Decoding the Pupil

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Pupillary examination is an important part of ocular examination as it often helps in identifying problems which may be local or may even involve central nervous system.

Anatomic and physiologic considerations

The size of the pupillary aperture is controlled by two opposing smooth muscles the pupillary constrictor muscle (innervated by parasympathetic autonomic nerves) and the dilator muscle (innervated by sympathetic autonomic nerves). Iris sphincter is much stronger than dilator.

Assessment of pupillary size, shape and function

Examination of pupil requires a meticulous history and a rigorous examination of pupil, which may often need pharmacologic testing.

History:

Patients with pupillary abnormalities are often not aware of their abnormalities as the symptoms are often insignificant, in most of the cases the spouse, friend or physician brings it to notice. Often, old photographs are required to identify the duration of illness. In some cases symptoms are associated with disturbance of pupil size and shape, like photophobia, blurring or "unclear" vision and difficulty in light/dark adaptation or difficulty in adapting to change in accommodative effort. Past history of pharmacologic use / misuse / accident should also be asked for. Past history of trauma, surgery, infections (Herpes etc) or migraine may point toward the cause of pupillary abnormality.

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Slit lamp anterior segment examination:

Ciliary congestion with small pupil may be due to intra-ocular inflammation.

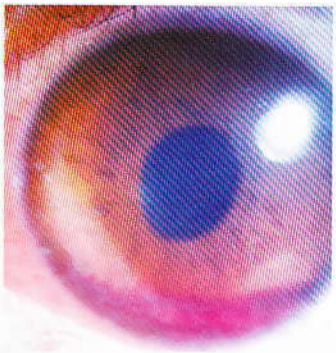


Figure 1: Traumatic mydriasis along with hyphema in a case of trauma.

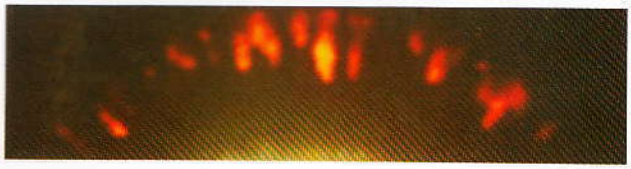


Figure 2: Transillumination defects seen in retro illumination

This also provides information regarding signs of trauma like, corneal abrasion, angle recession, transillumination defects in iris, sphincter tears, segmental defects and signs of inflammation responsible for abnormal pupil.

Figure 3: Pupillary rough irregularity and sphincter tears in case of trauma.

Measurement of pupil size:

The pupil can be measured using pupil

gauges or simple rulers in darkness, light and when the patient is focusing for near.

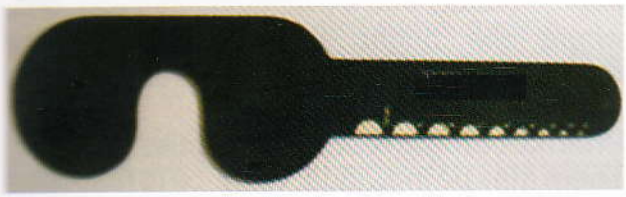


Figure 4: Commonly available pupil gauge.

A difference of more than 0.4mm between the two eyes is labeled as anisocoria and needs further evaluation. Physiologic anisocoria may be seen in 20% of general population.

Figure 5: Pupillary size being measured using pupil gauges held close to the eye.

Reaction to light:

This should be examined in dim quiet surroundings, distance fixation and there should *not* be an attempt to look for near or close the eye (this induces miosis). When the bright light is thrown in the eye being examined for a few seconds, it is the direct light reaction (Figure 6).

Figure 6: Assessment of direct light reaction.

In cases of retinal and optic nerve pathologies the pupil initially constricts and then slowly dilates to original size, "pupillary escape". This is more pronounced with a dim light. On shining light in one eye the pupil of the other eye constricts, this is consensual light response. This can be best assessed using a bright light source in one eye and dimmer light source in the contralateral eye shined obliquely. The consensual reflex is 0.1 mm less than direct reflex.

