

PRACTICING OPHTHALMOLOGISTS
CURRICULUM 2014-2016

Neuro- Ophthalmology/ Orbit

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Practicing Ophthalmologists Curriculum

Authors and Financial Disclosures

The Practicing Ophthalmologists Curriculum was developed by a group of dedicated ophthalmologists reflecting a diversity of background, training, practice type and geographic distribution.

Jeffrey A. Nerad, M.D., American Academy of Ophthalmology Secretary for Knowledge Base Development, serves as the overall project director for the acquisition and review of the topic outlines.

The Academy gratefully acknowledges the contributions of the North American Neuro-Ophthalmology Society.

Practicing Ophthalmologists Curriculum Panel

Roger E. Turbin, M.D., Chair

Matthew Dean Kay, M.D., Vice Chair

Sang H. Hong, M.D.

Flora Levin, M.D.

Todd A. Goodglick, M.D.

Timothy J. McCulley, M.D.

Anil D. Patel, M.D.

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Contributors who have disclosed financial relationships:

Contributors who state they have no significant financial relationships to disclose:

Todd A. Goodglick, M.D.

Sang H. Hong, M.D.

Matthew Dean Kay, M.D.

Flora Levin, M.D.

Timothy J. McCulley, M.D.

Jeffrey A. Nerad, M.D.

Anil D. Patel, M.D.

Roger E. Turbin, M.D.

Background on Maintenance of Certification (MOC)

Developed according to standards established by the American Board of Medical Specialties (ABMS), the umbrella organization of 24 medical specialty boards, Maintenance of Certification (MOC) is designed as a series of requirements for practicing ophthalmologists to complete over a 10-year period. MOC is currently open to all Board Certified ophthalmologists on a voluntary basis; time-limited certificate holders (ophthalmologists who were Board Certified after July 1, 1992) are required to participate in this process. All medical specialties participate in a similar process.

The roles of the American Board of Ophthalmology (ABO) and the American Academy of Ophthalmology relative to MOC follow their respective missions.

The mission of the American Board of Ophthalmology is to serve the public by improving the quality of ophthalmic practice through a process of certification and maintenance of certification that fosters excellence and encourages continual learning.

The mission of the American Academy of Ophthalmology is to advance the lifelong learning and professional interests of ophthalmologists to ensure that the public can obtain the best possible eye care.

The role of the ABO in the MOC process is to evaluate and to certify. The role of the Academy in this process is to provide resources and to educate.

Background on the Practicing Ophthalmologists Curriculum (POC)

At the request of the ABO, the Academy developed the Practicing Ophthalmologists Curriculum (POC), a knowledge base that identifies and defines areas of knowledge important to the delivery of quality eye care as a basis for the content of examinations for the MOC process. The content in the POC is comprised of the information deemed as the most relevant clinical information for a practicing ophthalmologist.

The ABO has agreed that their Periodic Ophthalmic Review Test (PORT) and closed-book Demonstration of Ophthalmic Cognitive Knowledge (DOCK) examinations will be based on the POC. The ABO is solely responsible for creating the PORT and DOCK exams and for certifying MOC candidates. The Academy has developed study tools based on the POC to assist doctors preparing to meet these MOC requirements.

Organization of the POC

The Practicing Ophthalmologists Curriculum comprises 10 practice emphasis areas (PEA), plus Core Ophthalmic Knowledge. The ABO has designated the following as practice emphasis areas:

- Comprehensive Ophthalmology
- Cataract/Anterior Segment
- Cornea/External Disease
- Glaucoma
- Neuro-Ophthalmology and Orbit
- Oculoplastics and Orbit
- Pediatric Ophthalmology/Strabismus
- Refractive Management/Intervention
- Retina/Vitreous
- Uveitis

In addition to two practice emphasis areas of choice, every diplomate sitting for the DOCK examination will be tested on Core Ophthalmic Knowledge. Core Ophthalmic Knowledge is defined as the fundamental knowledge every practicing ophthalmologist must have whatever their area of practice.

Each PEA is categorized into topics presented in an outline format for easier reading and understanding of the relevant information points by the reader. These outlines are based on a standard clinical diagnosis and treatment approach found in the Academy's Preferred Practice Patterns.

For each topic, there are Additional Resources that may contain journal citations and reference to textbooks. These resources are supplemental to the topic outline, and should not be necessary for MOC exam preparation purposes.

Creation of the POC

The POC was developed by panels of practicing ophthalmologists in each of the ten practice emphasis areas. The panels reflect a diversity of background, training, practice type and geographic distribution, with more than 90 percent of the panel members being time-limited certificate holders.

The panels ranked clinical topics (diseases and procedures) in terms of clinical relevance to the subspecialist or comprehensive ophthalmologist. The panelists created outlines for the topics deemed Most Relevant, based on what an ophthalmologist in a specific practice emphasis area needs to know to provide competent, quality eye care (i.e., directly related to patient care). These outlines were reviewed by subspecialty societies and the American Board of Ophthalmology.

Revision Process

The POC is intended to be revised every three years. The POC panels will consider new evidence in the peer-reviewed literature, as well as input from the subspecialty societies, the American Board of Ophthalmology and the Academy's Self-Assessment Committee, in revising and updating the POC.

Prior to a scheduled review the POC may be changed only under the following circumstances:

- A Level I (highest level of scientific evidence) randomized controlled trial indicates a major new therapeutic strategy
- The FDA issues a drug/device warning
- Industry issues a warning

Neuro-Ophthalmology/Orbit

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Confrontation visual field testing

I. List indications/contraindications

- A. Can be performed at the bedside or exam room**
- B. Functions as a screening test**
- C. Depends on ability of patient to understand instructions and cooperate**
- D. Field testing needs to be tailored to patient's age and attention span**
- E. Can miss visual field defects detectable with quantitative perimetry**

II. Describe pre-procedure evaluation

- A. Evaluate patient's ability to understand and follow directions**
- B. Evaluate level of visual acuity**

III. List the alternatives to this procedure

- A. Goldmann kinetic perimetry**
- B. Automated static perimetry**
- C. Tangent screen perimetry**
- D. Amsler grid testing**

IV. Describe the instrumentation and technique

- A. Examiner seated about 1 meter opposite patient**
- B. Patient is directed to cover one eye and fixate on examiner's opposite eye or nose**
- C. Patient is asked whether examiner's entire face is visible or specific portions are missing**
- D. Patient is asked to identify a target of one, two or five fingers presented at the midpoint of each of the four quadrants**
- E. The target should be presented in a plane halfway between the patient and examiner**
- F. Patient is asked to add the total number of fingers presented in opposing quadrants (double simultaneous stimulation)**
 - 1. In addition to visual loss, failure of this test may represent extinction phenomenon as the optic radiations pass through the parietal lobe, or it could reflect patient's inability to add (dyscalculia)**
- G. Subjective comparisons between temporal and nasal and superior and inferior hemifields using clarity of examiner's hands or color comparisons of red objects**
 - 1. This requires patient judgment; therefore interpretation is not clear-cut in patients with visual inattention or neglect**

- H. Moving stimuli are almost always appreciated better than static ones, so the latter are preferable for screening for subtle field defects**
- I. Expressive aphasic, uncooperative, sedated, intubated or very young patients can use finger mimicry, pointing, visual tracking or reflex blink to respond and allow gross appraisal of visual field integrity**
 - 1. If a patient saccades to a visual stimulus in a given quadrant, the visual field in that area can be considered to be *relatively* intact
- J. Check patient's ability to distinguish color of red object when looking directly at it**
 - 1. Check color of object to right and left of fixation (looking for central scotoma vs hemianopic defect too subtle to detect with finger-counting)

V. Describe the considerations in interpretation of this diagnostic procedure

- A. Subtle or small visual field defects can be missed, particularly if red desaturation is not tested**
- B. Limitations in patient comprehension and cooperation may limit usefulness of field testing**
- C. Inadequate cover of eye with hand or occluder (rather than patching) may allow patient to see or inadvertently peek with the covered eye and lead to inaccurate results**
- D. The visual field of the examiner is being compared to the patient**
 - 1. It is assumed the examiner's visual field is normal
- E. Finger wiggling visual field may lead to larger field than finger counting field**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
- 2. AAO, Visual Fields: Examination and Interpretation, 2nd ed., 1996; p.24-25.

Automated static perimetry

I. List indications/contraindications

A. Advantages

1. Reproducible
2. More objective (but still subjective test)
3. More standardized testing procedures
4. Less technician reliant and less inter-technician variability
5. More sensitive to subtle field loss than Goldmann perimetry
6. Numerical data can be used for statistical analysis and stored electronically
7. More sensitive to diffuse depression (usually anterior segment [cataract or surface problem] or refractive)
8. Examples of visual field defects

B. Disadvantages

1. Can be lengthy
2. Tedious
3. False positives, false negatives, and fixation losses may alter interpretation
 - a. Detection of scotomas may be impaired
4. May require several tests to establish reliability
5. Threshold test (by definition) more difficult
 - a. Stimuli not seen 50% of the time

II. Describe pre-procedure evaluation

A. Measure refractive error and determine near correction if appropriate

B. Assess ability of patient to perform static perimetry (mental status, comfort with sitting still for extended period of time, good attention span, good understanding of test)

III. List the alternatives to this procedure

A. Other means of perimetry include

1. Confrontation visual field
2. Kinetic perimetry

B. Various static perimetry stimuli and algorithms exist

1. Screening field rather than threshold in some cases
- C. Kinetic perimetry can be more appropriate than static automated perimetry for**
 1. Young children
 2. Patients who need frequent verbal redirection of attention

IV. Describe the instrumentation and technique

- A. Various automated perimetry devices are available, which typically test 10 to 30 degrees radius from fixation in each eye**
- B. Corrective lenses are supplied for testing according to the patient's refraction or current glasses**
- C. The patient fixates on a central target and presses buzzer when light is seen**
- D. The stimulus size is kept the same, but the stimulus intensity is varied**
- E. The computer records and estimates threshold (stimulus seen 50% of the time) at each test location**
- F. This threshold estimate is recorded in decibels, a unit on logarithmic scale of brightness, zero decibels being the inability to see the maximum stimulus of the perimeter**
- G. These threshold values are compared with age-matched normal values at each point, along with a statistical evaluation of the probability that each point value is abnormal and plotted on topographic grids**
- H. Patient reliability is recorded by means of fixation losses, false-positive and false-negative responses**

V. Describe the considerations in interpretation of this diagnostic procedure

- A. When the patient responds to a stimulus presented in the assumed blind spot location, a fixation loss is recorded**
 1. The number of fixation losses estimates how reliably the patient's gaze is maintained on fixation target. With defects around the blind spot or significant field loss fixation loss may be underestimated
 2. This may indicate that the eye is not aligned with the fixation target (improper patient positioning)
- B. A false-positive response occurs when the patient depresses the button when no light stimulus was presented**
 1. These errors can be reduced by technician-patient interaction during testing
 2. Can indicate an overanxious patient
 3. A false negative response is when a patient fails to depress the button when a stimulus of greater intensity is represented in the same location where threshold was already determined. These errors can indicate patient fatigue or inattention
 4. They increase with increasing visual field pathology.
- C. There may be a learning curve**
 1. The first static automated visual field is frequently less reliable than subsequent fields

- D. The mean deviation is a center-weighted summation of the differences from age corrected normal at all tested points**
 - 1. It is a measure of the overall height of the hill of vision relative to normal
 - 2. As the patient's visual field worsens, the mean deviation becomes more negative
 - 3. Serial visual fields can be compared by following the mean deviation.
- E. Mild ptosis or dermatochalasis can be associated with depression of the superior visual field**
 - 1. Improper head positioning can also cause the nose to produce an inferonasal defect or a trial lens-induced scotoma to appear.
- F. Increasing age, media opacities and pupillary miosis may cause diffusely decreased sensitivity**
- G. Pattern deviation**
 - 1. Uses methodology to reduce or filter out the effect of generalized depression i.e. possibly due to refractive error/cataract allowing identification of focal defects in the visual field

VI. Clinically relevant anatomic correlations

- A. Optic nerve disease causes monocular visual field defects**
 - 1. Paracentral scotoma
 - 2. Central scotoma
 - 3. Centrocecal scotoma
 - 4. Arcuate defects
 - 5. Nasal step defects
 - 6. Altitudinal defects
- B. Optic chiasmal disease causes bitemporal visual field defects**
- C. Retrochiasmal disease causes homonymous visual field defects**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
- 2. Oxford University Press, Optic Nerve Disorders, 2nd Edition, 2007.
- 3. AAO, Focal Points: A Primer on Automated Perimetry, Module #8, 1993.
- 4. AAO, Focal Points: Automated Perimetry in Neuro-Ophthalmology, Module 6, 1995.

Computed tomography

I. List indications/contraindications

A. Indications

1. Globe and orbital trauma
2. Assessment of bony abnormalities including fractures
3. Detection of calcification in lesions
4. Assessment of acute intracranial hemorrhage
5. When magnetic resonance imaging (MRI) is contraindicated
 - a. Ferromagnetic foreign body
 - b. Pacemaker
 - c. Recent cardiac stent; recently placed metallic implants
 - d. MRI - incompatible intracranial aneurysm clips
 - e. Cochlear implants
 - f. Claustrophobia, obesity (relative contraindications)
6. Neuro radiologic consultation may provide guidance for the application of CTA or MRA for specific clinical scenarios

B. Contraindications

1. Allergy to contrast media, if contrast is needed
2. Relative contraindication in pregnancy
 - a. Can shield fetus with lead apron
3. Repeated studies in childhood or when risk of radiation induced secondary tumors is increased
4. Renal insufficiency if using contrast

C. Disadvantages

1. Soft tissue details can be lost when in close proximity to bony structures such as the orbital apex, optic canal, and at the skull base
2. Dental fillings, braces may cause artifacts
3. Poor visualization of posterior fossa
4. Radiation risks to eye, orbit, head and neck

II. Describe pre-procedure evaluation

A. Need to assess for potential allergic reaction to contrast dye (iodine, shellfish)

- B. **Contraindications to ionizing radiation (need for frequent imaging, potential pregnancy)**
- C. **Renal function should be assessed before giving contrast dye**
- D. **Determine whether direct coronal images are required rather than reconstructed images for superior quality images (e.g., orbital fractures, extraocular muscle entrapment or vertical recti enlargement or abnormalities)**
- E. **Use of newer techniques, such as spiral CT, needs to be considered**
- F. **Desired thickness of sections may be discussed with the radiologist**
- G. **Clinical information invaluable in planning studies**

III. List the alternatives to this procedure

- A. **MRI**
- B. **Ultrasound**

IV. Describe the instrumentation and technique

- A. **CT scanning is based on ionizing radiation**

V. List the complications of the procedure, their prevention and management

- A. **Allergic reaction to iodinated contrast**
- B. **Contrast agent-induced renal failure**
 - 1. Risk is high in dehydrated patients and patients with renal or cardiovascular insufficiency
 - a. Risk is higher if creatinine is greater than 1.5 mg/dl
- C. **Neurotoxicity from contrast dye in conjunction with arteriography has been reported**

VI. Describe the considerations in interpretation of this diagnostic procedure

- A. **Lack of contrast administration may led to false normal radiologic interpretation**
- B. **Nonmetallic foreign bodies may not be well seen**
 - 1. Depends on hydration of the foreign body
- C. **Poor resolution at orbital apex or posterior fossa**
- D. **Artifact from metallic foreign bodies, beam hardening, and motion**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
- 2. AAO, Optic Nerve Disorders, 1996.
- 3. AAO, Focal Points: Neuroimaging for the General Ophthalmologist, Module #8, 1998.

4. AAO, Focal Points: Optic Atrophy, Module #2, 2006.

Magnetic resonance imaging

I. List indications/contraindications

A. Definition

1. Magnetic resonance imaging (MRI) is a method to generate cross-sectional images from the interior of the body based on nuclear magnetic resonance without using ionizing radiation

B. Indications

1. Most useful to image the full extent of inflammatory, ischemic and neoplastic processes, (including such areas more difficult to image with other modalities such as the skull base, orbital apex)
2. Confirmed nonmetallic foreign bodies

C. Contraindications

1. Trauma causing injury that could be exacerbated by manipulation of patient in scanner
2. Unstable medical condition logistically prevents patient from being scanned
3. Metallic foreign body
4. Cardiac pacemaker/defibrillator
5. Cochlear implants
6. MRI-incompatible aneurysm clips
7. Recent cardiac stent placement
8. Neurostimulators
9. Claustrophobia (relative contraindication)
10. Large body size (relative contraindication)
11. Pregnancy (relative contraindication)
12. No contrast with significant renal insufficiency

D. Technique may not be sensitive for acute hemorrhage

E. Expensive

II. Describe pre-procedure evaluation

A. Rule out contraindications

B. Specify anatomically where imaging needs to be performed: brain, orbits, neck, chest

C. Evaluate need for magnetic resonance angiography (MRA), magnetic resonance venography (MRV)

D. Discuss optimal sequences/technique for differential diagnosis with radiologist to insure proper technique

- E. For bony lesions

III. List the alternatives to this procedure

- A. Other imaging techniques
- B. In suspected large vessel disease, CT angiography or digital angiography are alternatives to MRA

IV. Describe the instrumentation and technique

- A. Mobile protons in biologic tissues align themselves and resonate along the direction of a strong static magnetic field at a known frequency. Resonating protons are exposed to a burst of radiofrequency energy that briefly excites them to a higher energy state.
- B. After excitation, protons spontaneously undergo a tissue characteristic process of relaxation and release weak radiofrequency energy, which is detected by a large antenna coil inside the MRI unit. The radiofrequency map is converted into a spatial signal map that appears as an image. Different tissues and disease processes may exhibit different tissue-specific relaxation properties that often allow one tissue to be distinguished from another
- C. MRI is sensitive to soft tissue changes in water content
 - 1. Pathologic processes in general have an increase in water content compared to normal tissues
- D. Gadolinium injection
 - 1. Paramagnetic substance
 - 2. Can cross disrupted blood-brain barrier as can occur in CNS disease
 - 3. Can help distinguish normal from abnormal tissue, whether inflammatory or neoplastic
 - 4. Not necessary for MRA of brain or of neck (but considered advantageous for a optimal quality MRA scan specifically of the neck)
- E. T1 weighted images
 - 1. Most useful for demonstrating anatomy
 - a. Fat is brightest and increasing water content in structures seen as darker image
- F. T2 weighted images
 - 1. Maximize differences in water content and most sensitive to inflammatory, ischemic or neoplastic alterations in tissue
 - a. Water containing structures brightest, fat containing structures less bright
- G. Fat-suppression techniques removes intense whiteness of fat signal that can obscure other signals
 - 1. Particularly useful for orbit imaging
- H. Fluid-attenuated inversion recovery (FLAIR)
 - 1. Disease processes which often show high T2 signal may be difficult to identify against the high signal of the CSF. FLAIR provides T2 weighted images without the high (white) cerebrospinal fluid signal

2. FLAIR imaging is CSF suppression, analogous to fat suppression on T1 images
3. FLAIR is thus ideal for viewing periventricular white matter changes
 - a. Demyelinating process such as multiple sclerosis
 - b. Edema
 - c. Changes from cortical stroke, and other white matter disease

I. Diffusion weighted images

1. Sensitive to acute ischemia causing cytotoxic edema appearing as high signal (white)
2. Similar changes with high signal seen in other forms of inflammation
3. Ideal for identifying acute ischemia

J. ADC map low (dark) signal confirms area seen on DWI is ischemic

K. MRA / MRV

1. Can be used to obtain images of the proximal large vessels of the chest and neck as well as CNS arteries and veins
2. Records signals from fast-moving particles such as blood, while signals from stationary tissues are suppressed

V. List the complications of the procedure, their prevention and management

A. Gadolinium allergy

B. Gadolinium induced nephrogenic systemic fibrosing syndrome

1. Seen mainly in patients with renal insufficiency
2. Scleroderma -like changes

VI. Describe the considerations in interpretation of this diagnostic procedure

- A. Provide details of patient clinical information, differential diagnosis and expected location of pathology to radiologist to make sure that the correct imaging sequences will be performed**
- B. When imaging study fails to demonstrate expected pathology or answer a clinical question, the first step is to re-examine the studies with a neuroradiologist to determine if the appropriate studies were performed and area of interest adequately imaged**
- C. Motion artifact may degrade quality of images**
- D. Presence of braces, mascara, permanent eyeliner or other metallic implants (including nonferromagnetic aneurysm clips or coils may also degrade quality of imaging**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Optic Nerve Disorders, 1996, p.48, 60-63, 82-83, 95-98, 102, 104, 107, 112-113, 118, 121,

203-206.

3. AAO, Focal Points: Multiple Sclerosis and Optic Neuritis, Module #12, 2003, p.3-5.
4. AAO, Focal Points: Neuroimaging for the General Ophthalmologist, Module #8, 1998.

Migraine

I. Describe the approach to establishing the diagnosis

A. List the pertinent elements of the history

1. Repetitive, stereotypic bouts of headache
2. Family history of headaches
3. History of motion sickness
4. Cold-induced vascular headache
5. Often temporal relationship to menstrual cycle
6. Typical headache features
 - a. Quality: pulsating or throbbing
 - b. Location: Unilateral head pain that may alternate sides; may include face pain
 - c. Precipitating factors: wine, cheese, menstrual cycle, physical activity
 - d. Age at onset: often begin in childhood, adolescence, or the second or third decade of life
 - e. Daily pattern (am or pm); headaches that awaken patients at night are rarely migraine
7. Associated symptoms
 - a. Nausea, emesis
 - b. Photophobia, phonophobia
 - c. Scintillating scotoma

B. Define the relevant aspects of epidemiology of the disease

1. Typically develops in childhood or adolescence
2. Women more commonly affected
3. Often (2/3) positive family history
4. If new onset elderly patients consider giant cell arteritis (GCA)

C. Describe pertinent clinical features

1. May be induced by hormonal changes, stress, relief of stress, certain foods or wines, or change in sleep pattern
2. Migraine with aura (previously termed classic migraine)
 - a. Preceded by aura < 45 minutes long
 - b. Imagery builds up over minutes with positive visual phenomena with movement (fortification spectrum)
 - c. Followed by severe contralateral throbbing headache

- d. Headache may occur in any location
- e. Last several hours
- f. Associated with photophobia, sonophobia and nausea
- 3. Migraine without aura (previously termed common migraine)
 - a. No preceding neurologic symptoms
 - b. Diffuse (global) headache
 - c. Unilateral or bilateral headache
- D. Describe appropriate testing and evaluation for establishing the diagnosis**
 - 1. Neuroimaging magnetic resonance imaging (MRI) of brain for atypical migraine features
 - a. Headache or aura always on same side
 - b. Neurologic deficits
 - c. Visual phenomenon not typical
 - d. Duration not typical
 - 2. Lumbar puncture to check opening pressure, cells, glucose and protein in the presence of signs and symptoms of raised intracranial pressure or meningitis

II. Define the risk factors

- A. Family history**
- B. Foods (chocolate, nitrates, monosodium glutamate, aged cheese, caffeine, wine, alcohol, aspartame, nuts and shellfish)**
- C. Stress or relief from stress**
- D. Change in sleep patterns**
- E. Cigarette smoke**
- F. A variety of environmental influences may precipitate migraine**

III. List the differential diagnosis

- A. Brain AVM or tumor**
- B. Increased ICP**
- C. Malignant hypertension**
- D. Vascular events**
- E. GCA in the elderly**
- F. Meningitis**
- G. Temporomandibular joint disorder**
- H. Tension headache and other headache syndromes, especially sympathetic pain syndromes**

IV. Describe patient management in terms of treatment and follow-up

A. Acute medications

1. Abortive
2. Analgesic

B. Prophylactic medications

C. Supportive measures

D. Maintain a headache log to assess headache (in terms of frequency and severity) and its response to medications and to identify precipitating factors

E. Eliminate precipitating environmental influences

V. List the complications of treatment, their prevention and management

A. Overuse of caffeine can result in rebound headaches

B. Analgesic rebound headache

C. Potential side effects of abortive, prophylactic or therapeutic migraine agents

VI. Describe disease-related complications

A. Loss of time from school and work

B. Stroke (rare)

C. Persistent visual field deficit (rare)

VII. Describe appropriate patient instructions

A. Avoid stress as much as possible

B. Avoid foods known to be triggers

C. Maintain consistent sleep schedule

D. Appropriate referral to headache specialist for management

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Electrophysiologic Testing, 2nd ed., 2001, p.257-258.
3. AAO, Ophthalmology Monographs 10. Optic Nerve Disorders, 1996.
4. AAO, Focal Points: Migraine, Module #1, 2000.
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6. Winterkorn JM, Kupersmith MJ, Wirtschafter JD, et al. Treatment of vasospastic amaurosis fugax with calcium-channel blockers. *N Engl J Med* 1993;329:396-398.
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9. Raskin NH. Acute and prophylactic treatment of migraine: practical approaches and pharmacologic rationale. *Neurology* 1993;43:S34-42.
10. AAO, Focal Points: Botulinum Toxin in Ophthalmology, Module #3, 2007.

Papilledema

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. History of familial cause of pseudopapilledema such as optic nerve head drusen

B. Define the relevant aspects of epidemiology of disease

1. Depends on the etiology of increased ICP
 - a. Brain tumor
 - i. Any age or gender possible
 - ii. Tumor type is correlated to age of patient
 - b. Pseudotumor cerebri (PTC)/idiopathic intracranial hypertension (IIH)
 - i. Obese women
 - ii. Higher incidence in women of childbearing age
 - iii. In prepubescent children the risk profile is different- no sex, body mass difference
 - c. Infection
 - i. Any age or gender possible
 - d. Inflammation
 - e. Sarcoidosis more common in African Americans and Scandinavians
 - f. Vascular: dural venous sinus thrombosis

C. List the pertinent elements of the history

1. Symptoms of increased ICP
 - a. Headache
 - b. Nausea & vomiting
 - c. Transient visual obscurations
 - d. Intracranial noises (humming or ringing) or pulsations
2. Double vision (VI N. palsy, VI N also in kids)
3. Decreased vision
4. Other neurologic symptoms suggestive of hydrocephalus or mass effect
5. Presence of systemic disease
 - a. Brain tumor or malignancy
 - b. Other neurologic symptoms or meningitic symptoms
 - c. Hypercoagulable state

- d. Autoimmune disease

D. Describe pertinent clinical features

1. Optic disc swelling - typically at the lower pole then upper, followed by nasal then temporal portions
2. Peripapillary nerve fiber layer opacification - usually bilateral but may be asymmetric
3. Lack of spontaneous venous pulsations (may be a normal finding)
4. Hyperemia from dilation and telangiectasia of the surface disc capillaries
5. Venous engorgement and tortuosity of the vessels
6. Obliteration of central cup (late finding)
7. Hemorrhages and exudates
8. Paton lines (circumferential retinal folds in the region surrounding the disc)
9. Choroidal folds
10. If chronic, optic atrophy may ensue, refractile bodies ("pseudodrusen") may be seen late
11. If chronic, optociliary shunt vessels (retinochoroidal collaterals)
12. Can be confused with pseudopapilledema due to optic nerve head drusen, hyperopic, anomalous discs, or myelinated nerve fibers
13. Afferent function usually normal early (central visual acuity, color, pupils and visual fields) but visual fields are key to management at all stages
14. Cranial nerve (CN) VI palsy may be present

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Neuroimaging (magnetic resonance imaging (MRI) preferred) - done urgently when papilledema is suspected
 - a. Must rule out a brain mass lesion
2. Ultrasound -B-mode or optic nerve head autofluorescence for buried drusen
3. Magnetic resonance venography (MRV) or other venous studies to rule out a dural venous sinus thrombosis as the cause of papilledema
4. Lumbar puncture to determine opening pressure and CSF composition including cells, protein and glucose if no contraindications
 - a. False opening pressure determinations assessed in other than lateral decubitus or prone patient position

II. Define the risk factors

A. Recent weight gain

B. Excess vitamin A intake

C. Medications (tetracycline, especially minocycline, retinoids, nalidixic acid, lithium, corticosteroid

withdrawal)

- D. Venous sinus thrombosis
- E. Possible role of other venous sinus abnormalities or jugular vein issues

III. List the differential diagnosis

- A. Pseudopapilledema (optic nerve head drusen, hyperopic or anomalous discs)
- B. Malignant hypertension
- C. Bilateral disc edema not due to increased ICP (i.e., other bilateral optic neuropathies)

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Ophthalmology Monographs 10. Optic Nerve Disorders, 1996.
3. AAO, Focal Points: Differential Diagnosis of Optic Disc Edema, Module #2, 1999.
4. Biousse V, Rucker JC, Vignal C, et al. Anemia and papilledema. *Am J Ophthalmol* 2003;135:437-46.
5. Friedman DI, Jacobson DM. Diagnostic criteria for idiopathic intracranial hypertension. *Neurology* 2002;59:1492-5.
6. Friedman DI. Papilledema and pseudotumor cerebri. *Ophthalmol Clin North Am* 2001;14:129-47,ix.
7. Friedman DI. Pseudotumor cerebri. *Neurosurg Clin N Am* 1999;10:609-21,viii.
8. AAO, Ophthalmology Monographs 10. Optic Nerve Disorders, 1996.
9. AAO, Focal Points: Optic Atrophy, Module #2, 2006.
10. AAO, Focal Points: Idiopathic Intracranial Hypertension (IIH, Pseudotumor Cerebri), Module #3, 2004.
11. AAO, Focal Points: Differential Diagnoses You Don't Want to Miss, Module #2, 1999.

