THE PUPIL -- A STUDY

Pete Caroselli

1997

INTRODUCTION

This paper will focus on the pupil - It's function, innervation, and anomalies. By carefully observing the pupils, a clinician can tell many things about the neurological pathways of the eye. He/she must become skilled at noticing subtle size differences between the pupils in different lighting conditions and abnormal reactions to light. These things can tell you about pathology (compressive lesions, aneurysms, inflammation) occurring behind the eye that is not observable with clinical equipment.

PUPIL FUNCTION

Although the pupil is considered an ocular structure, it is actually an optically empty space which acts as a diaphragm to control the amount of light entering the eye and reaching the retina. Without it, we would not be able to function visually. The size of this diaphragm is regulated by the dilator and sphincter muscles of the iris, controlled by sympathetic and parasympathetic innervation respectively. Think about waking up after a long night's sleep and the room is still dark. After turning on the bedroom lights, the brightness is almost unbearable. The pupils immediately constrict to protect the eyes from excessive light until retinal adaptation can occur. Through constriction, the pupil can also increase depth of focus and decrease spherical and chromatic aberrations of the eye to improve visual acuity. However, if the pupillary diameter is less than two millimeters, visual acuity may decrease because of diffraction.

THE NORMAL PUPIL

The pupils are small at birth and increase in size during the first decade of life. They remain stable until the second decade and then progressively decrease in diameter with age. The normal pupil ranges from 2.5 to 7 millimeters in diameter depending on the present lighting conditions, the state of convergence of the eyes when accommodating to view objects at near, motility of the iris, state of alertness, and the tonus of the sympathetic and parasympathetic nervous systems. In a normal situation the pupils are round, equal in size, and equally reactive to light and accommodation. About 25% of the population has a size difference (anisocoria) of one millimeter or less between the two pupils, which is a normal physiological phenomenon. An acquired anisocoria of recent onset can indicate a lesion within the efferent pathways. The pupils also play a part in the near triad (convergence, accommodation, and miosis) which occurs when someone looks at a near object. The somatic motor component of the oculomotor nerve innervates both medial rectus muscles. When innervated, these muscles contract causing the eyes to converge. The visceral motor component of the third nerve has fibers which lead to the muscles that control both accommodation and pupillary constriction. These are the ciliary muscle and iris sphincter, respectively. When innervated, the ciliary muscle contracts, thereby releasing some of the tension on the lens zonules. This increases the curvature of the lens, which results in accommodation. Finally, the iris sphincter is stimulated to contract causing the pupil to decrease in diameter. This helps to sharpen the image of a near object onto the retina. In a normal situation, the pupils constrict equally and briskly to a near stimulus, similar to the pupillary light reaction. Checking the pupil reactions to both light and accommodation is

important in detecting light-near dissociation which is an abnormal situation and will be discussed later.

SYMPATHETIC PATHWAY FOR PUPIL INNERVATION

Pupil size is sustained by the sympathetic and parasympathetic pathways. Proper neurological innervation to the pupils maintains that these pathways are intact and functional. The sympathetic pathway begins in the hypothalamus and descends through the mesencephalon and pons to the spinal cord where it synapses in the ciliospinal center of Budge in the cervical 8 - thoracic 2 region. The second-order neuron exits the spinal cord, passes over the apex of the lung, progresses through the stellate ganglion, and finally synapses in the superior cervical ganglion. A bifurcation of the internal and external carotid arteries occurs in this area near the upper angle of the jaw. From the superior cervical ganglion, the sympathetic pathway continues as the third-order neuron and accompanies the internal carotid artery after joining the carotid plexus. These fibers then leave the internal carotid artery in the cavernous sinus to accompany the fifth and sixth nerves and proceed through the superior orbital fissure to enter the orbit. Finally, they travel with the nasociliary nerve and break into long ciliary nerves to innervate the iris dilator muscle. Other branches of the sympathetic pathway supply Muller's muscles in the lids and lacrimal and sweat glands.

PARASYMPATHETIC PATHWAY FOR PUPIL INNERVATION

The parasympathetic pathway controls the pupillary light reflex by innervating the iris sphincter. This process begins though, with light entering the eye which triggers a neurological signal along the afferent pathway. This begins with a photochemical reaction that begins at the level of the photoreceptors when light impinges on the retina. The first neuron of the afferent pathway begins its journey through the optic nerve as impulses are collected by ganglion cells.

