Anisocoria ~ Now What?

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The Pupil

- Anatomical Considerations
- Pathway of the Pupil Light Reflex
  - Parasympathetic Pathway (Sphincter Muscle)
    - 4 Neuron Arc (afferent + efferent)
  - Sympathetic (Dilator Muscle of the Iris)
    - 3 Neuron Arc

Parasympathetic Pathway

- Light stimulates the retina then impulse travels with the ganglion cells through the chiasm into the optic tracts. 80% go to the LGN, 20% to the pretectal nuclei. They then hemidecussate and terminate at the EW nucleus.

Points of Interest

- Within the second order neuron there are 30 near response fibers for every light response fiber. This allows for light - near dissociation.
- The third order neuron runs with cranial nerve III from the brain stem to the ciliary ganglion. Superficially located prior to the cavernous sinus.
Sympathetic Pathway

- Three Neuron Arc
- Posterior hypothalamus to ciliospinal center of Budge (C8-T2)
- CSCB to Sup. Cervical Ganglion in the neck
- SCG to the dilator muscle

Pupil Examination Basics

Pupil Examination...

...Be Systematic

- What are the BCVA’s? ...And are the acuities equal either corrected or with pinhole?
- Are the patient’s pupils equal in size in bright and dim illumination?
- If not, is the anisocoria > in dim or bright illumination?
- Is the near accommodative reflex present and equal in both eyes?
- Are the accommodative amps = OU?

Pupil Examination (Cont.)

- If the pupils are equal in size, is the direct light reflex equally strong in both eyes?
- Is the consensual light reflex equally strong in both eyes?
True or False?
- A Cataract can cause an APD?
  - FALSE...If you are finding an APD, check your illumination source first.
  - If you still have a + APD, need to find other cause.

YES or NO?
- Is it possible to have optic nerve disease and NOT have an APD?
  - YES...if the disease is bilateral & EQUAL in BOTH eyes (i.e., toxic optic neuropathy)

True or False?
- Macular Degeneration can cause an APD?
  - TRUE...If the Macular Degeneration is unilateral & severe enough (Va +/- 20/400)

True or False?
- Visual Acuity does not necessarily correlate with an RAPD?
  - TRUE...a person with end-stage glaucoma can have an APD with good central acuity.

Identifying & Recording: Exam Clinical Pearls
- Ø PERRLA
- BIO >
  - Transilluminator >
  - Penlight
- Neutral Density Filters
- Fat Scan

Normal Pupillary Phenomena
- Pupillary Unrest vs. Hippus
- Near Synkinesis (The Near Triad)
- Direct & Consensual Responses
- APD / Marcus Gunn Defect
  - www.richmondeye.com
- Physiological Anisocoria
Anisocoria: Case History

- Temporal Aspects?
- Eye Pain?
- Decreased VA?
- Arm, Chest, Head, or Neck Pain?
- Nuchal Rigidity?
- Hx of Stroke, Cancer, or Surgery

- Diplopia?
- Hx of Trauma?
- Drops or Ung’s?
- Current Medications (including OTC’s)?
- STD’s, Shingles, MS, Thyroid Disease, Diabetes?
- Alcohol Usage?

Anisocoria: Exam Techniques

- VA’s
- External
  - Ptosis
  - Anyhydrosis
- EOM’s
- Color VA, Red Desaturation
- SLE & Tonometry

- Pupillary Assessment:
  - Iris Color
  - Pupil Size(s) & Shape
  - Reactivity
  - Dilation Lag
  - Near Response
  - Vermiform Changes
  - VF Testing & DFE

Which is the Abnormal Pupil?

- The pupil that reacts sluggishly to light
- If Aniso > in Bright => Larger Pupil
  - Parasympathetic Denervation
- If Aniso > in Dim => Smaller Pupil
  - Abnormal Sympathetic Innervation
**Physiological Anisocoria**
- Anisocoria of < 1mm (to 2mm)
- 20% of the US Population has Simple or Physiological Anisocoria.
- The degree of anisocoria can vary from day to day and even switch sides.
- Unequal supranuclear inhibition in EW nucleus. Fairly consistent across light levels.

**Pharmacological Anisocoria**
- Topical drugs (Visine)
- Systemic drugs: Heroin, morphine, codeine lead to miosis. Dramamine, cocaine, levodopa, and antihistamines lead to mydriasis. Belladona and jimson
- Angel’s Trumpet (Datura)
- Preparation H!!!!!! (2.5% phenyl)
- Scopolomine motion sickness patches
- Flea/tick control products
- 1% pilocarpine test. Will constrict a compressive or tonic pupil but not a pharmacological one
Pharmacology

- Flea and tick sprays / collars / powders
- Some cause mydriasis, some cause miosis!
- Permethrin: found in some sprays. Has sympathetic effects (dilation, normal near vision)
- Anticholinesterase products found in collars, powders, and foggers: heightened parasympathetic effect (miosis, accom. spasm)

Adie’s Tonic Pupil

Stats
- Females 3:1
- Age: 20-40
- 80% Unilateral Initially
- Becomes bilateral at rate of 1-4% / year
- Etiology
  - Idiopathic vs. Viral

Key Findings
- Dilated pupil with poor to absent direct response.
- Tonic near responses
- Reduced Accom Amps
- Look for segmental palsy of iris sphincter muscle

Normal Room Illumination
- Poor Direct Response
- Fair to Good Concensual

(+ ) Near Response After Prolonged Effort

Segmental Palsy Video
Adie’s Tonic Pupil: Additional Testing

- Dilute (0.125%) Pilocarpine
- Denervation Supersensitivity
- Parasympathetic defect occurs AFTER the fibers leave the Ciliary Ganglion.
- Exaggerated pupillary constriction in the Tonic pupil with little to no constriction of normal pupil.
- Diminished Deep Tendon Reflexes = Holmes-Adie Syndrome

Tonic Pupil with & w/o Pilo 0.12%

Adies Clinical Pearls

- With a higher concentration of 1% pilocarpine, even third-nerve palsy-related pupil will constrict. Pharm dilation likely will not.
- Most cases of the tonic pupil are idiopathic or caused by trauma.
- An acute tonic pupil in patients over 60 years of age warrants an erythrocyte sedimentation rate to rule out giant cell arteritis.
- Syphilis needs to be worked up if a patient is male, and has bilateral tonic pupils.
- The tonic pupil is distinguished from other causes of light-near dissociation by the presence of TONIC near response.
- Pharmacological testing, 0.125% pilocarpine or 2.5% methacholine causes denervation supersensitivity.

Isolated Third N. Palsy w/ Pupil Involvement

- Sudden Onset Unilateral Ptosis with Eye or Head Pain
- Acuity is Typically Unaffected unless damage is in Superior Orbital Fissure
- Eye is in non-comitant exotropic & hypotropic position ("down & out")
Isolated Third N. Palsy

Isolated Third N. Palsy w/ Pupil Involvement

- Posterior Communicating Artery Aneurysm (Most Common)
- Tumor or Trauma
- HZO
- Leukemia
- Uncal Herniation Syndrome
  - Space Occupying Lesion
  - Subdural Hematoma
- Pituitary Apoplexy
- Ischemic Vascular Disease (Rare)

Pupil sparing / Pupil involving

- Rule of thumb: Pupil sparing third nerve palsies tend to be ischemic while those involving the pupil tend to be due to aneurysms or tumors
- Not a firm rule
- Pupil sparing may become pupil involving so follow very closely

Pupil involving vs. pupil sparing
Pupil involving vs. pupil sparing

Third Nerve Management
- Immediate Gad enhanced MRI / MRA if any question of aneurysmal involvement. Patient may complain of a severe headache and will often have other neurological signs
- If patient is diabetic or hypertensive and the pupil is not involved they can be followed closely without imaging studies

Third Nerve Management
- Patient education and reassurance a must
- Diplopia relief with patching
- Most ischemic palsies resolve over several months

Isolated Third N. Palsy w/ Pupil Involvement
- Management
  - Hospital Neurosurgical Consult ASAP
  - CT/MRI/MRA
  - Lumbar Puncture
  - Cerebral Angiography

Horner’s Syndrome

Anatomy of the Sympathetic Pathway to the Eye
Horner’s Syndrome: Clinical Features

- **A. Moderate Ptosis (2-3mm)** due to paralysis of Muller’s muscle
- **B. “Upside Down Ptosis”** - Mild elevation of the lower lid due to paralysis of the smooth muscle attached to the inferior tarsal plate.
- **C. Apparent Enophthalmos** due to A & B above
- **D. + Dilation Lag (classic finding)**
- **E. Decreased IOP** on affected side

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Horner’s Syndrome: Clinical Features

- **F. Miosis**, more noticeable in dim illumination. Note: Pupil rxns to light and near are normal.
- **G. Anhydrosis** on Ipsilateral side of face if lesion is below the Superior Cervical Ganglion => Not a 3rd order neuron.
- **H. Increase in Amplitude of Accommodation** due to unopposed action of the parasympathetic.

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Horner’s Syndrome: Localization of Lesion

- **4% Cocaine**
  - + Test => Anisocoria will increase
- **Hydroxyamphetamine (Paradrine 1%)**
  - Preganglionic lesion => YES dilation
  - Postganglionic lesion => No dilation
- **If suspect pre-ganglionic lesion** => Chest CT or X-ray.

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Horner’s pupil (OS)

- Miosis with normal reaction to light
- Ptosis and upside down ptosis (loss of muscle tone)
- Heterochromia if congenital and anhydrosis if the lesion is below the SC ganglion but before the carotid bifurcation
- Hypotony
- Can occasionally get partial involvement with ptosis only (no miosis)
Horner’s

- Testing: 4% cocaine will dilation a normal pupil by blocking the re-uptake of epinephrine but will not dilate the Horner’s pupil. Shelf life of only six months if preserved and cost of $90.
- More practical: 1% Iopidine will dilate a Horner’s pupil after 30-45 minutes but will not dilate a normal pupil. 0.5% works also.
- 1% hydroxyamphetamine will dilate a first or second order Horner’s but not a third by releasing NE from postganglionic synapses. Must wait one hour to check and need 72 hour washout if cocaine was used.
- Ptosis only patients will get lid elevation with Naphazoline. Little pupillary mydriasis.

Horner’s Causes

- First order: Neoplasms, Wallenberg’s syndrome, trauma, vertebral-basilar insufficiency.
- Second order: Pancoast or thyroid tumor, neck trauma or surgery.
- Third order: Cluster headaches, cavernous sinus lesion, dissecting carotid aneurysm.
- Testing: MRI, MRA, and chest X-ray.

Wallenberg’s syndrome

- Stroke of vertebral or posterior inferior cerebellar artery in the brainstem.
- Difficulty swallowing
- Hoarseness
- Dizziness
- Nausea
- Gait disturbance
- Nystagmus
- Uncontrollable hiccups

Raeder’s syndrome

- Horner’s with pain in the distribution area of V1. Caused by a neoplasm compressing the trigeminal nerve. Differential for cluster headaches.

Argyll-Robertson Pupil

- Bilateral, asymmetrically miotic pupils which are irregular.
- Poor dilation with poor response to light but brisk near response.
- Hallmark of tertiary neurosyphilis.
Argyll-Robertson Pupil: Clinical Features

- Pupils are small and frequently irregular
- Key Finding: LND Pupil
- Bilateral Asymmetric Pupil Involvement
- VA's are typically NORMAL
- Poor dilation with Mydriatics

Argyll-Robertson Pupil: Work-up

- As this is a Hallmark Sign for Neurosyphilis, need to rule this out, as well as HIV:
  - FTA-Abs, VDRL
  - Neurological work-up
  - Consider MRI, Lumbar Puncture

Anisocoria Case Report

- 55 yr. Old caucasian female
- CC: droopy eyelid OD for 1 month, no other complaints or symptoms.
- Patient & Family Ocular & Medical Hx – Negative
- Medications: Evista, Calcium Sup.

Anisocoria Case Report

- Clinical Findings:
  - BVA: 20/20 OD, OS
  - Pupils:
    - (-) APD
    - Size (light): 2.5mm OD, 3.0mm OS
    - Size (dim): 3.0mm OD, 6.5mm OS
    - (-) LND
  - EOM’s / CT: Normal

Anisocoria Case Report

- Clinical Findings Continued:
  - Lid Eval
    - UL 2mm on cornea OD; IPF 5mm
    - UL 1mm above cornea OS; IPF 8mm
    - LL elevation OD
    - Iris Color Equal
Anisocoria Case Report

Clinical Findings
- TA: 10/12
- SLE: Normal
- DFE: C/D: 0.2 OD, 0.2 OS (good color)
- Macula & Retina: Normal OU

Q1: Which of the following tests is least appropriate to confirm the diagnosis?
1. 4-10% Cocaine test
2. 125% Pilocarpine test
3. Paradrine 1% test
4. All of the above
5. None of the above

Q2: Which of the following is the most likely diagnosis?
1. Congenital Horner's Syndrome
2. Acquired Horner's Syndrome
3. Adie's Tonic Pupil
4. CN III Palsy
5. Argyll-Robertson Pupil

Q3: Which of the following is NOT considered appropriate management for this condition?
1. Chest X-Ray
2. Brain Imaging
3. Referral to a Neurospecialist
4. All of the above are appropriate
5. None of the above are appropriate
Q3: Which of the following is NOT considered appropriate management for this condition?

1. Chest X-Ray
2. Brain Imaging
3. Referral to a Neurospecialist
4. All of the above are appropriate
5. None of the above are appropriate

Q4: Which of the following indicates the congenital / infantile form of this condition?

1. Mild Ptosis with excellent levator function
2. Miotic Anisocoria, most apparent in darkness
3. Lower Lid Elevation
4. Ipsilateral Anhydrosis
5. Heterochromia