Idiopathic intracranial hypertension (Pseudotumor cerebri)

I. Describe the approach to establishing the diagnosis

A. Define the relevant aspects of epidemiology of the disease

1. Majority of patients are obese women
2. Childbearing years
3. Exposure to agents associated with pseudotumor cerebri, including:
 - a. Nalidixic acid
 - b. Vitamin A, retinoids and other derivatives
 - c. Tetracyclines
 - d. Lithium
 - e. Steroids withdrawal
4. Systemic illnesses associated with IIH
 - a. Endocrine & metabolic disturbances
 - b. Severe anemia PCOS

B. List the pertinent elements of the history

1. Symptoms of increased ICP
 - a. Headache
 - b. Nausea, vomiting
 - c. Transient visual obscurations
 - d. Intracranial noises (humming or ringing) or pulsations
2. Double vision
3. Decreased vision
4. Other neurologic symptoms suggestive of hydrocephalus or mass effect
5. Presence of systemic disease
 - a. Brain tumor or malignancy
 - b. Other neurologic symptoms or meningitic symptoms
 - c. Hypercoagulable state
 - d. Systemic autoimmune, infectious or inflammatory diseases

C. Describe pertinent clinical features

1. Bilateral disc edema
2. Peripapillary/epipapillary hemorrhages and cotton wool spots
3. Paton's lines (circumferential retinal folds in the region surrounding the disc)
4. Visual field findings
 - a. Enlarged physiologic blind spot
 - b. Nerve fiber bundle defects
5. Unilateral or bilateral cranial nerve (CN) VI palsy
6. Atypical features
 - a. Non-obese adult
 - b. Male
 - c. Unilateral disc swelling
 - d. Multiple cranial neuropathies
 - e. Vitreous cells
 - f. Retinal hemorrhages beyond the peripapillary area
 - g. Acuity loss without atrophy

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Neuroimaging (magnetic resonance imaging (MRI) /magnetic resonance venography (MRV) or other venous studies preferred)
2. Lumbar puncture (opening pressure, cells, protein, glucose)
 - a. If the case is atypical (e.g. wrong age or gender-see I.C.6.) or the clinical symptoms are signs are not characteristic, additional work-up should include evaluations for infection, inflammation and/or neoplasia
3. Blood pressure
 - a. Should be checked, especially in cases with cotton wool spots, to exclude malignant systemic hypertension
4. Serologic testing: CBC for anemia

II. Define the risk factors

- A. Female predominance**
- B. Obesity**
- C. Child bearing years**

III. List the differential diagnosis

- A. Pseudopapilledema with headache**

- B. Secondary increased intracranial pressure**
 - 1. Meningitis: inflammatory, sarcoidosis, neoplastic
- C. Venous sinus thrombosis**
- D. Classic complete macular star and cotton wools spots are NOT characteristic and suggest an alternative cause such as infection or vasculitis/malignant hypertension, respectively**
- E. Dot blot hemorrhages may be seen out to the mid-periphery due to venous stasis from chronic papilledema, but need r/o CRVO with this finding.**
- F. Malignant hypertension**
- G. Functional overlay**
- H. Migraine headache**
- I. Other headache syndrome in conjunction with PTC not uncommon**

IV. Describe patient management in terms of treatment and follow-up

- A. Role of the visual field**
 - 1. Follow-up and intervention determined by severity of visual field defect and headache
- B. Weight reduction**
- C. Describe medical therapy options**
 - 1. Acetazolamide and other carbonic anhydrase inhibitors
 - 2. Role of corticosteroids
 - a. Limited application of IV corticosteroids in the management of advanced visual loss
 - 3. Additional therapy for headache as needed
- D. Describe surgical therapy options**
 - 1. Optic nerve sheath fenestration
 - a. For treatment of visual loss not responsive to medical therapy or severe and progressive
 - b. Not a primary therapy when headache is the dominant feature
 - 2. Cerebrospinal fluid (CSF) diversion procedures (lumboperitoneal shunt or ventriculoperitoneal shunt)
 - a. Serial lumbar punctures should be discouraged
 - b. For treatment of headache and visual loss
 - 3. Bariatric surgery
 - a. May be considered as an adjunct therapy for morbidly obese patients where diet and exercise have failed to result in weight loss

V. List the complications of treatment, their prevention and management

A. Acetazolamide

1. Nausea and emesis
2. Numbness and tingling of extremities/perioral area
3. Metabolic acidosis
4. Distaste for carbonated beverages
5. Kidney stones
6. Blood dyscrasias
7. Hypokalemia especially if used with other diuretics

B. Optic nerve sheath fenestration

1. Immediate or eventual fenestration failure
2. Visual loss
 - a. Due to direct optic nerve trauma or central retinal artery occlusion
3. Diplopia
 - a. Due to medial rectus muscle detachment and reattachment during medial approach to optic nerve
4. Tonic pupil
 - a. Due to ischemia or direct trauma to the ciliary ganglion or its innervation during lateral approach to the optic nerve

C. CSF diversion procedures

1. Immediate or delayed shunt failure
2. Infection (peritonitis or meningitis)
3. Abdominal or Back pain
4. Shunt Migration
5. Visual loss despite functioning shunt
6. Low pressure headache due to over shunting

D. Bariatric surgery

1. Immediate or eventual bypass failure
2. Nausea and vomiting
3. Diarrhea
4. Abdominal pain
5. Malabsorption

VI. Describe disease-related complications

- A. **Progressive visual field loss**
- B. **Central visual loss**
- C. **Optic atrophy**
- D. **Persistent headache despite normal ICP**
- E. **Depression**
- F. **Diplopia**

VII. Describe appropriate patient instructions

- A. **Encourage weight loss, by dieting or surgical methods**
- B. **Stress that compliance with follow-up examinations, to include visual field testing, is crucial**
- C. **Discuss why visual field testing is essential**
- D. **Educate about common acetazolamide side effects**
- E. **Consider checking electrolytes and complete blood count (CBC) shortly after starting acetazolamide**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Electrophysiologic Testing, 2nd ed., 2001, p.250.
3. AAO, Optic Nerve Disorders, 1996, p.48-52.
4. AAO, Focal Points: Neuro-Ophthalmic Problems Caused by Medications, Module #11, 1998, p.4-5.
5. Johnson LN, Krohel GB, Madsen RW. The role of weight loss and acetazolamide in the treatment of idiopathic intracranial hypertension (pseudotumor cerebri). *Ophthalmology* 1998;105:2313-7.
6. Skau M, Brennum J, Gjerris F, et al. What is new about idiopathic intracranial hypertension? An updated review of mechanism and treatment. *Cephalalgia* 2006;26:384-99.
7. Liu GT, Glaser JS, Schatz NJ..High-dose methylprednisolone and acetazolamide for visual loss in pseudotumor cerebri. *Am J Ophthalmol*. 1994 Jul 15;118(1):88-96.

Orbital cellulitis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Extension of infection from periorbital structures
 - a. Paranasal sinuses
 - i. Direct spread from an adjacent sinusitis in the majority of cases (most likely if no other obvious source)
 - ii. Rarely associated with orbital fracture
 - b. Face and eyelids
 - c. Dacryocystitis
 - d. Dental infection
 - e. Intracranial
 - f. Concomitant orbital abscess
 - g. Endophthalmitis
2. Exogenous
 - a. Direct inoculation following trauma or skin infection
 - i. Trauma
 - i) Need to rule out foreign body or orbital fracture
 - ii. Postsurgical (any orbital or periorbital surgery)
3. Endogenous
 - a. Bacteremic spread from a distant focus (otitis media, pneumonia) with septic embolization
4. Intraorbital
 - a. Endophthalmitis
 - b. Dacryoadenitis

B. Define the relevant aspects of epidemiology of the disease

1. In more than 90% of cases, orbital cellulitis occurs as a secondary extension of acute or chronic bacterial sinusitis
2. Organisms most commonly associated with orbital cellulitis include:
 - a. *Staphylococcus* species
 - b. *Streptococcus* species
 - c. *Bacteroides*

- d. Gram-negative rods (especially after trauma)
- e. Anaerobes
- f. Methicillin resistant staff aureus (MRSA)
- g. H.flu less common cause of childhood disease with Hib vaccine usage

C. List the pertinent elements of the history

- 1. Trauma
- 2. Ear, nose, throat or systemic infections
- 3. Diabetes mellitus
- 4. Immunosuppression
- 5. Ocular symptoms
 - a. Pain
 - b. Decreased vision
 - c. Diplopia
 - d. Swelling
 - e. Ptosis

D. Describe the pertinent clinical features

- 1. General (in only some cases)
 - a. Fever
 - b. Leukocytosis
- 2. Local
 - a. Proptosis
 - b. Conjunctival injection and chemosis
 - c. Eyelid edema, often tense edema
 - d. Ptosis,
 - e. Erythema, warmth
 - f. Orbital tenderness
 - g. Restriction of ocular motility
 - h. Pain with eye movement
 - i. Optic nerve dysfunction (decreased vision, afferent pupillary defect, visual field changes, dyschromatopsia)
 - j. Optic disc edema

E. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Evaluation of the orbits and paranasal sinuses with computed tomography (CT) scan or MRI

2. Otolaryngology consult if sinusitis is identified
3. Complete blood count with differential
4. Blood cultures (often negative)
5. Explore and debride any associated wound or skin lesion, culture any drainage

II. Define the risk factors

- A. Sinusitis
- B. Skin infection or preseptal cellulitis
- C. Diabetes mellitus
- D. Trauma (orbital fracture, foreign body in orbit)
- E. Systemic infection
- F. Immunosuppression

III. List the differential diagnosis

- A. Preseptal cellulitis
- B. Orbital inflammatory pseudotumor
- C. Trauma
- D. Mucormycosis
- E. Sarcoidosis
- F. Aspergillosis
- G. Carotid-cavernous fistula or dural AVM
- H. Cavernous sinus thrombosis
- I. Dysthyroid ophthalmopathy
- J. Necrotizing fasciitis
- K. Orbital tumors i.e. lymphoma
- L. In children: lymphangioma
- M. Ruptured dermoid

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options
 1. Broad spectrum IV antibiotics often for prolonged course
 2. Follow the patient
 - a. Vitals, CBC

- b. Visual acuity
 - c. Pupillary function (afferent and efferent)
 - d. Ocular motility
 - e. Degree of proptosis and globe displacement
 - f. External appearance
 - g. Corneal exposure
 - h. Intraocular pressure
 - i. Contralateral involvement
3. Abscesses in children under 9 years
 - a. More likely to resolve without surgery and with medical therapy alone
 - b. More likely to involve a single pathogen as opposed to similar infections in adults which tend to involve multiple organisms
 4. If worsening, the presence of an abscess should be suspected
 - a. Repeat CT scan of orbit and/or brain indicated
 5. If improving, can consider switch to oral antibiotics.

B. Describe surgical therapy options

1. Strongly consider draining affected sinuses if sinusitis present, especially in adults and older children
2. Incision and drainage of orbital abscess

V. List the complications of treatment, their prevention and management

- A. Abscess formation intraorbital or subperiosteal should be suspected if continuous improvement does not occur**
- B. Surgical complications include diplopia, ptosis, visual loss**

VI. Describe disease-related complications

A. Delay in treatment may result in

1. Progression of infection
2. Orbital apex syndrome
3. Cavernous sinus thrombosis
4. Blindness
5. Cranial nerve palsies
6. Meningitis

7. Intracranial abscess formation
8. Death

B. These can be avoided with aggressive management

VII. Describe appropriate patient instructions

- A. Patient instruction depends upon course of treatment agreed upon by the patient and ophthalmologist**
- B. Contact ophthalmologist, if new symptoms develop**
- C. Follow-up examinations important**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 7: Orbit, Eyelids, and Lacrimal System, 2013-2014.
2. AAO, Focal Points: Ocular and Periocular Pain, Module #2, 1996, p.5.

Aspergillosis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Aspergillus is a ubiquitous filamentous mold

B. Define the relevant aspects of the epidemiology of the disease

1. Contracted by
 - a. Inhalation or oral ingestion of spores

C. List the pertinent elements of the history

1. Review of patient general health including
 - a. Immunosuppression
 - b. Debilitation

D. Describe pertinent clinical features (several clinical variations)

1. Allergic aspergillosis affects bronchopulmonary system and paranasal sinuses
 - a. History of chronic sinusitis in immunocompetent host
 - b. Occasionally orbital and neuro-ophthalmic findings with involvement of sinuses
 - i. Optic neuropathy
 - ii. Proptosis
 - iii. Diplopia
 - iv. Headache
2. Saprophytic non invasive
3. Aspergillomas -fungus balls arising in poorly drained spaces such as the orbit, paranasal sinuses
 - a. Can occur in immunocompromised or immunocompetent patients
 - b. Symptoms of orbital mass
 - i. Proptosis
 - ii. Visual loss
 - iii. Diplopia
 - iv. Pain
4. Invasive aspergillosis in immunocompromised patients (cancer, acquired immune deficiency syndrome (AIDS), organ transplant, rheumatology patients on immunosuppressives)
 - a. Initial sinus or pulmonary involvement with subacute or acute progression
 - b. Central nervous system (CNS) infection occurs secondarily by either direct or

hematogenous spread of organisms

- c. Ophthalmic manifestations
 - i. Acute retrobulbar optic neuropathy
 - ii. Orbital apex syndrome
 - iii. Cavernous sinus syndrome
- d. Vascular invasion produces cerebral infarction or hemorrhage
- e. Meningitis, intracranial abscess, epidural and subdural hematomas and abscesses, mycotic aneurysm, encephalitis, cavernous sinus thrombosis, intracranial abscess

E. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Imaging studies of the brain or orbit as appropriate
- 2. Culture of tissue, blood, CSF may be negative
- 3. Biopsy of affected tissue essential and demonstrates tissue necrosis and vascular invasion

II. Define the risk factors

A. Aggressive acute disease, usually in immunocompromised

- 1. Diabetic
- 2. Elderly
- 3. Cancer patients
- 4. Immunocompromised patients of any nature

B. Infected paranasal sinus or nose

C. Early recognition is key to successful outcome of treatment

III. List the differential diagnosis

A. Mucormycosis or other fungal infection

B. Tumor (i.e., sinus, orbital)

C. Bacterial infection

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

- 1. Systemic immunomodulation for allergic fungal disease
- 2. Antifungal medication
 - a. Role in chronic allergic aspergillosis unclear
- 3. Correction of underlying metabolic abnormality

B. Describe surgical therapy options

1. Surgical debridement/excision of necrotic tissue is essential
2. Direct perfusion of involved tissue with antifungal agents has been described as a potential adjunctive therapy to systemic antifungal therapy and local debridement

V. List the complications of treatment, their prevention and management

- A. Post-surgical deformity**
- B. Loss of vision**
- C. Renal failure**

VI. Describe disease-related complications

- A. Endophthalmitis**
- B. Intracranial abscess**
- C. Cerebral infarcts**
- D. Necrosis**
- E. Mycotic aneurysms**
- F. Morbidity is high with CNS involvement**

VII. Describe appropriate patient instructions

- A. Patient instruction depends upon course of treatment agreed upon by the patient and physician**
- B. Contact physician if new neurological symptoms develop**
- C. Close follow-up for recurrence**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Orbital Cellulitis, Module #11, 1991, p.7.

Mucor

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Mucormycosis describes several different presentations of fungal infections of the class Zygomycetes

B. Define the relevant aspects of the epidemiology of the disease

1. Ubiquitous in environment
2. Fungus gains entry through respiratory tract
3. Iron potentiates growth of mucor
 - a. Mucor has an affinity for blood vessels
 - b. Mucor grows through blood vessel walls producing thrombosis, hemorrhage and ischemic tissue necrosis
 - c. Aneurysms or pseudoaneurysms may develop

C. List the pertinent elements of the history

1. Most cases limited to debilitated (elderly, cancer), injured (burn), diabetic or immunocompromised patients
2. Course is usually acute and rapid although a chronic indolent variation can occur

D. Describe pertinent clinical features

1. Mucormycosis in immunocompromised patients
 - a. Involvement of facial skin, nasal, sinus or hard palate mucosa and spreads to nearby blood vessels
 - b. Invasion of orbit causing cellulitis, orbital apex syndrome, cavernous sinus thrombosis, arterial thrombosis
 - c. Headache and facial pain or numbness
 - d. Facial swelling
 - e. Fever
 - f. Sinusitis
 - g. Pharyngitis
 - h. Nasal discharge
 - i. Eyelid swelling
 - j. Pain with eye movement
 - k. Redness

- l. Chemosis
- m. Proptosis
- n. Limitation of eye movement
- o. Painful diplopia
- p. Vision loss often related to retinal and choroid infarction or occlusion
 - i. Can also be due to fungal infiltration of optic nerve
- q. Cranial neuropathy can occur
 - i. Especially II, III, IV, V, VI
 - ii. Other cranial nerves including V if disease extends beyond orbital apex and cavernous sinus
- r. Neurologic manifestations of meningitis and parenchymal invasion
- s. Untreated rhinocerebral mucormycosis may bring about rapid deterioration leading to blindness and death within days
- t. Cutaneous with skin lacerations or burns or disseminated disease
- u. Gastrointestinal with extreme malnutrition or other gastrointestinal disease
 - v. Fungus gains entry to CNS from nose or paranasal sinus

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Computed tomography (CT) scan can show bony destruction, soft tissue alteration in paranasal sinuses and orbit, air-fluid levels in sinus and orbit, or brain abscess.
2. Magnetic resonance imaging (MRI)/magnetic resonance angiography (MRA)/angiography for thrombosis of major vessels
3. Biopsy is essential as imaging findings can be nonspecific and cultures can be negative. Pathology shows vascular invasion and tissue necrosis (seen clinically as a black eschar, which is a classic but late finding) , inflammatory cells and hyphae

II. Define the risk factors

- A. Rhinocerebral mucormycosis in patients with diabetes mellitus, particularly in those with ketoacidosis, in patients receiving corticosteroids, or neutropenia**
- B. Immunosuppressed and debilitated patients, such as cancer patients**

III. List the differential diagnosis

- A. Aspergillosis**
- B. Orbital cellulitis**
- C. Idiopathic orbital inflammatory disease or Wegner**
- D. Sino-orbital tumors**

IV. Describe patient management in terms of treatment and follow-up

- A. Invasive fungal infection is a life threatening as well as vision threatening emergency, and requires aggressive intervention by teams of specialists in inpatient settings**
- B. Describe medical therapy options**
 - 1. Identify and treat underlying systemic disease including hyperglycemia and acidosis
 - 2. Antifungal drugs, especially amphotericin
- C. Describe surgical therapy options**
 - 1. Debridement of devitalized tissues essential with possible intraoperative or postoperative irrigation
 - 2. Exenteration if needed but all efforts to avoid if it is possible to preserve useful vision

V. List the complications of treatment, their prevention and management

- A. Mortality is high with rhinocerebral and CNS mucormycosis**

VI. Describe appropriate patient instructions

- A. Patient instruction depends upon course of treatment agreed upon by the patient and physician**
- B. Contact physician if new neurological symptoms develop**
- C. Follow-up examinations important**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
- 2. AAO, Focal Points: Neuro-Ophthalmic Diagnoses You Don't Want to Miss, Module #9, 1999, p. 11-12.
- 3. AAO, Focal Points: Orbital Cellulitis, Module #11, 1991, p. 7.

Non arteritic anterior ischemic optic neuropathy

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Infarction of the optic nerve head in area of the short posterior ciliary arteries

B. Define the relevant aspects of the epidemiology of the disease

1. On average, patients present in the fifth decade and younger age than arteritic forms but significant crossover
2. Male = female

C. List the pertinent elements of the history

1. Acute painless visual loss often first noted on awakening
2. Absence of symptoms of GCA (e.g., malaise, headache, neck pain, jaw claudication, scalp tenderness, fever, chills, anorexia, weight loss, fatigue, myalgias, arthralgias, diplopia, antecedent amaurosis fugax, tenderness over the temporal arteries)

D. Describe the pertinent clinical features

1. Decreased visual acuity
2. Relative afferent pupillary defect if unilateral
3. Color vision usually less affected than in other optic neuropathies
4. Visual field defects
 - a. Typically altitudinal or arcuate, inferior most common
5. Optic nerve edema with or without associated peripapillary hemorrhages or cotton wool spots
 - a. Segmental swelling most common but may not consistently correspond to VF loss
 - b. Diffuse
6. Vision can worsen in the first 2 weeks and usually stabilizes by 2 months
7. Variable limited visual recovery

E. Pertinent anatomic correlations

1. The arterial supply in the region of the lamina cribrosa is derived from the branches of the short posterior ciliary arteries that form a dense capillary plexus
2. The prelaminar region is supplied mainly by the branches of the peripapillary choroidal vessels
3. The surface layer of the disc is supplied by the main retinal vessels and a large number of capillaries

F. Describe the appropriate testing and evaluation for establishing the diagnosis

1. Serologic
 - a. Complete blood count (CBC)
 - b. Erythrocyte sedimentation rate (ESR)
 - c. C-Reactive protein (CRP)
 - d. Assessment for diabetes mellitus
 - e. Lipid profile
 - f. Blood pressure evaluation
 - g. Sleep study if suggestion of sleep apnea in review of systems
2. Superficial temporal artery biopsy if elevated acute phase reactants or symptoms/ signs suggestive of GCA

II. Define the risk factors

A. Non-arteritic

1. Small to absent optic cup
2. Diabetes mellitus
3. Hypertension
4. Cigarette use
5. Elevated lipids
6. Possible role of sleep apnea
7. Possible role of nocturnal hypotension

III. List the differential diagnosis

- A. Arteritic ischemic optic neuropathy**
- B. Optic neuritis**
- C. Diabetic papillitis**
- D. Disc drusen / pseudopapilledema**
- E. Compressive optic neuropathy**
- F. Central retinal vein occlusion**
- G. Infiltrative optic neuropathy**
- H. Leber hereditary optic neuropathy**
- I. Progressive or sequential ischemic optic neuropathy**

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. No proven therapy
2. Persistent optic nerve edema beyond 6-10 weeks and progressive vision loss requires further evaluation

V. Describe disease related complications

A. Failure to recover vision

B. Describe appropriate patient instructions

C. Call immediately for worsening of vision, episodes of amaurosis, or development of symptoms of GCA

D. Control vasculopathic risk factors in NAION in coordination with primary care physician

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. Dickersin K, Manheimer E, Li T. Surgery for nonarteritic anterior ischemic optic neuropathy. *Cochrane Database Syst Rev* 2006:CD001538.
3. Mathews MK. Nonarteritic anterior ischemic optic neuropathy. *Curr Opin Ophthalmol* 2005;16:341-5.
4. AAO, Focal Points: Giant Cell Arteritis, Module #6, 2005.

Giant cell arteritis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Inflammatory thrombosis of medium-sized arteries with an elastic lamina

B. Define the relevant aspects of epidemiology of the disease

1. Age greater than 50, (generally greater than 60) years

C. List the pertinent elements of the history

1. Acute visual loss typically without eye pain
2. Visual loss may be preceded by amaurotic episodes
3. Diplopia
4. Symptoms of giant cell arteritis (GCA) (e.g. headache, jaw claudication, scalp tenderness, fever, weight loss, fatigue, myalgias, diplopia, antecedent amaurosis fugax)
 - a. May be absent - occult GCA
 - b. History of polymyalgia rheumatica (PMR)

D. Describe pertinent clinical features

1. Decreased visual acuity
 - a. Often severe visual loss
 - i. From counting fingers to no light perception
 - b. May be bilateral at presentation, however onset is usually sequential
2. Decreased color vision
3. Afferent pupillary defect
4. Visual field defects
 - a. Nerve fiber bundle defects
 - b. Altitudinal loss
 - c. Generalized depression
5. Pallid optic nerve edema with or without associated peripapillary hemorrhages or cotton wool spots
6. May have large cup: disc ratio of optic nerve
7. Retinal ischemia (e.g., CRAO, hemorrhages, cotton wool spots)
8. Choroidal ischemia may also be present
9. Involvement of individual or multiple extraocular muscles not corresponding to an isolated ocular motor nerve

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Serologic
 - a. Complete blood count (CBC) with differential and platelet count, looking for anemia of chronic disease and thrombocytosis
 - b. Erythrocyte sedimentation rate (ESR)
 - i. ESR may be normal
 - ii. Concurrent medications may artificially reduce ESR
 - c. C-reactive protein (CRP)
 - i. CRP may be normal
2. Use of fluorescein angiogram as adjunct test
 - a. Delayed/patchy choroidal filling
3. Superficial temporal artery biopsy if elevated acute phase reactants and/or symptoms/ signs suggestive of giant cell arteritis (GCA)
 - a. Obtain temporal artery biopsy as early as feasible
 - i. Large specimen (>2 cm best) due to skip lesions

II. Define the risk factors

- A. History of PMR
- B. Age

III. List the differential diagnosis

- A. Non-arteritic anterior ischemic optic neuropathy (AION)
- B. Disc drusen / pseudopapilledema
- C. Central retinal vein occlusion
- D. Infiltrative optic neuropathy
- E. Compressive optic neuropathy
- F. Other forms of visual loss from GCA

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options
 1. High dose corticosteroids, with slow taper over months to years
 2. Follow with serial clinical exams
 3. Monitor systemic symptoms of GCA

4. Imaging of the great vessels to exclude aneurysmal dilation/ valve compromise

V. List the complications of treatment, their prevention and management

- A. Medical monitoring of corticosteroid-induced side-effects as per discretion of internist (See Systemic corticosteroids in neuro-ophthalmology)

VI. Describe disease-related complications

- A. Blindness
- B. Systemic effects of arteritis
 1. Coronary arteritis
 2. Renal arteritis
 3. Stroke is rare
 4. Aorta aneurysm
- C. Local effects of arteritis
 1. Ocular ischemic syndrome
 2. Diplopia

VII. Describe appropriate patient instructions

- A. Call immediately for worsening of vision or development/worsening symptoms of GCA or of treatment complications

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
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Med 2001;134:106-14.

