



ANISOCORIA



Eye Learn

All about the Eye

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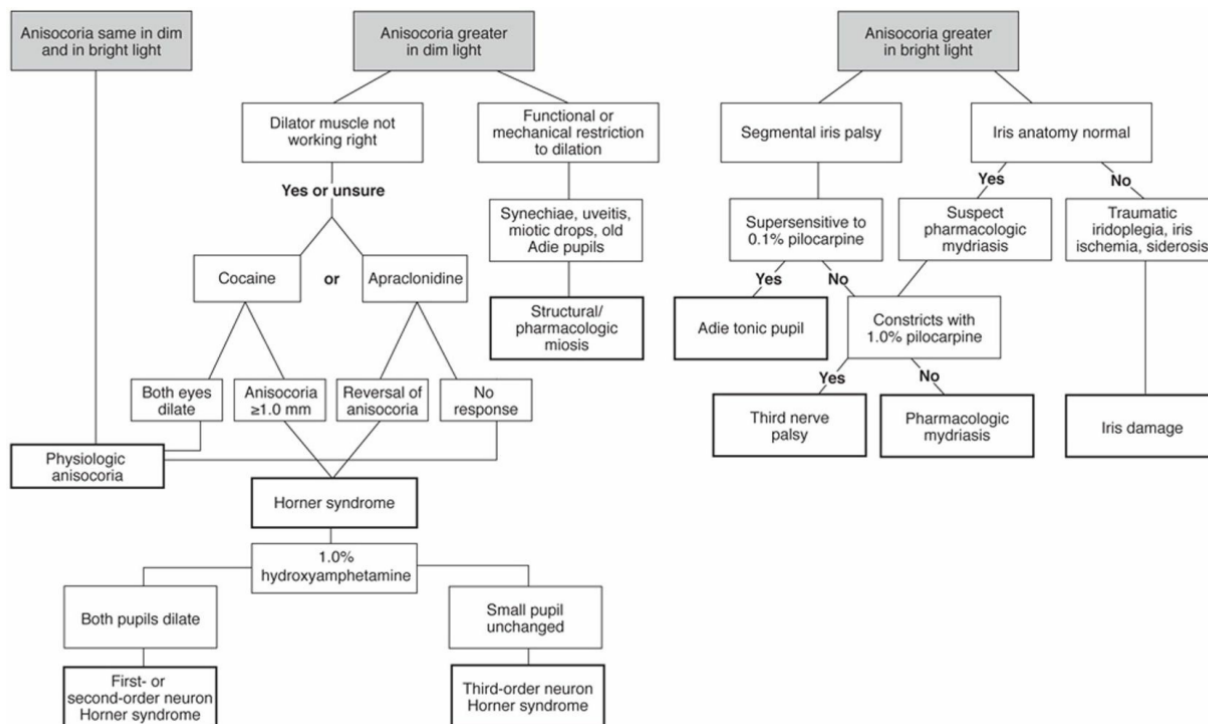
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ANISOCORIA

1. What is anisocoria and indications for its investigations? (1+3) J2018
2. Causes, differential diagnosis and clinical implications of anisocoria. (3+3+4) J2011
3. Discuss approach to diagnosis of anisocoria. (5) J2012
4. a) What is anisocoria and indications for its investigations? b) Give physiological basis and causes of light-near dissociation 1+3+4+2 J2018



Definition- Asymmetry of efferent signals to the iris muscles produces inequality in the diameters of the 2 pupils called anisocoria, which may be physiologic or pathologic.

- This is a condition characterized by an unequal size of the pupils.
- In the absence of any deformities of the iris or eyeball, anisocoria is usually the result of defects in the efferent nervous pathways controlling the pupil size, travelling in the oculomotor nerve (parasympathetic fibers) or the sympathetic pathways
- Physical lesions and drugs may also modulate these pathways.
- Anisocoria can be physiological or pathological.

Differential diagnosis of anisocoria

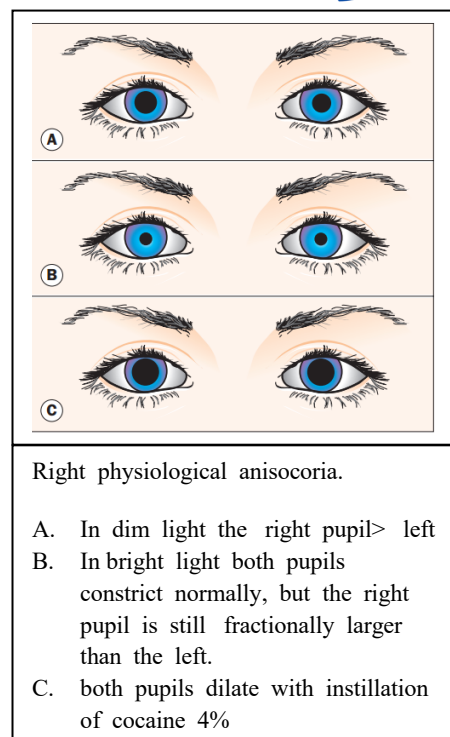
Pathological pupil is dilated	Pathological pupil is constricted
<ol style="list-style-type: none"> 1. Early stage of coma (brainstem herniation) 2. Traumatic mydriasis (non-reacting pupil; does not constrict with pilocarpine) 3. Mydriasis due to acute glaucoma (non-reacting pupil; constricts with pilocarpine) 4. Drug induced like with atropine (non-reacting pupil; the mydriasis may go away with time after the anticholinergic effect has been washed away but no constriction occurs with pilocarpine due to receptor blockade) 5. Oculomotor nerve palsy (non-reacting pupil; constricts with pilocarpine as the lesion is more central and hence, the receptivity to local pilocarpine exists) 6. Tonic pupil (non-reacting to light, reacts to near stimulus, shows supersensitivity to pilocarpine 0.125%) 	<ol style="list-style-type: none"> 1. Horner's syndrome (smaller pupil dilates less as compared to the normal pupil with 10% cocaine, thus increasing the anisocoria) 2. Unilateral pilocarpine use (history of glaucoma to be elicited) 3. Localizing for ipsilateral pontine bleed/lesion in early stage (recalcitrant to dilatation by topical mydriatics as the cause is central) 4. Early stage of opiate overdose where unilateral constriction may be there (recalcitrant to dilatation by topical mydriatics as the cause is central; may respond to naloxone) 5. Argyll Robertson pupil (usually bilateral; near reflex very markedly present; response to light reflex is very poor; recalcitrant to dilatation by mydriatics) 6. End stage tonic pupil



A. Anisocoria Equal in Dim and Bright Light

- **Physiological anisocoria/simple or essential anisocoria**

- Most common cause of a difference in pupil size of 0.4 mm or more.
- This is a benign condition characterized by slightly unequal pupils.
- This condition is common, occurring in 20 % of the population, especially in dim light.
- Patients with physiological anisocoria have:
 1. Difference of less than 1.0 mm between the pupils of both the eyes.
 2. Pupillary reactions being the same in both light adapted and dark adapted conditions.
 3. Anisocoria whose magnitude is equal in dim and bright light indicates that the relative function of the pupillary sphincter and dilator muscles is intact.
 4. There should be no light near dissociation.
 5. Occasionally the anisocoria may switch sides (called “alternating” or “seesaw” anisocoria).
 6. No associated features (e.g. diplopia, visual loss) are present.
 7. Old photographs are often helpful in dating the onset of anisocoria.
 8. Apraclonidine test- no response
 9. Cocaine- dilate testing may be needed to exclude Horner syndrome.
 10. Pilocarpine 0.1% has no effect.
 11. Once established, no further evaluation or therapy is required for the condition.



- **Pathological anisocoria:**

- The conditions that could lead on to pathological anisocoria and needs careful evaluation. They can at times indicate life threatening conditions.
- The localization as to whether the dilated pupil or the miosed pupil is pathological, is of importance.
 1. It is of importance to notice the pupillary reactions to light in such cases. If equal, sphincter denervation as in traumatic mydriasis or the pupil in angle closure glaucoma can be ruled out and a more central cause looked for.
 2. In case the pupil which is dilated or constricted, as the case may be, is not reacting to the light reflex, it is a good idea to check for the consensual reflex in the other pupil. Presence of the consensual reflex indicates that the integrity of the afferent system in that eye is normal and the small or the large pupil size is essentially due to efferent defect.
 3. The next step is to evaluate whether the anisocoria increases in bright light or dim light. This has localizing value.
 - a. **If the anisocoria increases in darkness**, it indicates that the smaller pupil is not able to react to the physiological dilatation that occurs in darkness in an attempt to keep the amount of light entering the eye constant and hence, it is the pathological eye.
 - b. **If the anisocoria increases in light**, it indicates that the larger pupil is not able to react to the physiological constriction that occurs in a bright background in an attempt to keep the amount of light entering the eye constant and hence, it is the pathological eye.

B. Anisocoria Greater in Dim Light

Assuming that only 1 pupil is faulty, anisocoria becomes more apparent in dim light under the following conditions.

1. Mechanical anisocoria

- Previous trauma (including surgery) or inflammation can lead to adhesions between the iris and the lens or IOL.
- Such adhesions may prevent pupillary dilation in conditions of dim illumination.
- Posterior synechiae should be visible with a magnifying lens or slit lamp.

2. Pharmacologic miosis

- The use of pilocarpine may result in a small, poorly reactive pupil.
- Anisocoria will not be present if both eyes have been treated, but the use of pilocarpine in 1 eye may lead to diagnostic confusion.
- Pharmacologic anisocoria is observed less often than it was in the past because of the wider range of choices in glaucoma medications.

3. Physiologic anisocoria may at times be greater in dim light

4. Horner's Syndrome



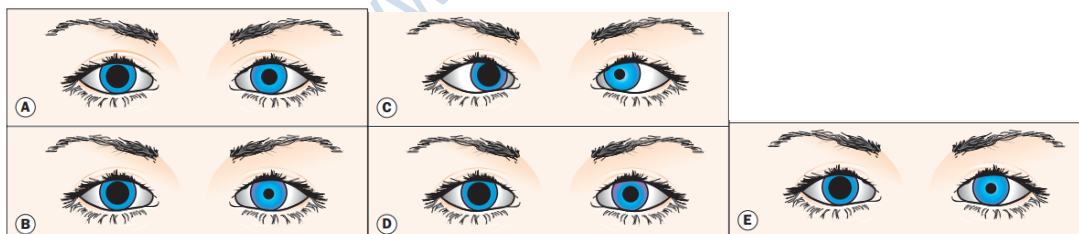
C. Anisocoria Greater in Bright Light

1. Iris damage

- Blunt trauma to the eye can cause miosis or mydriasis.
- The pupil may be relatively miotic after injury due to spasm, thereafter becoming midsized or mydriatic with poor responses to light and near stimulation.
- Evidence of sphincter damage is provided by notches in the pupillary margin or transillumination defects near the sphincter muscle.
- When iris injury occurs in patients with head trauma, the dilated pupil may be mistakenly identified as a sign of third nerve palsy due to uncal herniation.
- Mydriasis due to direct iris sphincter damage does not respond to topical pilocarpine (1% or 2%) and thus mimics pharmacologic mydriasis.
- Slit-lamp examination should help in differentiating traumatic from other types of mydriasis.
- Prolonged or recurrent angle closure can also impair pupillary function, as can intraocular surgery.

2. Pharmacologic mydriasis

- When mydriatic medications are instilled in the eye accidentally or intentionally, the pupil becomes dilated and its reactivity to light and near stimulation is lost.
- Use of eye drops prescribed for someone else, rubbing the eye after touching a car sickness scopolamine skin patch or deliberate for the purpose of malingering.
- The pupil does not constrict in bright light or on accommodation
- There are no other neurological features.
- Drug-induced dilation causes paralysis of the entire sphincter, in contrast to an Adie pupil, which causes segmental sphincter paralysis.
- When mydriasis is induced by an anticholinergic drug such as atropine, instillation of full-strength pilocarpine (1% or more) will not be able to reverse the mydriasis.
- Mydriasis due to neurologic disease such as Adie pupil or third nerve palsy is easily overcome with instillation of full-strength or even dilute pilocarpine.
- With adrenergic mydriasis, the pupil is large, the palpebral fissure is widened, and the conjunctiva may be blanched.
- Accommodation is not impaired.
- Medications such as those used to treat glaucoma may cause anisocoria if they are administered in only 1 eye or if absorption is asymmetric.



Right pharmacologic mydriasis. (A) Right mydriasis in dim illumination; (B) in bright light the right pupil does not constrict; (C) on accommodation the right pupil does not constrict; (D) neither pupil constricts after instillation of pilocarpine 0.1% into both eyes; (E) after instillation of 1% pilocarpine into both eyes the left pupil constricts but the right does not

3. Adie tonic pupil

- This pupillary dysfunction is an idiopathic form of internal ophthalmoplegia that results from denervation of the post-ganglionic supply to the sphincter pupillae and the ciliary muscle.
- Damage to the ciliary ganglion or short ciliary nerves (postganglionic parasympathetic nerve injury) produces a tonic pupil, which is characterized:
 - By poor reaction to light
 - Sectoral palsy of the iris sphincter
 - Accommodative paresis
 - Denervation cholinergic supersensitivity
 - A strong and tonic pupillary response to near vision (light–near dissociation) followed by slow redilation.
- May follow a viral illness.
- It is occasionally inherited in an AD pattern.
- Tonic pupils are unilateral in 80% of cases, although the second pupil may later become involved (4% per year).



- **Idiopathic tonic pupil** is known as Adie pupil; 70% of patients are female. Sites of dysfunction are presumed to be the ciliary ganglion in Adie pupil
- **Holmes-Adie syndrome**, the dorsal root ganglion involved in reflex pathways. Holmes-Adie syndrome includes other features, notably, diminished deep tendon reflexes and orthostatic hypotension.
- **Associations**- other features of autonomic nerve dysfunction such as excessive sweating (Ross syndrome), orthostatic hypotension and occasionally bowel obstruction or urinary retention.
- **Histologic examination** of the ciliary ganglion in patients with Adie tonic pupil has shown a reduction in the number of ganglion cells.

➤ **Symptoms**

- i. Patients may notice anisocoria.
- ii. May have blurring for near due to impaired accommodation
- iii. Photophobia
- iv. May have no symptoms and report that anisocoria was first noticed by a friend or relative.

➤ **Signs**

- i. Large, regular (irregularity sometimes reported) pupil
- ii. The direct light reflex is absent or sluggish.
- iii. Constriction is also absent or sluggish in response to light stimulation of the fellow eye (consensual light reflex)
- iv. On slit lamp examination, vermiform movements of the pupillary border are typically seen.
- v. Inspection of the iris using high magnification with the slit lamp can aid in distinguishing functional from nonfunctional sphincter segments.
- vi. Iris crypts stream toward areas of normal sphincter function, and the stroma bunches up along the pupillary border in such areas, whereas stromal thinning-even atrophy-is observed in areas of sphincter paralysis.
- vii. The pupil responds slowly to near, following which re-dilatation is also slow.
- viii. Accommodation may manifest similar tonicity, with slowed and impaired focusing for near and prolonged re-focusing in the distance.
- ix. In long-standing cases the pupil may become small ('little old Adie').
- x. Iris sector paralysis, iris stromal streaming and iris stromal spread.

➤ **Causes A tonic pupil can be caused by**

Local ocular or orbital processes	Part of widespread autonomic dysfunction
1. Surgery,	1. Diabetes mellitus,
2. Trauma,	2. Chronic alcoholism,
3. Laser procedure,	3. Dysautonomias,
4. Infection,	4. Neurosyphilis,
5. Inflammation,	5. Amyloidosis,
6. Ischemia.	6. Sarcoidosis,
	7. Miller-fisher variant of Guillain-Barré syndrome
	8. Charcot-Marie-tooth disease.

➤ **Pharmacological testing.**

- i. Instillation of 0.1–0.125% pilocarpine into both eyes leads to constriction of the abnormal pupil due to denervation hypersensitivity, with the normal pupil unaffected.
- ii. Some diabetic patients may also show this response and very occasionally both pupils constrict in normal individuals.
- iii. Syphilis serology should usually be checked in patients with bilateral tonic pupils.

➤ **Treatment**

- i. Treatment is not generally required, but reading glasses may be used to address near vision difficulties.
- ii. Accommodative symptoms are difficult to treat, they usually resolve spontaneously within a few months of onset.
- iii. Sunglasses or low concentration pilocarpine drops (0.1%) can be used to improve photophobia from a dilated pupil.
- iv. Thoracic sympathectomy can be considered for excessive sweating.

➤ **Denervation Hypersensitivity**

- i. During the acute denervation phase of a tonic pupil, the pupil is dilated and poorly reactive to light stimulation and accommodative effort.
- ii. As the damaged short ciliary nerves regenerate, misguided accommodative fibers sprout onto the iris sphincter, and the pupil recovers its ability to constrict to accommodative (or near) effort.
- iii. However, pupillary movement (both constriction to an accommodative stimulus and subsequent redilation) is delayed and slow; that is, tonic
- iv. This effect may account for patient reports of difficulty refocusing for distance.



- v. The pupillary light reflex typically remains severely impaired.
- vi. The denervated iris sphincter is supersensitive to weak parasympathomimetic - dilute pilocarpine eye drops (0.1%).
- vii. The denervation hypersensitivity and up-regulation results in a constriction response to 0.125 %pilocarpine.
- viii. This strength of pilocarpine can be obtained by diluting commercial 1% solution with sterile saline for injection.
- ix. After 60 minutes, the pupils are reexamined, and if parasympathetic denervation is present, the affected pupil will constrict more than the normal pupil.
- x. About 80% of patients with a tonic pupil show cholinergic denervation supersensitivity.

4. Third nerve palsy

- Pupillary involvement in third nerve palsy is almost always accompanied by ptosis and limited ocular motility.
- At times, the motility disturbance may be subtle, requiring careful quantitation with alternate cover testing.
- Pupillary dysfunction is an important factor in evaluating acute third nerve palsy.
- When the pupil is involved, an aneurysm at the junction of the internal carotid and posterior communicating arteries must be excluded.
- If the pupil is spared and all other functions of the third nerve are completely paretic, an aneurysm can likely be ruled out.
- Aberrant regeneration of the oculomotor nerve may cause mydriasis and a synkinetic pupillary reaction.

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