A Guide to the Isolated Dilated Pupil

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The poorly reactive and dilated pupil observed in a comatose patient is often thought to represent an acute third nerve palsy owing to brain herniation or aneurysm. In the well patient, however, the isolated dilated pupil is unlikely to be owing to a third nerve palsy. It is more commonly owing to other benign causes such as local iris sphincter abnormalities, pharmacologic dilation, tonic pupil syndrome, or sympathetic irritation. This article presents a diagnostic flowchart to help the primary care physician analyze this problem and prevent costly and unnecessary imaging of these patients.

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Several articles in the ophthalmologic literature have reviewed the management of anisocoria,[1-16] but little emphasis has been placed on the evaluation of the isolated dilated pupil. This is unfortunate because many of these patients initially present to the primary care physician and may undergo many unnecessary, expensive, and potentially hazardous tests.[5] This article outlines a simple stepwise diagnostic schematic (**Figure**) to guide the assessment of a patient with an isolated dilated pupil. The tests that need to be performed are shown as steps 1 through 7 in the Figure.

STEP 1: EXAMINATION OF LIGHT REACTION (FLASHLIGHT TEST)

Pupillary parasympathetic constriction to light is mediated by the third nerve as preganglionic efferent fibers to the ciliary ganglion and then as postganglionic fibers to the iris. Pupil dilation is mediated by the oculosympathetic pathway, which is not discussed in detail in this article. Therefore, careful examination of the pupillary response to light allows the clinician to determine whether the larger or the smaller pupil is abnormal. This is important because a difference in pupil size (anisocoria) is not always caused by an enlarged pupil (ie, the smaller pupil may be the abnormal pupil). If the larger pupil displays a poor light reaction, it is likely to be the abnormal pupil.[9,12,13] This finding suggests damage to either the iris or parasympathetic innervation to the iris. If, however, the light reaction is normal in both eyes, then the differential diagnosis includes physiological anisocoria, a contralateral oculosympathetic pathway disruption (ie, Horner syndrome involving the smaller pupil) or ipsilateral sympathetic overaction. Testing for the amount of relative anisocoria in bright or dim illumination gives similar information. Specifically, if the anisocoria is greater in bright light, then the larger pupil is abnormal because it is not constricting appropriately relative to the fellow eye. Conversely, if the anisocoria is greater in dim illumination, then the smaller pupil is abnormal because it is not dilating appropriately relative to the fellow eye. Abnormal pupillary light reaction may be subtle and difficult to recognize by the inexperienced examiner and appropriate ophthalmologic consultation should be considered in questionable cases.

STEP 2: EVALUATION OF EXTRAOCULAR MOTILITY

In theory, an extra-axial compressive lesion of the third nerve may cause an isolated dilated pupil without an extraocular motility deficit.[10] In practice, this rarely occurs. Intracranial aneurysms, espe-