9. AAO, Focal Points: Giant Cell Arteritis, Module #6, 2005.

Optic disc drusen

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Dynamic process progressing with age, important because of fundus appearance, differential diagnosis, and occasional occurrence of slow progressive visual loss
2. Progressive "fullness" of optic nerve head, especially in cases of non-surface "buried" optic disc drusen
3. "Hyaline" bodies of imprecisely determined etiology
4. These bodies enlarge, may calcify, and become more prominently localized on the surface of optic nerve head, making them more recognizable with increasing patient age
5. Early disc elevation of younger aged patients gives way to more calcified appearing focal excrescences in older patients
6. Long term compression of optic nerve fiber layer emerging from disc may lead to visual field loss, less common acuity loss, and other rare complications

B. Define the relevant aspects of epidemiology of the disease

1. Inheritance pattern
 - a. Sporadic
 - b. Occasionally autosomal dominant transmission
2. May be associated with other ocular and systemic disease
3. Does not preclude the possibility of concurrent true papilledema/optic nerve edema
4. Commonly bilateral
5. No known male/female preponderance

C. List the pertinent elements of the history

1. A commonly encountered entity in patients with the false appearance of papilledema (pseudopapilledema)
2. Typically lack signs and symptoms of raised intracranial pressure
3. May present with transient visual obscuration
4. Patients have typically undergone extensive workup as true papilledema or other causes of disc edema because of fundusoscopic features noted on a routine examination
5. Patients may not be aware of constricted visual field or abnormal acuity
6. Typically slowly progressive visual change, but may develop accelerated or rarely acute visual loss
 - a. AION
 - b. Peripapillary subretinal neovascularization with bleeding

D. Describe pertinent clinical features

1. Simulates the "full" optic nerve appearance of papilledema
2. Typically, optic nerve changes and loss of nerve fiber layer reflex are confined to disc rather than extending to peripapillary retina as a differentiating feature (i.e. no obscuration of retinal vessels at the disc margin, but may be present in some cases)
3. Anomalous retinal vascular branching pattern
4. Spontaneous venous pulsations may be present or absent. If present, the finding supports that the intracranial pressure is normal and the disc appearance represents pseudopapilledema rather than papilledema from raised intracranial pressure
5. Fullness of optic nerve with nerve fiber layer opacity may be replaced by coalescing refractile excrescences
6. Some or all of the features of true papilledema are occasionally present making absolute differentiation from true papilledema very difficult without serial observation
7. May have deep circumpapillary retinal hemorrhages (as opposed to radial nerve fiber layer hemorrhages of other optic neuropathies)

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Funduscopy features often diagnostic
2. Photographic documentation of appearance helps establish stability, a differentiating feature from other entities causing papilledema
3. Serial visual field testing appropriate for long term disease monitoring
4. Some cases very difficult to differentiate from other causes of pseudopapilledema, and diagnostic techniques (ultrasonography, fluorescein angiography, and other techniques) may not always aid in differentiation from other entities
5. The following may contribute to identifying the presence of disc drusen
 - a. Ultrasound features especially if calcified
 - b. Red free fundus photography (to follow nerve fiber layer defects)
 - c. Review of previously performed CT scans with axial images through the optic nerve head may identify calcified drusen with further investigation not required (presuming superimposed pathology not identified)
 - d. Autofluorescent photography (To visualize drusen)
 - e. Fluorescein angiography
 - f. Role of OCT unclear
6. Occasionally diagnosis may be established by examining other family members
7. Ancillary testing to differentiate from other disease that may cause raised intracranial pressure, optic neuropathy, and or infiltrative optic nerve disease, including a neurologic examination

II. Define the risk factors

- A. Family history
- B. Rare associations with other disease entities
- C. Concurrent ocular disease may lead to accelerated visual loss

III. List the differential diagnosis

- A. True papilledema with raised intracranial pressure
- B. Other causes of pseudopapilledema
- C. Other causes of optic disc swelling
- D. Infiltrative optic neuropathy
- E. Astrocytic hamartoma of tuberous sclerosis
- F. Concurrent neurologic disease -optic disc drusen AND true causes of papilledema may co-exist

IV. Describe patient management in terms of treatment and follow-up

- A. Describe the natural history, outcome and prognosis
 - 1. Slow progressive visual field constriction, or progressive nerve fiber layer defects with associated visual field defects
 - 2. Occasional occurrence of visual acuity loss
 - 3. May contribute to accelerated progression of other diseases associated with nerve fiber layer loss
- B. Describe medical therapy options
 - 1. None known to be effective for primary disease
 - 2. Control other risk factors of concurrent disease with disease specific therapy
- C. Describe surgical therapy options
 - 1. None known to be effective
 - 2. Control other risk factors or concurrent disease with disease specific therapy

V. List the complications of treatment, their prevention and management

- A. Not applicable

VI. Describe disease-related complications

- A. Visual field constriction and loss, often in nerve fiber bundle defects
- B. Prepapillary and peripapillary hemorrhages
- C. Rare cases of peripapillary neovascular disease
- D. Rare cases of secondary ischemic optic neuropathy in which disc drusen serve as a risk factor for NAION in otherwise healthy adults

VII. Describe appropriate patient instructions

A. Routine ophthalmologic examinations may include

1. Dilated funduscopy examination
2. Visual field testing
3. Ancillary testing to differentiate from other entities (See above)
4. The patient as their own advocate--Importance of patient to understand implication of papilledema versus pseudopapilledema, given this disease entity frequently presents confusion with other more serious neurologic diseases

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014

Optic atrophy

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Axonal degeneration
2. Retrograde degeneration is limited to the lateral geniculate typically without transsynaptic degeneration

B. Define the relevant aspects of epidemiology of the disease

1. Variable based upon specific etiology

C. List the pertinent elements of the history

1. Cadence of visual loss
 - a. Gradually progressive - toxic, compressive, infiltrative
 - b. Acute - ischemic, apoplexy
 - c. Subacute - inflammatory (both infectious and non-infectious), Leber hereditary optic neuropathy
2. Associated pain
3. Associated disorders
 - a. Vasculopathic diseases, multiple sclerosis, rheumatologic disease, malignancy, etc.
4. Family history of visual loss
5. Drug history (e.g., ethambutol)
6. Social history (e.g. diet, smoking, alcohol)

D. Describe pertinent clinical features

1. Pale optic nerve generally associated with nerve fiber layer loss
2. Optic nerve pallor out of proportion to cupping in most cases of non-glaucomatous optic atrophy
3. May have decreased visual acuity, which doesn't necessarily correspond to degree of pallor
4. Dyschromatopsia
5. Visual field defect
6. Relative afferent pupillary defect in unilateral or asymmetric cases
7. Alteration in retinal vessels (possible arteriolar attenuation)

E. Describe appropriate testing and evaluation for establishing the etiology

1. Imaging
 - a. Magnetic resonance imaging (MRI)

2. Serologic
 - a. Tailor based upon age, history, clinical features, associated diseases
3. Lumbar puncture
4. Electrophysiologic (e.g. visual evoked response, electroretinography)
5. Optic nerve pallor alone does not establish the etiology except
 - a. Pallid optic nerve swelling in arteritic optic neuropathy, that may resolve to mimic cupping that mimics glaucoma
 - b. Pale optic nerve with shunt vessels
 - c. Band or bow-tie optic atrophy in optic tract lesions

II. List the differential diagnosis

- A. Post-ischemic**
- B. Compressive**
- C. Post-inflammatory/demyelinating**
- D. Burned-out papilledema**
- E. Infiltrative**
- F. Toxic/metabolic**
- G. Post-traumatic**
- H. Hereditary (Leber and non-Leber)**
- I. Iatrogenic - radiation and post surgical**
- J. Infectious optic neuropathy i.e. syphilis**

III. Describe patient management

A. Describe medical therapy options

1. Treat underlying medical disorders if ischemic, inflammatory or metabolic
2. Discontinue exposure/consumption of offending agents if toxic/metabolic
3. Radiation as indicated (e.g., meningioma)
4. Corticosteroids/immunomodulating agents for inflammatory disorders
5. Follow-up clinical exams and visual fields
6. Change diet, offer nutritional supplementation, address malabsorption syndrome, etc. if nutritional in origin
7. Systemic evaluation for malignancy if metastatic or paraneoplastic disease is considered

B. Describe surgical therapy options

1. Orbital (orbital mass, thyroid eye disease)

2. Neurosurgical intervention for compressive or intracranial lesions

IV. List the complications of treatment, their prevention and management

A. Corticosteroids (See Systemic corticosteroids in neuro-ophthalmology)

B. Radiation

1. Optic neuropathy/retinopathy
2. Prevention
 - a. Limit dosimetry

C. Surgical

1. Direct injury to optic apparatus
2. Cerebral and/or optic nerve infarction
3. Cerebral hemorrhage
4. Hypopituitarism

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Electrophysiologic Testing, 2nd ed., 2001, p.101, 219-223, 252.
3. AAO, Ophthalmology Monographs 10. Optic Nerve Disorders, 1996.
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5. AAO, Ophthalmology Monographs 18. A Compendium of Inherited Disorders and the Eye, 2006.
6. AAO, Focal Points: Optic Atrophy, Module #2, 2006.

Multiple sclerosis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Immune-mediated demyelination of the central nervous system (CNS)
2. Underlying etiology unknown

B. Define the relevant aspects of epidemiology of the disease

1. Female predominance
2. Age 3rd to 5th decade
3. Increased prevalence in northern latitudes
 - a. Both genetic and environmental influence

C. List the pertinent elements of the history

1. Acute onset of neurologic or neuro-ophthalmologic disturbance
 - a. Multiple episodes separated in time and anatomic location

D. Describe pertinent clinical features

1. Neurologic dysfunction related to involved nerves/tracts with a myriad of presentations variably producing visual, motor, sensory, and autonomic disturbances
2. Worsening symptoms with heat/raised body temperature is called Uhthoff syndrome

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Magnetic resonance imaging (MRI) of brain and spinal cord
2. Administration of MRI contrast may improve sensitivity and provide info about the lesion
3. Cerebrospinal fluid (CSF) (oligoclonal bands, CSF immunoglobulin G index, myelin basic protein)
4. Electrophysiologic testing (visual evoked response, brainstem auditory evoked response, somatosensory evoked potential) in selected cases

II. Define the risk factors

- A. Female higher risk than male
- B. Family history increases the risk

III. List the differential diagnosis

- A. Stroke
- B. Vasculitis, especially lupus

C. Neuro-infectious diseases

1. Lyme disease
2. Syphilis

D. Sarcoidosis

E. Neuromyelitis optica

F. MS or MS like episodes may be precipitated by anti-tumor necrosis drugs (anti-TNF)

IV. Describe patient management in terms of treatment and follow-up

A. Acute neurologic disturbance

1. IV corticosteroids +/- oral corticosteroid taper

B. Chronic therapy with immunomodulating agents to decrease exacerbations, plaque number, volume, and enhancement, and disability

C. Follow-up clinical exams and MRI as per discretion of neurologist

V. List the complications of treatment, their prevention, and management

A. Corticosteroids (See Systemic corticosteroids in neuro-ophthalmology)

1. Uncommon acute side-effects as generally administered for only 2 weeks

B. Immunomodulating agents

1. Some side effects include flu-like symptoms, fever, chills, and myalgias

VI. Describe disease-related complications

A. Neurologic morbidity

B. Visual loss

C. Motility disturbance

D. Diplopia

E. Oscillopsia

F. Autonomic dysfunction

G. Late cognitive changes

H. Severe fatigue

VII. Describe appropriate patient instructions

A. Call physician for development of new neurological or visual deficits

B. Call physician for side effects of corticosteroids or immunomodulating agents

Additional Resources

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2. AAO, Electrophysiologic Testing, 2nd ed., 2001, p.100, 247-249.
3. AAO, Optic Nerve Disorders, 1996, p.60-61, 66.
4. AAO, Focal Points: Multiple Sclerosis and Optic Neuritis, Module #12, 2003.
5. Haegert DG, Marrosu MG. Genetic susceptibility to multiple sclerosis. *Ann Neurol* 1994;36:S204-S210.
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7. Poser CM. The epidemiology of multiple sclerosis: a general overview. *Ann Neurol* 1994;36:S180-S193.
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18. Arnold AC. Evolving management of optic neuritis and multiple sclerosis. *Am J Ophthalmol* 2005;139:1101-8.
19. Frohman EM, Frohman TC, Zee DS, et al. The neuro-ophthalmology of multiple sclerosis. *Lancet Neurol* 2005;4:111-21.

Demyelinating optic neuritis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Demyelination of the optic nerve

B. Define the relevant aspects of epidemiology of the disease

1. Typically patients are predominantly female in their 3rd to 5th decade

C. List the pertinent elements of the history

1. Acute, usually unilateral, visual loss
2. Preceding or concurrent pain around the eye and/or on eye movement lasting a few days
3. May have history of demyelinating symptoms or known diagnosis of multiple sclerosis (MS)

D. Describe pertinent clinical features

1. Decreased visual acuity
2. Decreased color vision
3. Visual field defect
4. Afferent pupillary defect (if unilateral or asymmetric bilateral)
5. Majority of cases do not have disc edema
6. Absence of vitreous cells
7. Deficits in the asymptomatic fellow eye
8. Lack of prominent disc hemorrhages is expected

E. Describe appropriate diagnostic/laboratory testing

1. Imaging

II. Define the risk factors

A. Female predominance

B. History of MS

III. List the differential diagnosis

A. Anterior ischemic optic neuropathy

B. Maculopathy in the presence of a normal appearing fundus

C. Infiltrative optic neuropathy

D. Compressive optic neuropathy

E. Leber hereditary optic neuropathy

F. Infectious optic neuropathy i.e. syphilis

G. Neuromyelitis optica

1. Acute or subacute optic neuropathy in one or both eyes, which may be preceded or followed by within days, weeks or years a transverse or ascending myelopathy
2. Primarily children and young adults, M=F
3. Clinical features
 - a. May have a mild febrile illness days-weeks before symptom onset
 - b. Rapid & severe vision loss, often bilateral
 - c. Pain in a minority of cases
 - d. Variable visual field loss
 - e. Mild disc swelling in most patients
 - f. Visual recovery
 - g. Usually acute, severe spinal cord involvement, involving multiple spinal segments
 - h. Findings may overlap demyelinating optic neuritis
 - i. Recurrent disease or relapse may help clinically differentiate from idiopathic demyelinating optic neuritis
4. Diagnosis
 - a. CSF usually shows an inflammatory process
 - b. NMO antibodies
5. Treatment
 - a. Corticosteroids
 - b. IVIG
 - c. Other chemical forms of immunosuppression

IV. Describe patient management in terms of treatment and follow-up

A. Magnetic resonance imaging (MRI) scan

1. Identify white matter abnormalities consistent with demyelinating neuritis
2. No treatment versus IV corticosteroids and immunomodulating agents based upon MRI findings supporting a diagnosis of demyelinating disease
 - a. IV corticosteroids may enhance rate of recovery but not visual outcome
 - b. IV corticosteroids may prevent conversion to MS in the short term

B. Referral to a multiple sclerosis specialist for the management of neurological disorders if abnormal MRI scan or consistent neurological examination and history

- C. Oral prednisone in standard doses contraindicated as primary therapy**
- D. Abnormal MRI with brain lesions should prompt consideration immunomodulatory therapy**
- E. Optic Neuritis Treatment Trial**
 - 1. Patients were randomized to oral (PO) prednisone, intravenous (IV) followed by oral corticosteroids (CS) and oral placebo
 - 2. There was no long-term difference in visual function between the 3 groups
 - 3. The IV/PO group had a more rapid visual recovery versus placebo
 - 4. The PO group had an increased risk of recurrent optic neuritis

V. List the complications of treatment, their prevention and management

- A. Complications of corticosteroids (See Systemic corticosteroids in neuro-ophthalmology)**

VI. Describe disease-related complications

- A. Failure to recover vision (10%)**
- B. Progression to MS**

VII. Describe appropriate patient instructions

- A. Medication instructions**
- B. Discussion of relation to MS, risk factors, and possible immunomodulation**
- C. Referral to neurologist**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
- 2. AAO, Optic Nerve Disorders, 1996, p.33-35, 55-73, 85.
- 3. AAO, Focal Points: Multiple Sclerosis and Optic Neuritis, Module #12, 2003, p.6-7.
- 4. Beck RW. The Optic Neuritis Treatment Trial. Three-year follow-up results. Optic Neuritis Study Group. *Arch Ophthalmol.* 1995;113:136-137.
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Hereditary optic neuropathy

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease.

1. Autosomal Dominant Optic Atrophy (ADOA)
 - a. Autosomal dominant transmission with variable penetrance and expressivity
 - b. Sporadic cases are frequent
2. Leber hereditary optic neuropathy (LHON)
 - a. Mitochondrial transmission - most patients will have a mutation in the mitochondrial DNA (positions 11778, 14484, 3460)

B. Define the relevant aspects of epidemiology of the disease

1. ADOA
 - a. Males and females equally affected
2. LHON
 - a. Male predominance (90%)

C. List the pertinent elements of the history

1. ADOA
 - a. Slowly progressive, painless, bilateral (possibly asymmetric) visual loss beginning in first decade and stabilizing by fourth or fifth decade
2. LHON
 - a. Onset of visual loss is typically between 10-30 years of age
 - b. Painless, acute to subacute loss of central vision, stabilizing after several months
 - c. Second eye involvement is typically weeks to months after first eye
 - d. Possible history of unexplained vision loss on maternal side of family

D. Describe pertinent clinical features

1. ADOA
 - a. Visual acuity loss can be variable, mild at onset but progresses to ~ 20/400
 - b. Visual fields show central or centrocecal scotoma; reduced foveal thresholds
 - c. Diffuse color vision loss
 - d. Optic atrophy, characteristically temporal wedge-shaped pallor with loss of papillomacular bundle
2. LHON
 - a. Visual acuity loss can be variable - 20/20 to no light perception

- b. Visual fields show central or centrocecal scotoma
- c. Relative afferent pupillary defect if asymmetric disease or early unilateral disease
- d. Diffuse color vision loss
- e. Early fundusoscopic changes include optic disc hyperemia, pseudoedema, and peripapillary telangiectatic vessels but not unusual to be normal initially
- f. Late fundusoscopic changes include diffuse optic disc pallor, nonglaucomatous cupping, diffuse nerve-fiber layer loss

E. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. ADOA
 - a. Complete neuro-ophthalmologic examination (including visual field and color vision testing)
 - b. Inquiry regarding family history (examine family members if indicated)
 - c. Neuroimaging may be necessary if atypical presentation
 - d. Genetic tests not widely available
- 2. LHON
 - a. Complete neuro-ophthalmologic examination
 - b. Inquiry regarding family history
 - c. Neuroimaging may be necessary if atypical presentation
 - d. Genetic testing for mitochondrial point mutation

II. Define the risk factors

A. ADOA

- 1. Positive family history

B. LH

- 1. Positive family history
- 2. Presence of genetic mutation

III. List the differential diagnosis

A. ADOA and LHON

- 1. Compressive optic neuropathy
- 2. Inflammatory optic neuropathy (i.e.; demyelinating disease)
- 3. Ischemic optic neuropathy
- 4. Toxic/metabolic optic neuropathy
- 5. Optic nerve hypoplasia

6. Functional visual loss

IV. Describe patient management in terms of treatment and follow-up

A. Describe the natural history, outcome and prognosis

1. ADOA
 - a. Natural history is generally stable or slowly progressive over a number of years
 - b. Loss of one or two lines of visual acuity per decade
2. LHON
 - a. Most experience visual loss of <20/200
 - b. Majority of patients will have second eye involvement within one year
 - c. Spontaneous improvement is uncommon

B. Describe medical therapy options

1. ADOA and LHON
 - a. No proven medical therapy

C. Describe surgical therapy options

1. ADOA and LHON
 - a. No proven surgical therapy

V. List the complications of treatment, their prevention and management

- ##### **A. None**

VI. Describe disease-related complications

A. ADOA

1. Bilateral visual loss

B. LHON

1. Bilateral visual loss
2. Associated neurological disorders (movement disorders, dystonia, brainstem syndromes, encephalopathic episodes and multiple sclerosis-like disease)
3. Cardiac conduction defects

VII. Describe appropriate patient instructions

A. ADOA and LHON

1. Genetic counseling
2. Low vision rehabilitation consultation/training

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-Ophthalmology, 2013-2014.
2. Cohn AC, Toomes C, Potter C, et al. Autosomal dominant optic atrophy: penetrance and expressivity in patients with OPA1 mutations. *Am J Ophthalmol* 2007;143:656-662.
3. Newman NJ. Mitochondrial disease and the eye. *Ophthalmol Clin North Am* 1992;5(3):405-424.
4. Newman NJ. Hereditary optic neuropathies: from the mitochondria to the optic nerve. *Am J Ophthalmol* 2005;140:517-523.
5. Newman NJ, Lott MT, Wallace DC. The clinical characteristics of pedigrees of Leber's hereditary optic neuropathy with the 11778 mutation. *Am J Ophthalmol* 1991;111:750-762.

Chiasmal syndromes

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Tumor
 - a. Pituitary macro adenoma
 - i. Tumor classification
 - i) Secretory
 - (i) Prolactinoma
 - (ii) Growth hormone
 - (a) Acromegaly
 - (b) Gigantism
 - (iii) Adrenal cortical tropic hormone (Cushing syndrome)
 - (iv) Other, rare
 - ii) Non-secretory
 - ii. Special clinical syndromes
 - i) Pituitary apoplexy
 - (i) Hemorrhage into pituitary gland
 - (ii) Occasional pre-existing pituitary tumor
 - (iii) May be associated with pregnancy
 - (iv) Acute visual loss, double vision, cranial neuropathy, and endocrine insufficiency
 - (v) Vision and occasionally life threatening emergency
 - b. Meningioma
 - c. Craniopharyngioma
 - d. Glioma
 - e. Rathke cleft cyst
 - f. Germ cell tumors
 - g. Bone and cartilage skull based tumors
 - h. Metastatic disease
 - i. Intrinsic chiasmal vascular lesions
2. Inflammatory

- a. Chiasmal neuritis
 - b. Sarcoidosis
 - c. Lymphocytic hypophysitis
 - d. Systemic lupus erythematosus/vasculitis
- 3. Infectious - particularly in immunocompromised individuals
- 4. Vascular
 - a. Aneurysm
 - b. Radiation chiasmopathy
- 5. Trauma—often with associated skull base fractures
- 6. Mechanical
 - a. Enlarged IIIrd ventricle
 - b. Iatrogenic—Surgical packing of sphenoid sinus
 - c. Chiasmal herniation

B. List the pertinent elements of the history

- 1. Symptoms referable to visual dysfunction
- 2. Symptoms referable to endocrine disturbance
 - a. Hyperfunction
 - i. Amenorrhea
 - ii. Galactorrhea
 - iii. Change in hat, shoe and glove size in patients with acromegaly
 - iv. Coarsening of facial features
 - b. Hypofunction
 - i. Loss of libido
 - ii. Polydipsia/polyuria
- 3. Headache and photophobia
- 4. Diplopia
- 5. Altered level of consciousness

C. Describe pertinent clinical features

- 1. Visual field loss with or without loss of visual acuity
 - a. Bitemporal hemianopsia - may be isolated to superior or inferior temporal quadrants
 - b. Junctional syndrome
 - i. Central scotoma

- ii. Contralateral superior temporal defect
- c. Bitemporal scotoma
- d. Homonymous hemianopsia when optic tract involved
- 2. Associated symptoms
 - a. Diplopia due to hemifield slip with dense bitemporal VF defect
 - b. Diplopia related to associated single or multiple cranial neuropathy
 - c. Signs of concurrent endocrine disturbance
- D. Describe appropriate testing and evaluation for establishing the diagnosis**
 - 1. Screening for Endocrine dysfunction
 - 2. Neuro-Imaging of chiasm and pituitary
 - a. Magnetic resonance imaging (MRI)
 - b. Computed tomography (CT)
 - c. Angiography in selected cases

II. Define the risk factors

- A. Pregnancy**
 - 1. Lymphocytic adenohypophysitis
 - 2. Growth of pituitary tumor
 - 3. Growth of tuberculum meningioma
- B. History of multiple sclerosis and other systemic inflammatory diseases**
- C. Change or withdrawal of hormonal medication**

III. List the differential diagnosis

- A. Pseudo-bitemporal visual field defect**
 - 1. Anomalous optic disc
 - a. Tilted disc
 - b. High myopia
 - c. Peripapillary coloboma
 - 2. Optic neuropathy with cecocentral field defects
- B. Bilateral optic nerve disease causing cecocentral field defects may simulate bitemporal visual field loss**
 - 1. Hereditary optic atrophy
 - 2. Toxic optic neuropathy

3. Nutritional optic neuropathy

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options— depend on underlying cause, etiology but could include:**
 1. Hormonal
 2. Immunosuppressive therapy
- B. Describe surgical therapy options**
 1. Transsphenoidal surgery
 2. Transcranial surgery
- C. Radiation therapy**
 1. Fractionated

V. List the complications of treatment, their prevention and management

- A. Optic neuropathy, including iatrogenic damage to optic apparatus**
- B. Radiation retinopathy or optic neuropathy**
 1. Limit fractionated and total dose to optic apparatus with conformal planning
- C. Worsening chiasmal syndrome postoperatively or with progressive chiasmal herniation**
- D. Cerebrospinal fluid leak spontaneously or after transsphenoidal surgery**
- E. Chiasmal prolapse after surgery or medical therapy**
 1. May respond to surgical repair
- F. Hypothalamic-pituitary axis failure**

VI. Describe disease-related complications

- A. Progressive visual loss**
- B. Optic atrophy**
- C. Endocrine disturbance**
- D. Hydrocephalus**
- E. Hypothalamic-pituitary disorders**

VII. Describe appropriate patient instructions

- A. Report worsening of vision**
- B. Report new visual field defects**
- C. Periodic afferent system assessment**

D. Pituitary endocrine status

E. Routine imaging follow-up

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Optic Nerve Disorders, 1996, p.64-65.