Fibers carrying impulses originating from the nasal retina decussate at the chiasm and eventually end at the contra-lateral pretectal nucleus. Impulses from the temporal retina are conducted by uncrossed fibers which eventually terminate in the ipsilateral pretectal nucleus. After the chiasm the fibers then continue along the optic tract where they exit prior to the lateral geniculate body and proceed to the brachium of the superior colliculus where they synapse in the pretectum. The second neuron connects each pretectal nucleus to both Edinger-Westphal (E-W) nuclei through intercalating fibers. Thus, impulses to the E-W subnuclei of the third nerve complex are crossed, and innervation of the pupillary sphincters is bilateral. This explains why a light stimulus to one eye results in a direct response from that eye and a symmetrical consensual response from the other.

At the Edinger-Westphal nuclei, the efferent portion of the parasympathetic pathway begins. These fibers travel with the third nerve through the cavernous sinus and enter the orbit with the inferior branch of the oculomotor nerve through the superior orbital fissure. Here, they synapse at the ciliary ganglion. The post-synaptic parasympathetic fibers run in the short ciliary nerves and end at the pupillary sphincter muscle and ciliary body. The pupillary parasympathetic fibers run superficially within the third nerve between the E-W nucleus and cavernous sinus, thus can be affected without third nerve involvement. After the third nerve passes through the cavernous sinus, the pupillary fibers occupy a more central position and therefor may be spared if a lesion occurs in this area. An aneurysm is usually the culprit when problems arise in the area between the E-W nucleus and cavernous sinus. When the aneurysm causes a significant amount of compression to the oculomotor nerve in this vicinity, the result may be a third nerve palsy with pupillary involvement. This is a medical emergency. Signs of this occurance are an eye pointing down and out, ptosis, and mydriasis on the side of the

lesion. In contrast, if the oculomotor nerve is involved without pupillary involvement, the cause is usually ischemic.

CLINICAL ASSESSMENT OF ANISOCORIA

An important part of the comprehensive vision exam should include careful pupil assessment in normal and dim lighting. The pupils should be equal in size in both of these conditions. If they are unequal, anisocoria is present. The next step is to determine if the size difference is pathological in nature or physiological. A good starting point would be to take a careful history. Ask when the anisocoria was first noticed, if there are any other signs or symptoms besides unequal pupils, and if there is any history of ocular trauma. Also ask about recent use of drops or ointments, history of syphilis, or recent complaints of decreased vision. Finally, check old photographs of the patient to identify if the anisocoria has always been there. Upon examination, if the anisocoria remains equal in both bright and dim illumination, it is probably physiological. Anisocoria greater in dim illumination suggests that the abnormal pupil is the smaller pupil and points toward a defect which involves the sympathetic nervous system or dilator muscle of the iris (See Fig. 1). Anisocoria greater in bright illumination suggests that the abnormal pupil is the larger pupil and points toward a defect which involves the parasympathetic system or iris sphincter (See Fig 2).

CLINICAL ASSESSMENT OF THE AFFERENT PUPILLARY DEFECT

Next, reactions of the pupils to a light stimulus are examined. This is accomplished by shining a transilluminator alternately into each pupil (the swinging flashlight test) and noting the reactions. Normally, both pupils should react equally and crisply. If the direct response in an eye is less than its consensual response, an afferent pupillary defect (APD) is present. Another term for an APD is a Marcus Gunn pupil. Clinically, this can be perceived by

observing both pupils constrict when a light is shined into the unaffected eye and noticing both pupils dilate when light is swung to the affected eye (See Fig. 3). Damage to either optic nerve in which the visual afferent fibers are affected prior to their crossing at the chiasm will result in these responses. Macular disease can cause an APD, however, these retinal lesions are obvious on examination and severely reduce visual acuity (20/200 or worse). With optic nerve lesions an afferent pupillary defect can be present with relatively good acuity. Although media opacities such as corneal scars, dense cataracts, and vitreal hemorrages filter a significant amount of incoming light, they do not cause an APD. Recent studies suggest that filtering of incoming light can be compensated by adaptation through increased sensitivity within the retina and possibly the midbrain.

CONDITIONS ASSOCIATED WITH AN AFFERENT PUPILLARY DEFECT

Optic neuritis is one condition that is associated with an afferent pupillary defect if the condition is unilateral. It is characterized by a loss of vision deteriorating over a period of hours to days. Visual loss can range from mild to profound. People affected are usually 18-45 years old and experience orbital pain on eye movement. In many cases, there is decreased color vision; decrease perception of light intensity; and central, centrocecal, arcuate, or altitudinal visual field defects. Optic neuritis may be associated with a swollen disc - more common in children and young adults; or a normal disc as in retrobulbar optic neuritis - more common in adults. Posterior vitreous cells may be observed in conjunction with an optic neuritis that is associated with a swollen disc because the inflammation involves the intraocular portion of the optic nerve. Its etiology may be idiopathic; due to multiple sclerosis; associated with viral infections such as herpes zoster, mononucleosis, measles, or mumps; and may be

secondary to intraocular or granulomatous inflammations such as tuberculosis, syphilis, or sarcoidosis.