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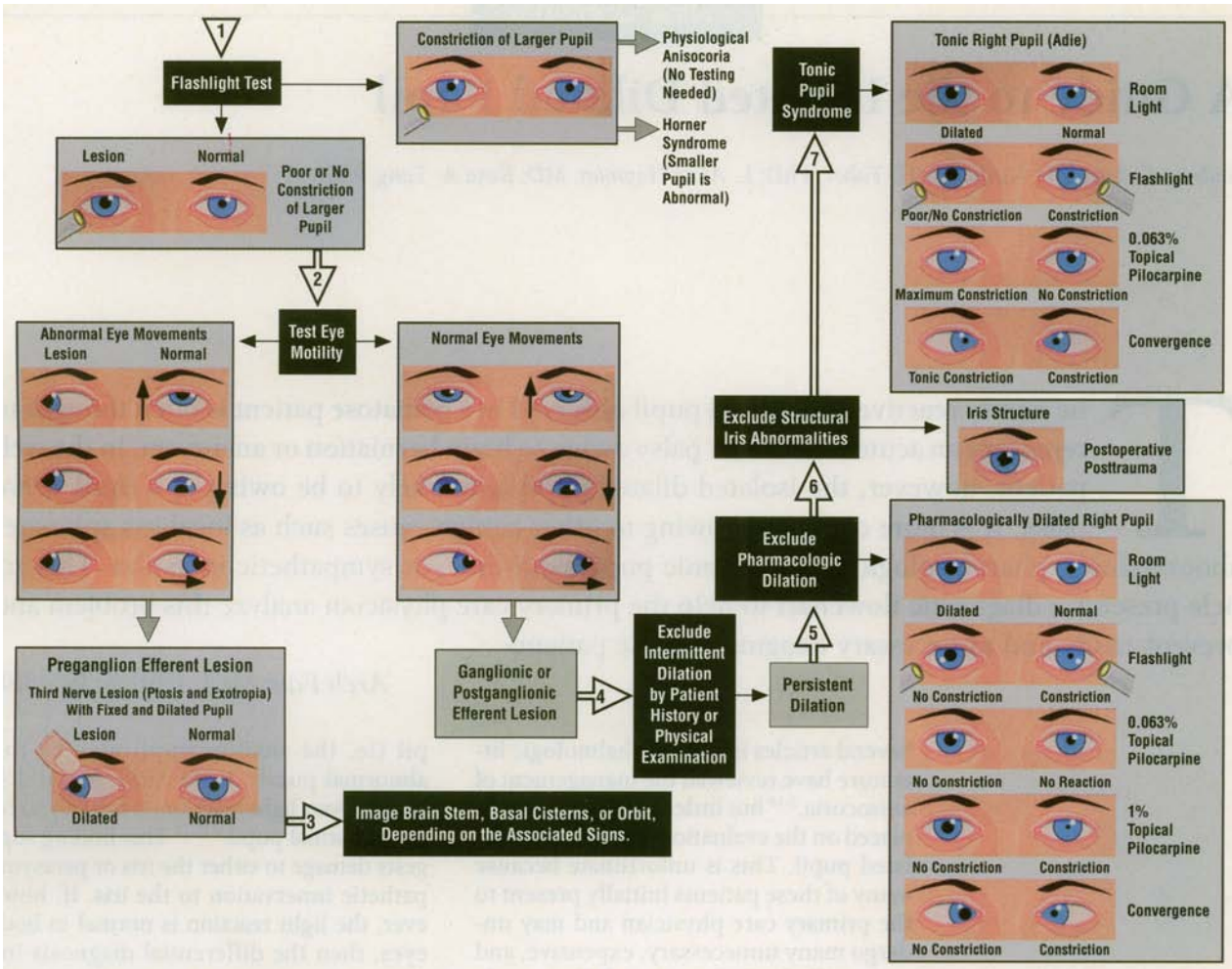

A guide to the isolated dilated pupil.

cially those involving the posterior communicating artery–internal carotid artery junction, often produce a fixed and dilated pupil and almost always produce other eyelid or extraocular motility signs of a third nerve palsy. Wilhelm et al[17] reviewed the literature on 6 cases with isolated dilated pupils owing to a third nerve palsy. Three patients had headaches and 1 patient had a seizure and headache. In 2 patients, signs or additional signs of a third nerve palsy developed early in the course of their illness, but in 1 patient these signs developed 1 year later. Rare cases of cryptococcal or tuberculous basal meningitis have also been described as presenting with an isolated dilated pupil, but other concomitant neurologic signs were present or additional features of a third nerve palsy appeared over time in most of these patients.[17] Thus, the patient with an isolated dilated pupil, without evidence of ptosis or extraocular motility deficit, is unlikely to have a third nerve palsy. Nevertheless, close follow-up for the development of additional signs of a third nerve palsy is mandatory and patients in the appropriate clinical setting, such as those in the intensive care unit with severe or acute onset headache, should have their condition evaluated immediately.

STEP 3: EVALUATION OF THIRD NERVE PALSY

In general, patients with a nontraumatic pupil-involved third nerve palsy should undergo screening for signs of subarachnoid hemorrhage (computed tomographic scan, lumbar puncture, or both) and subsequent cerebral arteriography to exclude aneurysm. The Figure shows that a third nerve palsy involves the preganglionic efferent lesion.

STEP 4: DIFFERENTIATE INTERMITTENT FROM PERSISTENT PUPIL DILATION

Transient dilation has been described in patients with migraine headaches[7,8,15] and even in otherwise normal individuals.[7,8] Tadpole-shaped pupils, owing to segmental spasm of the iris, may also be related to migraine phenomenon.[11] Some of these episodes may represent sympathetic irritation or excess, but there is still some controversy as to whether this is the true mechanism. Dysautonomic cephalgia after neck trauma may also result in sympathetic hyperactivity involving the pupil, sweating, and eyelid retraction.[18] If the transient or intermittent nature of the dilation can be established firmly by patient medical history or physical examination findings and the episodes occur in isolation in an otherwise healthy patient (or only with mi-

graine headaches), these patients should not undergo emergency arteriography. In addition, other neuroimaging may be deferred and the patient's condition should simply be followed up for improvement during the next 24 to 48 hours. Resolution of all signs suggests a benign origin for the pupil dilation.

