Pupil Testing
Back to the Basics

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Financial Disclaimer

- Speaker for Shire Ophthalmic

Overview

- Pupil anatomy and physiology
- Pupil testing
- Commonly encountered pupil disorders and how to detect them

Why evaluate the pupils

One of few objective *reflexes* that detect and quantify abnormalities of the retina, optic nerve, optic chiasm, optic tract, midbrain, and/or peripheral nerves

Why evaluate the pupils

- Pupil abnormalities can:
  - Reveal serious neuro-ophthalmic and retinal disease
  - Help aid in diagnosis and management of many conditions
  - Should be incorporated into every optometric examination

Eye and Pupil Anatomy

Pupil Anatomy and Physiology

- Hole in center of iris

- *Involuntarily* controls how much light enters the eye

- Improves vision by preventing irregular refraction from peripheral cornea

- Allows passage of aqueous from posterior to anterior chamber

Pupil Anatomy and Physiology

- Iris contains 2 groups of smooth muscle
  - Sphincter pupillae → circularly oriented
  - Dilator pupillae → radially oriented

- Dim light → sympathetic superior cervical ganglion stimulated → constriction of radial dilator pupillae muscles → pupil gets bigger

Bright light → parasympathetic short ciliary nerve innervated → constriction of circular sphincter pupillae muscles → pupil gets smaller

Pupil Anatomy and Physiology

- Average pupil size in normal illumination ~3.5mm
  - Range 1.0 - 10.0 mm
    - <2mm considered mitotic
    - >7mm considered mydriatic
  - Decrease with age due to senile miosis
    - Higher rate of atrophy of dilator muscle vs. constrictor muscles
  - Difference of >0.4mm is clinically significant

Pupil Anatomy and Physiology

- In a normal pupil, amount of light entering the eye governs the size of the pupil
    - Pupil size governed by
        - Amount of light entering the eye
        - Where patient if focusing
        - Mood
        - Drug use

Vocabulary Review

- Anisocoria - difference in pupil size between eyes
- Mydriasis - dilation of pupil
- Miosis - constriction of pupil
- Hippus - small constant changes in pupil size
- Afferent - signals going from the eye to the brain
- Efferent - signals going from the brain to the eye
- Bifurcation - divide into 2 equal branches

Vocabulary Review

- Light-Near Dissociation - pupil constricts to accommodation much more than to a light stimulus
- Afferent Pupil - pupil that responds poorly or not at all to a direct light but has a normal consensual response when light is shone into opposite eye

Pupillary Function

Pupil Anatomy and Physiology

- Pupil size is dependent on a balance between the sympathetic and parasympathetic innervation of the iris muscles

Parasympathetic Innervation

- Controlled by the parasympathetic system:
  - Pupil’s response to light (miosis / light response)
  - Pupil’s response to how close things are (near response/constriction)

Afferent Pupillary Pathway

light impulse → retinal photoreceptors → optic nerve → **optic chiasm (bifurcation of fibers)** → optic tract

Afferent Pupillary Pathway

after optic tract, fibers break off to go to

- Lateral geniculate nucleus (90%) → visual cortex
- Hypothalamus → circadian rhythm
- Superior colliculus → saccades
- **Pretectum → pupil**

Afferent Pupillary Pathway

After optic tract, fibers break off to **bilaterally** stimulate the **pretectal nuclei** in the midbrain

Internuclear Pathway

pretectal nuclei → **bifurcate again** → Edinger-Westphal nuclei of the oculomotor nerve (CN III)

Efferent Pupillary Pathway

Edinger-Westphal nuclei of the oculomotor nerve (CN III) → travel back towards orbit to the ciliary ganglion

- 97% innervate ciliary body → accommodation
- 3% innervate iris sphincter → pupil constriction

Pupillary Reaction to Near Response

- Fixation at near causes
  - Convergence
  - Accommodation
  - Pupillary constriction / Miosis
- If the direct pupillary light reaction is normal, the pupillary near response is always intact

Sympathetic Innervation

- EFFERENT ONLY system
  - Modulates pupil dilation via constriction of radial dilator muscles of iris
    - Less during drowsiness and sleep
      - During sleep pupils are partially constricted but still reactive to light
    - More during intense concentration, fright, and arousal

Sympathetic Innervation

- Hypothalamus 1st order neuron → descends through brainstem on each side (no bifurcation) → 1st synapse at ciliospinal center at C8 - T1 level

Sympathetic Innervation

- 2nd order neuron exit spinal cord → pass over apices of the lungs → synapse at superior cervical ganglion

- synapse at superior cervical ganglion → 3rd order neuron form a plexus around internal carotid artery → run along the internal carotid artery into the cavernous sinus

- Neurons traveling with ophthalmic artery → Mueller's muscle (eyelid control)
- Neurons traveling with V1 → through long ciliary ganglion → iris dilator (mydriasis)
- Neurons traveling to sweat glands of face

Sympathetic Innervation

- Pupil dilation
- Eyelid elevation
- Facial sweating

Interruption of ocular sympathetic pathway at any level will result in

Miosis

Ptosis

Facial anhidrosis

Pupillary Testing

Pupil Testing

Can objectively measure integrity of **afferent** and **efferent** pupillary pathways