Disorders of the retrogeniculate pathway

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. In the retrogeniculate structures, crossed nasal fibers from contralateral eye (temporal visual field) and uncrossed temporal fibers (nasal field) are grouped together
2. Lesions of these pathways nearly always produce homonymous field cuts that respect a vertical midline. Exceptions are discussed below.
3. Anatomy of optic radiations of geniculocalcarine tract
 - a. Parietal Superior fibers: Some fibers from lateral geniculate body course more directly posterior through the parietal lobe to ipsilateral calcarine fissure. These fibers represent contralateral inferior visual field
 - b. Temporal Inferior fibers: Some fibers from lateral geniculate course anteriorly in Meyer loop around the temporal horn of the lateral ventricle before turning posteriorly to reach the ipsilateral calcarine fissure. These fibers correspond to contralateral superior visual field
4. Anatomy of occipital lobe
 - a. Calcarine cortex- Located on the poles and medial surface of the occipital lobes containing typically homonymous, crossed, processed, representations from fibers with both a horizontal orientation and vertical orientation due to upper/lower/left /right orientation. Left visual field is represented in right calcarine bank. Upper visual field is represented in lower calcarine bank.
 - i. Macular fibers heavily represented
 - ii. Central macular field represented posteriorly
 - iii. Peripheral field represented more anteriorly
 - iv. Anterior monocular temporal crescent with monocular temporal representation of crossed nasal fibers (temporal field)

B. Pathophysiology

1. Vascular
 - a. Territorial infarcts of arterial vessels
 - i. Middle cerebral watersheds with PCA at posterior occipital tip
 - ii. Posterior cerebral
 - b. Thromboembolic
 - c. Proximal arterial dissection
 - d. Hemorrhagic events
 - e. Vasculitic disease

- f. Arteriovenous malformation
- 2. Neoplastic
 - a. Primary
 - b. Metastatic
- 3. Trauma
 - a. Surgically iatrogenic
 - b. Closed head injury (shearing)
 - c. Penetrating trauma
- 4. Inflammatory
 - a. Demyelinating disease
 - b. Infectious
- 5. Other
 - a. Developmental
 - i. Cortical dysplasia
 - ii. Sturge Weber
 - b. Metabolic
 - c. Toxic
 - d. Dementing illnesses
 - i. Alzheimer
 - e. Creutzfeldt-Jakob disease (CJD)

C. Define the relevant aspects of epidemiology of the disease

- 1. Vascular disease
 - a. Increasing age
 - b. Atherosclerosis
- 2. Inflammatory disease
 - a. Young patients
 - b. Autoimmune pathology
- 3. Neoplasia
 - a. Varies with tissue type

D. List the pertinent elements of the history

- 1. Loss of peripheral vision ,descriptions of which may be vague and represent visual field loss or loss of vision to one side that is not recognized by the patient
- 2. Hallucinations

E. Describe pertinent clinical features

1. Retrogeniculate lesions in general:
 - a. Variations of homonymous hemianopsia
 - i. Complete homonymous
 - ii. Homonymous with central sparing (keyhole)
 - iii. Homonymous central scotoma
 - iv. Non-homonymous monocular crescent
 - v. Reciprocal incongruous homonymous sparing temporal crescent
 - b. Preserved central acuity unless extensive bilateral lesions
 - c. Variations in congruity as above
 - d. Absent optic atrophy unless insult very early in development (congenital/intrauterine)
 - e. Occasional color vision loss, especially when bilateral
 - f. Associated neurologic disorders
 - i. Hemiparesis
 - ii. Hemisensory loss
 - iii. Pursuit deficit
 - iv. Seizures
2. Temporal radiations
 - a. Homonymous hemianopia
 - i. Typically superior (pie in the sky)
 - ii. May be homonymous congruous or homonymous partial incongruous
 - b. Temporal (Meyer loop)
 - i. Superior visual field defect ("pie in sky")
 - c. Relative incongruity
 - i. Associated symptoms
 - i) Partial complex seizures (uncinate fits)
 - ii) Auditory symptoms
 - iii) Visual hallucinations
 - ii. Etiology
 - i) Trauma (include surgical)
 - ii) Tumor
 - iii) Infarct

- iv) Arteriovenous malformation
- d. Parietal
 - i. Inferior visual field defect
 - ii. Associated symptoms
 - i) Pursuit deficit
 - (i) Ipsilateral
 - (ii) Optokinetic nystagmus (OKN) asymmetry (Cogan rule)
 - ii) Visual neglect
 - iii) Numbness
 - iv) Visual spatial abnormalities
 - iii. Etiology (vascular>mass)
 - i) Infarct
 - ii) Tumor
 - iii) Inflammatory
- 3. Calcarine cortex
 - a. May spare fixation
 - b. Homonymous with central sparing (keyhole)
 - i. Dual blood supply, with sparing due to MCA predominance over PCA
 - c. Highly congruous
 - d. May also preserve the horizontal meridian, relative to the upper or lower calcarine bank
 - e. Anterior temporal lesions may cause a monocular contralateral temporal crescent of field loss, or homonymous contralateral hemianopia sparing the temporal crescent of contralateral eye

F. Describe appropriate laboratory testing for establishing the diagnosis

- 1. Psychophysical testing
 - a. Quantitative static perimetry
 - b. Other forms of perimetry
- 2. Imaging
 - a. Computed tomography
 - b. Magnetic resonance imaging
 - c. Angiography

II. Define the risk factors

- A. Vasculopathic risk factors**
 - 1. Diabetes mellitus
 - 2. Systemic hypertension
 - 3. Elevated cholesterol
 - 4. Elevated triglycerides
- B. Immunosuppression**
- C. Systemic inflammatory disease**
- D. Infectious diseases**

III. List the differential diagnosis

- A. Bilateral optic neuropathy**
- B. Bilateral retinal disease**
- C. Optic tract or geniculate disease**

IV. Describe patient management in terms of treatment and follow-up

- A. Treat underlying condition**
- B. Vision rehabilitation, low vision aids, evaluation of associated cognitive impairment**
- C. Evaluate driving abilities**

V. List the complications of treatment, their prevention and management

- A. Worsen visual field defect**
- B. Other neurologic symptoms**

VI. Describe disease-related complications

- A. Progressive visual field defect**
- B. Development of other neurological symptoms**

VII. Describe appropriate patient instructions

- A. Follow visual fields**
- B. Periodic imaging studies**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.

2. AAO, Focal Points: Automated Perimetry in Neuro-Ophthalmology, Module #6, 1995, p.2.

Disorders of the lateral geniculate and optic tract

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Anatomic structure relates to clinical findings
 - a. Lateral geniculate and optic tracts relay crossed and uncrossed visual sensory and pupillary afferent impulses which project from retinal ganglion cell to a variety of pretectal and tectal nuclei
 - b. The geniculate has a complex laminar structure, and both the tract and geniculate preserve a retinotopic anatomy, the organization of which becomes increasingly more congruous as fibers course from retina to the layered geniculate, and more posteriorly to striate cortex. This arrangement leads to a variety of homonymous field cuts in diseases of these structures that may have varying congruity
2. Vascular supply
 - a. Lateral geniculate receives dual supply from anterior and posterior circulations of the brain, the anterior and lateral choroidal arteries respectively.
 - b. Optic tract blood supply is primarily from branches of the internal carotid artery
 - c. Anterior choroidal artery (wedge shaped homonymous defects)
 - d. Posterior choroidal artery (lateral to produce homonymous sectorial defects/homonymous wedge.) The latter have been described as keyhole field defects which straddle the horizontal meridian yet preserve the vertical meridian.
3. Pathophysiology
 - a. Vascular
 - b. Compressive tumor (primary intrinsic, secondary compressive)
 - c. Demyelination
 - d. Trauma
 - e. Other rare causes

B. Define the relevant aspects of epidemiology of the disease

1. Vascular disease is the most common cause of geniculate disorders, albeit rare
 - a. Increasing age
 - b. Atherosclerosis
2. Inflammatory disease
 - a. Young patients

- b. Autoimmune pathology
- 3. Neoplasia is the most common cause of lesions affecting the optic tract. Defects may not be pure and can occur in posteriorly located pituitary lesions
 - a. Varies with tissue type and age of patient

C. List the pertinent elements of the history

- 1. Blurry vision
- 2. Loss of peripheral vision
- 3. Abnormal color perception
- 4. Neurologic complaints referable to primary lesion and other structures involved

D. Describe pertinent clinical features

- 1. Optic tract clinical features
 - a. Homonymous hemianopsia, often incongruous, may be complete or wedge shaped defects, contralateral to the involved optic tract
 - b. Preserved central acuity
 - c. Variations in congruity
 - d. A particular pattern of bilateral optic atrophy ("bowtie atrophy"): A band of atrophy at the horizontal nasal and temporal pole to the optic nerve contralateral to the lesion and (variable) atrophy at the superior and inferior poles of the nerve ipsilateral to the lesion
 - e. Contralateral (or ipsilateral) afferent pupillary defect, dependent on completeness of lesion
 - f. Variable associated neurologic disorders
- 2. Lateral geniculate clinical features
 - a. Classically will display bilateral sectoral optic atrophy
 - b. Wedge shaped or keyhole shaped homonymous variably incongruous hemianopia
 - c. Because the lateral geniculate and optic tract share blood supply, the syndromes may have significant overlap

E. Appropriate testing for establishing the diagnoses

- 1. Neuroradiologic imaging when appropriate
- 2. Ancillary testing directed towards underlying disease process

II. List the differential diagnosis

- A. Bilateral optic neuropathy**
- B. Retrogeniculate cortical disease**

III. Describe patient management in terms of treatment and follow-up

- A. Treat underlying condition:
- B. Vision rehabilitation, low vision aids, evaluation of associated cognitive impairment
- C. Evaluate driving abilities

IV. List the complications of treatment, their prevention and management

- A. Worsening visual field defect
- B. Other neurologic symptoms

V. Describe disease-related complications

- A. Progressive visual field defect
- B. Development of other neurological symptoms

VI. Describe appropriate patient instructions

- A. Follow visual fields
- B. Periodic imaging studies

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Automated Perimetry in Neuro-Ophthalmology, Module #6, 1995, p.2.

Internuclear ophthalmoplegia

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Pathology affecting the medial longitudinal fasciculus

B. List the pertinent elements of the history

1. Double vision that resolves with occlusion of either eye
2. May be maximal at onset or gradually progressive, depending on etiology
3. Symptoms may be constant or intermittent
4. Double vision principally horizontal, but may have a vertical component secondary to accompanying skew deviation
5. Double vision may be worse or only occur in contralateral gaze or when making saccades to the contralateral side
6. Pertinent medical history
 - a. Diabetes mellitus
 - b. Systemic hypertension
 - c. Trauma
 - d. Cerebrovascular disease
 - e. Multiple sclerosis
 - f. Myasthenia gravis
7. Other neurological symptoms/history

C. Define the relevant aspects of epidemiology of this disease

1. Most commonly in adults (often demyelinating in younger adults and ischemic in older adults), but also seen in children

D. Describe pertinent clinical features

1. Impaired adduction or slowed saccades of affected eye on attempted adduction
2. Misalignment of eyes most pronounced on attempted gaze to the contralateral side
3. Abducting nystagmus may be observed in the contralateral eye
4. May be associated with skew deviation
5. May be associated with ipsilateral gaze palsy (one-and-a-half syndrome)
6. May be bilateral with large-angle exotropia (wall-eyed bilateral internuclear ophthalmoplegia (WEBINO syndrome))
7. Negative forced ductions

8. Convergence may be preserved

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Magnetic resonance imaging (MRI) with attention to the midbrain and pons assessing for pathology affecting the medial longitudinal fasciculus

II. Define the risk factors

A. Cerebrovascular disease

B. Multiple sclerosis

C. Vasculopathic risk factors

1. Diabetes mellitus
2. Systemic hypertension
3. Elevated cholesterol
4. Elevated triglycerides

III. List the differential diagnosis

A. Myasthenia gravis (i.e. pseudo-INO)

B. Incomplete oculomotor nerve palsy

C. Restrictive process

1. Infiltrative myopathies
2. Myositis
3. Orbital fracture with EOM entrapment
4. Orbital mass

D. Miller Fisher variant of Guillain-Barré

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Myasthenia Gravis, Module #4, 2003, p. 3.
3. AAO, Focal Points: Multiple Sclerosis and Optic Neuritis, Module #12, 2003, p.8.
4. Keane JR. Internuclear ophthalmoplegia: unusual causes in 114 of 410 patients. *Arch Neurol* 2005;62:714-7.

Restrictive strabismus and diplopia

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Tethered tissue of check muscles, tendons, intermuscular septum, and/or conjunctiva
2. Altered muscle histology from scarring
3. Acute or long standing orbital disease
4. Long standing non-restrictive strabismus may become restrictive strabismus
5. Space occupying orbital lesion
6. Trapdoor fractures
7. Iatrogenic causes
8. Intramuscular infiltration (e.g., inflammatory or neoplastic)

B. Define the relevant aspects of epidemiology of this disease

1. Varies by cause

C. List the pertinent elements of the history

1. Double vision that resolves with occlusion of either eye
2. May be maximal at onset or gradually progressive, depending on etiology
3. May be congenital
4. Symptoms may be constant or intermittent
5. Double vision may be horizontal, vertical, or oblique
6. Pertinent medical history
 - a. Thyroid disease
 - b. Orbital trauma
 - c. Past orbital inflammation
 - d. Previous ocular or orbital surgery
 - e. Retrobulbar injection
 - f. Family history of eye movement disorders
 - g. History of malignancy

D. Describe pertinent clinical features

1. Limitation of ductions
2. Incomitant deviations
3. Positive forced ductions

4. May have gaze evoked discomfort
5. Primary versus secondary deviations
 - a. Alternate prism cover testing may produce the smallest prism deviation when the prism is placed before the more restricted eye

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Sensorimotor examination
 - a. Duction and version testing
 - b. Measure ocular alignment in multiple fields of gaze
2. Gaze tonometry
 - a. Eye movement opposite the direction of action of restricted muscle may evoke elevation of IOP
3. Forced duction testing
4. Forced generation testing to differentiate from paralytic strabismus
5. Orbital imaging is employed in many cases
 - a. Computed tomography
 - b. Magnetic resonance imaging
 - c. Orbital ultrasound

II. Define the risk factors

- A. Thyroid disease
- B. Orbital trauma
- C. Orbital inflammation
- D. Orbital surgery
- E. Retrobulbar injection

III. List the differential diagnosis

- A. Paretic condition (nuclear, infranuclear, or supranuclear)
- B. Chronic progressive external ophthalmoplegia (CPEO)
 1. Kearns-Sayre syndrome
 2. Oculopharyngeal muscular dystrophy (OPMD)
- C. High myopia

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Occlusion
2. Prism therapy
3. Pharmacologic therapy
 - a. Steroids if acute inflammation (e.g. myositis)
 - b. Chemotherapy for malignancy
 - c. Radiation therapy (e.g. lymphoma)
4. Treatment of underlying medical condition (e.g. hyperthyroidism)

B. Describe surgical therapy options

1. Strabismus surgery
2. Correction of underlying disorder

V. List the complications of treatment, their prevention and management

A. Medical therapy complications

1. Complications from steroids, radiation or chemotherapy

B. Surgical therapy complications

1. Eyelid deformity
2. Ocular misalignment
3. Extraocular muscle (EOM) damage/restrictive strabismus/neuropathic damage
4. Postoperative or delayed visual loss/central retinal artery occlusion
5. Hypoesthesia
6. Abnormal pupil/accommodation loss
7. Orbital/ocular ischemia, compartment syndrome
8. Orbital cellulitis

VI. Describe disease-related complications

A. Diplopia

B. Loss of binocularity

C. Disease specific complications

VII. Describe appropriate patient instructions

A. Report worsening or change in symptoms

- B. Occlude eye to reduce diplopia**
- C. Report change in globe position (proptosis)**
- D. Report numbness or pain**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Myasthenia Gravis, Module #4, 2003.
3. AAO, Ophthalmology Monographs 17. Strabismus Surgery: Basic and Advanced Strategies, 2004.

Nuclear lesions of the oculomotor nerves

I. Describe the approach to establishing the diagnosis

A. Define the relevant aspects of epidemiology of this disease

1. Most commonly in adults, but also seen in children

B. List the pertinent elements of the history

1. Generally binocular oblique diplopia
2. May have bilateral ptosis
3. May be maximal at onset or gradually progressive, depending on etiology
4. Pertinent medical history
 - a. Vasculopathic risk factors
 - i. Diabetes mellitus
 - ii. Systemic hypertension
 - iii. Elevated cholesterol
 - iv. Elevated triglycerides
 - b. Multiple sclerosis
 - c. Brain tumor
 - d. History of malignancy
 - e. Systemic or central nervous system (CNS) infection or vasculitis
 - f. Other neurological symptoms and history

C. Describe pertinent clinical features

1. Involvement of all subnuclei from nuclear 3rd nerve palsy will result in bilateral ptosis, under action of contralateral superior rectus in addition to paresis of all extraocular muscles innervated by the ipsilateral oculomotor nerve and will also result in a mydriatic, poorly reactive pupil. Additionally there will often be involvement of surrounding midbrain structures if the lesion is extensive.
2. Ipsilateral limitation of infraduction, supraduction, and adduction in the affected eye, contralateral supraduction deficit, and bilateral ptosis if complete, +/- pupillary involvement
3. Incomplete involvement of the various subnuclei may spare any of the innervated ipsilateral extraocular muscles, the contralateral superior rectus, the levator palpebrae, and the pupil

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Magnetic resonance imaging (MRI) with attention to the midbrain or pons

II. Define the risk factors

- A. Multiple sclerosis**
- B. Vasculopathic risk factors**
 - 1. Diabetes mellitus
 - 2. Systemic hypertension
 - 3. Elevated cholesterol
 - 4. Elevated triglycerides

III. List the differential diagnosis

- A. Myasthenia gravis**
- B. Miller Fisher variant of Guillain-Barré**
- C. Peripheral third nerve palsy**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
- 2. AAO, Focal Points: Third, Fourth and Sixth Cranial Nerve Palsies, Module #8, 1996.

Isolated oculomotor nerve lesion

I. Describe the approach to establishing the diagnosis

A. Define the relevant aspects of epidemiology of this disease

1. Most commonly in adults, but also seen in children

B. List the pertinent elements of the history

1. Generally binocular oblique diplopia (may be vertical or horizontal; typically changes with gaze)
2. Ptosis of the ipsilateral upper eyelid
3. May be painful
4. May be maximal at onset or gradually progressive, depending on etiology
5. Pertinent medical history
 - a. Vasculopathic disease risk factors
 - i. Diabetes mellitus
 - ii. Systemic hypertension
 - iii. Elevated cholesterol
 - iv. Elevated triglycerides
 - b. History of aneurysm
 - c. Recent head trauma
 - d. Multiple sclerosis
 - e. Migraine (only relevant in children or in adults with history of ophthalmoplegic migraine when younger)
 - f. Recent viral infection or vaccination (relevant only in children)
 - g. Other neurological symptoms and history

C. Describe pertinent clinical features

1. Ipsilateral mydriasis and decreased pupillary activity
 - a. Common in patients with aneurysmal cranial nerve (CN) III palsy
 - b. Minority of patients with microvascular CN III palsy
2. Paresis of some or all of the EOMs innervated by the oculomotor nerve (medial, superior, and inferior recti and inferior oblique)
3. Ptosis secondary to levator palpebrae involvement
4. Aberrant regeneration (never in microvascular nerve palsy)(See Aberrant regeneration of the third cranial nerve)
 - a. May affect eyelid, pupil and/or extra ocular muscles

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Observation for 3-4 months is appropriate in adults > 50 years only if:
 - a. No pupil involvement
 - b. Complete external ophthalmoplegia of the superior, medial, and inferior rectus and inferior oblique muscles and complete ptosis
 - c. No history of malignancies with metastatic potential
2. Imaging is indicated for patients that do not fit into the above category, or in any patient with pupillary involvement or history of malignancy with metastatic potential, in patients with aberrant regeneration of the third cranial nerve and the absence of a history of trauma or an aneurysm, or in patients in whom the diagnosis is unclear:
 - a. Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) or computed tomography angiography (CTA)
 - b. Aberrant regeneration of the 3rd cranial nerve in absence of a history of trauma or aneurysm demands imaging to rule out compressive lesion
 - c. If MRI and MRA or CTA normal, and still high index of suspicion for aneurysm
 - i. Cerebral angiogram
 - i) Arteriography is almost never indicated in children less than 10 years old
 - d. If MRI and MRA or CTA normal, and other signs and symptoms are suggestive of infection, infiltration, or inflammation:
 - i. Lumbar puncture
 - e. If palsy does not resolve in 3-4 months or worsens beyond the first 2 weeks following onset:
 - i. Repeat imaging
 - ii. Consider lumbar puncture
 - f. In patients with signs and/or symptoms suggestive of vasculitis or giant cell arteritis obtain serological evaluation including:
 - i. Erythrocyte sedimentation rate
 - ii. C-reactive protein
 - iii. Complete blood count and platelets
 - iv. Additional serologic work up as indicated (e.g. ACE, ANA, etc.)

II. Define the risk factors

A. Vasculopathic risk factors

1. Diabetes mellitus
2. Hypertension
3. Elevated cholesterol

- 4. Elevated triglycerides
- B. Systemic disease known to be associated with the formation of aneurysms**
- C. History of malignancy with metastatic potential**
- D. History of head trauma**

III. List the differential diagnosis

- A. Myasthenia gravis**
- B. Miller Fisher variant of Guillain-Barré**

IV. Describe appropriate patient instructions

- A. Call for worsening diplopia or additional neurological signs and/or symptoms**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-Ophthalmology, 2013-2014.
- 2. AAO, Focal Points: Third, Fourth and Sixth Cranial Nerve Palsies, Module #8, 1996.

Aberrant regeneration of the third cranial nerve

I. Describe the approach to establishing the diagnosis

A. List the pertinent elements of the history

1. May or may not have previous history of cranial nerve (CN) III palsy
2. Pertinent medical history
 - a. History of traumatic IIIrd nerve palsy
 - b. History of aneurysm
 - c. History of cavernous sinus tumor
3. Pertinent family history
 - a. Family history of cerebral aneurysm
4. Other neurological symptoms and history

B. Define the relevant aspects of epidemiology of this disease

1. Most commonly in adults, but also seen in children

C. Describe pertinent clinical features

1. Eyelid synkinesis: eyelid elevation/ retraction upon attempted adduction or depression
2. Pupillary synkinesis: pupillary constriction upon attempted elevation, adduction, or depression
3. Never occurs in microvascular nerve palsy
4. Persistent vertical gaze limitation caused by co-contraction of the superior and inferior recti
5. Features of aberrant regeneration of CN III without a history of acute CN III palsy is known as primary aberrant regeneration and suggests a slowly expanding mass, compressing CN III. Common etiologies include
 - a. Carotid cavernous aneurysm, cavernous sinus meningioma

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Magnetic resonance imaging (MRI) with contrast
 - a. Particular attention should be paid to the cavernous sinus to evaluate for mass lesion (e.g. aneurysm, meningioma)
2. If the MRI does not reveal the cause, consider magnetic resonance angiography (MRA), computed tomographic angiography or cerebral angiography, based on the institution's capability and experience

II. Define the risk factors

- A. Previous CN III palsy
- B. Head trauma
- C. Cerebral aneurysm
- D. Previous intracranial surgery
- E. Cavernous sinus mass

III. List the differential diagnosis

- A. Mimickers of aberrant regeneration
 - 1. Duane syndrome

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.

Abducens nuclear lesion

I. Describe the approach to establishing the diagnosis

A. List the pertinent elements of the history

1. Inability to look toward the side of the lesion
2. May also have facial weakness
3. May be maximal at onset or gradually progressive depending on etiology
4. May be congenital, as part of the Möbius syndrome or Duane syndrome
5. Pertinent medical history
 - a. Vasculopathic risk factors
 - i. Diabetes mellitus
 - ii. Systemic hypertension
 - iii. Elevated cholesterol
 - iv. Elevated triglycerides
 - b. Multiple sclerosis
 - c. Cerebrovascular disease
6. Other neurological symptoms and history
 - a. Facial weakness
 - b. Change in facial sensation

B. Define the relevant aspects of epidemiology of this disease

1. Most commonly in adults, but also seen in children
2. May be congenital

C. Describe pertinent clinical features

1. Gaze palsy ipsilateral to the side of the lesion
2. May have ipsilateral facial weakness and/or changes in facial sensation
3. Contralateral adduction is preserved with convergence
4. Patient may have a head turn toward the side of the lesion
5. Vestibulo-ocular reflexes (VOR) (Doll's head maneuver) will not overcome the gaze palsy
6. Large lesions can result in complete loss of horizontal gaze with preservation of voluntary and involuntary vertical gaze if bilateral CN VI nucleus damage or a one-and-a-half syndrome if involvement of adjacent ipsilateral medial longitudinal fasciculus (i.e. ipsilateral horizontal gaze palsy and ipsilateral internuclear ophthalmoplegia)
7. Möbius syndrome: congenital bilateral CN VI palsies, bilateral facial weakness

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Magnetic resonance imaging with attention to the brainstem for acquired lesions

II. Define the risk factors

A. Cerebrovascular disease

B. Vasculopathic risk factors

1. Diabetes mellitus
2. Systemic hypertension
3. Elevated cholesterol
4. Elevated triglycerides

C. Multiple sclerosis

III. List the differential diagnosis

A. Miller Fisher variant of Guillain-Barré

B. Myasthenia gravis

C. Wernicke encephalopathy

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Third, Fourth and Sixth Cranial Nerve Palsies, Module #8, 1996, p.8-10.

Abducens nerve palsy

I. Describe the approach to establishing the diagnosis

A. List the pertinent elements of the history

1. Binocular horizontal diplopia worse in ipsilateral gaze
2. May be maximal at onset or gradually progressive, depending on etiology
3. Pertinent medical history
 - a. Vasculopathic risk factors
 - i. Diabetes mellitus
 - ii. Systemic hypertension
 - iii. Elevated cholesterol
 - iv. Elevated triglycerides
 - b. Multiple sclerosis
 - c. Elevated or low intracranial pressure
 - d. Meningitis
 - e. History of malignancies
 - f. History of head trauma
 - g. Symptoms of GCA
4. Other neurological symptoms and history
 - a. Facial weakness
 - b. Loss of facial sensation
 - c. Impairment of hearing or balance
 - d. Drooping eyelid

B. Define the relevant aspects of epidemiology of this disease

1. Most commonly in adults, but also seen in children

C. Describe pertinent clinical features

1. Limitation of abduction ipsilateral to the side of the lesion
2. Esotropia that is greatest with ipsilateral gaze
3. Patient may have a head turn toward the side of the lesion
4. Vestibulo-ocular reflexes (VOR) (Doll's head maneuver) will not overcome the palsy
5. In an isolated cranial nerve (CN) VI palsy, all other cranial nerves must be normal
6. Concurrent impairment of CN III, IV, and/or V with CN II suggests an orbital apex lesion

7. Concurrent impairment of only CN III, IV, and/or V suggests cavernous sinus lesion
8. Concurrent impairment of cranial nerves V, VII, and VIII suggest a tumor of the cerebellopontine angle (e.g. acoustic neuroma, meningioma) or infiltration of the petrous bone (e.g. nasopharyngeal carcinoma, mastoiditis)
9. Concurrent ipsilateral facial nerve paresis, localizes to genu of facial nerve (intra-axial pontine lesion)
10. Ipsilateral Horner syndrome suggests lesion of cavernous sinus (less often of brainstem)

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. If palsy is truly isolated (i.e. no other cranial neuropathies; no evidence of Horner syndrome; no accompanying neurologic signs/symptoms), observation for 3-4 months is appropriate in adults > 50 years of age who have a new onset unilateral VIth nerve palsy without progression beyond the first 2 weeks following onset and with no history of malignancies with metastatic potential (e.g. breast, lung, prostate, lymphoma) (presumed microvascular)
 - a. Assess for vasculopathic risk factors (blood pressure, HgbA1c, glucose, lipid profile)
2. For patients with systemic symptoms suggestive of giant cell arteritis, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and CBC with platelets may be indicated
3. Magnetic resonance imaging (MRI), +/- lumbar puncture, +/- serologic testing (e.g. ACE, ANA, RPR, FTA, Lyme) for all patients with accompanying neurologic signs/symptoms, all patients younger than 50 years old, patients with progressive motility deficit beyond 2 weeks following onset, patients with persistent paresis > 3-4 months, and any patient with history of malignancies with metastatic potential (e.g. breast, lung, prostate, lymphoma)

II. Define the risk factors

A. Vasculopathic risk factors

1. Diabetes mellitus
2. Systemic hypertension
3. Elevated cholesterol
4. Elevated triglycerides

B. Multiple sclerosis

C. Head trauma

D. Malignancy with metastatic potential

E. Elevated or low intracranial pressure

III. List the differential diagnosis

A. Neural causes

1. Duane syndrome

2. Miller Fisher variant of Guillain-Barré

B. Myopathic causes

1. Giant cell arteritis (can also be neurogenic)
2. Restrictive myopathy (e.g. thyroid eye disease (Graves ophthalmopathy, thyroid orbitopathy), trauma, fracture)
3. Extraocular muscle infiltration and orbital myositis
4. Convergence spasm

C. Neuro-muscular Junction Disease

1. Myasthenia gravis

IV. Describe patient management in terms of medical treatment and follow up

A. Management depends upon the underlying condition

B. Lesions due to small vessel ischemia will almost always completely resolve spontaneously within approximately 6-12 weeks without specific treatment

1. These patients should be referred to their primary care physician for vasculopathic risk factor assessment

V. Describe appropriate patient instructions

A. Call for worsening diplopia or additional neurological signs and/or symptoms

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Third, Fourth and Sixth Cranial Nerve Palsies, Module #8, 1996.

