

Cardinal Direction of Gaze	Extraocular Muscle	Cranial Nerve
Upper-Outer Gaze	Superior Rectus	III
Upper-Inner Gaze	Inferior Oblique	III
Temporal Gaze	Lateral Rectus	VI
Nasal Gaze	Medial Rectus	III
Lower-Inner Gaze	Superior Oblique	IV
Lower-Outer Gaze	Inferior Rectus	III

Now, we are humble practitioners of Emergency Medicine here on CRACKCast, so to simplify things, you can think about it this way:

- Every extraocular movement is controlled by CN III (oculomotor nerve) EXCEPT for looking toward the temple (CN VI or the abducens nerve) or at the tip of the nose (CN IV or the trochlear nerve)

[4] Outline the physical exam for the patient with monocular and binocular diplopia.

So, let's break it down. Here is our approach to the physical examination for the patient seeing double.

Monocular Diplopia

- Remember, this is exclusively a problem of the eye itself. So, you are going to do a thorough ophthalmologic examination including:
    - Visual acuity

- Cardinal directions of gaze
- Peripheral field testing
- Intraocular pressure testing
- Pupillary examination
    - Direct response
    - Consensual response
    - Swinging light test
- Fundoscopy
- Slit Lamp Exam

Binocular Diplopia

- Now things get a little more complex, but if you think about the four mechanisms that cause binocular diplopia, things get a little easier
- Remember, binocular diplopia can be caused by:
    - Mechanical orbitopathies
    - Cranial nerve palsies
    - Neuraxial lesions
    - Systemic processes
- Knowing this, we here at CRACKCast recommend the following:
    - Detailing neurologic examination, evaluating
        - Cranial nerve testing
        - Cerebellar testing
        - Examination of the motor system
        - Examination of sensation
        - Reflex testing
        - Head and neck examination

[5] Outline the DDx for monocular diplopia?

While not an all-inclusive list, the following is a good DDx for monocular diplopia:

1. Keratoconjunctivitis sicca
2. Corneal abrasions/defects
3. Cataracts
4. Lens dislocation
5. Macular Disruption

[6] Outline the DDx for binocular diplopia? [Table 18.1]

The following is taken from Rosen's 9th Edition. Please see the text for a more complete table.

Diplopia-causing Entity	Mechanism and Mortality	Distinguishing Features
Tier 1 - Critical		
Basilar Artery Thrombosis	Impending thrombosis of the basilar artery with brainstem ischemia; untreated mortality 70-90%	Vertigo, dysarthria, other cranial nerve involvement; risk factors for stroke
Botulism	Toxins inhibit release of acetylcholine at cholinergic synapses and presynaptic myoneural junctions; untreated mortality 60%	Dysarthria, dysphagia, autonomic dysreflexia, pupillary dysfunction
Basilar Meningitis	Infection; untreated mortality, close to 100% if bacterial, (15-20% if treated)	Headache, meningismus, fever
Aneurysm	Enlarging aneurysm directly compresses cranial nerve; untreated rupture risk = 1% per year (3.5%/yr for previously ruptured); mortality 26-67% for rupture	CN III palsy with pupillary involvement
Tier 2 - Emergent		
Vertebral Dissection	Dissection causes vertebrobasilar ischemia; acute untreated mortality 28% (2-5% if neurologically asymptomatic)	Neck pain, vertigo; risk factors for vertebral dissection
Myasthenia Gravis	Autoantibodies develop against ACh nicotinic postsynaptic receptors; untreated crisis mortality 42% (5% if treated)	Fluctuating muscle weakness, ptosis, and diplopia worsens with activity, improve with rest
Werkicke's Encephalopathy	Thiamine-dependent metabolic failure and tissue injury; untreated mortality 20%	Nystagmus, ataxia, altered mental status, ophthalmoplegia; alcoholism and nutritional deficiency
Orbital Apex Syndrome, Cavernous Sinus Process	Inflammation or infection in the orbital apex or cavernous sinus directly affects oculomotor cranial nerves; acute mortality low unless complicated by meningitis	Combination of palsies of the CN III, IV, VI, with retro-orbital pain, conjunctival injection, possible periorbital/facial numbness

Tier 3 - Urgent		
Brainstem Tumor	Tumor involvement in the supranuclear level, acute mortality low (long-term mortality variable)	Skew deviation, vertical diplopia, internuclear ophthalmoplegia
Miller-Fisher Syndrome	Autoantibodies develop to the cranial nerve ganglioside, GQ1b; acute mortality low (if fully differentiated from GBS, 2-12% if GBS)	Ophthalmoplegia, ataxia, areflexia
MS	Demyelinating lesions; acute low mortality	Internuclear opthalmoplegia
Thyroid Myopathy	Autoimmune myopathy; acute mortality low in regard to ocular complications	Proptosis, restriction of elevation and abduction of the eye, signs of Grave's Disease
Ophthalmoplegic Migraine	Inflammatory cranial neuropathy; low mortality, self-limited disease	Ipsilateral headache, CN (usually III) palsy
Ischemic Neuropathy	Microvascular ischemia, mortality, low-limited disease	Isolated CN palsy (pupil-sparing if CN III
Orbital Myositis, Pseudotumor	Autoimmune or idiopathic myositis; acute mortality low in regard to ocular complaints	Eye pain, restriction of movement, periorbital edema; exophthalmos and chemosis when more severe
Orbital Apex Mass	Tumor, infiltration, or mass effect in orbital apex or cavernous sinus directly compresses oculomotor cranial nerves; acute mortality low	A combination of palsies of CN III, VI VI and possible periorbital, facial numbness, with retro-orbital pain, proptosis, signs of venous congestion

[7] Detail the different oculomotor palsies. [Figure 18.3]

This table was adapted from Figure 18.3 in Rosen's 9th Edition. Please see the textbook for the accompanying images.

Nerve Palsy	Muscles **OFF**	Symptoms
CN III	Medial, inferior, and superior rectus muscles Inferior oblique Levator palpebrae Ciliary and constrictor pupillae muscle	Multidirectional horizontal and vertical diplopia, except on lateral gaze to affected side Eyelid droop
CN IV	Superior oblique muscle	Rotational diplopia that worsens when looking down and toward the nose
CN VI	Lateral rectus muscle	Horizontal diplopia on gaze toward the affected side

[8] Detail the various lacunar stroke syndromes. [Box 18.1]

This is a box, folks. Strap in for some intense neurology learning!

This table is adapted from Box 18.1 in Rosen's 9th Edition. Please reference the textbook for more information.

Lacunar Stroke Syndrome Presenting with Diplopia

Weber Syndrome	Midbrain Lacune Ipsilateral CN III Palsy Contralateral Hemiparesis
Benedikt Syndrome	Midbrain Lacune Ipsilateral CN III Palsy Contralateral Tremor or Dysmetria
Claude Syndrome	Midbrain Lacune Ipsilateral CN III Palsy Contralateral Weakness, Tremor, and Ataxia
Millard-Gubler Syndrome	Pontine Lacune Ipsilateral CN VI Palsy Ipsilateral Facial Weakness Contralateral Arm and Leg Weakness
Foville's Syndrome	Pontine Tegmentum Ipsilateral CN VI Palsy Ipsilateral Facial Weakness Contralateral Ataxia and hemiparesis

One-and-a-half Syndrome	CN VI Nuclei, Paramedian Pontine Reticular Formation Bilateral CN VI Palsies Unilateral Adduction Palsy

[9] Define internuclear ophthalmoplegia.

As per Rosen's 9th Edition:

An internuclear ophthalmoplegia is defined as having an inability to adduct the eye on one side in the contralateral direction during lateral gaze that resolves during convergence, implicates a lesion in the medial longitudinal fasciculus

This physical examination finding is typically seen in patients with multiple sclerosis. The long and short of it is, the affected eye is unable to adduct when looking to the side opposite it (i.e., one cannot adduct the right eye when following the examiners finger laterally to the left, and vice versa)

[10] What ancillary tests are required for the patient presenting with diplopia? [Figure 18.4]

Ancillary tests ordered are largely dependent on whether or not the patient has monocular or binocular diplopia.

In patients with monocular diplopia, you may not need ANY ancillary testing. If present, they will likely simply need a referral to your friendly neighbourhood Ophthalmologist.

Rosen's 9th Edition has a pretty tight diagnostic algorithm for patients with diplopia presenting to the ED (reference the textbook for the original figure), but it basically states the following:

1. **For patient with a suspected restrictive mechanical orbitopathy:**
    a. Get a contrast-enhanced CT or MRI of the orbits
2. **For patients with isolated nerve palsies:**
    a. If they have typical microvascular ischemia CN III palsy (sparing of the pupil, Hx DM/HTN, no other focal neurological deficits), you can consider discharge with referral to neuro-Ophthalmology
    b. If they have exam features not consistent with CN III palsy or other oculomotor cranial nerve palsies, MRI/CT of the brain
3. **For patients with multiple CN palsies of the III/IV/VI:**
    a. Get a contrast-enhanced CT or MRI of the brain/orbits
4. **For patients with diplopia and other neurologic deficits confined to the brainstem:**
    a. Get a MRI/MRA brain or CT/CTA brain and neck
    b. Consider LP for meningitis

5. **For patients with neurologic deficits consistent with neuropathic syndrome with brainstem and cranial nerve involvement:**
    a. Treat empirically for the suspected entity (e.g. botulism, Wernicke's, Miller Fisher Syndrome)
    b. Consider screening MRI
    c. Consider LP for MFS
6. **For patients with symptoms consistent with a neuromuscular disorder:**
    a. Perform the ice test or Tensilon test

Wisecracks:

[1] What are the most common oculomotor palsies and what causes them?

Answer:

The most common oculomotor nerve palsy is CN VI (abducens nerve). Second is CN III (oculomotor nerve). Third most commonly affected oculomotor nerve palsy is CN IV (trochlear nerve).

CN VI is most commonly affected by tumors, elevated ICP, and microvascular ischemia. It's particularly long course makes it vulnerable to damage.

CN III is most commonly affected by diabetic or hypertensive vasculopathies as well as aneurysms of the posterior communicating, basilar, superior cerebellar, posterior cerebral, and cavernous internal carotid arteries.

CN IV is most commonly affected by trauma, abutting against the tentorium, and vascular causes.

[2] What is orbital apex syndrome?

Answer:

Orbital Apex Syndrome is a poorly-defined term, but generally refers to a constellation of multiple oculomotor nerve palsies, diminished vision, and inflammation caused by masses and/or venous congestion in the ocular apex or cavernous sinus

[3] What is the "rule of the pupil" and how reliable is it?

Answer:

According to Rosen's 9th Edition, the rule of the pupil states that in the patient with an otherwise complete CN III palsy (complete ptosis, completely down-and-out orientation of the afflicted eye), if the pupil has normal size and reactivity, there is no compressive source (e.g., expanding aneurysm) of the nerve palsy.

This being said, this is more of a guideline, because clinical medicine is never perfect. You cannot use this to "rule in" a compressive cause of a neuropathy. Up to 50% of patients with diabetic or hypertensive microvascular ischemia will have will have pupillary involvement. This is thought to be because these patients have some degree of autonomic neuropathy.

[4] Detail the physical exam maneuvers used to identify patients with myasthenia gravis.

Answer:

1. Fatigability of Upward Gaze
    a. First, the patient is to maximally close their eyes and hold it for 5-10 seconds. Then, have the patient fix their gaze upward at your finger and hold it there. The patient's degree of ptosis will worsen if the test is positive.
    b. 80% Sensitive
    c. 63% Specific
2. Ice Test
    a. Based on the fact that neuromuscular transmission occurs faster at lower temperatures
    b. As per UpToDate:
        i. In the ice pack test, a bag (or surgical glove) is filled with ice and placed on the closed lid for two minutes. The ice is then removed and the extent of ptosis is immediately assessed. Improvement in ptosis is a positive test result (defined by a > 2mm improvement in palpebral opening). Make sure to provide forehead pressure to prevent contribution from the frontalis muscle.
    c. 80% Sensitive
    d. 25% Specific