An APD can also be a critical sign of arteritic or non-arteritic ischemic optic neuropathy. These are initially unilateral but may rapidly become bilateral and are characterized by a sudden, painless, non-progressive severe visual loss. The arteritic form occurs in people older than fifty years of age and is combined with a simultaneous headache, pain with chewing, scalp tenderness, polymyalgia rheumatica, and an elevated erythrocyte sedimentation rate (ESR). The non-arteritic form is different in that it occurs in people 40-60 years of age, has a normal ESR, and is not associated with the scalp pain and headache. These neuropathies are also characterized by an altitudinal or central visual field defect. A compressive optic neuropathy is characterized in most cases, by a slowly progressive visual loss, a central visual field defect, and a relative APD. Other signs include proptosis and optociliary shunt vessels. All patients displaying progressive visual loss and optic nerve dysfunction should undergo either an MRI of the orbit and brain or CT scan. These can reveal possible plaques found in Multiple Sclerosis or rule-out a possible intraorbital mass.

Finally, an amaurotic eye is a totally blind eye with no light perception. Thus, an amaurotic pupil shows no direct response to light, and the normal eye has no consensual response. When light is shined in the good eye however, both pupils constrict normally. This may be the case after an optic nerve glioma. The optic nerve, or possibly both nerves, may be severed in the excision of the tumor, causing amaurotic eyes.

PARASYMPATHETIC PATHWAY LESIONS

Light-near dissociation, the instance of pupils not reacting well to light but normally to near, is seen in Adie's tonic pupil, Argyll-Robertson pupil, Parinaud's Syndrome, and aberrant

third nerve regeneration. Adie's tonic pupil is the result of a lesion of the ciliary ganglion. Someone with this affliction may present with a chief complaint of blur at near because accommodation is decreased. In the early stages one pupil is irregularly dilated with minimal or no reaction to light, shows slow constriction to convergence, and slowly re-dilates as the patient shifts gaze from near to distance. It is most commonly found in young women (second to fourth decades) and demonstrates supersensitivity to pilocarpine 0.125% (see Table 1). A pathogneumonic sign of an Adie's pupil is iris sector palsy with segmental veriform movements - in other words, wavy portions at the iris/pupil border. Over time, this condition may extend bilaterally, and the pupils may become more miotic. The diagnosis then becomes much more difficult. If the pupil signs are in conjunction with Adie's Syndrome, deep tendon reflexes of the knees and ankles are often absent. The first thing that may be noticed clinically in the early stages of Adie's is a greater anisocoria in bright lighting (See Fig 4).

Table 1.

Dilution of Commercially Available Pilocarpine

percentage of commercially available pilocarpine	Desired final concentration (%)	
	0.1	0.125
1	1/9	1/7
2	1/19	1/15

Dilutions are prepared by mixing the indicated number of drops of commercially available drug (numerator) with the indicated number of drops of saline (denominator). Equal drop sizes should be used.

The Argyll-Robertson pupil is the hallmark sign of neurosyphilis and is usually asymptomatic with normal vision. It presents as a miotic and irregular pupil that reacts poorly or not at all to light but constricts normally when looking at a near object. The anisocoria will

be greater in dim lighting. This, in most cases, is a bilateral condition although asymmetric. Also, the pupils dilate poorly upon instillation of a mydriatic. The light-near dissociation in this case is theorized to be secondary to a lesion of the intercalating neurons between the pretectal nuclei and the Edinger-Westphal subnucleus (See Fig 5). Other ocular signs of syphilis are interstitial keratitis, chorioretinitis, retinal vasculitis, papillitis, and uveitis. Laboratory tests that confirm the diagnosis of syphilis include FTA-ABS and VDRL. FTA-ABS is a specific test in all stages of syphilis to detect antitreponemal antibodies. If positive, the test remains positive throughout the patient's life regardless of treatment. VDRL becomes positive shortly after the development of the primary chancre. In many cases, it will become negative after adequate antisyphilitic therapy.

Parinaud's Syndrome is another abnormality that may be suspected when light-near dissociation is identified. It is caused by a pineal tumor or midbrain infarction. Parinaud's can be differentiated from the other abnormalities that have been discussed because the light-near dissociation associated with this syndrome is part of a triad of signs that help in its distinction. The two other cardinal signs are paresis of upward gaze, particularly with saccades, and retraction nystagmus. This is characterized by spurts of convergence and retraction of both eyes, especially when attempting an upward saccade. These unusual signs can be accompanied by accommodative spasm and lid retraction (Collier's sign) on attempted upgaze.