STEP 5: EXCLUDE PHARMACOLOGIC DILATION

In cases with persistent pupil dilation, a careful patient history is often all that is required to detect inadvertent or intentional exposure to topical dilating agents (mydriatics). Specific questioning should be directed toward the use of topical medications by the patient or patient's family members (especially postcataract drops) or the use of transdermal scopolamine patches for motion sickness (which have been unavailable recently, but will be reintroduced in 1997). Nurses, physicians, and other health care workers, in particular, may be inadvertently or intentionally exposed to topical mydriatics.[9,12,13] To establish this diagnosis, the dilated pupil may be tested for a pharmacologic blockade with topical 1% pilocarpine.[1,14] A pupil that is dilated owing to a third nerve palsy will constrict, but a pupil with a parasympathetic pharmacologic blockade (such as with topical atropine) will not. Adrenergic pharmacologic dilation (such as with topical phenylephrine hydrochloride) often may be clinically distinguished from parasympatholytic blockade by blanched conjunctival vessels, residual light reaction, and a retracted upper eyelid owing to sympathetic stimulation of the upper eyelid retractor muscle. Convergence effect and 0.063% pilocarpine also will not constrict a pharmacologically dilated pupil.

In most cases, the patient history and a simple confirmatory pharmacologic test result are all that are required for the diagnosis. Reassuring the patient along with close follow-up as the dilatory effect wears off are sufficient.[9,12,13] An acute tonic pupil may be unreactive to either light or near stimuli and may be difficult to distinguish from a pharmacologically dilated pupil or a case of acute traumatic iridoplegia.[9,12,13]

STEP 6: EXCLUDE STRUCTURAL IRIS ABNORMALITIES

Ophthalmologic consultation is particularly helpful in patients with a suspected orbital or intraocular pathologic condition. Patients may present with a history of ocular trauma, loss of vision, a red eye, or ocular pain. Slit-lamp biomicroscopy is far superior to gross inspection with a handlight for the detection of iris transillumination defects and sphincter tears at the pupillary margin, which may cause a dilated pupil.

Increased intraocular pressure owing to angle-closure glaucoma may also cause an acute sphincter paresis and a unilateral dilation. These patients often have ocular pain, conjunctival hyperemia, or corneal edema, but these features are variable and may be missed without a complete ophthalmologic examination.[9,12,13] Finally, iris ischemia such as carotid occlusion may also result in a dilated pupil.[19]

STEP 7: CONSIDER TONIC PUPIL SYNDROME

The clinical features of the tonic pupil include a diminished or absent pupillary reaction to light stimulus, segmental palsy of the iris sphincter, a tonic pupillary near response producing a "light-near dissociation" of the pupil, cholinergic supersensitivity to low-dose (0.125%-0.063%) topical pilocarpine of the denervated sphincter, and a variable accommodation paresis.[2-4,6,16] The pathophysiological feature of the Adie tonic pupil is most likely damage to the ciliary ganglion or postganglionic efferent nerves.[2,3,6,11,16] More than 90% of the ciliary ganglion cells serve the ciliary body and only 3% serve the iris sphincter. After damage to the ciliary ganglion, aberrant regeneration of fibers originally destined for the ciliary body now innervate the iris sphincter. Accommodative effort stimulates these fibers and produces a tonic near response.[2,3,6,11,16] Some patients may have decreased limb deep tendon reflexes. The syndrome is benign and does not usually require further evaluation or treatment.

STEP 8: CONSIDER SYPHILIS

Fletcher and Sharpe[4] reported that 5 of 60 consecutive patients with tonic pupils had positive serologic results for syphilis. Of these patients, all had a bilateral tonic pupil and none presented with acute mydriasis or cycloplegia. We, therefore, perform syphilis serologic testing on all patients with a bilateral tonic pupil and on patients with a monocular tonic pupil.

CONCLUSIONS

The primary care physician should be familiar with the most common causes for the isolated dilated pupil in the ambulatory setting. Neuroimaging and other laboratory studies are usually unnecessary in the evaluation of the isolated dilated and poorly reactive pupil. A careful stepwise patient medical history and physical examination, as well as prompt ophthalmologic consultation, may spare the patient unnecessary, expensive, and potentially hazardous or invasive diagnostic testing.

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