Trochlear nerve palsy

I. Describe the approach to establishing the diagnosis

A. List the pertinent elements of the history

1. Binocular vertical or oblique diplopia
2. May describe torsion
3. May be painful
4. May be maximal at onset, gradually progressive, or intermittent depending on etiology
5. Pertinent medical history
 - a. Vasculopathic risk factors
 - i. Diabetes mellitus
 - ii. Systemic hypertension
 - iii. Elevated cholesterol
 - iv. Elevated triglycerides
 - b. Multiple sclerosis
 - c. Head trauma
 - d. History of head tilt
6. Other neurological symptoms and history

B. Define the relevant aspects of epidemiology of this disease

1. Most commonly in adults, but also seen in children

C. Describe pertinent clinical features

1. Hypertropia that increases when the hypertropic eye is in adduction
2. Hypertropia that increases when the patient's head is tilted toward the hypertropic eye
3. Patient may have a head tilt away from the hypertropic eye
4. Patient may have a head turn away from the hypertropic eye
5. Excyclotorsion (if > 10 degrees, indicates bilateral)
6. If caused by a nuclear lesion, the involved eye will be contralateral to the side of the lesion
7. If caused by a peripheral nerve lesion, the hypertropia will be ipsilateral to the side of the lesion
8. If caused by a nuclear lesion, there may be an associated Horner syndrome contralateral to the involved eye (i.e. ipsilateral to the lesion)
9. Bilateral traumatic cranial nerve (CN) IV palsy
 - a. Small hypertropia in primary gaze

- b. Right hypertropia in left gaze
 - c. Left hypertropia in right gaze
 - d. V-pattern esotropia
 - e. Excyclotorsion of >10degrees
 - f. Marked torsional diplopia in downgaze
10. May be congenital (increased vertical fusional amplitudes)

D. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Review of old photographs for evidence of previous head tilt
 - a. Implies congenital or longstanding CN IV palsy
- 2. Assess for presence of spontaneous head tilt on clinical exam
- 3. Measurement of vertical fusional amplitudes
 - a. Patients with congenital CN IV palsy may have large vertical fusional amplitudes
- 4. Observation of adults > 50 years old with new onset *isolated* CN IV palsy for 3-4 months for presumed microvascular origin is appropriate if patient exhibits
 - a. Normal vertical fusional amplitudes
 - b. No progression beyond 2 weeks following onset
 - c. No history of malignancy of metastatic potential
- 5. Assessment for vasculopathic risk factors if felt to be microvascular in origin (blood pressure, HgbA1c, glucose, lipid profile)
- 6. Observation for presumed decompensated congenital or longstanding CN IV palsy is appropriate in patients with evidence of longstanding head tilt or increased vertical fusional amplitudes
- 7. Magnetic resonance imaging (MRI) for non-trauma related cases that do not fit into the above categories

II. Define the risk factors

A. Vasculopathic risk factors

- 1. Diabetes mellitus
- 2. Systemic hypertension
- 3. Elevated cholesterol
- 4. Elevated triglycerides

B. Multiple sclerosis

A. Head trauma

III. List the differential diagnosis

- A. Skew deviation
- B. Myasthenia gravis
- C. Miller Fisher variant of Guillain-Barré
- D. Thyroid eye disease

IV. Describe patient management in terms of medical treatment and follow up

- A. Management depends upon the underlying condition
- B. Patching or fogging of one eye to alleviate diplopia
- C. Prisms for alleviation of diplopia
- D. Strabismus surgery
- E. Monitoring for resolution, worsening, or stability with serial motility examinations
- F. Additional serologic and imaging investigations as indicated if atypical course for microvascular cranial nerve palsy

V. Describe appropriate patient instructions

- A. Call for worsening diplopia or additional neurological signs and symptoms

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Third, Fourth, and Sixth Nerve Palsies, Module #8, 1996, p. 5-8.

Myasthenia gravis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Neuromuscular transmission deficit
2. Autoantibodies to neuromuscular receptors
3. Antibodies more commonly identified in systemic than in ocular
4. Post synaptic neuromuscular blockade
5. Congenital myasthenia has different mechanisms

B. Define the relevant aspects of epidemiology of the disease

1. Associated conditions
 - a. Thyroid abnormalities
 - b. Thymoma
 - c. Other autoimmune diseases
2. Generalization
 - a. Incidence increases with length of follow-up

C. List the pertinent elements of the history

1. Variable diplopia
2. Variable eyelid droop
3. Difficulty with swallowing
4. Change in tone of voice
5. Shortness of breath
6. Systemic weakness
 - a. Trouble climbing stairs
 - b. Trouble arising from a chair
7. Fatigability
8. Variability over longer periods of time
9. Diurnal variation

D. Describe pertinent clinical features

1. Ophthalmic signs & symptoms
 - a. Ptosis
 - i. Almost all at some time in their course

- ii. Worse with prolonged up gaze
 - iii. Cogan lid twitch sign
- b. Diplopia
- c. Extraocular muscle (EOM) motility disturbance (often without pattern of isolated cranial neuropathy)
 - i. Saccades frequently abnormal and may be too rapid or too slow
 - ii. Gaze paretic nystagmus
- d. Orbicularis weakness
- e. Facial diplegia
- f. Fatigability
- g. Variability
- h. Pupil not clinically involved
- 2. Neurologic signs & symptoms
 - a. Muscle weakness, especially bulbar and facial
- 3. Associated
 - a. Thyroid eye disease (thyroid orbitopathy)
 - b. Other autoimmune diseases

E. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Office testing
 - a. Rest/ice test (mainly for ptosis)
 - b. Tensilon test
 - c. Prostigmin test
 - d. Serial ocular motility and eyelid examinations
- 2. Laboratory testing
 - a. Acetylcholine receptor antibody/muscle-specific receptor tyrosine kinase (MuSK), low sensitivity
 - b. Electromyography (EMG)
 - i. Repetitive stimulation: decremental response
 - ii. Single fiber
 - c. Chest computed tomography (CT) or magnetic resonance imaging (MRI) (rule out thymic abnormalities)

II. Define the risk factors

- A. Autoimmune diseases**
- B. Thyroid eye disease (thyroid orbitopathy)**

III. List the differential diagnosis

A. Other neuromuscular transmission deficit

- 1. Lambert-Eaton syndrome
 - a. Ptosis
 - b. Diplopia rare
- 2. Toxic effect on neuromuscular transmission
 - a. Botulism
 - i. Clinical syndromes
 - i) Food borne
 - ii) Wound botulism
 - iii) Infantile botulism
 - ii. Clinical symptoms
 - i) Fixed (poorly reactive) pupils
 - ii) Ptosis
 - iii) Ophthalmoplegia
 - b. Medications
 - i. Iatrogenic neuromuscular blockade especially succinylcholine in patients at risk
 - ii. Anticholinesterase especially organophosphates
 - iii. Iatrogenic botulinum toxin injections
 - iv. Many agents may exacerbate myasthenia gravis including beta and calcium channel blockers, muscle relaxants

B. Other causes of ptosis

- 1. Levator dehiscence
- 2. Mechanical ptosis

C. Other causes of diplopia

- 1. Restrictive strabismus
- 2. Skew deviation
- 3. Ophthalmoplegia
 - a. Pupil sparing cranial nerve (CN) III palsy
 - b. Multiple cranial nerve palsies

IV. Describe patient management in terms of treatment and follow-up

A. Pyridostigmine (Mestinon®)

B. Functional

1. Lid crutches
2. Patch
3. Prism

C. Immunomodulation

1. Corticosteroids
2. Corticosteroid sparing agents
3. Plasmapheresis
4. IV immune globulin
5. Thymectomy

D. Strabismus or ptosis surgery

1. Less predictability
2. Postoperative corneal exposure may be difficult to manage with concurrent facial weakness

V. List the complications of treatment, their prevention and management

A. Worsen weakness

1. Possibly less likely with slow build up dose

B. Gastrointestinal (GI) symptoms

1. Diarrhea
2. Abdominal cramping

C. Complications of corticosteroid/immunosuppressive therapy (See Systemic corticosteroids in neuro-ophthalmology)

D. Corneal exposure with ptosis surgery

VI. Describe disease-related complications

A. Progression of ocular to systemic myasthenia gravis

1. 50% patients initially with isolated ocular involvement
2. Rarely progress beyond 2-3 years

B. Respiratory failure

C. Severe ptosis with visual impairment

D. Aspiration

VII. Describe appropriate patient instructions

A. See medical attention immediately for

1. Shortness of breath
2. Difficulty swallowing

B. Avoid medications that exacerbate myasthenia gravis

C. Report GI side effects of pyridostigmine

D. Inform all your physicians that you have myasthenia gravis

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Myasthenia Gravis, Module #4, 2003.
3. AAO, Focal Points: Third, Fourth and Sixth Cranial Nerve Palsies, Module #8, 1996.
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8. Gajdos P, Chevret S, Toyka K. Intravenous immunoglobulin for myasthenia gravis. *Cochrane Database Syst Rev* 2006:CD002277.
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Dorsal midbrain syndrome (pretectal or Parinaud syndrome)

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Lesions of the dorsal mesencephalon region
 - a. Extrinsic pressure on dorsal mesencephalon- tumors in the pineal region are most common, obstructive hydrocephalus, intraventricular hemorrhage, aqueductal stenosis
 - b. Intrinsic lesions of the dorsal midbrain such as vascular, inflammatory, infectious, and neoplastic
 - c. Midbrain stroke
 - d. Multiple sclerosis

B. Define the relevant aspects of epidemiology of the disease

1. Affects all demographics

C. List the pertinent elements of the history

1. Inability to look up
2. Blurred vision, often at near
3. Diplopia

D. Describe the pertinent clinical features

1. Best described as abnormalities of eye movements and pupil dysfunction. May have some of the following signs:
 - a. Upgaze paresis —most common feature
 - b. Mid-dilated pupils
 - c. Light-near dissociation of pupils
 - d. Convergence-retraction nystagmus on attempted upgaze from co-contraction of extraocular muscles, which causes retraction and convergence of the globes
 - e. Neurogenic eyelid retraction (Collier sign)
 - f. Impaired conjugate vertical pursuit (usually upgaze)
 - g. Other neuro-ophthalmologic findings vary with severity and etiology
 - h. Papilledema
 - i. Skew deviation
 - j. Convergence spasm or palsy
2. Tonic downgaze in premature newborns, combined with eyelid retraction = setting sun sign

- a. Can be caused by intraventricular hemorrhage expanding the third ventricle, compressing the pretectum

E. Describe the appropriate testing and evaluation for establishing the diagnosis

1. Check saccades by having the patient shift gaze between two targets in the vertical plane
2. Check pursuit by having the patient follow a vertically moving target
3. Check the pupils for light and near response (will usually react better to accommodation than to light)
4. Check for convergence-retraction nystagmus by looking for both eyes to make a convergence movement while simultaneously being retracted into the orbit
 - a. Elicit during upward saccades exaggerated by using an optokinetic stimulus rotating downward
5. Check for retraction of the upper eyelid
6. Check the fundus for papilledema

II. Define the Risk Factors

- A. None**

III. List the Differential Diagnosis

- A. Accommodative spasm/spasm of near reflex**
- B. Other disorders of light-near dissociation**
- C. Thyroid eye disease**
- D. Wernicke encephalopathy**
- E. Miller-Fisher Syndrome**

IV. Describe the patient management in terms of treatment and follow-up

A. Describe the natural history, outcome and prognosis

1. Natural history dependent on etiology
2. Can improve signs and symptoms with treatment of the underlying cause

B. Describe medical therapy options

1. Avoid upgaze
2. Prisms to move targets into inferior field
3. Radiation

C. Describe surgical therapy options

1. Shunt placement for raised intracranial pressure

2. Surgery for tumor
3. Muscle surgery usually ineffective

V. List complications of treatment, their prevention and management

- A. Complications related to shunt failure, which may include vision loss from high intracranial pressure
- B. Complications related to strabismus surgery including persistent diplopia

VI. Describe disease-related complications

- A. Diplopia
- B. Gaze paresis
- C. Other complications related to inciting disease

VII. Describe appropriate patient instructions

- A. Treat underlying disease with appropriate medical specialist

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-Ophthalmology, 2013-2014.
2. Baloh RW, Furman JM, Yee RD. Dorsal midbrain syndrome: clinical and oculographic findings. *Neurology* 1985;35:54-60.
3. Miller NR, Newman NJ. Walsh & Hoyt's Clinical Neuro-Ophthalmology 5th ed. Maryland, Williams & Wilkins, 1998;1867-1874.
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Nystagmus

I. Describe the approach to establishing the diagnosis

A. Abnormal eye movement may occur due to

1. Inability to maintain fixation
 - a. Fast phase is always in the direction of gaze
 - b. Alexander's law
2. Loss of the normal inhibitory influences on the eye movement control system
3. Loss of the normal symmetric input from the vestibular pathways to the oculomotor nuclei

B. List the pertinent elements of the history

1. Age of onset
2. Family history of abnormal eye movements
3. Oscillopsia
4. Associated neurologic and/or vestibular symptoms
5. Medications

C. Describe pertinent clinical features

1. Congenital nystagmus (CN)
 - a. Recognized in the first few months of life
 - b. May have positive family history
 - c. No oscillopsia
 - d. Acuity may be normal or diminished
 - e. Jerk and/or pendular pattern
 - f. Conjugate horizontal movements that remain horizontal in up- and downgaze
 - g. Null point
 - h. Increasing velocity of slow phase
 - i. Accentuated by distant fixation; diminished by convergence
 - j. Concurrent strabismus common
 - k. Abolished in sleep
 - l. Reversal of optokinetic reflex (OKN)
 - i. In normal pursuit the nystagmus consists of initial slow phases in the direction of the stimulus, followed by fast, corrective phases. In congenital nystagmus, this may be reversed. This may be due to shifting of the null point

- m. Differential diagnosis
 - i. Afferent visual pathway disorder
 - ii. Ocular albinism
 - iii. Achromatopsia
 - iv. Leber's Congenital Amaurosis
 - v. Aniridia
- 2. Latent nystagmus (LN)
 - a. Appears early in life
 - b. Horizontal conjugate jerk nystagmus that is accentuated or appears only with monocular viewing conditions
 - c. Fast phase toward the viewing eye
 - d. Congenital esotropia (ET) common
 - e. Poor stereopsis
 - f. May be present with CN
 - g. Manifest latent nystagmus
 - i. Present under binocular viewing conditions
- 3. Monocular nystagmus of childhood
 - a. Monocular vertical or elliptical small amplitude movements
 - b. May occur with optic neuropathy or amblyopia
 - c. Warrants neuroimaging when found in an infant to exclude optic nerve/chiasmal tumor (glioma)
- 4. Spasmus nutans
 - a. First year of life
 - b. Intermittent, binocular, very small amplitude, high-frequency (shimmering) horizontal, pendular nystagmus
 - c. May be dissociated or monocular
 - d. Subtle head nodding
 - e. Torticollis
 - f. Benign, head movement and torticollis usually resolve by the end of the first decade
 - g. Differential diagnosis
 - i. Monocular nystagmus of childhood
 - ii. Retinal dystrophies
 - iii. Lesions of chiasm

5. Gaze-evoked nystagmus
 - a. Clinically insignificant when in extremes of far horizontal gaze (end-gaze) with no other features
 - b. Should prompt further evaluation when asymmetric or sustained
 - i. Metabolic
 - ii. Toxic
 - iii. Brainstem or cerebellar lesion (CVA, MS, tumor)
 - iv. Rebound nystagmus in cerebellar disease
 - v. Extraocular myopathies, MG
6. Vestibular nystagmus
 - a. Peripheral vestibular nystagmus
 - i. Vertigo, nausea, vomiting
 - ii. Symptoms exacerbated by head movements or postures
 - iii. Oscillopsia, tinnitus, hearing loss
 - iv. Usually unilateral unless toxic
 - v. Horizontal-torsional nystagmus that changes with gaze and dampens on fixation
 - vi. Acute onset followed by gradually waning symptoms
 - i) Dysfunction of the vestibular system end organ (semicircular canals, otolithic structures, vestibular nerve) - Meniere disease, BPPV, systemic autotoxins (AG, chemo Rx), CPA tumors
 - b. Central vestibular nystagmus
 - i. Downbeat nystagmus
 - i) Arnold-Chiari type I
 - ii) Tumors at foramen magnum
 - (i) Spinocerebellar degenerations
 - ii. Upbeat nystagmus
 - (i) Posterior fossa (medulla) lesions
 - iii. Periodic alternating nystagmus (PAN)
 - i) Strictly horizontal
 - ii) Congenital or acquired
 - (i) Acquired form: cycle 2-4 minutes
 - iii) Cerebellar dysfunction
7. Acquired pendular nystagmus

- a. Poor localizing value
 - b. Oculopalatal myoclonus
 - i. Lesions affecting the transmission between the cerebellum (flocculus) and the inferior olive
 - ii. Hypertrophy of the inferior olivary nucleus
8. See-Saw nystagmus
- a. One eye elevates and intorts while the other eye depresses and extorts
 - b. Typically slow and pendular
 - c. Congenital
 - i. Congenital achiasma
 - d. Acquired
 - i. Parasellar region tumors (craniopharyngioma)
 - ii. Trauma
9. Dissociated nystagmus
- a. INO
 - i. Lesion of the MLF
 - ii. Ipsilateral slowing of adduction +/- abducting nystagmus
10. Saccadic Intrusions
- a. Square-wave jerks and macro square wave jerks
 - i. May be seen in normal elderly when small and low frequency
 - ii. May be seen with movement disorders (i.e. PSP, Parkinson's)
 - b. Ocular flutter
 - i. Bursts of horizontal movements with small amplitude but very high frequency
 - ii. No inter-saccadic interval
 - c. Opsoclonus (saccadomania)
 - i. Multidirectional, high frequency, larger amplitude
 - ii. No inter-saccadic interval
 - i) Paraneoplastic etiology must be excluded in flutter and opsoclonus
 - ii) Neuroblastoma in children
 - iii) Small cell lung ca or breast/ovarian in adults
 - iv) Anti-Ri/ANNA-2 (breast/ovary) & anti-Hu/ANNA-1 (NB) antibodies in serum or CSF
 - iii. May be "idiopathic"

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Assessing ocular stability in primary and 9 cardinal positions of gaze
2. Pursuit, saccades
3. Monocular or binocular
4. Conjugate or disconjugate
5. Direction (horizontal, torsional, mixed)
6. Continuous or induced by a certain position
7. Pattern
 - a. Pendular
 - b. Jerk
 - c. Saccadic intrusion
8. Null point
9. Present under monocular versus binocular condition (latent nystagmus)

II. Differential Diagnosis

- A. Demyelination**
- B. Stroke**
- C. Drugs**
- D. Toxins (EtOH)**
- E. Tumors**
- F. Trauma**
- G. Degenerative diseases**
- H. Encephalitis**

III. Describe patient management in terms of treatment and follow-up

A. Medical treatments

1. Discontinue any causative medications
2. Correct refractive errors
3. Prisms
 - a. Convergence (base-out) prisms for congenital nystagmus or when nystagmus suppressed by near viewing
4. Image stabilization methods
5. Pharmacologic

- a. Gabapentin
 - b. Baclofen
 - c. Memantine
 - d. Clonazepam
 - e. Valproate
6. Botox injection

B. Surgical treatment

1. Extraocular muscle surgery to shift the null point into primary condition

IV. List the complications of treatment, their prevention and management

A. Complications associated with medications

B. Complications associated with surgery

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.

Benign essential blepharospasm

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Idiopathic
2. Similar spasms can be associated with Parkinson disease

B. Define the relevant aspects of epidemiology of the disease

1. Many patients present in the sixth decade
2. Gender: female>male

C. List the pertinent elements of the history

1. Begins with excessive blinking
2. Variable periods of blepharospasm lasting seconds to minutes
3. May be asymmetric
4. Progress to complete eyelid closure with functional blindness in some patients
5. Photophobia and dry eye symptoms are common
6. Some patients have inability to open the eyelids (apraxia of eyelid opening)
7. Triggers include sunlight, stress, wind, noise, reading, and fatigue

D. Describe pertinent clinical features

1. Severe, bilateral involuntary spasms of the orbicularis oculi muscles
2. Some patients learn techniques to diminish the spasm temporarily such as tongue thrusting, humming, mouth opening, extending the neck, closing one eye, touching around the eye, or rubbing the face. Sleep and rest may improve symptoms
3. Progression is the rule although usually not to complete incapacitation
4. Social withdrawal with inability to work or drive may result
5. Eventually the eyelids may clamp shut and must be pried open with fingers
6. Brow spasm can also be seen
7. Associated anatomic problems can result or accompany essential blepharospasm
 - a. Brow ptosis
 - b. Blepharoptosis, associated levator disinsertion
 - c. Entropion or ectropion
8. Some patients develop lower facial dystonia - orofacial cervical dystonia (Meige syndrome)

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Typical presentation without neurological signs makes imaging unnecessary in most cases.

II. List the differential diagnosis

A. Hemifacial spasm (See Hemifacial spasm)

B. Facial myokymia (pontine lesion, multiple sclerosis (MS))

C. Benign facial fasciculations

1. Risk factors include
 - a. Caffeine
 - b. Stress
 - c. Physical exertion
 - d. Fatigue

D. Reflex blepharospasm

1. Risk factors include
 - a. Corneal/ocular surface irritation
 - b. Anterior uveitis
 - c. Dry eye syndrome
 - d. Medications causing facial dystonia
 - e. Photophobia

E. Tic disorders

III. Describe patient management in terms of treatment and follow-up

A. Botulinum toxin

1. Average duration of therapeutic effect is 3 months, so patients require repeat injections to control spasms. The frequency and dosage of injections may need to be titrated by clinical response, i.e., individualize treatment
2. Discuss use of ocular lubricants and occlusive (moisture chamber) eyewear or goggles after injection if eyelid closure may be impaired

B. Orbicularis myectomy

1. Reserved for patients with an inadequate response to botulinum toxin
2. May continue to need botulinum toxin injections after surgery

C. Oral medications demonstrate limited success and may have significant side effects

D. Address any causes of secondary blepharospasm which may accompany essential blepharospasm (e.g. dry eye syndrome, stress)

E. FL-41 lenses may be of use in some patients to decrease photophobia and increase comfort

IV. List the complications of treatment, their prevention and management

A. Botulinum toxin

1. Complications may involve levator muscle and extraocular muscles
 - a. Ptosis (avoid central upper eyelid)
 - b. Diplopia
2. Injection should be remote from these muscles and superficial
3. Complications usually will resolve as the medication effects subside
4. Bruising, epiphora, ectropion, lagophthalmos
1. Relative contraindications include pregnancy, lactation, myasthenia gravis
5. Respiratory suppression and other complications may be seen with the use of non-approved forms of botulinum toxin, especially in young patients

B. Orbicularis myectomy

1. Recurrence
2. Necrosis of overlying skin
3. Lymphedema, lagophthalmos, lower eyelid retraction, ectropion, ptosis

V. Describe disease-related complications

A. Visual dysfunction with lifestyle limitations

VI. Describe appropriate patient instructions

A. Recommend treatment when functioning becomes limited

B. Refer to local/regional/national support groups

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-Ophthalmology, 2013-2014.
2. Bradley EA, Hodge DO, Bartley GB. Benign essential blepharospasm among residents of Olmsted County, Minnesota, 1976 to 1995: an epidemiologic study. *Ophthal Plast Reconstr Surg* 2003;19:177-81.
3. AAO, Ophthalmology Monographs 8. Surgery of the Eyelid, Orbit and Lacrimal System, Vol. 2, 1994.
4. AAO, Focal Points: Essential Blepharospasm and Related Diseases. Module 5, 2000.
5. AAO, Basic and Clinical Science Course. Section 7: Orbit, Eyelids, and Lacrimal System, 2013-2014.

6. Ben Simon GJ, McCann JD. Benign essential blepharospasm. *Int Ophthalmol Clin* 2005;45:49-75.
7. Costa J, Espirito-Santo C, Borges A, et al. Botulinum toxin type A therapy for blepharospasm. *Cochrane Database Syst Rev* 2005:CD004900.
8. AAO, Focal Points: Botulinum Toxin in Ophthalmology. Module 3, 2007.