Abberant regeneration of the third nerve sometimes occurs after a total third nerve palsy. After oculomotor nerve fibers are disrupted by trauma, they can grow back in the direction of any of the pathways of ocular muscles innervated by this nerve. Following a third nerve palsy, the pupil may remain permanently fixed and dilated, return back to normal, or remain fixed and dilated, but react curiously secondary to aberrant regeneration of fibers. This pupil does not

constrict to light but reacts somewhat upon convergence. However, it also constricts on adduction of the eye due to a misdirection of fibers after re-growth. Retraction and adduction of the globe on attempted up-gaze may also occur. As the superior rectus is innervated for up-gaze, the inferior rectus and medial rectus are also aberrantly innervated. So, instead of going up, the eye retracts a little and adducts a little. If a misdirection syndrome is observed, you know it has been about 3-6 months since the lesion occurred, which is the approximate time frame for this process to take place.

HORNER'S SYNDROME (SYMPATHETIC PATHWAY LESION)

Yet another abnormality that may be encountered is a miotic pupil that does not dilate nearly as well as the normal pupil. It is secondary to a lesion along the sympathetic pathway which means that the anisocoria is greater in dim illumination due to decreased pupillary dilation. When the abnormal pupil is accompanied by ptosis, anhydrosis, apparent enophthalmos, increased accommodation, and decreased intraocular pressure, it may indicate Horner's Syndrome. A congenital Horner's Syndrome also displays iris heterochromia with the lighter iris on the affected side secondary to decreased sympathetic stimulus to melanin formation.

Localizing the lesion along the sympathetic pathway is important because the prognosis for a postganglionic lesion is far better than that for one that is preganglionic. Preganglionic lesions may be the result of CNS disease, bronchial carcinoma, or thoracic aortic aneurysms. The most common tumor is the Pancoast apical lung lesion and may be ruled out through a chest X-ray. This lesion secondary to an apical tumor is usually a second order neuron defect associated with arm and hand pain. Horner's Syndrome secondary to a vascular lesion is probably located higher in the neck where it is associated with arteriosclerotic disease of the

carotid artery. This is usually a third order neuron lesion. The Horner's Syndrome may be associated with a third nerve palsy if a lesion occurs near the cavernous sinus. Involvement near the cavenous sinus may also involve the sixth nerve causing a conjugate sixth nerve palsy and Horner's. These postganglionic lesions are usually idiopathic or associated with vascular headaches and are almost always benign.

Using 10% cocaine is the classic definitive test for Horner's. It acts by blocking the re-uptake of norepinephrine from postsynaptic terminals. Pupil dilation after instillation indicates a negative test, and no pupillary reaction indicates a positive Horner's. Although 10% cocaine is useful in the diagnosis, the drug does not localize the lesion.

Paradrine (Hydroxyamphetamine 1%) is the drug of choice for determining whether the lesion is preganglionic or postganglionic. It acts by stimulating the release of norepinephrine from the presynaptic neuron. The postganglionic sight along the sympathetic pathway is the only synapse that uses norepinephrine as its neurotransmitter. Therefor, if the postganglionic cleft is functioning properly, the result is pupil dilation. A non-functioning postganglionic sight will give rise to a pupil that does not dilate upon administration of paradrine. So, paradrine will cause the pupil to dilate poorly in the presence of a postganglionic lesion and normally in the case of a central or preganglionic lesion (See Fig. 6). Paradrine is produced by the Smith, Kline, and French Laboratories in Philadelphia, PA.

At present, there is no pharmacological test that can differentiate a central from a preganglionic lesion. This is done on the basis of other clinical data. A central lesion may be associated with the presence of hypothalamic, brain stem, or spinal cord symptoms. A preganglionic lesion may be associated with signs and/or symptoms that deal with the chest or neck.

ABNORMAL PUPIL SHAPES

A distortion of the pupil can indicate congenital and developmental anomalies of the iris. Aniridia is one that is characterized by the absence of the iris. This can range from a totally absent iris to a small iris coloboma. This condition is usually bilateral and the patient experiences photophobia. Other characteristics include foveal hypoplasia, nystagmus, decreased visual acuity, and secondary glaucoma. Aniridia can be managed with artificial pupil contact lenses and tinted lenses to regulate the amount of light that reaches the retina. Low vision devices can also be used to improve acuity. Corectopia is the displacement of the pupil. This can be congenital or secondary to surgery. Corectopia was common after earlier cataract surgeries before the advent of the no-stitch procedures. Dyscoria is the abnormality in pupil shape. A fairly common abnormality is a keyhole shape. It can arise secondary to a sphincter tear that might occur following blunt trauma to the eye. Posterior synechiae can also cause dyscoria. Polycoria means multiple pupils. Vera polycoria is one type in which each pupil has an iris sphincter. Spuria polycoria is another variety in which only one of the openings has an iris sphincter. This type, in many instances, is a pseudopolycoria because holes develop in the iris due to iris atrophy causing pigment dispersion and possibly pigmentary glaucoma (See Table 2).

TABLE 2.

Aniridia - The absence of the iris.
Corectopia - Displacement of the pupil.
Dyscoria - Abnormal pupil shape.
Polycoria - Muliple pupils.

CONCLUSION

In summary, unequal and abnormally responding pupils can indicate many things about the neurology behind the eye. A miotic pupil can point to a sympathetic pathway lesion. However, this must be differentiated from such conditions as iritis, unilateral use of miotic eye drops, and physiological anisocoria. Miosis secondary to an iritis may also be associated with a painful red eye, photophobia, and slightly decreased vision. The hallmark of anterior uveitis is the presence of cells and/or flare in the anterior chamber. Other possible signs include posterior synechiae, low IOP, and circumlimbal vessel injection.

A miotic pupil may be secondary to certain pharmacological agents. To decrease intraocular pressure, many glaucoma patients are prescribed pilocarpine which acts to increase aqueous outflow. Pilocarpine is a parasympathomimetic which stimulates the pupil to constrict. Other instances occur with people who work in hospitals or nursing homes. They may accidentally come in contact with medications that will constrict the pupil. These types of cases may be ruled out by taking a careful patient history.

A dilated pupil may indicate a lesion along the parasympathetic pathway. However, this must be differentiated from such conditions as iris sphincter damage secondary to trauma, pharmacological mydriasis, or physiological anisocoria. The sphincter muscle can rupture or tear secondary to blunt trauma to the eye. Iatrogenic trauma, such as cataract extraction or iridectomies are also possibilities. Sphincter trauma can also result from ischemia. A dilated pupil may be seen in vascular occlusion or local vascular compromise secondary to narrow angle glaucoma.

The pharmacologically dilated pupil can be detected by instilling a drop of 1% pilocarpine. A mydriatic pupil caused by a lesion to the third nerve will constrict. A pharmacologically dilated pupil will not because the mydriatic agent will block the postganglionic cholinergic receptors, thus making pilocarpine ineffective.

When the abnormal pupil indicates a neurological dysfunction, a few general rules, in many cases, hold true. Lesions in the midbrain area cause dilated pupils and lesions in the pontine area cause miotic pupils. Lesions of the dorsal midbrain often give rise to pupillary light-near dissociation. The most frequent cause, in this case, is a pineal gland tumor.

The pupil evaluation is an important part of the comprehensive vision and eye health examination. It should not be overlooked or passed over quickly. In many instances, an abnormal pupil may be the first clue in making an accurate clinical diagnosis.

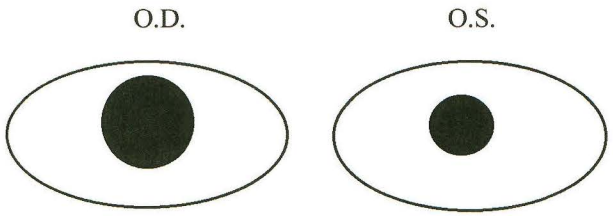


Fig. 1 Anisocoria greater in dim illumination. Left eye defect suggesting sympathetic lesion.

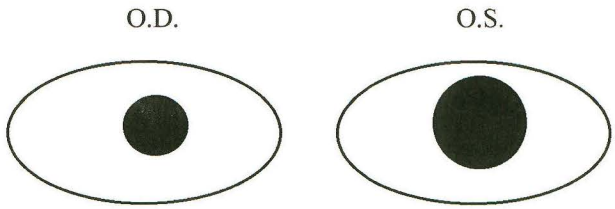


Fig. 2 Anisocoria greater in bright illumination. Left eye defect suggesting parasympathetic lesion.

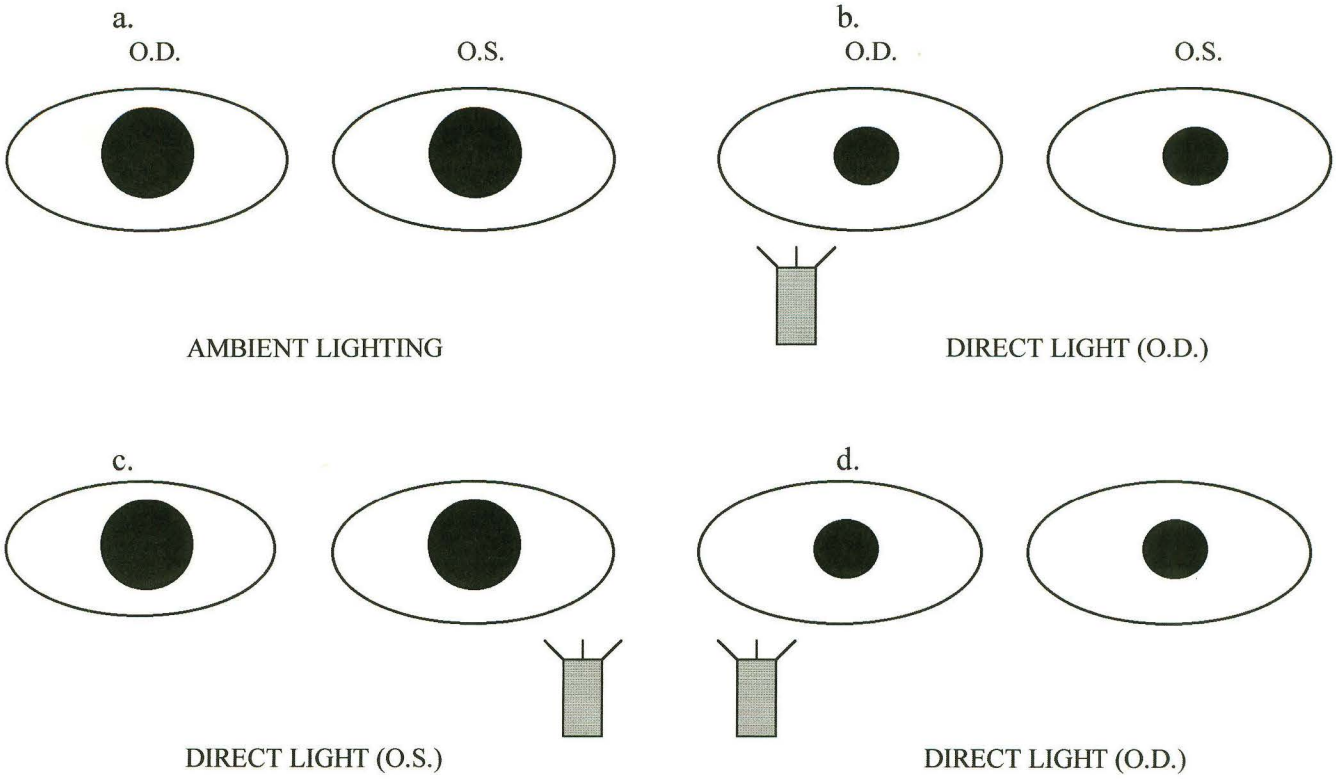
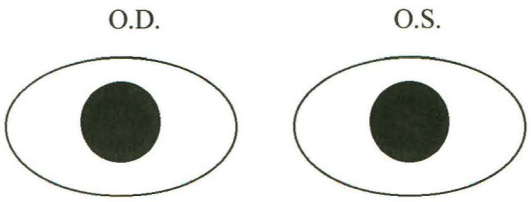
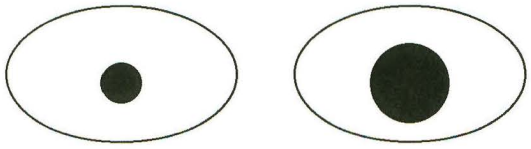


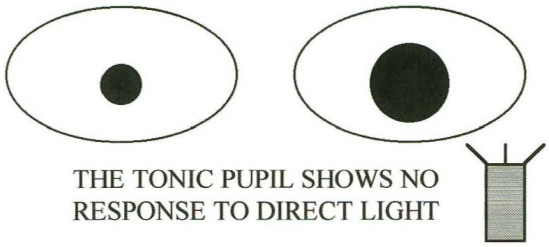
Fig. 3. APD (O.S.) shown by the swinging flashlight test.