Pupil Testing

- Comprehensive and detailed case history is key to reach appropriate diagnosis
  - Recent contact with medications or agents that can affect pupil size
  - History of trauma
  - History of surgery
  - Ocular history of inflammation
  - Use old photos to evaluate possible onset and duration

Pupil Testing

- Purpose is to evaluate pupil:
  - Symmetrical Size (bright and dim)
  - Symmetrical Shape (round)
  - Similar Location (central)
  - Strength of *direct* pupillary light response compared to strength of *consensual* pupillary light response - the in the same eye

Pupil Testing

- Pupils should be round
  - Non-round pupillary shape can be due to

Surgery

Trauma

Inflammation

Iris atrophy from age

Ischemia

Posterior synechiae

Congenital

Pupil Testing

- Pupils should be
  - Symmetrical in Size
    - Anisocoria - unequal size between pupils
      - Physiologic anisocoria
        - 20% of people, benign
        - Difference in pupil diameter less than 1.0mm
        - Difference is *same* in dark and bright illumination

Pupil Testing

- Pupils should be Symmetrical
  - Pupillary inequality (anisocoria) usually results from an *iris innervation* (efferent) problem
    - But can also be due to trauma, inflammation, synechia
      - Must check iris sphincter and iris dilator muscles - best in slit lamp

Pupil Testing

- Remove glasses
- Fixate on a non- accommodative distance target (or pupils constrict)
- Stand off to the side
- Observe pupils in light
- Then perform in dim room (able to visualize pupils)

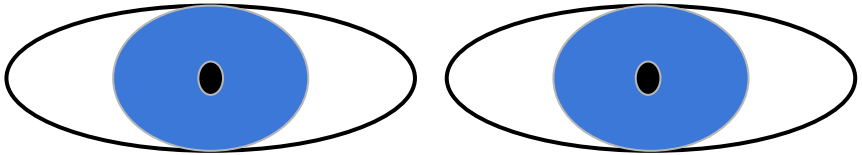
Pupil Testing

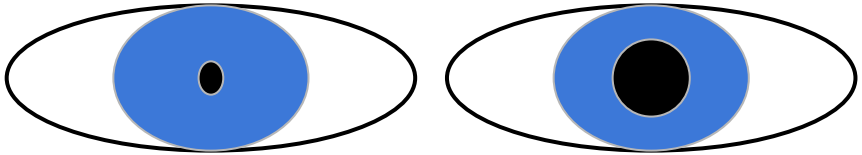
- Measure using a mm ruler
    - Some new auto refractors
    - Pupillometer
    - Keep below visual axis to avoid accommodation and miosis
- Can use O-scope to simultaneously observe red reflexes-easier to evaluate symmetry of pupil size

Anisocoria worse in dim light

Bright

Dim





Anisocoria Testing - too small

- Small Pupil is the problem
  - Anisocoria greater in the dark (unable to dilate in the dark)
  - Impairment of oculo-sympathetic system

Anisocoria Testing - too small

- Small Pupil is the problem

Pharmacologic

Horner’s syndrome

Argyll-Robertson

Anisocoria Testing - too small

- Pharmacologic constriction
  - Morphine, Heroin, Codeine, Oxycodone
    - usually bilateral
  - Cholinergic agonist / Anticholinesterase
    - Antipsychotics, antidepressants, MAOI
    - Clonidine and tetrahydrozoline (for HTN)
    - Pilocarpine, flea/tick control products
      - Spray or patch

Anisocoria Testing - too small

- Horner's Syndrome / Oculo-sympathetic paresis
  - Interruption along oculo-sympathetic pathway between hypothalamus (origin) and iris dilator (destination)
  - Classic triad - Ipsilateral
    - Unilateral ptosis
    - Miosis
    - Facial anhidrosis

Anisocoria Testing - too small

- Horner's Syndrome / Oculo-sympathetic paresis
  - 33% are idiopathic
  - 4 - 13% are congenital
    - Iris heterochromia - lighter iris = affected eye

Anisocoria Testing - too small

- Horner's Syndrome / Oculo-sympathetic paresis
- Acquired causes - central (1st order)
  - Stroke
  - Trauma to neck
  - Surgery
  - Aortic or carotid artery dissection
  - Otitis media

Anisocoria Testing - too small

- Horner's Syndrome / Oculo-sympathetic paresis
- Acquired causes
  preganglionic (2nd order)
  - Pancoast tumor
  - Tuberculosis
  - Neck trauma or surgery
  - Thyroid surgery/neoplasm

Anisocoria Testing - too small

- Horner's Syndrome / Oculo-sympathetic paresis
- Acquired causes - postganglionic (3rd order)
  - Trauma /surgery
  - Raeder's syndrome
    - painful cluster migraine
  - Giant cell arteritis
  - Cavernous sinus/superior orbital fissure lesion
  - Nasopharyngeal carcinoma

Anisocoria Testing - too small

- Horner’s Syndrome / Oculo-sympathetic paresis

Detailed history and diagnostic imaging can help with differential diagnosis

Anisocoria Testing - too small

- Horner's Syndrome / Oculo-sympathetic paresis
  - Evaluation
    - Look for 'dilation lag' - Horner's pupil will be delayed in its dilation in dim illumination
      - Anisocoria most evident 4-5 seconds after turn off lights and will equalize 10-15 seconds after

Anisocoria Testing - too small

- Horner's Syndrome / Oculo-sympathetic paresis
  - In most instances, imaging takes precedence over localization via drops
    - Diplopia
    - Cranial nerve palsy
    - Numbness
    - Headache
    - Pain

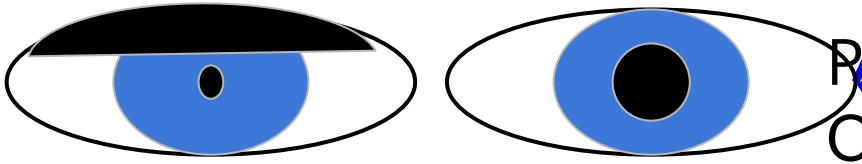
Anisocoria Testing - too small

- Horner's Syndrome / Oculo-sympathetic paresis
  - Pharmacologic testing can help localize lesion and aid in differential diagnosis
    - apraclonidine / Iopidine (Alcon)
      - Alpha-adrenergic receptor agonist
      - One drop of 0.5% or 1% will dilate a Horner's pupil with no/minimal effect on normal pupil
      - Must have 1.0mm or more dilation after 30-45 minutes

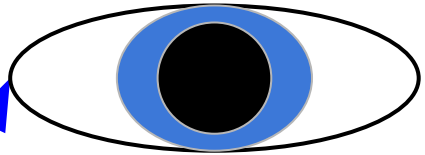
Anisocoria Testing - too small

- Allow 48 hours for Iopedine to dissipate
  - Two drops of 1% hydroxyamphetamine (Paredrine) Akorn - difficult to obtain
    - Will dilate first or second order neuron lesion and normal pupils only
      - Release stored norepinephrine from postganglionic axon terminals into neuromuscular junction at iris dilator
      - Can not differentiate between first or second order lesions

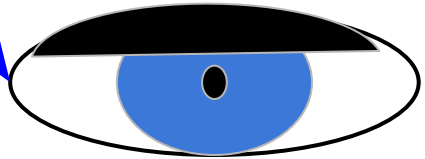
Right Horner's



Paredrine
OU



Horner's due to first or second order neuron lesions



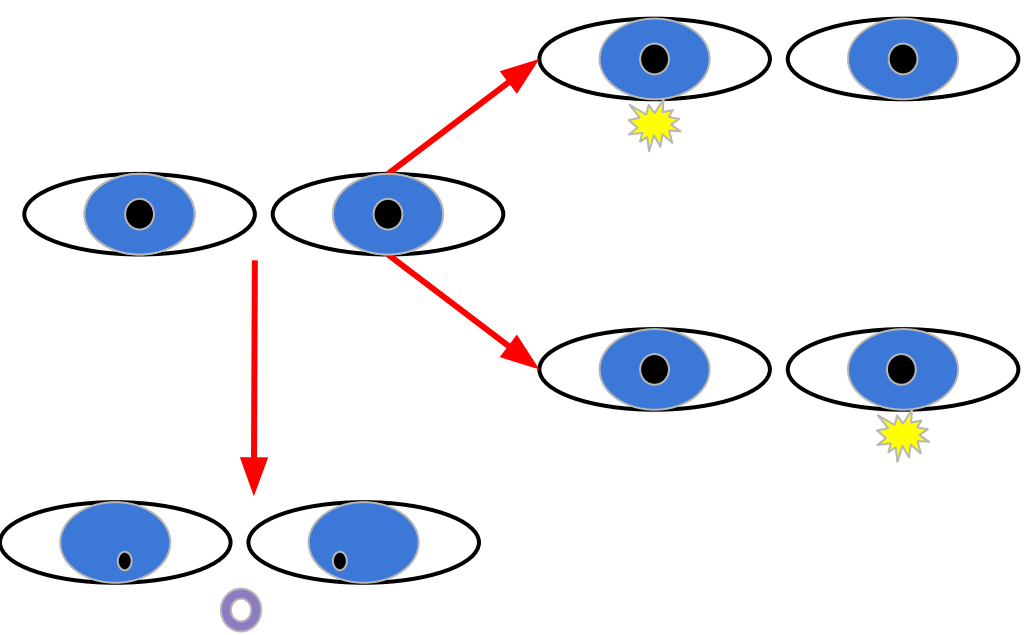
Horner's due to 3rd order

Anisocoria Testing - too small

- Horner's Syndrome / Oculo-sympathetic paresis
  - No treatment for Horner's itself
  - Resolution is often possible if/when underlying cause is cured
    - Few weeks to few months
  - Can use 2.5% phenylephrine to resolve anisocoria

Anisocoria Testing - too small

- Argyll-Robertson Pupils
  - Asymmetrically, bilateral small and irregular pupils that
    - Respond poorly to light
    - Respond poorly to dilation
  - Light-Near Dissociation = pupil constriction to near response markedly better than to light response