Facial nerve paresis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Peripheral facial weakness
 - a. Usually unilateral
 - b. Idiopathic (some may relate to viral infection, up to 60-70% have been estimated to relate to HSV-1)
 - c. Auto-immune (SLE, Miller Fisher variant of Guillain-Barre syndrome)
 - d. Infectious (HSV, Lyme disease, Zoster, especially with VIII N. involvement- Ramsey-Hunt otitis media, syphilis)
 - e. Traumatic
 - f. Neoplastic (parotid gland tumors, acoustic neuroma, meningioma)
 - g. Inflammatory (sarcoid)
 - h. Iatrogenic (botulinum toxin injection, acoustic neuroma resection, parotid gland surgery, face/brow lifting)
2. Central facial weakness
 - a. Often bilateral
 - b. Frequently associated with long tract signs and VI nerve dysfunction (Foville syndrome, Millard-Gubler syndrome)
 - c. Pathophysiology
 - i. Vascular (vertebrobasilar insufficiency)
 - ii. Inflammatory (demyelinating)
 - iii. Neoplastic (glioma, metastatic)

B. Define the relevant aspects of epidemiology of the disease

1. Peripheral idiopathic (Bell palsy) most common type of facial neuropathy
2. Increase risk in diabetes, pregnancy, positive family history

C. List the pertinent elements of the history

1. Mild pain, usually retroauricular may precede development of palsy

D. Describe pertinent clinical features

1. facial weakness
2. Cutaneous sensation is intact
3. Increased tearing may be noticed

4. Ectropion
5. Diminished taste may be present - the facial nerve provides taste to the anterior 2/3 of tongue
6. Dysacusis may be noted - the facial nerve innervates the stapedius muscle of the inner ear
7. External auditory canal may show a vesicular dermatitis in patients with herpes zoster (Ramsey Hunt syndrome)
8. Recovery typically begins at 3 weeks and is complete by 3 to 4 months

E. Anatomy of cranial nerve VII (facial nerve)

1. Supranuclear
 - a. Ganglion cells reside within the cerebral cortex
 - b. Motor axons travel within the corticobulbar tract via the internal capsule.
 - c. Lesions affect the upper and lower face variably based on the following
 - i. Axons to the upper face synapse bilaterally within the pons.
 - ii. Axons to the lower face synapse only within the contralateral nucleus.
2. Nuclei
 - a. Clinical findings of brain stem lesions depend on level of involvement
 - i. Motor nucleus: located in pons
 - ii. Superior salivary nucleus: visceromotor located in the pontine tegmentum
 - iii. Solitary nucleus: special sensory (taste) embedded in the medulla oblongata
3. Major motor branches of the facial nerve
 - a. Temporal branch
 - i. Crosses the over the zygomatic arch and is at risk of injury with some periocular surgery
 - b. Zygomatic branch
 - c. Buccal branch
 - d. Marginal mandibular branch
 - e. Cervical branch

F. Describe appropriate testing and evaluation for establishing the diagnosis

1. Distinguish upper and lower motor neuron abnormalities
 - a. Upper motor neuron does not involve the forehead due to bilateral (crossed and uncrossed) innervation
 - b. Lower motor neuron involves the entire face including the forehead
 - c. This distinction is helpful in defining etiology and planning evaluation/management
2. Consider imaging with computed tomography (CT) or magnetic resonance imaging (MRI) (See Computed tomography) (See Magnetic resonance imaging)

- a. If facial weakness continues to progress after three weeks or failure to improve after 4-6 months
 - b. Associated neurologic abnormalities
 - i. Other cranial nerve palsy (VI,VIII)
 - ii. Weakness, ataxia
 - c. Signs of meningitis
 - d. Facial twitch or spasm preceding paralysis which may be indicative of nerve irritation by tumor
- 3. Consider serologic testing for Lyme, syphilis, human immunodeficiency virus (HIV)
 - 4. Consider screening for sarcoidosis

II. Define the risk factors

- A. History of tick bites suggests an underlying diagnosis of Lyme disease**
- B. History of sarcoidosis or pulmonary problems**
- C. Immune suppression (HIV)**

III. Describe patient management in terms of treatment and follow-up

- A. Describe the natural history, outcome and prognosis**
 - 1. Most patients with isolated idiopathic palsy experience a satisfactory spontaneous recovery
- B. Describe medical therapy options**
 - 1. Corticosteroids likely have a positive effect on speed and degree of recovery.
 - 2. Antivirals including acyclovir may play a role, but have unclear efficacy
 - 3. Artificial tears and lubricants for corneal exposure
 - 4. Taping eyelid shut for exposure
- C. Describe surgical therapy options**
 - 1. Tarsorrhaphy for exposure
 - 2. Gold weight implant
 - 3. Surgical correction of lower eyelid malposition
 - 4. Facial nerve reconstruction/re-innervation

IV. List the complications of treatment, their prevention and management

- A. Steroid complications (See Systemic corticosteroids in neuro-ophthalmology)**
- B. Gold weight may become infected or extrude**

- C. Ectropion repair is often ineffective unless combined with midface lifting

V. Describe disease-related complications

- A. Exposure keratopathy (Corneal ulcer, etc.)
- B. Development of aberrant regeneration

VI. Describe appropriate patient instructions

- A. Call for redness, irritation
- B. Call for decrease vision
- C. Call for dry eye symptoms

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-Ophthalmology, 2013-2014.
2. Dresner SC. Ophthalmic Management of Facial Nerve Paralysis. Module 4, 2000.
3. Grogan PM, Gronseth GS. Practice parameter: steroids, acyclovir, and surgery for Bell's palsy (an evidence-based review). *Neurology* 2001;56:830-836.
4. Jackson CG, von Doerstan PG. The facial nerve: current trends in diagnosis, treatment, and management. *Med Clin North Am* 1999;83:179-95.
5. Grogan PM; Gronseth GS. Practice parameter: Steroids, acyclovir, and surgery for Bell's palsy (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2001 Apr 10;56(7):830-6.

Hemifacial spasm

I. Describe the approach to establishing the diagnosis

A. Pathophysiology

1. Ephaptic transmission
2. Vascular compression of facial nerve root at exit from brainstem (99%)
 - a. Normal vessel in aberrant location (e.g. AICA, PICA)
 - b. Dolichoectatic vertebral or basilar artery
3. Cerebellar pontine angle (CPA) mass (rare) (e.g. meningioma, acoustic neurinoma)
4. Post-paralytic (i.e. s/p Bell Palsy)

B. Symptoms

1. Paroxysmal painless synchronous contraction of muscles innervated by facial nerve
2. Almost always unilateral
3. Present during sleep (unlike blepharospasm)

C. Signs

1. Clonic or tonic episodic contraction of muscles innervated by CN VII
2. Lid closure
3. May be associated with facial paresis

D. Work-up

1. Imaging to identify vascular anomaly or rare tumor in CPA

II. Define the risk factors

- A. Age - most common in middle age, though may develop at any age
- B. Posterior fossa tumor
- C. Dolichoectatic vertebral or basilar artery
- D. Normal artery in abnormal location
- E. Previous facial palsy

III. List the differential diagnosis

A. Blepharospasm

1. Essential
2. Secondary (corneal disease, dry eye)

B. Facial myokymia

1. Pontine demyelination (e.g. multiple sclerosis)
2. Pontine tumor

C. Benign facial fasciculations

1. Caffeine
2. Stress

D. Facial tic

E. Aberrant regeneration of the facial nerve

IV. Describe the patient management in terms of treatment and follow-up

A. Describe the natural history, outcome and prognosis

1. Usually progressive (worsening with time)
2. Often starts with contractions around the eye and spreads to involve the lower facial musculature
3. May be associated with facial paresis

B. Describe medical therapy options

1. Botulinum toxin chemodenervation (>90% effective)
 - a. Avoid the upper lip and central upper eyelid
 - b. Concentrate around orbicularis oculi and cheek
 - c. Onset of effect 2-3 days after injection
 - d. Maximal effect in 10-14 days

C. Describe surgical therapy options

1. Neurovascular decompression of the facial nerve

V. List the complications of treatment, their prevention and management

A. Botulinum toxin

1. Complications may involve levator muscle, extraocular muscles, and muscles innervated by the facial nerve where botulinum toxin is injected
 - a. Ptosis (avoid central upper eyelid)
 - b. Diplopia
 - c. Facial droop/excessive facial weakness, drooling
2. Injections should be superficial and remote from the extraocular muscles, the central portion of the levator palpebrae, and the orbicularis oris
3. Complications usually will resolve as the medication effect subsides

4. Bruising, epiphora, ectropion, lagophthalmos
5. Relative contraindications include pregnancy, lactation, myasthenia gravis
6. Respiratory suppression and other complications may be seen with the use of non-approved forms of botulinum toxin, especially in young patients

B. Surgical neurovascular decompression

1. Persistent or recurrent spasm
2. Facial nerve palsy
3. Stroke
4. Hearing loss
5. Death

VI. Describe disease-related complications

A. Difficulty with visual activity

1. Driving
2. Reading

B. Social problems

VII. Describe appropriate patient instructions

- A. Feed back on effectiveness of botulinum toxin injections (either re-evaluate 2-4 weeks after initial injection or inquire at follow-up visit)**
- B. Call for side-effects (e.g. ptosis, diplopia, ocular irritation/tearing)**
- C. Call if recurrent symptoms**
- D. Referral for a discussion of surgical options**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-Ophthalmology, 2013-2014.
2. AAO, Focal Points: Botulinum toxin in ophthalmology. Module 3, 2007.
3. Samii M, Gunther T, Iaconetta G, et.al. Microvascular decompression to treat hemifacial spasm; long-term results for a consecutive series of 143 patients. *Neurosurgery* 2002;50:712-718.

Idiopathic orbital inflammatory disease (non-specific orbital inflammation)

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Orbital inflammation may occur as
 - a. "Idiopathic", isolated orbital process not associated with identifiable disease
 - b. Local manifestation of a widespread systemic disease
 - c. May be initial manifestation of previously unidentified systemic disease
2. Several classification systems in
 - a. Pathologic (e.g., type of cellular infiltrate)
 - b. Anatomic (e.g., myositis, perineuritis, scleritis, dacryoadenitis, fat involvement, orbital apex/cavernous sinus (Tolosa-Hunt syndrome))
 - c. Radiologic (e.g., localized, diffuse, anterior, posterior)
 - d. Time course (e.g., acute, subacute or. chronic)
 - e. Sclerosing orbital pseudotumor
 - i. Subtype distinguished histologically by degree of fibrosis
 - ii. May be refractory to treatment with prednisone, requiring additional immunosuppressive agents

B. Define the relevant aspects of epidemiology of the disease

1. In adults, usually unilateral
2. If bilateral, more likely associated with systemic disease
3. May be associated with other systemic inflammatory conditions
4. In children, more often bilateral and not associated with systemic disease

C. List the pertinent elements of the history

1. The symptoms often vary by the tissue affected
 - a. Acute or chronic recurrences
 - b. Pain (local, diffuse, tenderness, pain with eye movement)
 - c. Diplopia
 - d. Blurred or otherwise reduced vision
 - e. Red eye
 - f. Signs of orbital inflammation (e.g., swelling, chemosis, proptosis)

2. May have signs/symptoms of associated systemic disease (e.g., SLE, sarcoidosis, rheumatoid arthritis, Wegener granulomatosis, Symptoms may wax and wane, have multiple recurrence over years, or worsen in a crescendo fashion
3. Systemic constitutional symptoms common in children
4. Dramatic improvement of symptoms to corticosteroid therapy
5. Symptoms frequently recur if corticosteroids are tapered too rapidly

D. Describe pertinent clinical features

1. Anterior segment inflammation
 - a. Dilated scleral and episcleral vessels
 - b. Conjunctival chemosis
 - c. Cell and flare
 - d. Inflammatory scleral reaction
2. Posterior segment inflammation
 - a. Papillitis
 - b. Scleral thickening or choroidal folds
 - c. Retinal edema
3. Adnexa
 - a. Eyelid edema/erythema
 - b. Lacrimal gland enlargement
4. Orbital
 - a. Proptosis
 - b. Resistance to retropulsion
 - c. Ophthalmoplegia Point tenderness

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Magnetic resonance imaging (MRI) (T1 fat suppressed with and without contrast)
2. Computed tomography (CT), with contrast
3. Ultrasound (especially scleritis, Tenon's thickening, T sign junction of optic nerve and sclera)
4. Surgical biopsy, especially in atypical or recurrent cases
5. Ancillary evaluation for concurrent disease
 - a. Guided by the review of symptoms
 - b. Selected cases warrant hematologic/oncologic consultation for lymphoproliferative disease or other malignancy
 - c. Selected cases warrant rheumatologic/immunologic consultation, or rare parasitic evaluation

- d. Give consideration to ANA, RPR, FTA, ANCA, ACE, CBC

II. Define the risk factors

- A. **Bilaterality in adults makes one think of systemic disease; whereas children can have bilateral disease in the absence of an underlying systemic disorder**
- B. **Parasite infection (historical risk)**
- C. **Concurrent immunologic or rheumatologic disease (especially vasculitis, sarcoidosis, polyarteritis nodosa, connective tissue disease, Wegener granulomatosis)**

III. List the differential diagnosis

- A. **Orbital cellulitis**
- B. **Thyroid eye disease (Graves ophthalmopathy)**
- C. **Orbital vasculitis (Wegener granulomatosis, polyarteritis nodosa, giant cell arteritis)**
- D. **Orbital sarcoid, granulomatous disease**
- E. **Neoplastic**
- F. **Fistula (dural arteriovenous malformation/ carotid cavernous fistula)**
- G. **Polyclonal/monoclonal orbital infiltrates**
- H. **Fungal disease**
- I. **Parasitic (myopathy)**
- J. **Orbital ischemia**

IV. Describe patient management in terms of treatment and follow-up

- A. **Describe medical therapy options**
 - 1. **Corticosteroids**
 - 2. **Adjuvant immunosuppression (especially alkylating agents)**
 - 3. **Control of concurrent systemic disease**
- B. **Describe surgical therapy options**
 - 1. **Biopsy for histology, assess for lymphoproliferative disease or findings characteristic of known inflammatory disease**
- C. **Radiation therapy (when refractory to medications)**

V. List the complications of treatment, their prevention and management

- A. **Corticosteroid-induced side effects (See Systemic corticosteroids in neuro-ophthalmology)**
- B. **Complications of other immunosuppression**

1. Myelosuppression
2. Genitourinary toxicity (cyclophosphamide: hemorrhagic cystitis)
3. Risk of sterility
4. Secondary malignancy
5. Teratogenic effect
6. Musculoskeletal system
7. Gastrointestinal

C. Radiation effects

1. Radiation retinopathy (diabetes mellitus is relative contraindication)
2. Optic neuropathy (unlikely with standard radiation dose)
3. Dry eye
4. Secondary tumor risk
5. Cataract development
6. Anterior segment ischemia-neovascular glaucoma

D. Avoidance of radiation effects

1. Limit radiotherapy (dose)
2. Consult with radiation therapist
3. Treatment of complications as necessary
4. Monitor patients during and after radiation period

VI. Describe disease-related complications

A. Specific to underlying disease

1. Manifestation of lymphoproliferative disease
2. Systemic rheumatologic disease

B. Infiltration of adjacent structures

1. Intracranial spread

C. Orbital deformity

D. Extraocular muscle damage

1. Ocular misalignment
2. Paretic, restrictive or both

E. Visual loss

1. Optic nerve involvement
2. Ocular involvement

- 3. Retinal (choroidal) involvement
- F. Hypoesthesia
- G. Abnormal pupil/accommodation loss
- H. Orbital ischemia/compartment syndrome/ orbital infarction
- I. Exposure syndrome with severe proptosis
- J. Chronic pain

VII. Describe appropriate patient instructions

- A. Discussion of risks of therapy
- B. Discussion signs of clinical progression
- C. Importance of ancillary care to avoid complications

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
- 2. Zborowska B, Ghabrial R, Selva D, et al. Idiopathic orbital inflammation with extraorbital extension: case series and review. *Eye* 2006;20:107-13.

Thyroid eye disease (thyroid orbitopathy)

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Euthyroid or dysthyroid concurrent disease
2. Systemic autoimmune disease with potential target cells within orbit

B. Define the relevant aspects of epidemiology of the disease

1. Associated with other systemic autoimmune disorders, notably myasthenia gravis in roughly 1% of patients
2. Female predominance
3. Slight familial predominance

C. List the pertinent elements of the history

1. Eyelid retraction
2. Proptosis
3. Diplopia
4. Symptoms related to ocular surface exposure
5. Insidious or rapid visual loss in minority of patients
6. May exhibit signs/symptoms of hypothyroidism/hyperthyroidism
7. Position dependent orbital edema
8. Orbital discomfort and pressure sensation
9. Describe pertinent clinical features
10. Orbital inflammatory signs including injection over muscle insertions and chemosis (may be diffuse)
11. Eyelid lag, eyelid retraction, lagophthalmos
12. Exposure keratopathy
13. Restrictive strabismus (most commonly esotropia/hypotropia)
14. Exophthalmos (resistant retropulsion)
15. Elevated intraocular pressure (IOP) which may increase in upgaze
16. Loss of vision without marked proptosis may exist
17. Pattern of extraocular muscle (EOM) enlargement: Inferior > Medial > Superior > Lateral
18. Muscle tendon relatively spared

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Imaging (may not be uniformly necessary)
 - a. Computed tomography of orbits (non-enhanced is usually adequate)
 - b. Magnetic resonance imaging (MRI)
2. B scan ultrasonography
3. Forced duction testing
4. Gaze-evoked IOP elevation
5. Consider referral to endocrinologist
6. Thyroid function testing
7. Thyroid antibody testing

II. Define the risk factors

- A. Smoking**
- B. Other autoimmune diseases**
- C. Treatment with radioactive iodine for hyperthyroidism may exacerbate orbital disease**
 1. Concomitant use of steroids may mitigate this effect

III. List the differential diagnosis

- A. Dural arteriovenous malformation**
- B. Carotid-cavernous fistula**
- C. Non-specific orbital inflammation**
- D. Orbital tumor (lymphoma/leukemic infiltrate/single or multiple metastasis)**
- E. Ocular myasthenia gravis (possibly concurrence)**
- F. Orbital cellulitis**
- G. Orbital myositis**

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options**
 1. Endocrine consultation
 2. Corticosteroids
 - a. controversial
 3. Other immune suppressive agents
 - a. Controversial and unproven
 4. Smoking cessation

5. Role of thyroid ablation and orbitopathy progression
6. Modalities to treat symptoms such as dry eyes, e.g., lubricants

B. Describe surgical therapy options

1. Surgical planning
 - a. Unless medical necessity requires otherwise, surgery should be performed in the following order
 - i. Orbital
 - ii. Strabismus
 - iii. Eyelid
 - b. Unless medical necessity requires otherwise, surgery should be postponed until patients are clinically stable. The exact duration recommended, varies among surgeons
2. Orbital decompression for optic neuropathy
 - a. Indications for surgical decompression
 - i. Optic neuropathy
 - ii. Severe proptosis with exposure keratopathy
 - iii. Unacceptable cosmesis
 - b. Techniques
 - i. Bony decompression
 - i) Decompression of orbital apex for compressive optic neuropathy
 - ii) Open vs. endoscopic
 - iii) Decompression of the medial, inferior and lateral walls may be performed in isolation or in any combination. Opinions vary and are currently evolving regarding the best technique
 - ii. Orbital fat excision
 - iii. Complications
 - i) Visual loss
 - (i) Hemorrhage
 - (ii) Direct injury to optic nerve
 - ii) Diplopia
 - (i) Rates vary, but have been reported to range from 5 to 20%
 - (ii) May be less apt if decompression of the orbital floor is avoided
3. Strabismus surgery when motility exam is stable
 - a. Recession of tight muscle, not resection, should be employed
4. Eyelid malposition

- a. Indications
 - i. Ocular surface exposure
 - ii. Cosmetic rehabilitation (should be postponed until clinically stable)
- b. Technique
 - i. Upper eyelid retraction
 - i) Levator recession
 - ii) Blepharotomy
 - ii. Lower eyelid retraction
 - i) Posterior lamellar spacer
 - ii) Correction of laxity (tarsal strip) if present
 - iii) Midface elevation
 - iv) Orbital rim augmentation
 - iii. Tarsorrhaphy (consider as a last resort) but can effectively manage exposure secondary to both upper and lower retraction

C. Radiation therapy

- 1. Indications are controversial
- 2. May have a role in patients with optic neuropathy or active inflammation in the orbit

V. List the complications of treatment, their prevention and management

A. Corticosteroids (See Systemic corticosteroids in neuro-ophthalmology)

B. Surgery

- 1. Eyelid deformity
- 2. Ocular misalignment
- 3. EOM damage/restrictive strabismus/neuropathic damage
- 4. Postoperative or delayed visual loss/central retinal artery occlusion
- 5. Hypoesthesia
- 6. Vision loss

C. Abnormal pupil/accommodation loss

D. Orbital cellulitis

E. Dry eye and retinopathy may result from radiation therapy

VI. Describe disease-related complications

A. Anterior segment

- 1. Corneal exposure problems
- B. Ocular motility abnormalities**
- C. Raised IOP**
 - 1. Glaucoma may be overlooked
- D. Optic neuropathy**
- E. Cosmetic deformity**

VII. Describe appropriate patient instructions

- A. Smoking cessation**
- B. Report any progression in symptoms**
- C. Report any change in therapeutic plan by endocrinologist**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
- 2. AAO, Focal Points: Thyroid-Associated Orbitopathy, Module #1, 1997.
- 3. Bartley GB, Fatourehchi V, Kadmas EF, et al. Long-term follow-up of Graves ophthalmopathy in an incidence cohort. Ophthalmology 1996;103:958-962.
- 4. Prummel MF, Terwee CB, Gerding MN. A randomized controlled trial of orbital radiotherapy versus sham irradiation in patients with mild Grave's ophthalmopathy. J Clin Endocrinal Metab 2004;89:15-20.

Optic nerve sheath meningioma

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Benign tumor arachnoid cap cells

B. Define the relevant aspects of epidemiology of the disease

1. One of the two most common optic nerve tumors
2. Female predominance except in children where it is equal

C. List the pertinent elements of the history

1. Visual disturbance (usually monocular)
2. Transient complaints (transient visual obscurations) versus slowly progressive visual loss
Gaze-evoked complaints, e.g., gaze evoked visual loss

D. Describe pertinent clinical features

1. Progressive loss of visual acuity, color or field
2. Pattern of field loss
3. May produce any pattern of visual field loss
4. Optic atrophy and/or edema if located immediately posterior to the globe
5. Optociliary vessels (enlargement of retinochoroidal collaterals)

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Orbital computed tomography (CT) with contrast to look for:
 - a. Calcification or thickening nerve sheath (tram track)
 - b. Enlargement of optic canal
 - c. Adjacent bony hyperostosis
 - d. Contrast enhancement
2. MRI scan of orbit/optic nerve: fat suppressed with and without contrast is superior to CT in defining the extent of the tumor
3. Biopsy is not necessary to establish the diagnosis in most cases with characteristic findings on imaging studies and may result in visual loss

II. Define the risk factors

A. Increased prevalence with neurofibromatosis

B. Potential role for hormonal (estrogen) influences

III. List the differential diagnosis

- A. Other optic neuropathy (unobserved nonarteritic anterior ischemic optic neuropathy (NAION))**
- B. Optic neuritis**
 - 1. Typical course of progression over 7 to 10 days with recovery over following weeks to months
 - 2. Associated neuroradiographic findings in demyelination
- C. Sarcoidosis**
- D. Inflammatory disease of optic nerve**
 - 1. Perineuritis
 - 2. Systemic lupus erythematosus
 - 3. Therapeutic corticosteroid trial might be used to differentiate this from optic nerve sheath meningioma (ONSM)
- E. Spread of skull base meningioma**
- F. Neoplastic**
- G. Glioma (with arachnoid gliomatosis growth pattern), neurofibroma, schwannoma, lymphoproliferative**
 - 1. Nerve vs. nerve sheath
 - 2. Infiltrative optic neuropathy

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options**
 - 1. Observation may be the most appropriate therapy
- B. Describe surgical therapy options**
 - 1. Biopsy typically unnecessary
 - 2. May cause visual loss by disrupting blood flow
 - a. May be indicated in atypical cases
 - 3. Surgical debulking of tumor for disfiguring proptosis
 - a. Consider in cases with severe visual loss
 - b. Excision may be used to prevent extension to the chiasm
- C. Role of radiation**
 - 1. Consider in progressive cases
 - 2. Considered treatment of choice by most clinicians
 - 3. May improve prognosis
 - a. Improvement in vision may be seen

- b. may slow but not stop progression

V. List the complications of treatment, their prevention and management

A. Radiation effects

1. Optic neuropathy
2. Radiation retinopathy
3. Dry eye
4. Secondary tumor risk
5. Cataract development
6. Anterior segment ischemia-glaucoma
7. Rare complications

B. Avoidance of radiation effects

1. Limit radiation therapy (XRT dose)
2. Consult with radiation therapist to choose appropriate delivery model
3. Treatment of complications as necessary
4. Monitor patients during radiation period

C. Surgical risks

1. Related to approach used
2. Risks of anesthesia
3. Disruption of pial blood supply (may cause complete visual loss)
4. Cranial neuropathy
5. Cerebrospinal fluid leak
6. Spread of tumor

VI. Describe disease-related complications

A. Visual loss

B. Intracranial spread

C. Little risk for contralateral spread

D. Strabismus

E. Exposure keratopathy

VII. Describe appropriate patient instructions

- A. Appropriate patient follow-up**
- B. Scanning regimen in follow-up**
- C. Seek attention for episodes of rapid change, pain**
- D. Discussion of radiation risks**
- E. Treatment of dry eye post radiation**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Optic Nerve Disorders, 1996, p.115-121.

