THE PUPILLARY REFLEXES
and THEIR NEUROLOGICAL IMPORTANCE

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The pupil is a circular opening in the center of the iris, its shape and size controlled by the iris. Usually three to four millimeters in diameter in normal room light, it may reach eight to nine millimeters when maximimly dilated.

The function of the pupil is mostly optical. It regulates the amount of light reaching the retina. It increases the depth of focus and decreases the chromatic and spherical aberration caused by the lens and cornea.

The pupil is in constant motion which varies with the amount of light present. In bright light, these oscillations are small and regular, in dim light, they are larger and slower. Termed pupillary unrest, the bilateral oscillations are caused by a dynamic equilibrium between the sympathetic and parasympathetic systems and are considered non-pathological. Hippus is an extensive degree of bilateral unrest and its importance is not known.

The pupillary size is controlled by both the sympathetic and parasympathetic systems. The iris muscles play a very important part, and any pathology or atrophy of the iris will affect the pupillary size and shape. For example, an iritis may cause unequal contractions in the sphincter.

The iris, and hence the pupil, is controlled by two muscle masses, the dilator and the sphincter. The sphincter, located in the stromal layers, is composed of fully developed smooth muscle cells. It is about one millimeter wide and forms a ring around the pupillary border. Derived from ectoderm, it is inervated by the parasympathetic Oculomotor nerve via the Short Ciliary Nerve.
The dilator, by contrast, is a loosely arranged muscle composed by myoepithelial cells. The cells are part of the epithelium in one end and are contractile at the other end. They are also of ectodermal origin, and are interlaced with the edge of the sphincter muscle. It is under the control of the sympathetic system innervated by the Long Ciliary Nerves.

The sympathetic pathway, controlling dilation of the pupil, begins in the posterolateral hypothalamus and descends through the tegmentum and the pons. A few fibers may partially cross in the decussation of Forel. They cross the pre-rubal field and terminate in the intermediolateral cell column at the level of C8 through T2. This area is called the ciliospinal center or the center of Budge and Waller. Fibers leave T1 via the white rami communicantes in the para vertebral sympathetic chain. They follow the stellate ganglion and are in near proximity to the pleura at the pulmonary apex. They travel in the anterior loop of the ansa subclavia of Vieussens through the Inferior and Medial Cervical Ganglion to synapse in the Superior Cervical Ganglion. The Superior Cervical Ganglion is the largest of the sympathetic ganglion, being about two to three centimeters long. It is located below the base of the skull between the jugular vein and the internal carotid artery. The post-ganglionic fibers exit as a thick bundle and accompany the carotid artery through the carotid canal and the foramen lacerum to the Casserian Ganglion and the cavernous sinus. It continues on to the orbit near the ophthalmic division of the Trigeminal nerve. They reach the eye as the Long Ciliary Nerve and end in the dilator muscle. This pathway is responsible for the fright or fight response of the pupil.

The light reflex is controlled by the parasympathetic system and is considered to be a three neuron arc. The afferent arc begins in the retinal ganglion cells to the pretectal nucleus, where there is a synapse. The second order neuron arises from the pretectal nucleus...
to the parasympathetic Edinger-Westphal nucleus. The efferent arc begins at the Edinger-Westphal nucleus via the Oculomotor nerve to the Ciliary Ganglion, where there is a synapse. From there, the fibers proceed to the sphincter.

The light reflex is termed a retinomesencephalic pathway and begins in the rod and cone layer of the retina. It is uncertain if there is a different set of ganglion cells that mediate vision than those controlling pupillary reactions. It is known, however, that the ganglion cells do carry pupillomotor information from the eye via the optic nerve, and partially cross in the optic chiasm. They extend into the posterior one third of the optic tract and exit into the superior brachium conjunctium. They do not enter the Superior Colliculus. The fibers then enter the pretectal nucleus in the midbrain and synapse. They exit via the intercalated neurons, partially crossing in the posterior commissure. From here, they enter the Edinger-Westphal nucleus and synapse. The efferent arc begins in the Edinger-Westphal nucleus via the Oculomotor nerve. They exit in the midbrain in the interpeduncular space. Here they lie superficially, just internal to the epineurium and are very vulnerable to compression. At the superior orbital fissure, the oculomotor nerve divides into a superior and inferior division. The pupillomotor fibers follow the inferior division, which also carries innervation to the inferior oblique. These parasympathetic mylineated fibers enter the ciliary ganglion where they synapse. The fibers which control accommodation also synapse in the ciliary ganglion, also having origin in the Edinger-Westphal nucleus. Studies have estimated that there are thirty fibers for accommodation control for every one fiber for pupillary constriction. Fibers exit from the ciliary ganglion via the short ciliary nerves to the sphincter.

The Edinger-Westphal nucleus receives information form higher centers which help to control the light reaction. It receives inhibitory input from the cortex via the corticomesencephalic pathway
and the hypothalamus. These tend to keep the pupil slightly dilated. For example, during sleep these supranuclear influences are decreased and miosis results. The pupil remains reactive during sleep.

The pretectal nucleus in the midbrain cannot differentiate which retina is being stimulated. Therefore the efferent impulses to each sphincter muscle is equal and gives rise to an equal direct and consensual response. Some studies state that the constriction of the fixating eye is greater than the non-fixating eye, especially in amblyopia. However, recent information indicates this may not be true. It is certain that when both eyes are stimulated, the reaction that occurs is a summation from the two eyes.

The retina shows a variable response to light dependent upon the area of the retina stimulated and the intensity of the stimulus.

With a bright stimulus, the macular and perimacular areas are the most sensitive and the nasal retina responds stronger than the temporal retina. With a low intensity stimulus, the peripheral areas of the retina are the most sensitive. However, the amplitude is lower than the amplitude of the macular area to a bright stimulus. Some authors advocate stimulating different areas of the retina to compare the temporal reaction form one eye to the temporal area in the other eye. Others feel that without a pupilllograph, precise measurements cannot be made and the test is useless for general practice.

Lesions which affect the afferent arc generally show a miotic fixed pupil where a lesion of the efferent arc generally show a dilated fixed pupil.

In a unilateral afferent defect, both pupils react sluggishly when the pupil on the defective side is stimulated. The intact eye reacts with a normal brisk response to direct stimulation. The swinging flashlight test shows the release of the strong pupillary response from the intact eye as the light is moved from the intact
to the defective eye. This is called the Marcus Gunn pupil.

A lesion of the optic nerve will show a Marcus Gunn pupil with an intact near reflex. In their resting state both pupils may appear equal in size or the pupil on the affected side may be larger if his fellow is occluded. Some possible causes are optic neuritis, vascular accidents, tumors, and trauma.

In an optic chiasm lesion, the pupils are usually equal in size. Since the nasal hemi-retinal fibers are interrupted, the response from the temporal field will be less than that from the nasal field. The near reaction is normal.

An anterior junction syndrome occurs when the chiasm and the optic nerve are both involved. The defective optic nerve causes a Marcus Gunn in the affected eye, while the fellow eye shows a chiasmatic hemianoptic reaction. Some causative factors may be tumors or aneurysms.

An optic tract lesion can be defined by the use of visual fields. It will cause an incongruous homonymous hemianopsia. Also a homonymous hemianoptic pupillary problem which is termed Wernicke's hemianopic reaction. The pupils are equal in size and the near reaction is present.

A lesion above the level of the lateral geniculate body will not affect the pupillary fibers. It will produce a homonymous hemianopsia. That is why patients with cortical blindness will show a normal pupillary response.

A lesion in the intercalated neurons causes an alternating contraction anisocoria. A light stimulus into the temporal retina will cause a homolateral response, but no contralateral response. If the nasal retina is stimulated, the homolateral response is absent with the contralateral response intact. These are difficult to observe without the use of a pupillograph. This type of defect causes an Argyll Robertson pupil and may also cause lid retraction.
The near reflex mediated by the occipitomesencephalic pathway is an associated convergence, accommodation, and constriction. It is not a true reflex, but is more properly termed a synkinesis and arises from awareness of a near object. The near triad can be disassociated by the use of lenses and prism with the constriction still occurring. It is believed to be mediated by the cortex in area 19.

From area 19, fibers descend to the Edinger-Westphal nucleus. Some authors feel that the caudal section is associated with pupillary constriction while the rostral section is associated with accommodation and the mid portion is concerned with both. The fibers concerned with constriction exit the nucleus via the oculomotor nerve to the ciliary ganglion. The post-ganglionic fibers exit the ganglion via the short ciliary nerves to the sphincter.

In normals, the light reaction and the near reaction are both present, and summate. When the light reaction is not present, but the near reaction is, a number of conditions, such as syphilis or Parinaud's syndrome.

The dark reaction, dilation following the removable of a light stimulus, is elicited by a short interval of darkness after the eye is light-adapted. It is a bilateral reaction and the latent period is a little longer than the latency of the near reaction. It may be due to a simple cessation of the light-induced constriction, however some authors believe it is due to active inhibition of the Edinger-Westphal nucleus due to the "off" discharge in the retina.

The lid-closure reflex is the dilation of the pupil during closure and constriction following the blink. With the opening of the lid, a constriction takes place and is due to an increased retinal sensitivity during the brief period of darkness. It is dependent upon the duration of the lid closure, the room illumination, and the amount of psychosensory stimulation.
The trigeminal reflex, also called the oculosensory pupillary reflex, is a bilateral transient dilation followed by a sustained constriction. The reaction of the stimulated eye is usually greater. It is caused by stimulation of the cornea, conjunctiva, or eyelid by an irritating source. It indicates that the trigeminal fibers stimulate the third nerve nucleus by connections in the midbrain. It is an axon reflex mediated by the fifth cranial nerve.

The orbicularis reflex, also known as the forced lid-closure reflex and the Westphal-Piltz pupillary reaction, is the unilateral miosis that occurs with contraction of the orbicularis oculi muscle. It may be responsible for the pupillary reaction of an eye with no light perception. It is present in eighty per cent of normals and shows the efferent pathway is intact. It can be helpful in diagnosis of the Argyll Robertson pupil.

The vestibular reflex is a bilateral wide dilation, preceded by a constriction, which finally manifests into hippus. It is due to stimulation of the labyrinth by a thermal, rotation, or air compression. The iris increases in volume, causing constriction and is due to two possible mechanisms. The release of histamine causes vasodilation of the iris blood vessels and prostaglandins may also play a vasoactive role.

The psychosensory reflex is a mydriasis produced by an emotional stimulation. It is a result of two possible mechanisms. One is caused by the stimulation of the sympathetic nerve and is termed active. The passive mechanism results from the inhibition of the Edinger-Westphal nuclei by cortex, thalamus and hypothalamus. With prolonged or intense stimulation humoral control of adrenergic substances may enhance the reaction. It is known that norepinephrine from the heart reaches the eye in two to five seconds and dilates the pupil. It is believed that most catecholamines released during severe
stress may reach the pupil in twelve to fifteen seconds and possibly causes the pupil to remain dilated for several seconds.

It should be kept in mind during a pupillary examination that the psychosensory reflexes may be playing a major role in the size and reactivity of the pupils. It is especially noted that young females may be over anxious and will present with a fixed dilated pupils. If the pupillary reactions are repeated later, they will appear normal if the patient is relaxed.

Several phenomenon have been associated with the psychic aspect of pupillary reactions. They will result in pupillary dilation.

- Ciliospinal- the skin of the neck is pinched
- Cochleopupillary- tuning fork is held to the ear
- Flatau’s Neck mydriasis- the neck is flexed
- Redlich’s Phenomenon-from vigorous sustained muscle activity
- Meyer’s iliac- pressure on McBurney’s point

In a schizophrenic patient, the pupil will appear normal and reactive at times, and dilated and fixed at other times. The non-reactive phase is termed spasmus mobilis and is believed to be an exaggerated psychosensory response from inner turmoil.

Bumke’s Anxiety pupil is the term given to a maximally dilated non-reactive pupil due to the psychosensory reflex. It is seen in neurotic individuals.

It is also believed that a few individuals can voluntarily dilate their pupils and is due to psychosensory reaction.

Anisocoria is present in almost everyone to some degree. It is present in a clinically significant amount in about twenty to twenty-five per cent of otherwise normal individuals and is called essential anisocoria. One characteristic of essential anisocoria is that the amount of anisocoria remains the same regardless of the room illumination. Old photos may be helpful in determining the time of onset.
The tonic pupil, also known as Adie's pupil, myotonic pupil, and pupiliotonic psuedotabes, is a pupillary abnormality in which the reaction to a light stimulus is very slow and reduced in amplitude. The pupillary constriction associated with accommodation is also slow and accommodation itself may be normal or tonic. There may be episodes of painful ciliary spasms. The amplitude of accommodation may also be reduced. It is usually of acute origin and the reaction to near and accommodation may recover, but the reaction to light rarely does.

It occurs most often in females between the age of thirty and fifty and is unilateral in eighty per cent of the cases. The affected pupil is larger in regular room illumination. It will be smaller in dim illumination or after prolonged accommodative effort, as the pupil also re-dilates very slowly. About one half of the patients have an associated loss of deep tendon reflexes which may involve the ankle only, or the ankle and the knee. If present, it is termed the Holmes-Adies Syndrome.

The tonic pupil is considered to be due to a lesion at the ciliary ganglion or to the post-ganglionic pathway to the sphincter. It is thought that the ganglion cells to the ciliary ganglion are decreased in number or absent. The fibers subserving the ciliary muscle, being more numerous than those serving the pupillary sphincter, are the most likely to be re-innervated. This accounts for the re-instatement of accommodation with the absence of the light reflex.

It is usually considered to be a benign condition, and may follow a viral illness or orbital trauma. It has been reported to follow retinal detachment surgery where there is damage to the long ciliary nerve. It is usually not considered to be hereditary, but has rarely been reported among members of the same family. The tonic pupil may be associated with such severe conditions as orthostatic hypotension, progressive segmental hyphidrosis, or forme fruste familial dysautonomia.
Riley-Day Syndrome which includes symptoms such as excessive sweating, emotional problems, vomiting, absence of tearing with associated trophic corneal lesions, may be associated with the tonic pupil.

Useful diagnostic tests include observation of the tonic reaction to light and near. Veriform movements will be seen with the slit lamp and are due to portions of the sphincter muscle contracting independently of other portions of the muscle.

Due to denervation supersensitivity, 2.5% Mecholyl or .125% pilocarpine will constrict the pupil.

Horner's Syndrome, also called the oculosympathetic defect, is due to a partial or total interruption of the sympathetic pathway at any location from the hypothalamus through the orbit.

The clinical features include:

1.) Miosis on the affected side. It is due to a paretic dilator muscle. Therefore the amount of anisocoria is more marked in dim illumination. The pupil may become larger than its fellow during extreme excitement due to circulating andrenergics. With moderate excitement, only the unaffected eye dilates. A painful stimulus or sudden noise may increase the amount of anisocoria by .5 to 1.0 mm. Also with fatigue, the amount of anisocoria may decrease due to a decreased amount of hypothalamic sympathetic outflow. In summary, the amount of anisocoria varies with the completeness of the injury, the point of fixation, the degree of denervation supersensativity, and the concentration of circulating andrenergics, the alertness of the patient, the brightness of the light, and the extent of the re-innervation of the dilator.

2.) Ptosis of the upper lid on the involved side. It is due to paralysis of Mueller's muscle. The lower lid may be slightly elevated. Therefore the palpebral fissure will be narrowed and the eye may appear enophthalmic.
3.) Anhidrosis of the affected side. This is due to denervation of the fibers from the External Carotid and causes a decrease in the amount of vasoconstriction. This results in a warm face with no sweating. The earlobe and conjunctiva on the affected side may be hyperemic.

4.) The intraocular pressure may be slightly decreased on the affected side. This is usually transient.

5.) The amplitude of accommodation may be decreased immediately after onset, but will return to normal quite quickly.

6.) Pigmentary anomalies. If Horner's is congenital, the affected side will be lighter in color due to the failure of pigment to develop in the iris. It is rare in adults.

7.) The reaction to light and near is normal. Diagnosis is made by use of pharmacological tests. 4% cocaine or 1% Pareidine will not dilate the affected eye.

Horner's syndrome may be associated with other anomalies depending upon the site of the lesion.

If the site of the involvement is at the brainstem or spinal cord, any of these could result.

1. Wallenberg Syndrome', caused by a cerebrovascular accident, is characterized by a falling tendency, rotary nystagmus, and laryngeal and pharyngeal paralysis. Analgesia of the face and extremities is also present.

2.) Syringomyelia is associated with trophic changes in the upper extremities, and a rotary or vestibular nystagmus.

3.) Scleroderma with facial hemiatrophy is characterized by heterochromia, asymmetries of the face, distortion of the face, and anomalies of the sternum. It is due to developmental defects in the cervical cord, medulla, or both.
An interruption in the para-veterbral pathways could have the following associated conditions.

1.) Bronchiogenic carcinoma is the most common cause, with pain in the neck, shoulders, and arm. There may also be atrophy of the homolateral hand muscles.

2.) Klumpke's paralysis of the homolateral arm which is due to traction on the brachial plexus at the ventral root. It may be caused by birth trauma.

3.) Thoracic aneurysms are associated with increasing pain in the chest, neck, and shoulder. There may be a dry cough and progressive hoarseness. There is unequal blood pressure in the two arms.

Lesions at the base of the skull can be caused by a tumor of the nasopharynx, or a jugular foramen. There is a paralysis of the tongue. It could also be caused by a tonsillectomy, a mandibular tooth abscess, or inflammation of the cervical lymph nodes.

An intracranial lesion might show these.

1.) Rader's Syndrome often called painful Horner's, which is associated with cluster headaches, lacrimation, conjunctival chemosis, and rhinorrhea.

2.) Carotid thrombosis with facial anhidrosis

3.) Cavernous Sinus Thrombosis. There is no facial anhidrosis and a palsy of the third is likely.

There are a few tests which can be helpful to localize the area of interruption. Besides the associated neurological signs and symptoms, the distribution of anhidrosis may be of value. If the lesion is at the brain stem, the anhidrosis may be over half of the body. The ventral root of the cervicothoracic or the sympathetics of the neck, the anhidrosis will affect the face, neck and possibly the upper extremities. If the lesion involves the post-ganglionic
at the base of the skull, only part of the forehead may be involved.

The Claude Bernard’s syndrome is the physiological opposite of Horner’s syndrome. It is usually short-lived and often progresses to destruction and Horner’s. There is a unilateral mydriasis, lid retraction, pseudoexophthalmus, and flushing and sweating of the face on the same side. There are slight pupillary reaction present, both direct, consensual and near.

Argyll Robertson is a pupillary abnormality which is characterized by very small (2.5 mm or less) pupils which are irregular. They show either a slight or no reaction to light with an intact near reaction. With prolonged time, the pupils may become non-reactive and are termed immobile pupils. It may begin unilaterally, but generally becomes bilateral. Visual acuity is good indicating an intact visual pathway. Anisocoria is frequent and the pupils may be oval, tear-shaped, eccentric, or serrated. The reaction to atropine is poor if iris atrophy is also present. The pupils may constrict further with the instillation of Physostigmine. The orbicularis reaction is normal or increased, however, the ciliospinal reaction is absent.

It is thought that the cause of Argyll Robertson pupils is a lesion of the intercalated neurons so that the pupillary information never reaches the Edinger-Westphal nucleus. This is consistent with the finding of good visual acuity as the visual and pupillary fibers separate before this area.

Syphillis is the cause in about ninety per cent of the true Argyll Robertson pupil. Some authors state that diabetes, and von Economo encephalitis may cause Argyll Robertson pupils. Although most authors do not consider these to cause a true A-R pupil, others feel chronic alcoholism, herpes zoster, midbrain tumors, and multiple sclerosis may be factors.
The inverse Argyll Robertson pupil is characterized by a normal reaction to light, but no reaction to near. Some feel it is caused by a lesions of Perlea's nucleus. Others doubt its existence, stating that the patient may not be accommodating properly and therefore has a poor constriction to near.

Parinaud's Syndrome is characterized by a absent light reaction and a normal near reaction. It is due to a pineal tumor. There is a supranuclear paralysis of upward gaze and lid retraction, called Collier's Sign. Convergence is defective with nystagmus on upward gaze. There may be an accommodative spasm and paresis present. There is usually moderate mydriasis and anisocoria.

A fixed dilated pupil may be associated with a neurological disturbance or a pharmalogical paralysis. If the pupil is eight to nine milimeters in diameter, it must be pharmalogical, as a neurological cause would not dilate the pupil that much. A frequent offender is the belladonna alkloids from plants, especially in farmers which is termed corn picker's pupil. Other possible offenders are perfume or cosmetics. The possibility of accidental self-innocation with such drugs as atropine must be considered. One differential test is the use of 1% pilocarpine. Pilocarpine will constrict a neurologically dilated pupil, but will not constrict a drug-induced pupil.

Some possible neurological causes of a fixed dilated pupil are midbrain tumors, third nerve nucleus lesions, ciliary ganglion lesions, short ciliary nerve lesions, eye trauma, and posterior synechiae. A pineal tumor will affect both eyes, where a midbrain tumor tends to be incomplete and unilateral. If the cause is vascular disease, or a demyelinating disease, there will be associated findings such as nuclear ophthalmoplegia, paralysis of upward gaze, loss of convergence with exotropia. If the ciliary ganglion is involved, there may be an isolated internal ophthalmoplegia. If the trigeminal fibers are involved, there will be retrobulbar pain. Some other causes are
herpes zoster, chicken pox, scarlet fever, measles, sinusitis, and small pox.

A total paralysis of constriction and accommodation is termed internal ophthalmoplegia and is caused by supranuclear lesions, a nuclear lesion, oculomotor lesion, ciliary ganglion lesion, or a short ciliary nerve lesion.

In summary, careful observation of the pupillary reflexes can give the clinician valuable information about the patient. Used in conjunction with other tests, the integrity of the various pathways can be assessed.


Bibliography