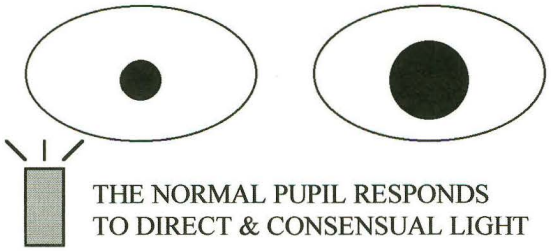
DIM ILLUMINATION



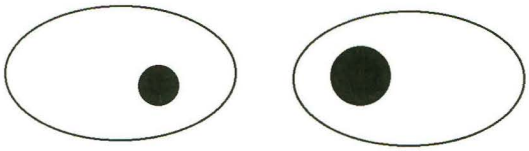
BRIGHT ILLUMINATION



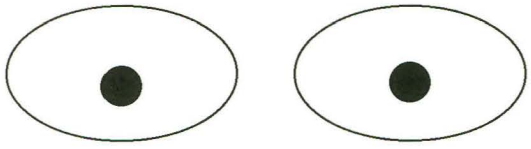
THE TONIC PUPIL SHOWS NO RESPONSE TO DIRECT LIGHT



THE NORMAL PUPIL RESPONDS TO DIRECT & CONSENSUAL LIGHT

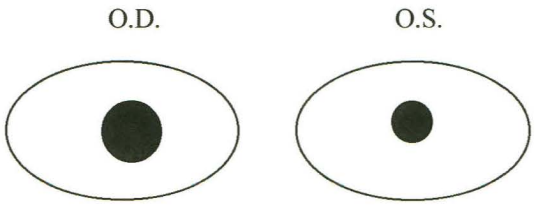


BOTH PUPILS CONSTRICT WITH CONVERGENCE.

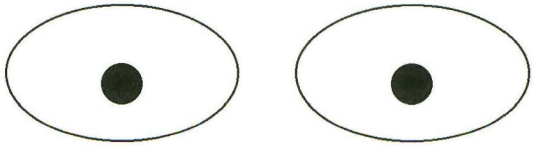


ADIE'S PUPIL IS SUPERSENSITIVE TO 0.125% PILOCARPINE

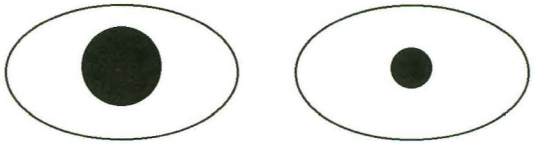
Fig. 4 Adie's Tonic Pupil (O.S.)



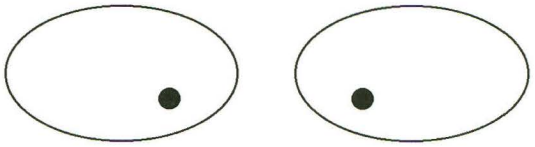
AMBIENT LIGHTING



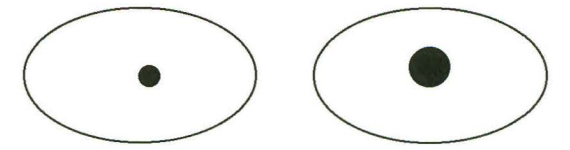
LESS ANISOCORIA IN BRIGHT ILLUMINATION



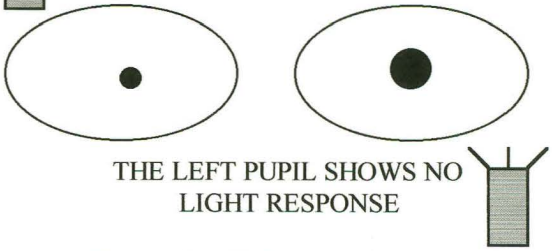
GREATER ANISOCORIA IN DIM ILLUMINATION



BOTH PUPILS CONSTRICT DURING CONVERGENCE

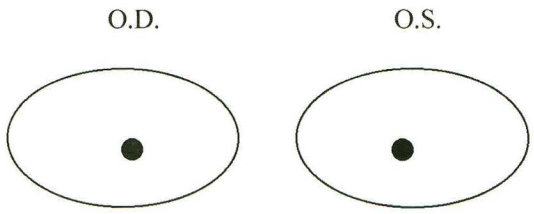


THE NORMAL PUPIL RESPONDS TO DIRECT & CONSENSUAL LIGHT



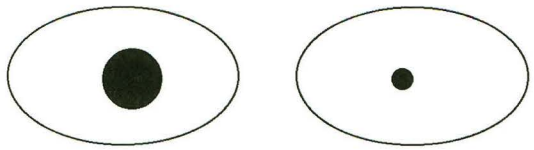
THE LEFT PUPIL SHOWS NO LIGHT RESPONSE

Fig. 5. Argyll-Robertson Pupil (O.S.)



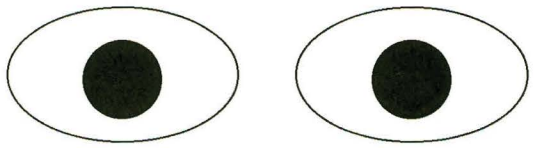
BRIGHT ILLUMINATION

MIMIMAL OR NO ANISOCORIA



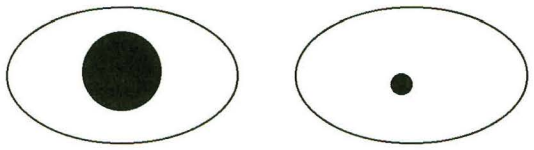
DIM ILLUMINATION

GREATER ANISOCORIA - SUGGESTS SYMPATHETIC PATHWAY LESION



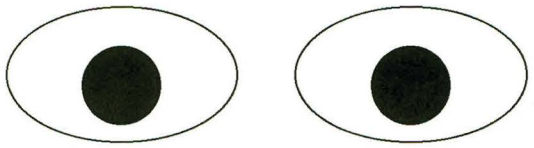
NEGATIVE 10% COCAINE TEST

NEGATIVE HORNER'S - SUSPICIOUS PUPIL DILATES WITH COCAINE



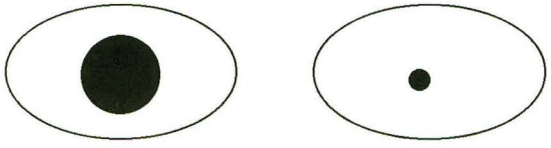
POSITIVE 10% COCAINE TEST

POSITIVE HORNER'S - SUSPICIOUS PUPIL SHOWS NO DILATION



POSITIVE 1% PARADRINE TEST

DILATION OF SUSPECT PUPIL SUGGESTS POSTGANGLIONIC LESION



NEGATIVE 1% PARADRINE TEST

SUSPECT PUPIL SHOWS NO DILATION - SUGGESTS PREGANGLIONIC LESION

Fig. 6. Horner's Syndrome (O.S.)

Table 3.

	APD	ADIE'S	LONG STANDING ADIE'S	ARGYLL-ROBERTSON	HORNER'S
SIZE	NORMAL	DILATED	MIOTIC	MIOTIC	MIOTIC
SHAPE	ROUND	IRREGULAR	IRREGULAR	IRREGULAR	ROUND
REACTION TO LIGHT	PUPIL DILATION	MINIMAL TO NONE	MINIMAL TO NONE	MINIMAL TO NONE	NORMAL
BRIGHT ILLUM.	LARGER THAN NORM	DILATED	MIOTIC	MIOTIC	MIOTIC
DIM ILLUM.	NORMAL	DILATED	MIOTIC	MIOTIC	MIOTIC
REACTION TO NEAR	NORMAL	CONSTRICTS SLOWLY	CONSTRICTS SLOWLY	NORMAL	NORMAL

BIBLIOGRAPHY

Bartlett, Jimmy D., O.D., D.O.S. and Jaanus, Siret D., Ph.D. Neuro-Ophthalmic Disorders. Clinical Ocular Pharmacology 3rd Edition. 1995; 523, 527.

Burde, Ronald M., M.D., Savino, Peter J., M.D., and Trobe, Jonathan, D., M.D. Anisocoria and abnormal pupillary light reactions. Clinical Decisions in Neuro-Ophthalmology. 1985: 7;224-243.

Burde, Ronald M., M.D. and Slamovitz, Thomas L., M.D. The Pupil. Neuro-Ophthalmology - Textbook of Ophthalmology Vol. 6. 1994: 5;1-24.

Burt, Alvin M., Ph.D. Textbook of Neuroanatomy. 1993: 225, 226, 397.

Chang, Benjamin and Cullom, R. Douglas Jr. The Wills Eye Manual 2nd Edition. 1994: 11;241-248;395-398.

Kanski, Jack J. Neuro-Ophthalmology. Clinical Ophthalmology 2nd Edition. 1989: 15; 472-475.

Newman, Nancy M. The Pupil. Neuro-Ophthalmology - A Practical Text. 1992: 16;239-252.

Smith, J.L., M.D. The Pupil.

Spalton, David J., Hitchings, Roger A., and Hunter, Paul A. Neuro-Ophthalmology. Atlas of Clinical Ophthalmology 2nd Edition. 1994: 19.14-19.17.

Wilson-Pauwels, Linda, A.O.C.A., B.Sc. AAM., Akesson, Elizabeth J., B.A., M.Sc., and Stewart, Patricia A., M.Sc., Ph.D. Cranial Nerves - Anatomy and Clinical Comments. 1988: 26-36.