Orbital tumor causing neuro-ophthalmic manifestations

I. Describe the approach to establishing the diagnosis

A. Describe the etiology and epidemiology of this disease (only the most common/relevant neoplasms are listed)

1. Cavernous hemangioma
 - a. Most common benign orbital tumor of adulthood
 - b. Usually intraconal
 - c. Slow growing
 - d. Most often presents with proptosis without other findings
 - e. May be found incidentally
2. Meningioma
 - a. Most common intrinsic optic nerve tumor in adulthood
 - b. May also invade the orbit secondarily from intracranial location
 - c. More common in women
 - d. Usually benign but rarely can be malignant
3. Glioma
 - a. Most common intrinsic optic nerve tumor in childhood
 - b. May be associated with neurofibromatosis
 - c. Two distinct growth patterns
 - i. May grow within the nerve itself
 - ii. May grow primarily as arachnoid gliomatosis
 - d. May have a benign course and do not always require intervention
4. Schwannoma
 - a. Benign tumor of oligodendrocytes
 - b. In the orbit, may arise from any peripheral nerve
 - c. May have intracranial component hindering complete excision
5. Lymphoproliferative disease
 - a. MALT type lymphoma most common
 - b. May involve any or multiple orbital structures

- c. Predilection for lacrimal gland involvement
 - d. May be bilateral
- 6. Metastatic disease
 - a. Breast cancer most common in women
 - b. Lung cancer most common in men
 - c. Consider metastatic evaluation for poorly differentiated orbital tumor of unclear origin
- 7. Cutaneous tumor with secondary spread
 - a. Squamous cell carcinoma is most common via perineural invasion
 - b. Basal cell usually invades orbit directly but may also spread along sensory nerves
 - c. Melanoma
- 8. Dermoid
 - a. Common benign congenital tumor
 - b. Age
 - i. Usually recognized in childhood
 - ii. May rarely present in adulthood
 - c. Most often located adjacent the frontozygomatic suture
 - i. May have an orbital component "dumbbell lesion"
 - ii. May be located entirely within the orbit
 - d. May present as inflammatory lesion if keratin ruptures through cyst wall
- 9. Capillary hemangioma
 - a. Congenital tumor
 - b. Enlarges during first one to two years followed by involution
 - c. Amblyopia may result from a number of mechanisms
 - i. Occlusive
 - ii. Astigmatic
 - d. Intervention is usually indicated with visual compromise
- 10. Plexiform neurofibroma
 - a. Seen almost exclusively in the setting of neurofibromatosis 1
 - b. Diffusely infiltrative
- 11. Lymphangioma
 - a. Benign tumor
 - b. Composed primarily of lymphatics but may have vascular components to varying degree

- c. Features may overlap with orbital varix
- d. Spontaneous hemorrhage may occur (chocolate cyst)
- e. May enlarge with upper respiratory or other infections
- 12. Rhabdomyosarcoma
 - a. Most common soft tissue malignancy in children
 - b. May present rapidly resembling a cellulitis
 - c. Treated with radiation and chemotherapy
- 13. Neuroblastoma
 - a. May result in characteristic "raccoon eye" hemorrhage
- 14. Pleomorphic adenoma
 - a. Benign epithelial lacrimal gland neoplasm with malignant potential
 - b. Usually presents with several years history of proptosis or infra-medial globe displacement
 - c. If characteristic imaging findings are seen complete excision is indicated
 - d. Incomplete excision may increase risk of recurrent disease or malignant degeneration
- 15. Adenoid cystic carcinoma
 - a. Most common malignant epithelial tumor of the lacrimal gland
 - b. Often presents with pain due to sensory nerve invasion
- 16. Adjacent invasion from sinuses/bone structures
 - a. Mucocele/mucopyocele
 - b. Osteoma
 - c. Fibrous dysplasia
 - d. Sinus tumors
 - i. Carcinoma and adenocarcinoma
 - ii. Lymphoma

B. List the pertinent elements of the history

- 1. Blurred vision, distorted images
- 2. Painful, painless
- 3. Red desaturation, dim vision
- 4. Globe malposition
- 5. Double vision
- 6. Disease of adjacent tissue (brain, sinus, facial structures)
- 7. Numbness

8. Bloody tears
9. Headache
10. Hyperopic shift
11. Nasal congestion (chronic), epistaxis
12. Known history of other malignancy
13. Known history of genetic syndrome
14. Gaze-evoked vision loss

C. Describe pertinent clinical features

1. Optic nerve compression (abnormal acuity, afferent pupillary defect, visual loss)
2. Restrictive, paralytic, or mechanical strabismus
3. Proptosis
4. Globe dystopia
 - a. Direction of globe displacement affects differential diagnosis as it often determines anatomic region of tumor origin
5. Cranial nerve (CN) dysfunction (I, II, III, IV, V1, V2, VI)
6. Anterior segment
 - a. Chronic eyelid abnormalities or proptosis may lead to cornea exposure and scarring
7. Posterior segment abnormality (retinal striae, choroidal folds), optic nerve swelling or pallor
8. Facial deformity, eyelid deformity

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Magnetic resonance imaging (MRI) with T1 fat suppressed images with and without contrast
2. Computed tomography (CT)
3. Orbital ultrasound

II. Define the risk factors

- A. Known malignancy
- B. Genetic predisposition (xeroderma pigmentosa, neurofibromatosis, other name syndromes)
- C. Previous ocular or orbital tumor (malignant or benign)
- D. Sun exposure (eyelid tumors)
- E. Smoking and other risk factors of systemic disease which metastasize
- F. Advancing age

III. List the differential diagnosis

- A. **Nonspecific orbital inflammation (inflammatory or sclerosing)**
- B. **Vascular malformations**
- C. **Scleritis**
- D. **Carotid-cavernous fistula**
- E. **Thyroid eye disease (Graves ophthalmopathy)**
- F. **Loculated infection (abscess, tuberculosis, parasitic, acute fungal, chronic fungal)**
- G. **Orbital manifestation of systemic disease (vasculitis, sarcoidosis)**

IV. Describe the patient management in terms of treatment and follow-up

A. General principles

1. Individualized treatment and follow-up varies greatly with disease etiology
2. Treatment often requires consultation from neurosurgical, ear, nose and throat, facial plastic surgeons as well as oncologist and internists
3. Observation may be indicated for benign tumor with low likelihood of causing compressive or other damage
4. Some tumors are managed surgically: needle biopsy, excision biopsy, incisional biopsy, limited orbital approach, cranio-facial approach
5. Other lesions are best treated using radiotherapeutic techniques
6. Other lesions are best treated using chemotherapy
7. Serial monitoring (clinical, radiographic, and visual field examination)

B. Surgical management of benign lesion

1. Indication
 - a. Progressive growth documented and/or expected
 - i. Surgical removal of an asymptomatic benign lesion, while small, may be preferential to waiting until the lesion is symptomatic, when larger and likely more difficult to excise
 - b. Compressive optic neuropathy
 - c. Motility abnormalities
 - i. May result from muscle displacement, compression of innervation, or direct involvement of muscle
 - d. Proptosis
 - i. Cosmesis
 - ii. Ocular surface exposure

C. Surgical management of malignant lesion

1. Indication

- a. Diagnostic
- b. Irradiation of disease, when isolated to the orbits
- c. Palliative
 - i. Pain control
 - ii. Reduce functional consequences of tumor which parallel those outlined for benign lesions

D. Potential complications of surgery

- 1. Cosmetics
 - a. Incision related scarring
 - b. Related to soft tissue loss
 - i. Enophthalmos
 - ii. Eyelid and/or conjunctiva involvement
 - c. Disfigurement should bone be excised (and not replaced)
- 2. Ocular motility abnormality
 - a. Injury to muscles or their innervation
 - b. Displacement of muscles, through bony defects or into space previously occupied by neoplasm
 - c. Scarring with restriction to movement
- 3. Visual loss
 - a. Orbital hemorrhage
 - b. Direct injury to nerve
 - i. Related to tumor involvement
 - ii. Injury to blood supply to nerve
 - iii. Excessive intraoperative retraction or pressure on optic nerve
- 4. Failure to achieve goals of surgery

V. List the complications of treatment, their prevention and management

- A. Orbital hemorrhage**
- B. Motility disorder (mechanical or neurologic)**
- C. Ptosis**
- D. Facial sensory disturbance**
- E. Spread of tumor (local or distance metastasis)**
- F. Facial-orbital deformity**

- G. Visual loss
- H. Corneal exposure
- I. Secondary tumor, cataract, dry eye or retinopathy (chemotherapy or radiotherapy)
- J. Change in refractive error

VI. Describe disease related complications

- A. Orbital hemorrhage
- B. Motility disorder (mechanical or neurologic)
- C. Ptosis
- D. Facial sensory disturbance
- E. Spread of tumor (local or distance metastasis)
- F. Facial-orbital deformity
- G. Visual loss
- H. Corneal exposure

VII. Describe appropriate patient instructions

- A. Varies with type of lesion
- B. Report progressive loss of function, new visual symptoms, and new systemic symptoms
- C. Obtain appropriate ancillary consultation
- D. Reinforce the necessity of adequate high quality radiographic imaging

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.

Orbital hemorrhage

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Traumatic
 - a. Suspect coagulation abnormality if occurs with minor trauma
2. Anticoagulation
 - a. May contribute to hemorrhage with surgery (blepharoplasty, orbital surgery)
3. Perioperative (e.g. retrobulbar injection)
4. Orbital vascular malformation
5. Neoplasm
6. Iatrogenic (sinus and neurosurgery complication)

B. List the pertinent elements of the history

1. Proptosis
2. History of trauma
3. Prior orbital or systemic disease
4. Pain
5. Diplopia
6. Decreased vision
7. Previous similar episodes
8. Abnormal bleeding diathesis

C. Describe pertinent clinical features

1. Painful or painless
2. Proptosis
3. Conjunctival hemorrhage
4. Signs of optic neuropathy
5. Strabismus
6. IOP is reflective of orbital pressure and should be monitored

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Diagnostic tools
 - a. Computed Tomography
 - i. Usually preferred with trauma

- b. Magnetic resonance imaging
 - i. If neoplasm is suspected
- c. Serologic evaluation if coagulation disorder suspected

II. Define the risk factors

- A. Trauma**
- B. Bleeding diathesis**
- C. Underlying orbital disease**
- D. Anticoagulation**
- E. Orbital vascular anomaly**

III. List the differential diagnosis

- A. Vascular malformations without hemorrhage**
 - 1. Lymphangioma
 - 2. Venous malformations/varix
- B. Orbital cellulitis**
- C. Air in orbit**
- D. Retained foreign body**
- E. CC fistula**

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options**
 - 1. Observation
 - 2. Elevated intraocular pressure management
 - 3. Frequent re-evaluation
 - 4. Hospitalization may be indicated
 - a. Close monitoring
 - b. expedited access to surgical facilities
- B. Describe surgical therapy options**
 - 1. Lateral canthotomy/cantholysis indication
 - 2. Urgent decompression/drainage
 - 3. Surgical control of bleeding

V. List the complications of treatment, their prevention and management

A. Complications

1. Related to orbital decompression
 - a. Visual loss
 - b. Enophthalmos or other orbital deformity
 - c. Ocular misalignment
 - d. Pupillary abnormalities
2. Related to canthotomy/cantholysis
 - a. Ectropion
 - b. Scar formation

B. Prevention

1. Early intervention to prevent consequences of elevated orbital pressure
2. Appropriate observation for progression may require hospitalization

VI. Describe disease-related complications

A. Visual loss

1. Optic neuropathy
2. Central retinal artery occlusion

B. Ocular misalignment

C. Orbital ischemia/compartment syndrome/orbital infarction

D. Abnormalities related to underlying cause

VII. Describe appropriate patient instructions

A. Describe signs/symptoms of delayed postoperative hemorrhage

B. Emergent reconsultation for worsening pain, proptosis, ecchymosis, motility, or visual loss

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-Ophthalmology, 2013-2014.
2. AAO, Focal Points: Management of Orbital Trauma: Fractures, Hemorrhage, and Traumatic Optic Neuropathy, Module #7, 1994, p. 6-8.

Orbital fractures

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Blunt direct trauma
 - a. Orbital rim fractures
 - b. Medial wall fractures associated with blunt nasal impact (blow in fracture)
 - c. Tripod fractures
 - d. Le Fort
2. Indirect hydraulic blowout (e.g. medial wall and floor fractures,

B. Define the relevant aspects of epidemiology of the disease

1. High prevalence in young men

C. List the pertinent elements of the history

- a. Adults
 - b. Diplopia
 - c. Hypesthesia of cheek and upper teeth
 - d. Pain with eye movement
 - e. Malocclusion (of teeth)
 - f. Pain with jaw movement
2. Pediatric (trapdoor fractures/white-eyed blowout fracture)
 - a. Pain with eye movement
 - b. Nausea
 - c. Vasovagal symptoms (e.g. bradycardia)
 - d. Visual loss due to injury to the eye (various mechanisms) or optic nerve
 - e. diplopia

D. Describe pertinent clinical features

1. Globe dystopia
2. Exophthalmos (from edema/hemorrhage/emphysema)
3. Enophthalmos
4. Abnormal ocular motility
5. Sensory hypoesthesia
6. Facial deformity

- a. orbital rim step-off
 - b. depression of the malar eminence
- 7. Orbital emphysema
- 8. Bony sinus opacity
- 9. Associated injuries
 - a. AV fistulas (e.g. carotid cavernous fistula)
 - b. Ocular trauma
 - c. Head injury/cerebrospinal fluid (CSF) leak (especially roof fractures)
 - d. Trismus, jaw malocclusion

E. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Role of computed tomography (CT), axial/coronal images
- 2. Motility testing
- 3. Forced duction testing
- 4. Recognition of concurrent skull base fractures, trimalar fractures, jaw malocclusions
- 5. IOP to assess orbital pressure (may be elevated with hemorrhage)

F. Anatomy of orbital bones

- 1. Clinically relevant dimensions
 - a. Globe to canal: 18mm
 - b. Optic nerve: 25mm+
 - c. The length of the optic nerve allows for ocular motility and explains why optic nerve stretch is not encountered with small degrees of proptosis
- 2. Orbital roof
 - a. Injury may occur in conjunction with injury of the following structures and their contents
 - i. Landmarks
 - i) Lacrimal gland fossa
 - ii) Superior oblique tendon
 - iii) Supraorbital notch or foramen
 - ii. Adjacent structures
 - i) Frontal sinus
 - ii) Anterior cranial fossa
- 3. Lateral orbital wall
 - a. Injury may occur in conjunction with injury of the following structures and their contents
 - i. Landmarks

- i) Lateral orbital tubercle
 - ii) Zygomaticofacial foramen
 - iii) Zygomaticotemporal foramen
 - ii. Adjacent structures
 - i) Middle cranial fossa
 - ii) Temporalis fossa
- 4. Orbital floor
 - a. Injury may occur in conjunction with injury of the following structures and their contents
 - i. Landmarks within the orbit floor
 - i) Infraorbital groove, canal, foramen
 - ii. Adjacent structures
 - i) Maxillary sinus
- 5. Medial orbital wall
 - a. Injury may occur in conjunction with injury of the following structures and their contents
 - i. Landmarks
 - i) Ethmoid arteries: anterior and posterior
 - ii) Cribriform plate: level of frontoethmoid suture
 - ii. Adjacent structures
 - i) Ethmoid and sphenoid sinuses
 - ii) Nasal cavity

II. Define the risk factors

- A. Trauma (direct or indirect)**
- B. Muscle entrapment/significant diplopia in primary gaze**
- C. Muscle ischemia in trapdoor fractures**
- D. Enophthalmos with large fractures**
- E. Jaw malocclusion in trimalar fractures**
- F. Midface instability in Le-Forte fractures**

III. List the differential diagnosis

- A. Diplopia**
 - 1. Mechanic

- a. Soft tissue edema/ hemorrhage
- 2. Paretic
 - a. Traumatic cranial neuropathy
- 3. Muscle entrapment/malposition
 - a. Entrapped muscle
 - b. Displaced muscle
 - c. Severe globe malposition (enophthalmos)
- 4. Traumatic carotid-cavernous fistula

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

- 1. Observation for small fractures without entrapment
- 2. Possible role of preoperative or perioperative corticosteroids
- 3. Consider systemic antibiotics
- 4. Instruct patients not to blow their nose (avoid emphysema)
- 5. Pain management

B. Describe surgical therapy options

- 1. Indications
 - a. Enophthalmos with large fractures
 - i. More likely to develop if greater than 50% of the orbital floor is involved
 - ii. Dependent on degree of soft tissue prolapse through the fracture
 - b. Diplopia
 - i. When persists with prolonged observation
 - ii. Urgent repair is indicated for abnormal motility in the setting of a trapdoor fracture
 - c. Timing of repair
 - i. Trapdoor fractures with muscle entrapment should be repaired urgently
 - ii. The best time to repair of comminuted fractures is controversial
- 2. Repair of fracture with repositioning of entrapped tissue
 - a. May not solve motility problem
- 3. Strabismus surgery for persistent diplopia after fracture repair

V. List the complications of treatment, their prevention and management

A. Complications

1. Eyelid deformity
2. Implant migration
3. Ocular misalignment
4. Extraocular muscle damage
5. Visual loss
6. Chronic sinusitis
7. Orbital hemorrhage (compartment syndrome)
8. Hypoesthesia
9. Abnormal pupil/accommodation loss
10. Infected implant

VI. Describe disease-related complications

- A. Late enophthalmos**
- B. Persistent restrictive strabismus**
- C. Sinus disease**
- D. Jaw malocclusion**
- E. Hypoesthesia**
- F. CSF leak**

VII. Describe appropriate patient instructions

- A. Discussion of postoperative anticipated temporary worsening**
- B. Describe long term risks**
- C. Describe signs/symptoms of sinus infection**
- D. Describe signs/symptoms of postoperative hemorrhage**
- E. Emergent reconsultation for worsening motility, visual loss or pain**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 7: Orbit, Eyelids, and Lacrimal System, 2013-2014.
2. AAO, Focal Points: Management of Orbital Trauma: Fractures, Hemorrhage, and Traumatic Optic Neuropathy, Module #7, 1994, p. 2-6.

Approach to anisocoria

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Characterized by inequality in the diameter size of the 2 pupils
 - a. Disruption of the oculosympathetic pathway
 - b. Parasympathetic dysfunction in or distal to the ciliary ganglion causing diminished pupillary constriction
 - c. Pharmacologic
 - d. Dysfunction of the parasympathetic fibers of the cranial nerve (CN) III causing the pupil to be larger and poorly reactive
 - e. Physiologic (essential)
 - f. Local pupil /iris abnormality

B. List the pertinent elements of the history

1. Physiologic or essential anisocoria
 - a. Onset
 - b. Variability
2. Anisocoria secondary to Horner
 - a. Presence of pain, neck pain or headache especially, in setting of trauma
 - b. Recent neck trauma or manipulation
 - c. Other neurologic symptoms to suggest brainstem localization in central first order disease
 - d. Pulmonary or shoulder symptoms in second order disease
 - e. Headache syndrome suggestive of cluster
 - f. If associated with amaurosis fugax, assess for an ipsilateral carotid artery dissection.
3. Anisocoria secondary to Adie
 - a. Onset
 - b. Blurred near vision
4. Anisocoria secondary to third nerve palsy
 - a. Droopy eyelid
 - b. Oblique/horizontal diplopia
 - c. Headache or orbital pain
5. Pharmacologic mydriasis

- a. Exposure to systemic medications, drops or other agents that may cause a dilated pupil
- b. Occupational history

C. Define the relevant aspects of epidemiology of this disease

1. Physiologic or Essential Anisocoria
 - a. Approximately 20% of individuals have > 0.4 mm anisocoria
 - b. The amount of anisocoria and laterality of anisocoria can be variable, but is usually not greater than 1 mm
 - c. More apparent with advancing age
2. Pupil-involving CN III palsies occur in the following settings
 - a. Compression (aneurysm or tumor)
 - i. Especially posterior communicating aneurysm
 - b. Severe head trauma
 - c. Microvascular ischemia in patients with vasculopathic risk factors, although typically these are not pupil involving
 - d. Other inflammatory, infiltrative and infectious causes
3. Horner
 - a. Congenital
 - b. Early acquired (rule out neuroblastoma)
 - c. Young adult with syndrome of carotid dissection associated with minor trauma
 - d. Presenting as apical chest tumor in patient with risk factors for cancer
 - e. Idiopathic: no identifiable cause in majority
 - f. Incidence typically increases with advancing age
4. Adie
 - a. Almost all cases are idiopathic
 - b. Majority of patients are females
5. Pharmacologic
 - a. Intentional or accidental exposure

D. Describe pertinent clinical examination approach

1. Step 1 - Measure degree of anisocoria
2. Step 2 - Perform a slit lamp biomicroscopic examination to determine the presence of local structural factors as possible cause of the anisocoria
 - a. Determine if there are iris sphincter tears
 - b. Determine if there are pupillary synechiae

- c. Look for iris retroillumination defects, or areas of iris atrophy
 - d. Look for sluggish, segmental pupillary response (vermiform movements)
 - e. Gonioscopy as indicated
3. Step 3 - If a local structural factor is not identified then, examine the patient in bright and dim illumination
- a. If relative anisocoria remains the same in bright and dim lighting then, it represents physiologic or essential anisocoria
 - i. Benign condition characterized by inequality in the diameter size of the 2 pupils (usually less than 1 mm)
 - b. Both pupils react well to direct light
 - c. Both pupils dilate in the dark
 - d. Both pupils react well to near
 - e. Absence of other neurologic/eye signs or symptoms
 - i. Normal eyelid examination
 - ii. Normal motility examination
4. Step 4 - If the anisocoria is greater in dim illumination, then the miotic pupil is the abnormal pupil; and, work up for Horner syndrome is necessary (See Horner syndrome)
- a. Efferent, sympathetic mediated usually mild paralytic ptosis of upper eyelid
 - b. Efferent, sympathetic mediated usually very mild paralytic reverse ptosis of lower eyelid, causing eyelid position to be higher than other side
 - c. Variable lack of or diminished sweating (anhidrosis) on side of smaller pupil, especially in more central lesions
 - d. Lighter iris color on side of smaller pupil in congenital Horner syndrome
5. Step 5 - If the anisocoria is greater in bright illumination then the mydriatic or larger pupil is abnormal, and the clinician must consider:
- a. Adie (See Adie pupil)
 - i. Light-near dissociation
 - ii. On refixation from near to distance, pupil redilation is slow (tonic)
 - iii. Sectoral palsy of the pupillary sphincter
 - iv. Vermiform movements at slit-lamp biomicroscope
 - v. Atrophy of pupillary ruff with time
 - vi. In Adie syndrome, decreased deep tendon reflexes
 - vii. Decreased near vision unless preexisting presbyopia
 - viii. Over time, mydriasis decreases but reactivity does not recover
 - b. Third nerve palsy

- i. Pupillary dilation almost always accompanied by ptosis and limited ocular motility
- ii. Poor or no reaction of pupil to light
- iii. Mid-dilated (not widely dilated) size is typical
- iv. No light-near dissociation, i.e., poor near reaction as well
- v. Paradoxical movements (constriction of pupil with adduction or depression of eye) suggest aberrant regeneration of CN III (always from either compressive lesion or previous trauma)
- vi. Decreased accommodation and subsequent difficulty with near vision (symptomatic if pre-presbyopic)
- vii. Ptosis (incomplete or complete)
- viii. Isolated pupillary dilation
 - i) In an awake adult patient essentially never a manifestation of CN III palsy
 - ii) In a comatose patient may be due to uncal herniation, if ocular motility and eyelid position can not be assessed
- c. Pharmacologic mydriasis (See Pharmacologic mydriasis)
 - i. Isolated pupillary mydriasis
 - ii. No light or near response (anisocoria worse in light)
 - iii. Often widely dilated (> 7 mm)
 - iv. No ptosis
 - v. Normal motility

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Horner Syndrome (See Horner syndrome)
 - a. Pharmacologic testing with cocaine (4% or 10%), hydroxyamphetamine (1%), and apraclonidine (0.5% or 1%)
 - b. Imaging (Brain, neck, carotid and/or chest)
 - c. Acquired childhood Horner needs evaluation for neuroblastoma (abdominal imaging and urine catecholamines)
2. Adie Syndrome (See Adie pupil)
 - a. Dilute pilocarpine testing
3. Patients with a Large Pupil due to aneurysmal compression of pupillomotor fibers of CN III require an urgent referral
 - a. Magnetic resonance imaging (MRI) or CT of brain (stroke and tumor) and MRA or CTA to rule out aneurysm
 - b. Pupil will not constrict or show signs of denervation supersensitivity to dilute pilocarpine
4. Pharmacologic Mydriasis (See Pharmacologic mydriasis)

- a. Pharmacologic dilation by anticholinergics does not respond to 1% pilocarpine unless performed near the termination of the pharmacologic blockade, in which case there is incomplete constriction of affected pupil

II. List the differential diagnosis

- A. Adie tonic pupil
- B. Horner syndrome
- C. Cranial nerve (CN) III palsy
- D. Pharmacologic mydriasis/miosis
- E. Benign episodic pupillary mydriasis (may occur in patients with history of headaches)
- F. Previous globe/iris trauma
- G. Iris coloboma or other structural abnormality
- H. Diabetic tonic pupil (symmetric or asymmetric)

III. Describe patient management in terms of treatment and follow-up

- A. Medical therapy
 - 1. Determined based on etiology of the anisocoria
 - 2. All patients need a comprehensive eye examination with measurement of pupillary light responses in dim and bright illumination as discussed above
 - 3. Review of old photographs may be helpful
 - 4. Pharmacological testing, if indicated, to rule out other diagnoses
 - 5. Imaging, when appropriate

IV. Describe appropriate patient instructions

- A. Etiology specific
 - 1. Physiologic anisocoria
 - a. Reassurance
 - b. Report any new symptoms - diplopia, ptosis
 - 2. Adie pupil
 - a. Reassurance
 - b. Report new neurologic symptoms
 - c. Tonic pupil may become smaller over months to years
 - d. If necessary, appropriate refractive correction for near work

- e. Instillation of dilute pilocarpine to help symptomatic photosensitivity and accommodative difficulties
 - f. Colored contact lenses
- 3. Anisocoria secondary to third nerve palsy
 - a. Failure to resolve or development of aberrant regeneration findings requires further evaluation
 - b. Reassurance, if negative emergent work-up
 - c. If necessary, appropriate refractive correction for near work
 - d. Instillation of pilocarpine to help symptomatic photosensitivity and accommodative difficulties
 - e. Colored contact lenses
 - f. Follow-up clinical examination
- 4. Horner syndrome
 - a. Etiology specific
 - b. Report new neurologic symptoms
- 5. Pharmacologic mydriasis
 - a. Reassurance
 - b. Observation, expect resolution without development of any other evidence of CN III palsy

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Clinical Importance of Pupillary Inequality, Module #10, 1992, p.4.
3. AAO, Focal Points: Neuro-Ophthalmic Problems Caused by Medications, Module #11, 1998.

Pharmacologic mydriasis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Instillation into eye of anticholinergic (atropine-like) substance may cause unilateral or bilateral mydriasis
2. Systemic medications such as sympathomimetics and parasympatholytics may cause bilateral mydriasis

B. Define the relevant elements of the epidemiology of this disease

1. Intentional or accidental exposure

C. List pertinent elements of history

1. Try to identify exposure (medications or other chemicals)
 - a. Handling red top eye drops
 - b. Use of scopolamine patch
 - c. Previous treatment for iritis
 - d. Visit to the emergency room (ER)
 - e. Exposure to botanicals and anticholinergics
 - f. After cardiopulmonary resuscitation
2. Blurred near vision
3. No ptosis
4. No double vision

D. Describe pertinent clinical features

1. Isolated pupillary mydriasis and abnormal accommodation
2. No light or near response (anisocoria worse in light)
3. Often widely dilated (> 7 mm)
4. No ptosis
5. Normal motility

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Pharmacologic dilation does not respond to 1% pilocarpine unless performed near the termination of the pharmacologic blockade, in which case there is incomplete constriction of affected pupil

II. Define the risk factors

A. Handling anticholinergic medication

- B. Scopolamine patches for nausea**
- C. Handling foliage**
- D. Handling of tick and flea pesticide products**
- E. Secondary gain (intentional instillation)**
- F. Previous episodes of functional medical problems**

III. List the differential diagnosis

- A. Cranial nerve (CN) III palsy (always accompanied by some degree ophthalmoplegia plus/minus ptosis)**
- B. Tonic pupil**
- C. Widespread dysautonomia**
- D. Previous iritis/primary iris pathology/secondary iris pathology/traumatic mydriasis**
- E. Diabetes mellitus**
 - 1. Autonomic pupillary dysfunction
 - 2. Previous panretinal photocoagulation

IV. Describe appropriate patient instructions

- A. Reassurance**
- B. Observation, expect resolution without development of any other evidence of CN III palsy**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
- 2. AAO, Focal Points: Neuro-Ophthalmic Problems Caused by Medications, Module #11, 1998.

Horner syndrome

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Disruption of the oculosympathetic pathway
 - a. First order neuron
 - i. Central disorders of the nervous system or cervical disease associated with other defects
 - b. Second order neuron
 - i. Apical lung tumors (Pancoast syndrome)
 - ii. Neck mass
 - iii. Chest surgery
 - iv. Brachial plexus trauma
 - c. Third order neuron
 - i. Carotid artery dissection
 - ii. Cavernous sinus tumors

B. Define the relevant elements of the epidemiology of this disease

1. Idiopathic
 - a. No identifiable cause in majority of third order (post ganglionic)
2. Secondary
 - a. Etiology determined with appropriate use of imaging
3. Age dependent difference in the diagnosis of Horner

C. List the pertinent elements of the history

1. Different sizes of both pupils- smaller pupil
2. Drooping of upper eyelid
3. Lower eyelid higher than other side
4. Lack of facial sweating on side of smaller pupil
5. Lighter iris color on side of smaller pupil (congenital Horner)
6. Presence of facial pain, neck pain or headache, especially in setting of trauma
7. Recent neck trauma or manipulation
8. Other neurologic symptoms to suggest brainstem localization
9. Pulmonary or shoulder symptoms

10. Headache syndrome suggestive of cluster
11. Diplopia

D. Describe pertinent clinical features

1. Classic triad of ipsilateral ptosis, miosis and anhidrosis
 - a. Anisocoria greater in dim light with the affected pupil being smaller
 - b. Affected pupil demonstrates dilation lag
 - i. Anisocoria worse immediately after turning off lights than when reassessed after a delay
2. Light and near pupillary reactions are intact
3. Ptosis of upper eyelid
4. "Upside down" ptosis of lower eyelid (lower eyelid rising)
5. Anhidrosis of ipsilateral face/forehead
6. Conjunctival injection
7. Involvement of CN III, IV, V or VI localizing lesion to cavernous sinus
8. Congenital form usually due to birth trauma to brachial plexus
9. Iris heterochromia with the affected iris lighter in color in congenital Horner

E. Clinically relevant anatomic correlations

1. Sympathetic activity originates in the posterior region of the hypothalamus
2. Sympathetic fibers destined for the orbit: divided into 1st, 2nd, and 3rd order neurons
 - a. First order neuron
 - i. Posterior Hypothalamus
 - ii. Descends through brainstem to spinal cord
 - iii. Within the spinal cord sympathetic fibers synapse and exit from C8 to T2 level
 - b. Second order neuron
 - i. Exits spinal cord from C8 to T2: can be involved in brachial plexus injury in this region
 - ii. Sympathetic chain passes just above the lung apex: can be affected by Pancoast (apical lung) tumor in this location
 - iii. Ascends to synapse in the superior cervical ganglion
 - c. Third order neuron
 - i. Postganglionic third-order fibers continue in the wall of the internal carotid: can be affected in carotid artery dissection
 - ii. In the posterior cavernous sinus, sympathetic fibers destined for the pupillary dilator leave the carotid artery and join CN 6: therefore, a concurrent Horner and ipsilateral 6th nerve palsy localizes the process to the cavernous sinus

- iii. In the anterior cavernous sinus, the sympathetic fibers join the ophthalmic division of the trigeminal nerve
- iv. In the orbit, the fibers pass through the ciliary ganglion (without synapsing) and travel with the long ciliary nerves to reach the pupillary dilator
- v. Fibers destined for the Mullers muscle travel along the ophthalmic artery and subsequent branches

F. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Cocaine testing: blocks the re-uptake of norepinephrine
 - a. Confirm presence of Horner syndrome
 - b. Normal pupil will dilate; affected pupil dilates poorly or not at all
- 2. Hydroxyamphetamine testing: releases norepinephrine from presynaptic terminal
 - a. Differentiate between a pre or postganglionic lesion
 - b. Normal pupil will dilate and affected pupil will not dilate in postganglionic lesion (3rd order Horner)
 - c. Normal and affected pupil will dilate in preganglionic lesion
- 3. Apraclonidine testing: apraclonidine effect on pupillary dilator muscle is amplified by denervation hypersensitivity secondary to the upregulated postsynaptic alpha receptors
 - a. Reversal of anisocoria is interpreted as a positive test. The miotic pupil dilates, and the normal pupil constricts a little
- 4. Imaging
 - a. Brain, neck, carotid and/or chest
- 5. Acquired childhood Horner needs evaluation for neuroblastoma

II. Define the risk factors

- A. Recent history of neck trauma/surgery**
- B. Recent history of chest trauma/surgery, central line placement**
- C. History of lung cancer**
- D. Congenital due to birth trauma to the brachial plexus and acquired in childhood raises possibility of neuroblastoma**
- E. List the differential diagnosis**
- F. Physiologic (essential) anisocoria with unrelated ptosis**
- G. Adie pupil**
- H. Pharmacological mydriasis/miosis**
- I. Argyll Robertson pupil**

III. Describe patient management

A. Describe medical therapy options

1. Determined by etiology of syndrome
2. Acute management of carotid dissection since stroke is a possible complication
3. Cluster headache/migraine management
4. Stroke management when recognized
5. Tumor management when recognized
6. Apraclonidine drops can be used to reverse ptosis

B. Describe surgical therapy options

1. Consideration of ptosis surgery

IV. Describe the disease-related complications

A. Carotid dissection - stroke

B. Lung cancer

C. Otherwise based upon underlying cause

V. Describe appropriate patient instructions

A. Etiology specific

B. Report new neurologic or visual symptoms

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.

Adie pupil

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of the disease

1. Parasympathetic dysfunction in or distal to ciliary ganglion causing diminished pupillary constriction to light

B. List the pertinent elements of the history

1. Large pupil with patient occasionally complaining of light sensitivity
2. Loss of accommodation with decreased near vision
3. No diplopia or ptosis

C. Define the relevant elements of the epidemiology of this disease

1. Almost all cases are idiopathic
2. Majority of patients are females

D. Describe pertinent clinical features

1. Large pupil
2. Anisocoria is greatest in light
3. Light-near dissociation
4. The near response is tonic as the pupil will constrict to near effort with a slow tonic constriction while accommodative response and pupillary redilation are tonic upon resuming distance fixation, therefore involved pupil maybe the smaller pupil if patient was reading just prior to your exam
5. Sectoral palsy of the pupillary sphincter
 - a. Vermiform movements at slit-lamp biomicroscope
 - b. Atrophy of pupillary ruff with time
6. In Adie syndrome, decreased deep tendon reflexes are present
7. Decreased near vision unless preexisting presbyopia
8. Over time, mydriasis decreases but reactivity does not recover

E. Clinically relevant anatomic correlations

1. Adie tonic pupil arises from damage to the postsynaptic parasympathetic fibers arising from the ciliary ganglion
2. There are a significantly greater number of fibers associated with accommodation innervating the ciliary body as there are fibers destined for the pupillary sphincter
 - a. This preponderance of accommodative fibers may be one of the reasons for development of light-near dissociation after aberrant regeneration of the postsynaptic accommodative fibers to the pupillary sphincter

3. The postsynaptic parasympathetic fibers travel with the nerve to the inferior oblique muscle to join the posterior ciliary nerves to reach the pupillary sphincter

F. Describe appropriate testing and evaluation for establishing the diagnosis

1. Dilute pilocarpine testing
 - a. Denervation supersensitivity -- dilute pilocarpine constricts pupil
 - b. Test will be negative acutely before supersensitivity develops

II. Define the risk factors

- A. The presence of a contralateral Adie pupil
- B. Systemic dysautonomias
- C. Other neurologic disorders (rare)

III. List the differential diagnosis

- A. Essential anisocoria
- B. Horner syndrome (contralateral eye)
- C. Dorsal midbrain syndrome (differentiate from bilateral Adie pupil)
- D. Pharmacological mydriasis/miosis
- E. Widespread (systemic dysautonomia)
- F. Previous iritis
- G. Diabetes mellitus
 1. Autonomic pupillary dysfunction
 2. Previous panretinal photocoagulation
- H. Cranial nerve (CN) III palsy
- I. Iris atrophy
- J. Tonic pupils
 1. Recent history of orbit trauma/surgery
 2. Panretinal photocoagulation (PRP)

IV. Describe patient management

- A. Dilute Pilocarpine for miosis if light sensitive
- B. Reading prescription for near vision may be asymmetric (stronger on Adie side)
- C. Tinted lenses
- D. Colored contact lenses

V. Describe appropriate patient instructions

- A. Reassurance**
- B. Report any double vision or ptosis**
- C. Tonic pupil may become smaller over months to years**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Clinical Importance of Pupillary Inequality, Module #10, 1992, p.4.

Relative afferent pupillary defect

I. Describe the approach to establishing the diagnosis

A. Describe etiology of the disease

1. Hallmark of unilateral or asymmetric optic nerve disease
 - a. Relative difference in midbrain light input because of unilateral or asymmetric optic nerve dysfunction results in difference between direct and indirect or consensual light reflex
2. Large macular lesions or other extensive retinal disorders (e.g.. retinal detachment)
3. Asymmetric chiasmal disease
4. Optic tract or lateral geniculate lesions
5. Relative afferent pupillary defect may be contralateral in optic tract syndromes
6. Amblyopia (usually low magnitude)

B. Define the relevant elements of the epidemiology of this disease

1. Specific for each optic nerve disorder

C. List the pertinent aspects of the history

1. Specific for each optic nerve disorder
2. Complaints of decreased vision may be present, highlighted by:
 - a. Reduced brightness sense
 - b. Diminished color vision
 - c. Visual field loss

D. Describe pertinent clinical features

1. This is best demonstrated by the swinging flashlight test in which pupillary escape or early redilation (of either pupil) is demonstrated when a light is brought to the eye with the afferent defect and constriction (of either pupil) occurs when the light is returned to the "good" eye

E. Clinically relevant anatomic correlations

1. Afferent limb of pupillary light reflex
 - a. Optic nerve
 - b. Hemidecussation of fibers at optic chiasm
 - c. Optic tract: pupillary tract fibers leave optic tract in the brachium of the superior colliculus just prior to the lateral geniculate nucleus
 - d. Pretectal nucleus
 - e. Bilateral Edinger-Westphal nuclei
 - i. Ipsilateral

- ii. Contralateral via posterior commissure
- 2. Efferent limb of pupillary light reflex
 - a. Edinger-Westphal nucleus (part of CN III nuclear complex in midbrain)
 - b. CN III (pupil fibers run in the medial superficial surface)
 - c. Inferior division of CN III
 - d. Ciliary ganglion (synapse)
 - e. Postsynaptic fibers travel with the nerve to the inferior oblique
 - f. Posterior ciliary nerves
 - g. Pupillary sphincter muscle

F. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Swinging flashlight test
 - a. The affected eye's pupillary response is less brisk than the unaffected eye
- 2. Quantification with neutral density filters
 - a. Neutral density filters are placed in front of the "good" eye and the swinging flashlight test is performed. Increasing amounts of neutral density filters are added until the RAPD is no longer observed with the swinging flashlight test
- 3. A relative afferent defect can still be detected in the presence of a unilateral efferent defect (i.e., in an immobile or obscured pupil) by comparing the consensual pupillary response from contralateral light stimulation to the direct pupillary response from ipsilateral light stimulation

II. Define the risk factors

- A. The magnitude of the RAPD does not necessarily correlate with the loss of visual acuity**

III. List the differential diagnosis

- A. Unilateral or asymmetrical optic nerve disease**
- B. Severe retinal disease**
- C. Asymmetric chiasmal disease**
- D. Optic tract syndrome**
- E. Occasionally seen with amblyopia**

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
- 2. AAO, Optic Nerve Disorders, 1996; 44,56,126,186.
- 3. Enyedi LB, Dev S, Cox TA. A comparison of the Marcus Gunn and alternating light tests for

afferent papillary defects. *Ophthalmology* 1998;105:871-3.

Thromboembolic phenomena

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Atherosclerotic disease
 - a. Carotid - plaque, and/or bruit
 - b. Cardiac - valvular or mural thrombus
 - c. Aortic arch disease
2. Hypercoagulable states (genetic vs acquired)
3. Other
 - a. Surgery
 - b. Venous stasis
 - c. Right-to-left cardiac shunt
 - d. Intravenous drug use

B. Define the relevant aspects of epidemiology of the disease

1. Family history of thrombosis
2. Previous episodes of thrombosis in other territory

C. List the pertinent elements of the history

1. Acute neurologic deficit or visual loss
2. Monocular visual loss suggests ocular ischemia
3. Binocular visual loss or homonymous visual field defect, suggests retrochiasmal ischemia in carotid or vertebrobasilar territory
 - a. with vertebrobasilar territory, may have other symptoms related to posterior circulation deficit - such as dizziness or diplopia

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Extent of laboratory work-up varies with patient's clinical presentations (venous vs arterial thrombosis), site of thrombosis (large vs. small vessel), patient's characteristics and family history
2. Referral to appropriate medical specialist for evaluation and treatment of any underlying disorders and diseases

II. Define the risk factors

A. Family history of thrombosis

B. Personal history of thrombosis

- C. Pregnancy or postpartum state
- D. Oral contraceptives
- E. Smoking
- F. Surgery, trauma, travel
- G. Advancing age
- H. Hyperlipidemia
- I. Diabetes
- J. Hypertension
- K. Intravenous drug use
- L. Hematologic diseases predisposing to thromboembolism

III. List the differential diagnosis

- A. Other causes of vascular disease (embolic, vasculitis, atheroma, etc.)

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Anticoagulants vs antiplatelets
2. Short term or prolonged
3. Depends on the type of thrombosis and work-up
4. Prevention of pulmonary embolism
5. Discontinue oral contraceptive
6. Prevention of thrombosis during pregnancy or postpartum state
7. Smoking cessation
8. Treat hyperlipidemia
9. Control diabetes
10. Control hypertension

B. Describe surgical therapy options

1. Clot lysis in situ (endovascular approach)
2. Treat underlying cardiac disorder - dysrhythmia, mural thrombus, valvular disease
3. Consider carotid endarterectomy in cases of significant ipsilateral carotid stenosis
4. Prevention of pulmonary embolism depending on site of clot

V. List the complications of treatment, their prevention and management

- A. Complications of anticoagulants and antiplatelets
- B. Complications of intravascular surgery (e.g. stroke, death)

VI. Describe disease-related complications

- A. Propagation of clot
- B. Recurrent thrombosis
- C. Pulmonary embolism

VII. Describe appropriate patient instructions

- A. Risk factor modification
- B. Genetic counseling where appropriate

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.

Cerebrovascular disease/stroke

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Ischemic (embolic or hypoperfusion) vs. hemorrhagic (intraparenchymal, subarachnoid, subdural, or epidural)
2. Arterial vs. venous -

B. Define the relevant aspects of epidemiology of the disease

1. Typically an elderly patient with atheromatous disease, cardiac disease, or atrial fibrillation
2. In young patients, suspect arterial dissection or coagulopathy

C. List the pertinent elements of the history

1. Acute neurologic deficit or visual loss
 - a. Patients with posterior ischemic cerebrovascular accident (CVA) may only have visual field loss and may not be acutely aware of visual field defect
2. If monocular visual loss, suggests ocular ischemia in the ipsilateral carotid territory (or anterior calcarine disease)
3. If binocular visual loss or homonymous hemifield defect, suggests retrochiasmal lesion either in carotid or vertebrobasilar territory
4. Headache common in hemorrhagic stroke
5. Headache also common if arterial dissection, vertebrobasilar infarction or venous disease
6. Blood pressure, palpitations
7. consider giant cell arteritis in the elderly
8. Facial pain or trauma with dissection

D. Blood supply of the brain

1. Anterior (carotid circulation)
 - a. Anterior visual pathway and optic radiations
2. Posterior (vertebral circulation)
 - a. Posterior visual pathway and occipital cortex
 - b. Brainstem (including cranial nerve nuclei)
3. Collateral circulation
 - a. Circle of Willis

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. If retinal ischemia

- a. Dilated fundus examination looking for emboli
 - b. Fluorescein angiography
2. Consider CT, CTA, MRI with diffusion weighted images (DWI), or MRA
3. Carotid and vertebral ultrasonography and transcranial Doppler are very helpful but are not adequate to definitively rule out disease
4. Conventional angiography only obtained preoperatively or in special circumstances to be determined by stroke neurologist
5. Cardiac evaluation, electrocardiogram, event monitor/Holter monitor
6. Transesophageal echocardiogram for cardiac and proximal large vessel atheroma, valvular disease or intracardiac clot
7. Evaluate for cardiovascular risk factors
8. Look for giant cell arteritis if elderly (especially with amaurosis fugax)
 - a. Erythrocyte sedimentation rate
 - b. C-reactive protein
 - c. Complete blood count, platelet evaluation
 - d. Possible temporal artery biopsy
9. Look for ocular ischemic syndrome if severe carotid occlusive disease
 - a. Mid peripheral dot-and-blot retinal hemorrhages
 - b. Ocular hypotension
 - c. Anterior chamber cells
 - d. Rubeosis
 - e. Corneal edema

II. Define the risk factors

A. Atheroma is most common cause of cerebrovascular disease

1. Age
2. Systemic hypertension
3. Tobacco
4. Dyslipidemia
5. Diabetes mellitus
6. Hyperhomocysteinemia
7. Obesity

B. Cardiac disease

1. Embolic disease
2. Dysrhythmia

C. Hypercoagulable states

III. List the differential diagnosis

- A. Any acute or fluctuating neurologic disease (multiple sclerosis, migraine, seizures)**
- B. If transient monocular visual loss presumed of vascular mechanism, transient visual obscurations from:**
1. Optic nerve head anomalies
 2. Orbital tumors
 3. Subacute angle closure glaucoma
 4. Dry eye syndrome
 5. Keratoconus
 6. Hyphema
 7. Serous retinal detachment

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options**
1. Consult appropriate medical specialist regarding anticoagulation, antiplatelets, thrombolysis, secondary prevention, risk factor modification
- B. Describe surgical therapy options**
1. Carotid endarterectomy
 2. Carotid or vertebral angioplasty/stenting
 3. Vena Caval filters

V. List the complications of treatment, their prevention and management

- A. Thrombolysis, anticoagulants and antiplatelet agents**
1. Bleeding
- B. Surgery**
1. Directly related surgical complications
 2. CVA
 3. Myocardial infarction

VI. Describe disease-related complications

- A. Other localization of atheroma (coronary artery disease), peripheral vascular disease**
- B. Blindness if ocular stroke**
- C. Ocular ischemic syndrome**

VII. Describe appropriate patient instructions

- A. Secondary prevention**
- B. Referral to stroke neurologist**
- C. Consult if transient ischemic attacks/transient visual loss**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Neuro-Ophthalmic Complications of Cardiac Surgery, Module #6, 2001.
3. Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, Bushnell CD, Culebras A, DeGraba TJ, Gorelick PB, Guyton JR, Hart RG, Howard G, Kelly-Hayes M, Nixon JV, Sacco RL; American Heart Association; American Stroke Association Stroke Council. Primary prevention of ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council: cosponsored by the Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Stroke* 2006; 37: 1583-1633.
4. Sacco RL, Adams R, Albers G, Alberts MJ, Benavente O, Furie K, Goldstein LB, Gorelick P, Halperin J, Harbaugh R, Johnston SC, Katzan I, Kelly-Hayes M, Kenton EJ, Marks M, Schwamm LH, Tomsick T; American Heart Association/American Stroke Association Council on Stroke; Council on Cardiovascular Radiology and Intervention; American Academy of Neurology. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke: co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. *Stroke* 2006; 37: 577-617.

Cerebral aneurysms

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Defects in arterial wall
2. Congenital predisposition, but aneurysms are acquired lesions

B. Define the relevant aspects of epidemiology of the disease

1. Most common in middle aged females
2. May present with neuro-ophthalmic symptoms and signs alone or in combination with other neurological symptoms
3. Risk of rupture varies depending on age, size of aneurysm, location, family history and clinical presentation
 - a. Risk to be estimated by neurosurgeon/neurologist/interventional neuroradiologist with expertise with aneurysms

C. List the pertinent elements of the history

1. Sudden headache suggesting subarachnoid hemorrhage
2. Diplopia - cranial nerve (CN) palsies
 - a. CN III pupil involving palsy classic for posterior communicating, posterior cerebral or superior cerebellar artery aneurysm) -
 - b. CN VI - cavernous sinus aneurysm
 - c. CN IV - rare with aneurysm
3. Visual loss may occur if there is compression of visual pathway

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Computerized tomography (CT) without contrast to diagnose subarachnoid hemorrhage
2. Lumbar puncture to confirm subarachnoid hemorrhage if not seen on scan
3. May be seen on head CT or magnetic resonance imaging with contrast
4. Magnetic resonance angiography (MRA) and computerized tomographic angiography (CTA) often helpful, sometimes in combination
5. Conventional catheter angiography remains the gold standard
 - a. To be obtained if MRA and/or CTA negative and clinical suspicion high
 - b. Done at the time of treatment if endovascular treatment planned and MRA or CTA positive

II. Define the risk factors

- A. Family history
- B. Trauma (dissection)
- C. Polycystic kidney disease
- D. Elastic tissue disease (e.g. Ehlers Danlos)

III. List the differential diagnosis

- A. All causes of headache
- B. All causes of CN palsies
- C. All causes of optic neuropathies
- D. Other causes of homonymous hemianopia (e.g. migraine)

IV. Describe patient management in terms of treatment and follow-up

- A. Describe medical therapy options
 - 1. Treat symptom (diplopia, headache)
 - 2. Management of subarachnoid hemorrhage, vasospasm
 - 3. Recognize Terson syndrome if subarachnoid hemorrhage
 - 4. Genetic counseling
 - 5. Monitor sensory afferent and motor efferent vision abnormalities
- B. Describe surgical therapy options
 - 1. Endovascular treatment (e.g. coils)
 - 2. surgical clipping

V. List the complications of treatment, their prevention and management

- A. Aneurysmal rupture
- B. Stroke
- C. Cranial nerve compression (diplopia, optic neuropathy)
- D. Visual field defect
- E. Recurrence (incomplete occlusion)
- F. Death

VI. Describe disease-related complications

- A. Rupture with devastating subarachnoid hemorrhage
- B. Terson syndrome if rupture

- C. Spasm with ischemic stroke
- D. Compression (cranial nerves, brain parenchyma) if unruptured
- E. Pain, headache
- F. Death

VII. Describe appropriate patient instructions

- A. Genetic counseling in familial aneurysms
- B. Precautions if aneurysm left untreated (risk of rupture with Valsalva, trauma)

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Optic Nerve Disorders, 1996, p.91, 119-128.
3. Brisman JL, Song JK, Newell DW. Cerebral aneurysms. *N Engl J Med* 2006;355:928-39.

Dissecting aneurysms

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Trauma (neck rotation, cervical manipulation, etc.)
2. Elastic tissue disease (Ehlers Danlos syndrome, Marfan syndrome, fibromuscular dysplasia)

B. Define the relevant aspects of the epidemiology of the disease

1. common cause of ischemic stroke in young patients

C. List the pertinent elements of the history

1. Sequence of "trauma - pain - stroke" is highly suggestive
2. Painful postganglionic Horner syndrome or Horner with amaurosis fugax are suggestive of carotid dissection
3. Alterations in taste sensation (lower cranial nerve dysfunction)
4. Facial and/or neck pain

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Ultrasound, MRI, MRA, CTA, &/or conventional catheter angiogram of the carotid circulation

II. Define the risk factors

A. Trauma

B. Elastic tissue disease

C. Association with migraine

III. List the differential diagnosis

A. Any cause of stroke

B. Acute painful Horner syndrome is considered a carotid dissection until proven otherwise

C. Certain migraine syndromes such as cluster headache

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. consult with appropriate medical specialist regarding anticoagulation

B. Describe surgical therapy options

1. possible angioplasty or arterial stenting

V. List the complications of medical treatment, their prevention and management

A. Anticoagulants and antiplatelets

1. Bleeding

B. Angioplasty/Stenting

1. Procedure related complications

VI. Describe the disease-related complications

A. Cerebral infarction

B. Retinal or optic nerve or arterial ischemia

C. Horner syndrome

D. Development of a pseudoaneurysm

E. Chronic carotid or vertebral artery occlusion

F. Poorer prognosis if intracranial dissection

VII. Describe appropriate patient instructions

A. Avoid cervical manipulations

B. Consult if recurrent pain or neurologic symptoms develop

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Optic Nerve Disorders, 1996, p.91, 119-128.
3. Biousse V, Touboul PJ, D'Anglejan-Chatillon J, Levy C, Schaison M, Bousser MG. Neuro-ophthalmological manifestations of internal carotid artery dissections: a series of 146 patients. *Am J Ophthalmol.* 1998;126:565-577.

Cerebral venous sinus thrombosis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Occlusion of a venous sinus or cortical vein secondary to
 - a. Trauma, surgery
 - b. Hypercoagulable states (genetic and acquired)
 - c. mass lesion causing secondary compression of venous outflow
 - d. Infection e.g. otitis
 - e. Vasculitis e.g. Behçet disease

B. Define the relevant aspects of epidemiology of the disease

1. Occurs at any age
2. Often overlooked

C. List the pertinent elements of the history

1. Headache
2. Any focal neurologic symptoms and signs
3. Seizures
4. Confusion, coma
5. Symptoms of raised intracranial pressure - headache, pulse-synchronous tinnitus, transient visual obscurations

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. CT, MRI, MRV, catheter venogram
2. Lumbar puncture to measure the cerebrospinal fluid (CSF) opening pressure and analyze the CSF
3. Extensive etiological work-up if diagnosis confirmed

II. List the differential diagnosis

A. Any cause of stroke, seizures, coma

B. Any cause of raised intracranial pressure (ICP)

1. venous sinus thrombosis should be considered when diagnosing idiopathic intracranial hypertension

III. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Close observation
2. Anticoagulation
3. Thrombolysis
4. Treat seizures
5. Treat raised ICP
6. Follow visual function
 - a. Treat underlying disorders

B. Describe surgical therapy options

1. Ventricular drainage if hydrocephalus
2. optic nerve sheath fenestration if visual loss from papilledema

IV. List the complications of treatment, their prevention and management

A. Fibrinolytics, anticoagulants and antiplatelet agents

1. Bleeding

V. Describe disease-related complications

- A. Cerebral infarction, cerebral hemorrhage**
- B. Death**
- C. Pulmonary embolism**
- D. Seizures**
- E. Raised ICP**
- F. Visual loss from papilledema**

VI. Describe appropriate patient instructions

- A. Discontinue oral contraceptive**
- B. Consult physician if recurrent headache**
- C. Precautions during pregnancy and post-partum state**
- D. Monitor visual function (formal visual fields)**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-Ophthalmology, 2013-2014.
2. Ferro JM, Lopes GC, Rosas MJ. Do randomized clinical trials influence practice? The example of

cerebral vein and dural sinus thrombosis. *J Neurol.* 2002;249:1595-6.

Dural cavernous fistula and traumatic carotid cavernous fistula

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Direct fistula/high flow (trauma, rupture of carotid cavernous aneurysm, elastic tissue disease)
2. Indirect fistula/low flow (spontaneous, postmenopausal women)

B. Define the relevant aspects of epidemiology of the disease

1. Majority of direct carotid cavernous fistula (CCF) from trauma
2. Majority of indirect DCF are insidious

C. List the pertinent elements of the history and clinical examination

1. Headache, orbital pain
2. Orbital bruit
3. Proptosis
4. Red eye (arterialization of episcleral vessels)
5. Decreased vision
6. diplopia/ophthalmoplegia
7. Elevated intraocular pressure (IOP) with increased pulse pressure
8. Retinal hemorrhages, venous engorgement, optic disc edema
9. Fistula may be contralateral to signs/symptoms
10. Chemosis

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. CT, CTA, MRI, MRA
2. Orbital ultrasound - enlarged superior ophthalmic vein and/or extraocular muscles (reversal of flow in superior ophthalmic vein)
3. Conventional angiography is gold standard

II. Define the risk factors

A. Trauma

B. Hypertension

C. Elastic tissue diseases

D. Cavernous sinus aneurysm

III. List the differential diagnosis

A. Orbital process

1. Thyroid eye disease
2. Myositis (orbital pseudotumor)
3. Tumor

B. Cavernous sinus thrombosis or cavernous sinus infiltrative process/neoplasm/infection

C. Chronic conjunctivitis

IV. Describe patient management in terms of treatment and follow-up

A. Describe medical therapy options

1. Treat corneal exposure
2. Treat elevated IOP
3. Correct diplopia
 - a. Occlusion
 - b. Prism
 - c. Muscle surgery when stable

B. Describe surgical therapy options

1. Endovascular treatment of the CCF
2. Surgical treatment if endovascular treatment fails

C. Indications for treatment

1. Absolute
 - a. Cortical venous hypertension
 - b. Progressive optic neuropathy
2. Relative
 - a. Intractable ophthalmoplegia
 - b. Intractable chemosis/exposure keratopathy
 - c. Uncontrolled glaucoma
 - d. Central retinal vein occlusion

V. List the complications of treatment, their prevention and management

A. Aneurysm, stroke, recurrence, cranial nerve palsy with diplopia

VI. Describe disease-related complications

- A. Visual loss (corneal exposure, corneal edema, glaucoma, central retinal vein occlusion, vitreous hemorrhage, proliferative retinopathy, optic neuropathy, exudative retinal detachment, choroidal effusion)**
- B. Diplopia**
- C. Intractable pain**
- D. Intracranial hemorrhage**

VII. Describe appropriate patient instructions

- A. