



Deciphering DIPLOPIA

The symptom is diplopia. But what's the diagnosis?

When your patient sees two images, you may need to consider 20 possible causes, and ruling out 19 of those can be a headache.

The various etiologies of diplopia comprise one of the most sweeping differential diagnoses in all of ophthalmology. The patient who complains of double vision can have something as benign as dry eye or as life-threatening as an intracranial tumor. The cause may be as rare as Wernicke encephalopathy or as common as convergence insufficiency. “It’s a huge differential diagnosis,” said Nurhan Torun, MD, director of the neuro-ophthalmology service at Beth Israel Deaconess Medical Center and an instructor of ophthalmology at Harvard Medical School in Boston. “Diplopia tends to be intimidating for many practitioners.”

Intimidation may even turn to dread. “When most ophthalmologists see a patient with a chief complaint of diplopia, they hate it,” said Michael S. Lee, MD, associate professor of ophthalmology, neurology and neurosurgery at the University of Minnesota in Minneapolis. “They often don’t know what to do with the patient.” What they do know, of course, is that the proper workup will take longer than a standard office visit.

A multidisciplinary monster. Eric Eggenberger, DO, professor of neurology at Michigan State University in East Lansing, noted that diplopia challenges neurologists as well. “Ophthalmologists are not as comfortable with it as they are with vision loss because many of the diagnoses are neurologic. And neurologists are not comfortable with it

because they’re not trained in techniques to measure ocular alignment.” But the consequences of a delayed or incorrect diagnosis are not comfortable, either. “Most double vision is not dangerous. But some is super dangerous,” said Andrew G. Lee, MD. “You have to do a complete and thorough exam to look for the distinctive dangerous sign. That sign could suggest a life-threatening diagnosis. It’s a red flag,” he said. Dr. Lee is professor of ophthalmology, neurology and neurosurgery at Weill Cornell Medical College in New York as well as chairman of ophthalmology at The Methodist Hospital in Houston, adjunct professor of ophthalmology at the University of Iowa in Iowa City and clinical professor of ophthalmology at the University of Texas in Galveston.

The exam of a diplopic patient demands a meticulous history and the posing of questions pertinent to the disposition of double images in various positions of gaze: Is the diplopia monocular or binocular? Are the images horizontal or vertical? Answers to these may determine whether the pathology is neurological or mechanical—involving a nerve, an extraocular muscle or a neuromuscular junction.

Question: Monocular or Binocular?

The first step in cornering diplopia is to determine whether it is monocular or binocular, said Karl C. Golnik, MD, professor of ophthalmology, neurology and neurosurgery at the University of Cincinnati.

- If it’s monocular, the patient sees double with only one eye open, and the extra image typically appears as a ghost, Dr. Golnik said. Causes of this include media or refractive

problems, dry eye, warped cornea, cataract, unstable tear film, IOL decentrations, media opacities, the wrong glasses and even uveitis.

- With binocular diplopia, however, the patient sees double only if both eyes are open. Cover either eye and the patient's problem disappears—though the physician's trouble may have just begun.

Surprisingly, many doctors assume the diplopia is binocular, without considering monocular, though the differential diagnosis is different for each, Dr. Golnik said. In fact, he explains to referring colleagues that he does not need to see patients with monocular double vision because they typically don't require a neurological evaluation. "Once you've determined it's monocular, your level of anxiety goes down and your diagnostic techniques switch."

Dr. Michael Lee agreed. "It's really reassuring if someone has monocular double vision," he said, explaining that the cause must be within the eye itself.

Binocular Dangers

Binocular diplopia can be a cause for alarm. It may be a symptom of aneurysm, stroke, neoplasm, myasthenia gravis or trauma. Even certain infections, such as sinus disease with a fungal infection, can present with double vision, especially in an immune-compromised patient. "There are

literally hundreds of potential diagnoses," Dr. Eggenberger said, and many of them are life-threatening.

"Begin by localizing," he said. "Once you've determined location you need to incorporate the patient's age, demographics, history and other findings on exam to help with understanding the pathophysiology. This keeps you from jumping to conclusions."

Dr. Torun added that an assessment of ocular motility will help narrow things down. "That requires a very careful exam of the misalignment in different positions of gaze and looking for restriction of motility in any position of gaze," she said. "Unless we make a correct diagnosis of the underlying eye movement problem, our differential is not going to be appropriate."

Dr. Golnik agreed. After the physician establishes binocular diplopia, the next step is to figure out whether there's a pattern to the misalignment. For example, he said, if it's comitant—the double vision is the same no matter where the patient turns his head—the problem is less worrisome. On the other hand, if it's incomitant—the double vision goes away when the patient turns his head to the left but remains bad when turned right—then it's time to worry. There are exceptions and nuances, but, said Dr. Golnik, "You can guide diagnostic evaluation better if you can find the pattern."

Five to Fear

"There are clearly some life-threatening causes of double vision. Those are the ones an ophthalmologist can't afford to miss," Dr. Andrew Lee said. Following are five especially worrying possibilities.

1 **Dangerous Sign:** Pupil involvement suggesting third-nerve palsy.

Dangerous Diagnosis: Aneurysm.

Dangerous Prognosis: "The one that's going to kill you is the third-nerve palsy," said Dr. Michael Lee, explaining it's the most common presentation of an aneurysm of the posterior communicating artery. Dr. Golnik added that a third-nerve palsy with a large and poorly reactive pupil is a big red flag, and he doesn't let the technician dilate the patient until he does the exam. Sometimes, however, the red flag turns out to be a false alarm. While third-nerve palsy is a warning sign for aneurysm, it could also be associated with high blood pressure or diabetes. For example, Dr. Eggenberger said, an 85-year-old with high blood pressure, diabetes and normal pupils is probably not harboring a compressive lesion, but in a 25-year-old with pain and pupil involvement, the safer assumption would be that it's compressive. As for those in-between cases, he said, "There's no cookbook answer. It takes some time. It's not a quick evaluation. And it's very individualized. The challenge is in knowing which patient is going to get better in three months and which harbors a life-threatening diagnosis."

2 **Dangerous Sign:** Problem with more than one of the following: lid, pupil or eye movement.

Dangerous Diagnosis: Horner syndrome (ptosis with small pupil), third-nerve palsy (ptosis with big pupil) or inflammatory disease, such as Guillain-Barré or Miller Fisher variant.

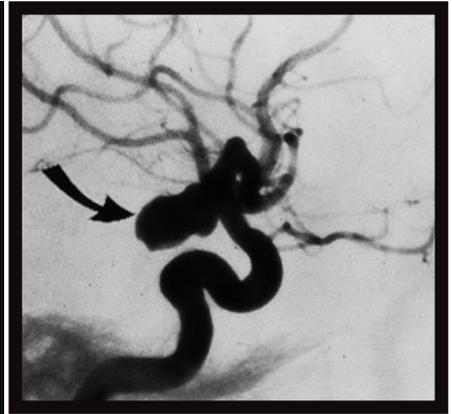
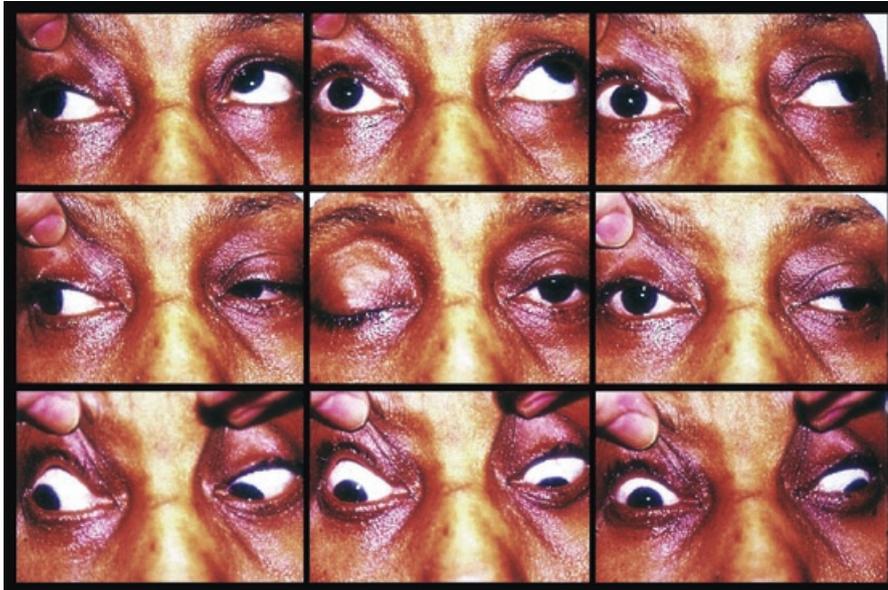
Dangerous Prognosis: If any one of the lid, pupil or motility appears abnormal, you have to check the other two, said Dr. Andrew Lee. "You're not allowed to have more than one of these neuro-ophthalmic problems at a time." More than one abnormality requires a referral or a more aggressive evaluation for the life-threatening etiologies, he said. The biggest dangers are aneurysmal third-nerve palsy and Horner syndrome from carotid dissection. Even mild third-nerve palsy could be due to aneurysm, which can kill the patient. Guillain-Barré also can cause death, or systemic paralysis.

3 **Dangerous Sign:** More than one cranial nerve palsy.

Dangerous Diagnosis: Multiple cranial neuropathy.

Dangerous Prognosis: Intracranial or meningeal-based tumors, meningitis or polyneuropathy. Involvement of more than one nerve is a huge red flag, Dr. Andrew Lee said. Sixth-nerve involvement by itself in a diabetic patient probably indicates an ischemic mononeuropathy. Likewise, an isolated, complete and pupil-spared third nerve may indicate a benign and isolated ischemic palsy. But involvement of both the third and the sixth is dangerous and could be a cavernous sinus lesion.

Dr. Golnik remembers one patient referred to him with



TROUBLE. A 62-year-old woman with right-side ptosis, nonreactive, dilated pupil and severely limited extraocular movement was found to have a posterior communicating artery aneurysm.

a diagnosis of unilateral sixth-nerve palsy who actually had metastatic lung cancer in the skull base. Dr. Golnik’s exam found involvement with the fifth and seventh nerves, something the referring physician might have found by checking facial sensation and facial muscle strength.

4 **Dangerous Sign:** Weakness or fatigue, often variable. **Dangerous Diagnosis:** Myasthenia gravis. **Dangerous Prognosis:** Respiratory failure or aspiration. Myasthenia gravis can mimic almost any ophthalmoplegia and should be considered in the differential diagnosis of any pupil-spared motility disturbance, said Dr. Andrew Lee. “An ophthalmologist doesn’t have to be a neurologist but does have to ask the neurologic questions,” he said. Those include: Do you have other symptoms? Do you experience weakness in the arms or legs? Hoarseness? Difficulty swallowing?

Dr. Torun described a patient who had transient diplopia and a presumed diagnosis of internuclear ophthalmoplegia. Multiple brain scans revealed nothing so the patient was referred to her. Initially, she agreed with the presumptive

diagnosis. “But I also saw she had quite variable eye movements. She had difficulty holding her eyes in an eccentric position, with the eyes drifting toward the center, which is a feature of myasthenia.” The workup for myasthenia was positive, and the patient was later admitted to the hospital in myasthenic crisis. The case illustrated the importance, Dr. Torun said, of early diagnosis of an ocular motility problem, which may be the initial presentation of a serious systemic disorder.

5 **Dangerous Sign:** Onset of new kind of headache, scalp tenderness, pain with chewing. **Dangerous Diagnosis:** Giant cell arteritis. **Dangerous Prognosis:** GCA is a life- and sight-threatening disease that is associated with aortic dissection, cerebral and myocardial infarction. “Remember that giant cell arteritis can cause double vision, either constant or transient,” said Dr. Golnik, who asks every patient over the age of 50 a few giant-cell questions: Have you experienced a new kind of headache? Scalp tenderness? Pain or weakness with chewing? Unexplained weight loss?

Scans Don’t Think, Doctors Do

Given the rigors of the diplopia differential diagnosis, it might be tempting to order a scan and let the machine figure it out. But in many situations, costly imaging may not catch a serious problem. For example, myasthenia gravis and giant cell arteritis aren’t apparent on imaging. Alternatively, imaging may indeed yield a life-saving diagnosis but only if the correct scan is aimed at the correct anatomy.

Good scan, bad interpretation. CT scans of the orbit can rule out diplopia secondary to thyroid eye disease and orbital tumors, according to Dr. Golnik. “But beware the reportedly ‘normal’ MRI or CT scan when you are looking for an extraocular muscle abnormality,” he warned, because he

routinely sees scans that are misread as normal.

Pointless scan, pinhole better. What’s more, Dr. Golnik frequently sees patients with monocular diplopia who had had an MRI. “Thousands of dollars were spent, and all I needed was a pinhole test to tell it’s not a neurological problem,” he said. “If you just throw up the pinhole and the second image is gone, the patient can understand they don’t have a brain tumor.”

Two bottom lines. So when are scans warranted?

1. “If it’s not neurologically isolated, you have to image,” Dr. Andrew Lee said. “For example, if you identify a sixth-nerve palsy, you have to also check the fifth and seventh nerves. If one of those is also affected, you have to image.”

2. Age is a guide. In a patient under the age of 50, an image is advised unless there's a long history of vasculopathic problems, Dr. Golnik said.

Conversely, an isolated cranial nerve palsy in a patient over 50 who has high blood pressure and vascular risk factors but no other findings is probably not urgent, Dr. Golnik said. But he advised a six-week follow-up exam. "Hopefully they'll start to improve. If not, then you need to image."

Etiologies Overlooked

Some causes of diplopia are easily missed, including:

- **An extra hole in the iris** from an iridotomy may cause diplopia, said Dr. Michael Lee. Double vision may occur if the laser hole falls within the palpebral fissure rather than being hidden underneath the upper lid or if the prismatic effect of the tear meniscus allows light into a superiorly placed iridotomy. "I don't think it's something someone would normally think of," he said. "When you talk about the major causes of monocular double vision, you think of refractive error, dry eye, warped cornea, cataract. The iridotomy is less common."
- **Thiamine deficiency** can cause double vision, Dr. Torun said. Diplopia may be the earliest symptom of Wernicke encephalopathy, which consists of confusion and ataxia, along with ophthalmoplegia. The disease is typically associated with malnutrition and alcoholism, but it can also be seen in patients with gastric bypass procedures, as well as those with eating disorders—bulimia and anorexia. "These patients may have nystagmus or what mimics a sixth-nerve palsy. In severe cases, they may not be able to move their eyes at all," Dr. Torun said. Untreated, the condition can lead to coma and eventually death. If treated too late, it can cause neurological problems. But timely administration of intravenous thiamine (vitamin B₁) may prevent permanent neurologic sequelae.
- **Convergence spasm** is a nonorganic cause of double vision, but it might easily be mistaken for a unilateral or bilateral sixth-nerve palsy or myasthenia, said Dr. Michael Lee. On first glance, the patient's eyes are crossed and the complaint is double vision. But if the pupils are constricted,

TRANSIENT DIPLOPIA: Dr. Torun's Differential Diagnosis

Decompensated phoria
Convergence or divergence insufficiency
Myasthenia gravis
Spasm of accommodation
Ischemia of extraocular muscles (as in temporal arteritis)
TIAs involving the vertebrobasilar system
Superior oblique myokymia
Ocular neuromyotonia
Cyclic esotropia

it's likely the patient is deliberately crossing his eyes. "Miotic pupils, in a patient with variable esotropia and abduction deficits, can suggest convergence spasm," Dr. Lee said. "When evaluating versions, there may be an abduction deficit and the pupils are miotic from convergence. When ductions are performed, the abduction deficit resolves." He once saw a patient on referral who had undergone a few strabismus surgeries, but the diagnosis was convergence spasm.

- **Skew deviation** is a prenuclear vertical misalignment that results from brainstem or cerebellar lesions. It may be comitant or incomitant, but a diagnostic feature is a marked decrease in the vertical misalignment with the patient in supine position.

Patients may give history of a stroke before onset of diplopia, said Dr. Torun. "If there are no associated brainstem signs and the misalignment is relatively small, it is easy to overlook, especially since motility is usually full."

- **An epiretinal membrane** in one or both eyes can sometimes cause central binocular vertical diplopia, Dr. Torun said. Visual acuity could be quite good, though patients typically describe distortion on an Amsler grid. Motility is full. "This is easy to overlook if the maculopathy is subtle."

For "Pearls for Diagnosing Diplopia" go to this story online at www.eyenetmagazine.org.

Meet the Experts

Eric Eggenberger, DO Professor and vice chairman of neurology at Michigan State University in East Lansing.

Karl C. Golnik, MD Professor of ophthalmology, neurology and neurosurgery at the University of Cincinnati.

Andrew G. Lee, MD Professor of ophthalmology, neurology and neurosurgery at Weill Cornell Medical College in New York; chairman of ophthalmology at The Methodist Hospital in Houston; adjunct professor of ophthalmology at the University of Iowa in Iowa City; clinical professor of ophthalmology at the



University of Texas Medical Branch in Galveston.

Michael S. Lee, MD Associate professor of ophthalmology, neurology and neurosurgery at the University of Minnesota in Minneapolis.

Nurhan Torun, MD Director of the neuro-ophthalmology service at Beth Israel Deaconess Medical Center and instructor of ophthalmology at Harvard Medical School in Boston.