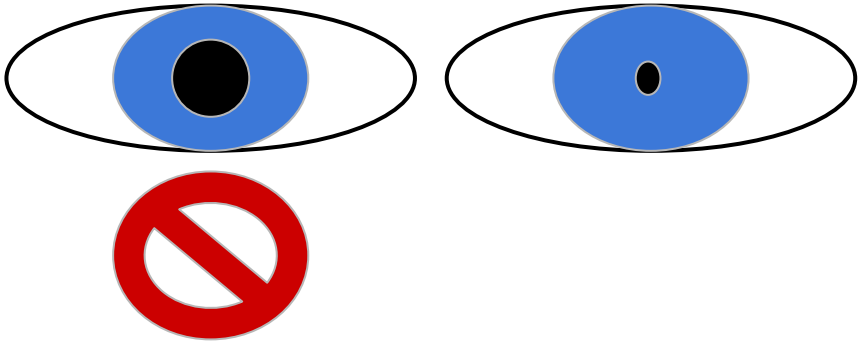
Argyll-Robertson Pupils

- Due to lesion in the Edinger-Westphal nucleus
- Associated with chronic syphilis, MS, DM, wernicke's encephalopathy
  - Bloodwork indicated
    - CBC
    - FTA-Abs
    - RPR/VDRL

Anisocoria worse in bright light

Bright

Dim



Pupil Testing

- Anisocoria - worse in bright light
  - Larger pupil is not constricting properly
  - Parasympathetic problem
    - Pharmacologic dilation
    - Trauma
    - Cranial nerve III palsy
    - Adie’s tonic pupil

Anisocoria Testing - too big

- Pharmacologic Dilation - bi or unilateral
  - Anticholinergics
    - Scopolamine - motion sickness patches
    - Permethrin - insecticide
  - Plants
    - Angel’s trumpet, jimson weed, belladonna
  - OTC products
    - Phenylephrine - antihistamines, ‘get the red out’ drops, anti-itch creams, nose spray

Anisocoria Testing - too big

- Pharmacologic Dilation
  - Recreational drugs
    - Alcohol
    - Stimulants - cocaine, crack, methamphetamines
    - Ecstasy, LSD, Acid, Hallucinogens
    - Marijuana, inhaled propellants

Anisocoria Testing - too big

- Pharmacologic Dilation
  - Fixed or sluggish and dilated
  - Will not constrict to 1% pilocarpine

Anisocoria Testing - too big

- Trauma
  - Trauma / surgery to circular iris sphincter at edge of pupil
    - Can be full or sectoral

Anisocoria Testing - too big

- Cranial Nerve III Palsy
  - CN III palsy signs
    - Moderate-Large ptosis
      - levator palpebrae
    - Exotropia and hypotropia (down and out)
      - Medial, superior, inferior recti, inferior oblique
        - Eye does not adduct on EOM testing
    - Pupil dilation
    - Unilateral accommodative dysfunction

Anisocoria Testing - too big

- Cranial Nerve III Palsy
  - Pupillary fibers are close to surface of CN III → susceptible to compression via mass or aneurysm at or close to CN III
    - Inability for pupil to constrict
    - Poor accommodation

Anisocoria Testing - too big

- Cranial Nerve III Palsy
  - Posterior communicating artery aneurysm presents with a CN III palsy 30-60% of the time
  - Other causes:
    - Tumor
    - Trauma

Anisocoria Testing - too big

- Cranial Nerve III Palsy
  - Ptosis, down and out eye, *with* pupil involvement
    - IMMEDIATE ER / Neuro consult with neuroimaging and angiography
      - Notify hospital by phone of incoming patient

Anisocoria Testing - too big

- Cranial Nerve III Palsy
  - A CN III palsy with *no* pupil involvement is usually ischemic in nature (DM, HTN)
    - Pupil-sparing may become pupil-involving over time
      - 14% of CN III palsies due to aneurysm may not have pupil involvement in early stages
      - Follow very closely with neurologist

Anisocoria Testing - too big

- Adie's Tonic Pupils
  - Lesion to ciliary ganglion or short posterior ciliary nerve which innervate iris constrictor
  - Most common cause is postviral denervation of pupil sphincter

Orbital trauma	Virus
Diabetes	Giant cell arteritis
Syphilis	Varicella-Zoster

Anisocoria Testing - too big

- Tonic Pupils
  - Adie’s tonic pupil
    - Idiopathic tonic pupil found in 20-40yo females
    - Markedly diminished or absent deep tendon reflexes in knee and ankle frequently found

Anisocoria Testing - too big

- Tonic Pupils
  - Unilateral
  - Can become bilateral at rate of 4% / year
  - Anisocoria diminishes with time as larger tonic pupil becomes more miotic with age
    - Long standing Adie’s pupil will be miotic and remain constricted

Anisocoria Testing - too big

- Characteristic findings
  - Sluggish, segmental pupillary sphincter palsies
  - Light-near dissociation
    - Better (but still poor) pupil constriction to near with slow redilation
      - Vs. Argyle-Robertson where the constriction to near is quick and normal
  - Denervation hypersensitivity - supersensitive constriction to diluted pilocarpine (0.125%)

Anisocoria Testing - too big

- Tonic Pupils
  - No treatment available
  - Mild miotics may help for symptomatic glare
    - Brimonidine
    - Low-dose pilocarpine
  - Bifocal for accommodation
  - Cosmetic CL for aniso

Defects of Pupillary Light Response

Pupillary Light Response

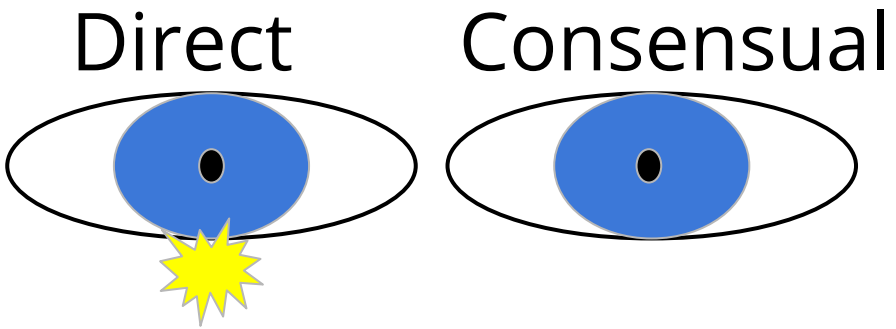
- Observe pupils before introducing light for anisocoria
- Use transilluminator or light from BIO (penlight too dim) shone ~1 inch away
- Dim room, patient fixates at distance with glasses off
- Point light directly into eye
  - Stray light can cause non-tested pupil to constrict
- Hold light for 2-4 seconds
  - Observe both tested and non-tested pupil response

Swinging Flashlight / Marcus Gunn Test

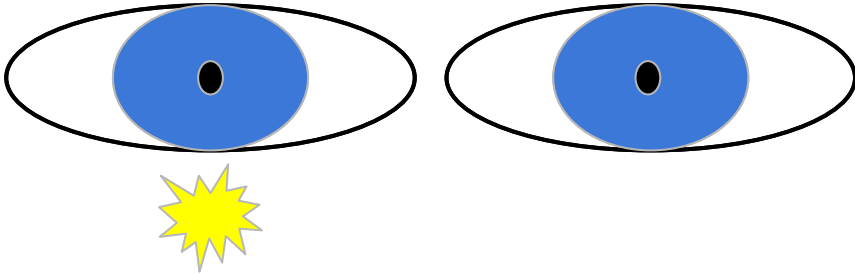
- Direct light into right eye
- Hold 2 - 4 seconds
- Quickly move light to left eye in a “U” motion
  - Avoid stimulating accommodation
- Hold 2 - 4 seconds
- Repeat 3 - 4 times
- Magnitude and duration must be constant

Swinging Flashlight / Marcus Gunn Test

Direct → Consensual → Swinging Flashlight

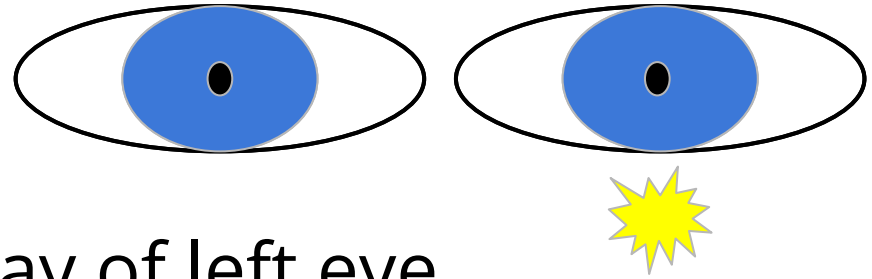


Pupillary Light Response



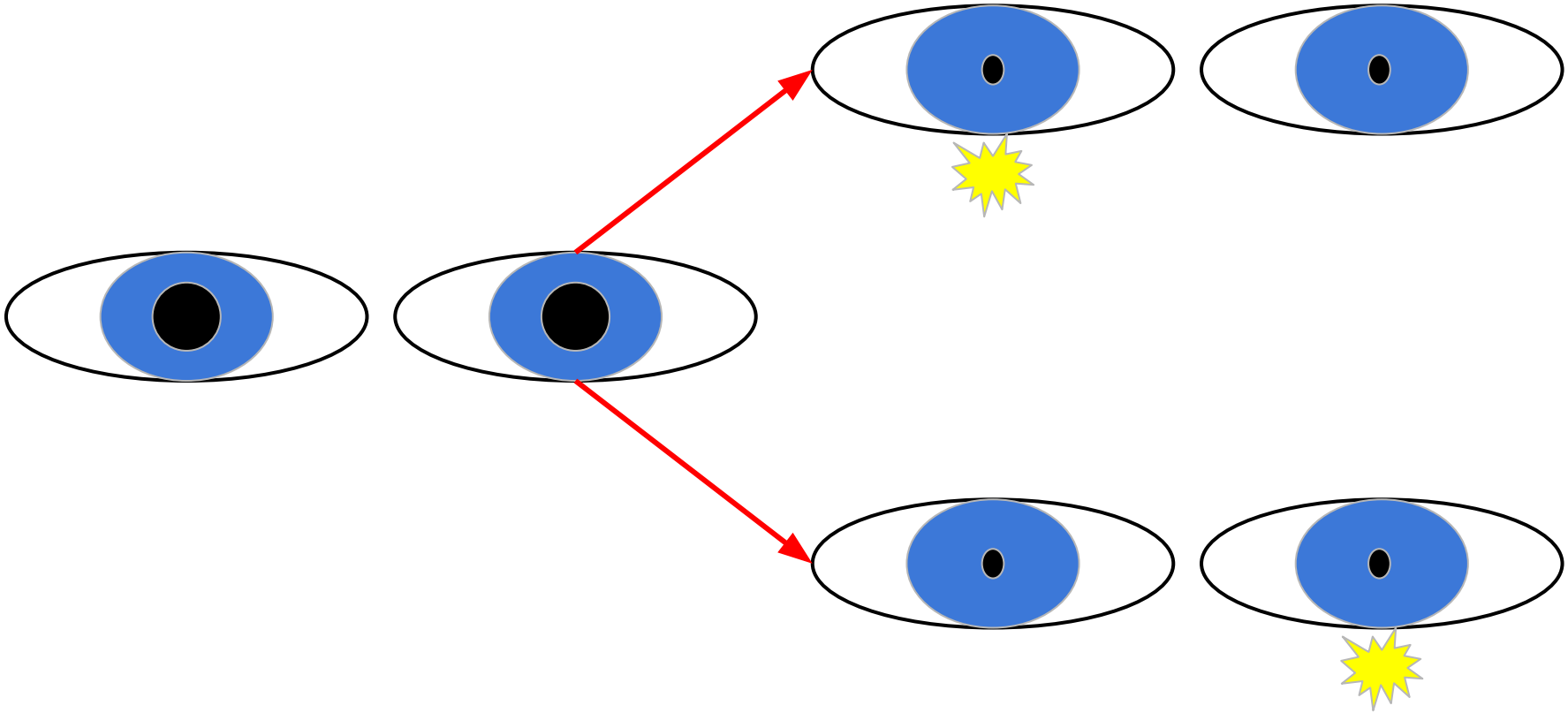
- Light pointed into right eye
- Measuring afferent pathway of right eye
  - Observe direct response of right eye
  - Observe consensual response of left eye
    - Constriction amount (quantity), rapidity (quality), and time to release should be the same

Pupillary Light Response



- Light pointed into left eye
- Measuring afferent pathway of left eye
  - Observe direct response of left eye
  - Observe consensual response of right eye
    - Similar quantity, quality, and release

Normal pupil response



Swinging Flashlight / Marcus Gunn Test

- RAPD alone does not cause anisocoria
  - Due to consensual response pupils will look the same size
    - Anisocoria is due to an efferent, traumatic, mechanical, or pharmacological etiology

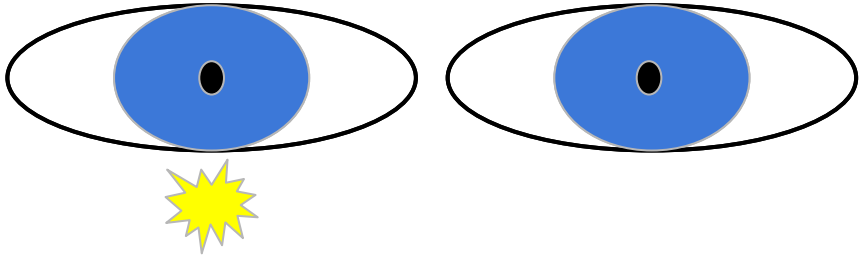
Swinging Flashlight / Marcus Gunn Test

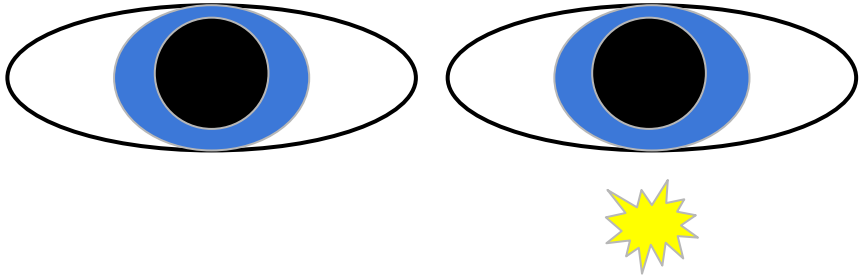
- Afferent Pupillary Light Reflex-Optic Nerve and Tract
  - Strength of direct pupillary light response compared to strength of consensual pupillary light response in the SAME EYE - a RELATIVE comparison
    - Relative Afferent Pupillary Defect (RAPD)
      - Damage at or before the Pretectum / Midbrain

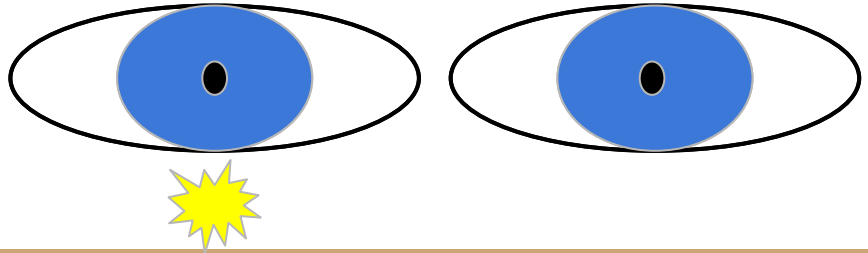
Swinging Flashlight / Marcus Gunn Test

- Relative Afferent Pupillary Defect
  - *Consensual* response of an eye is greater than *direct* response of the same eye
    - Unilateral or asymmetric damage to anterior visual pathway (afferent) on that side

Left AD







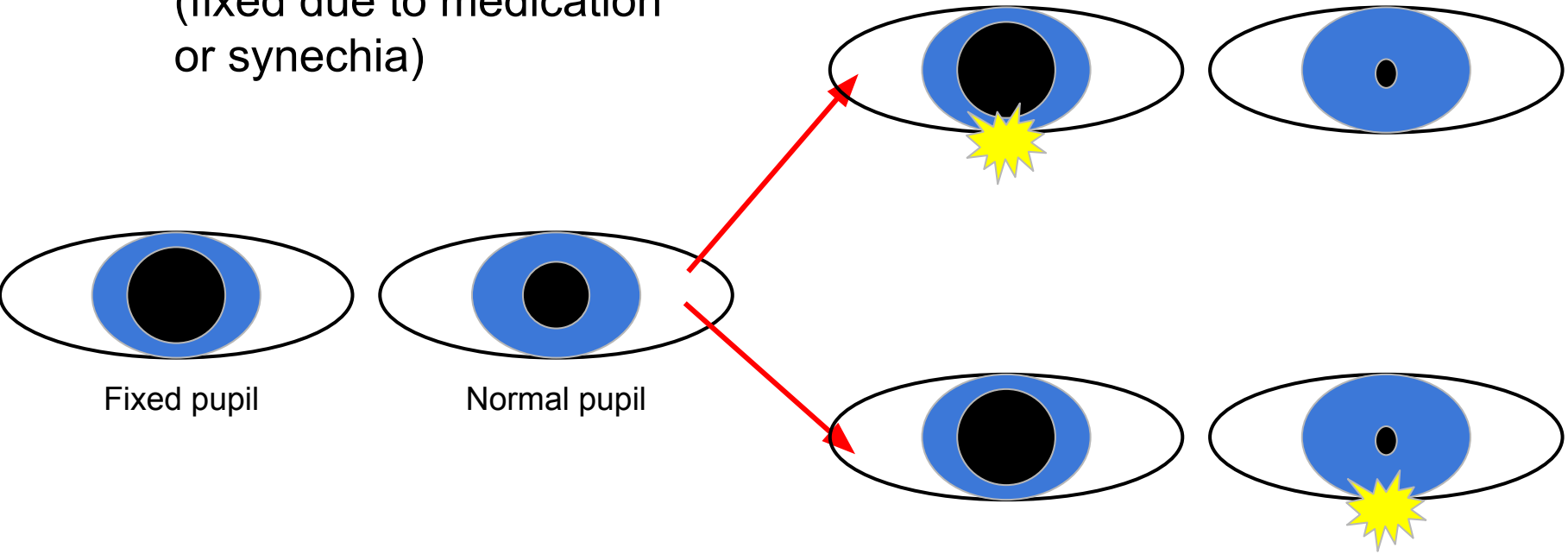
Swinging Flashlight / Marcus Gunn Test

- Consensual Response
  - Only one functioning pupil or one visible pupil needed to test for RAPD in **either** eye
    - Surgical / traumatic / pharmacologic pupil
    - Obscured view of pupil
    - Anisocoria

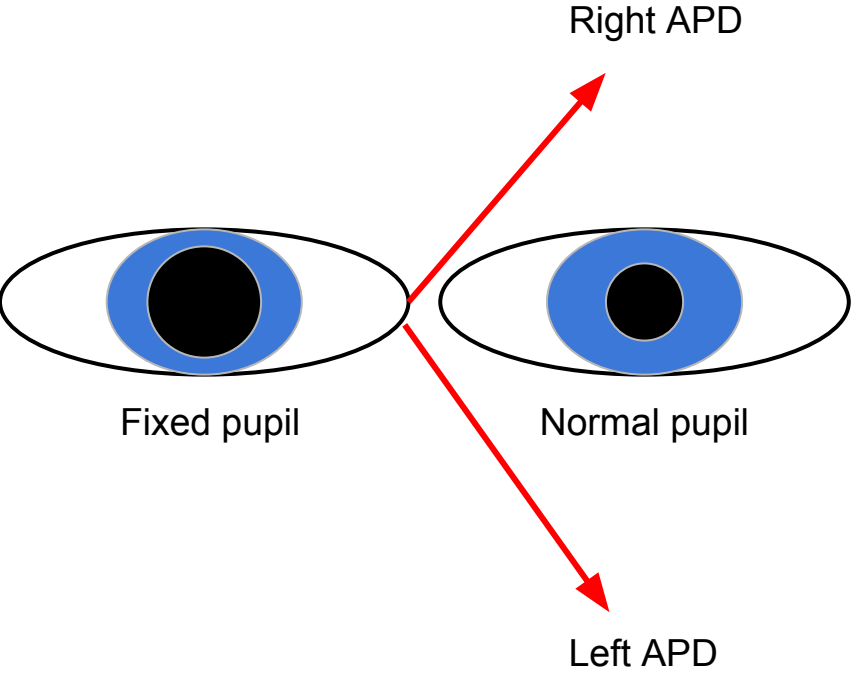
Swinging Flashlight / Marcus Gunn Test

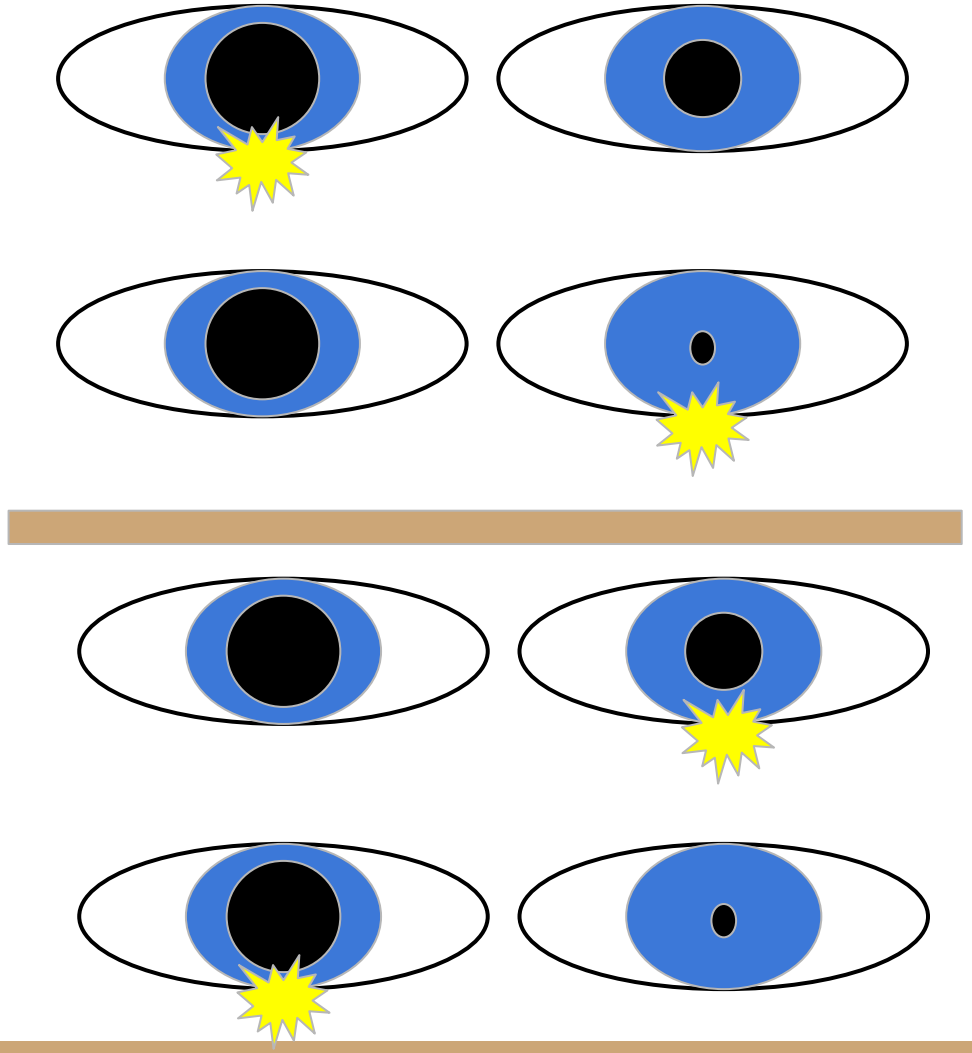
- Consensual Response
  - Perform as usual but observe ONLY the VISIBLE / REACTIVE pupil
    - Compare *that* eye's direct response to *that* eye's consensual response
    - If working pupil constricts more with direct illumination than with consensual, RAPD is present in the *opposite*, unreactive or unobservable eye

Pupil with no APD/MG (fixed due to medication or synechia)



do not spend longer on one eye than the other





Swinging Flashlight / Marcus Gunn Test

- Grading an APD can help identify
  - Subtle defects
  - Monitor progression
- Visual acuity does not necessarily correlate with RAPD
  - However, always look carefully for an APD in cases of reduced BCVA in one eye

Swinging Flashlight / Marcus Gunn Test

Grading Scale of RAPD

- Grade 1+: weak initial pupillary constriction followed by greater redilation
- Grade 2+: initial pupillary stall followed by greater redilation
- Grade 3+: immediate pupillary dilation
- Grade 4+: no reaction to light (amaurotic)

Swinging Flashlight / Marcus Gunn Test

- Neutral density filter

  Dim amount of light entering the ‘better’ eye until the afferent responses are equal and RAPD is resolved

P.E.R.R.L.A (+ / - RAPD / MG)

- PE: pupils are equal
- R: pupils are round
- RL: pupils are equally reactive to light
    - Direct and Consensual
- A: pupils are responsive to accommodation
- + or - relative afferent pupillary defect
    - Note grade and which eye if positive

Conclusion

- Pupillary testing is an important component of every comprehensive eye examination
- Careful observation may reveal important information about the anterior visual pathway as well as the autonomic nervous system

Conclusion

A comprehensive history can be key in proper diagnosis

Loss of vision / BCVA
Loss of visual field
Pain
Diplopia
Ptosis / Proptosis
Color vision / Red desat

Surgical history
Trauma history
Medication history
Medical history

tumor, aneurysm, HA, ear infection, inflammation

Thank You

?Questions?

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