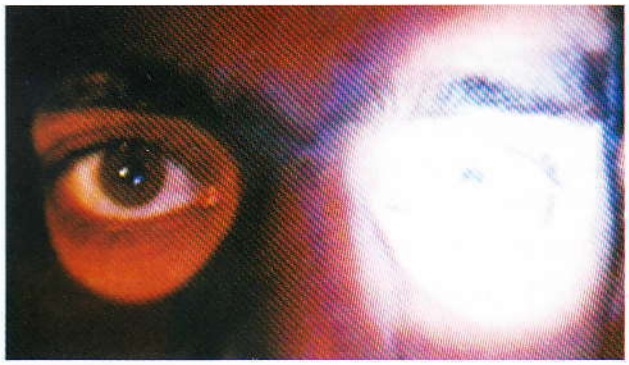


Figure 7: Assessment of consensual reflex.

Near response:

The near triad consists of pupillary constriction, accommodation and convergence. To be tested in adequately lighted room and the patient is asked to look at the accommodative target.

Assessment of Pupillary dilatation:

Pupils dilate after constriction due to light or near response, with sudden noise or pinching the back. While assessing the dilation, note "dilatation lag", which is seen commonly in defective sympathetic pathway. In such cases anisocoria is more at 4-5 seconds after constriction than 15 seconds post constriction. Rarely such a phenomenon may be seen in normal individuals.

Light near dissociation:

There is dissociation between the light response and near stimulation. In almost all cases there is impaired pupillary response to light whereas the response to near stimulation is present. In cases where the light response is present but the near response is absent, it is most likely due to lack of accommodative effort on patients part.

Argyll Robertson Pupils:
Here the pupils are very small, associated with normal pupillary constriction for accommodation, but poor response to light. This was seen more often in the past and was considered pathognomonic of neurosyphilis.

Testing for RAPD:
This can be demonstrated with alternate cover of either eye, as described by Kestenbaum. In cases with optic atrophy or asymmetrical optic atrophy, alternate cover of eyes reveal that on uncovering the normal eye or on covering the normal eye the pupil of abnormal eye dilates.

This is "Marcus Gunn or Gunn phenomenon" or "relative afferent pupillary defect". This can also be tested with a swinging flash light test, where the bright light accentuates the differences in the pupillary response.

Pharmacologic testing of pupils:
There may be individual variation in response to the pharmacologically instilled drug (due to squeezing, tearing, corneal penetration, and iris color); hence if the condition is unilateral then the drug should be instilled in both eyes so that the other eye acts as a control. When the disease is bilateral, the drop should be instilled in one eye so that the response can be compared with the other eye.

Table 1: Drugs used in pharmacologic testing for common pupillary disorders

Drug	Purpose	Dose	Time	Lighting	Measure
Dilute pilocarpine	Supersensitivity testing	0.625%	30 min	Dim light or darkness	Change in pupil diameter
Pilocarpine	Pharmacologic pupil blockage	2%	40 min	Darkness	Change in pupil diameter
Cocaine	Sympathetic defect	10%	60 min	Light	Post –cocaine anisocoria
Hydroxyampheta-mine	Detect post ganglionic sym-pathetic defect		50-60 min	Light	Absolute dilation OU or anisocoria > 1mm or change in anisocoria >1mm

Anisocoria:

Table 2: Common causes of Anisocoria

	More Anisocoria in Darkness
1	Simple (physiologic)
2	Inhibition of sympathetic pathway a. Horner's Syndrome b. Pharmacologic (thymoxamine, dapiprazole)
3	Stimulation of sympathetic pathway a. Tadpole pupils b. Intermittent dilatation caused by intermittent sympathetic hyperactivity c. Pharmacologic (adrenergic, ocular decongestants, cocaine)
4	Pharmacologic stimulation of parasympathetic pathway (pilocarpine, serine, methacholine, organophosphates etc)

More Anisocoria in Light	
1	Damage to parasympathetic outflow to the iris sphincter muscle a. Oculomotor nerve paresis b. Tonic pupil syndromes (including Adie's) c. Intermittent dilatation of one pupil caused by inhibition of the parasympathetic pathway
2	Trauma to iris sphincter
3	Acute glaucoma, siderosis
4	Pharmacologic inhibition of parasympathetic pathway (atropine, scopolamine)

Horner's syndrome:
It is caused by the interruption of sympathetic supply which causes the weakening of the retractor muscle (drooping of eye lid and lower lid to rise) & the iris dilator is weakened (small pupil). The Anisocoria is more in dark, as the normal pupil dilates well and early. Clinical features include ptosis, miosis, anhydrosis (seen only in central and preganglionic types of Horner's syndrome), apparent enophthalmos, paradoxical pupillary dilatation at the time of emotional excitement due to denervation super-sensitivity, dilatation lag, depigmentation of iris (seen in congenital Horner's).

The diagnosis of Horner's syndrome can be made using cocaine test (as described in table). Clinically, it may be useful to differentiate into central (first-order), preganglionic (second-order) and post ganglionic (third-order) variety. The actual anisocoria in cases of Horner's syndrome varies and may be affected by following conditions.

Table 3: Various conditions affecting the anisocoria of Horner's syndrome

1 Resting pupil size	2 Whether the injury is complete or not?
3 Adrenergic circulation in the blood	4 Re-innervation extent of the dilator muscle
5 Point of fixation of patient (distance or near)	6 Extent of denervation supersensitivity
7 Difference in the brightness of ambient light and examiner's light source	8 Degree of alertness or tiredness of the patient at the time of examination

Central Horner's Syndrome:
The Horner's due to damage to the central neuron is almost always unilateral and is often associated with other neurological deficits.

Preganglionic Horner's Syndrome:
This is a disorder of second order neuron in thorax and superior cervical region. Thecharacteristic anhydrosis is in the half of head, face, neck down to clavicle. The cause of this form of Horner's syndrome may be malignancy (lung/breast), accident or surgery.

Case:
A12 year old boy, presented with history of drooping right eye lid and absence of sweating in right side of face and neck for 2 years.

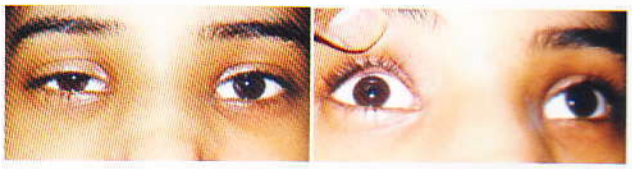
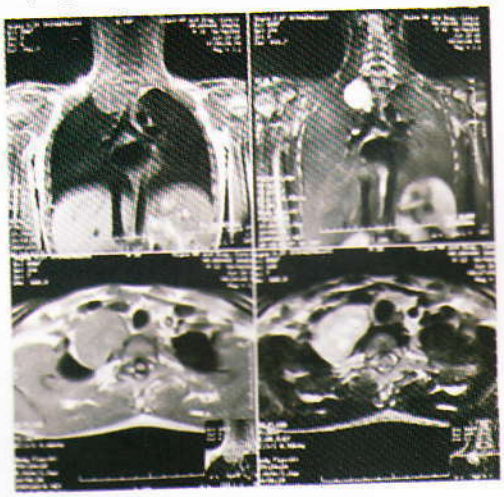


Figure 8: A case of 12 year old boy with mild ptosis and right pupil smaller than the left. The anisocoria increases in dark.

Ophthalmic evaluation revealed anisocoria more in dark with right pupil smaller than the left (figure 8), rest of the examination was unremarkable. He was advised MRI upper thorax, CT brain and Ultrasound Abdomen. MRI upper thorax revealed a large mass lesion (Figure 9).



Figue 9: MRI thorax showing a large 4.8 x 4.6 x 4.4 cm mass in right paraspinal area (D1-D3), in the apical region close to trachea and main vessels.

The patient underwent cardiothoracic surgery and the mass was histo-pathologically found as benign nerve sheath tumor (Schwannoma) with cystic changes. The photographs of the same patient before and after surgery show improvement in ptosis and decrease in anisocoria (Figure 10).

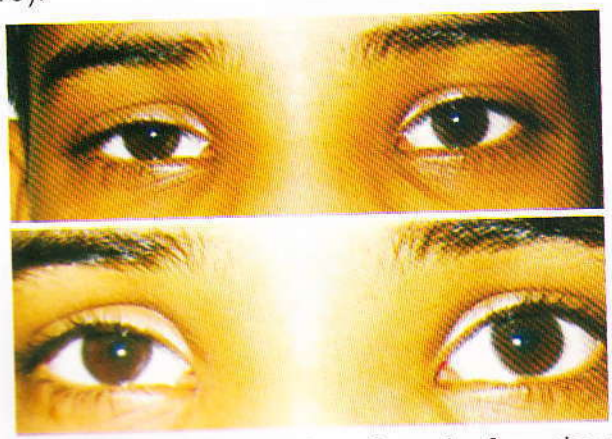


Figure 10: Before (above) and after chest surgery (below), the improvement in ptosis and decrease in anisocoria is evident.

Postganglionic Horner's Syndrome:
The is seen with involvement of third order neuron which travels "the Carotid plexus" and enters the orbit with nasocilliary nerve and divides into two long ciliary nerves and supply anterior segment of the eye and innervate the iris dilator muscle.

Pharmacologic causes of anisocoria:
Anisocoria could be caused by either stimulation of iris sphincter or stimulation of dilator muscles of the eye. Cocaine, oxymetazoline, phenylephrine may dilate pupil, but their effect is very mild and the anisocoria would be more evident in dark.

Anisocoria more in light:
In these cases the anisocoria is more in the light, this signifies the dilated or the larger pupil is abnormal and poorly constricts in response to bright light (Table 2).

Damage to parasympathetic outflow or iris sphincter:
Lesion anywhere in this pathway from the brain to the iris can produce absolute/partial paralysis of pupillary constrictor, which can result in dilated and non-reactive pupil. The pupillary constrictor paralysis may be associated with loss of accommodation in some cases.

Tonic Pupils:
Damage to ciliary ganglion or its roots may lead to poor light reaction, Paresis of accommodation, cholinergic super sensitivity, strong & tonic near reaction and slow re-dilatation this is termed as Tonic pupil. It can be of various types.

Local Tonic Pupil:
This may be caused by a variety of inflammatory, infectious and infiltrative process of ciliary ganglion which may be in isolation or as part of systemic process.

Neuropathic Tonic Pupil:
Usually a part of generalized neuropathy which may involve the ciliary ganglion or the short ciliary nerves or both.

Holmes-Adie (Adie's) Syndrome:
It consists of unilateral or bilateral tonically reacting pupils developing in otherwise healthy persons. This is more common as a unilateral disease in females between the age group of 20 to 50 years. The tonic pupils may be associated with Areflexia or hyporeflexia of deep tendon reflexes.

Patients may complain of photophobia, blurred near vision, enlarged pupil and headache. In most patients, accommodative paresis resolves over a few days to months. In few patients, aberrant regeneration within ciliary muscle- accommodative paresis that may persist until presbyopia develops and diminishes the symptoms. Segmental contraction or "vermilliform" movements are observed in all forms of tonic pupil which is a critical diagnostic observation. Almost every Adie's pupil that has any reaction to light (90%) has such segmental palsy of sphincter.

With time accommodative paresis sets and affected pupil gradually become smaller, the pupillary light reaction may even weaken, deep tendon reflexes tend to become increasingly hyporeflexic and there is tendency for patients with unilateral Adie's syndrome to develop a tonic pupil in opposite eye with time. The diagnosis is made with the use of pharmacological test with 0.1% pilocarpine. The cause of Adie's syndrome is obscure. Pharmacologic and pathologic studies indicate ciliary ganglion, short-ciliary nerves, or both as the location of lesion.

Case:
A 48 year old male presented with difficulty in reading and opening the left eye in light for 20 days. On examination, left pupil was larger than the right. The anisocoria increased in bright light and decreased in dark. On asking the patient to read continuously for 5 minutes, his symptoms improved and also the anisocoria decreased. Vermilliform movements of pupil were also noted.

Diagnosis of Adie's pupil was made and advised asymmetric near glasses and photochromatic glasses for distance.

Damage to iris sphincter:
Blunt trauma to the eyes may result in tears in the iris sphincter which may lead to dilated pupil. In such cases other tell-tale signs of trauma like Vossius ring, traumatic cataract, choroidal rupture, commotio retinae, retinal hemorrhages, angle recession etc may be seen.

Pharmacologic blockade (parasympatholytics):
The mydriasis due to drugs is extreme (usually >8mm) and may respond poorly to 1% pilocarpine solution.

Few Facts

- *Octopus has rectangular pupils.*
- *Mosquitoes like the scent of estrogen, hence, women get bitten by mosquitoes more often than men do.*
- *A person could grow 600 complete eyelashes in a life time.*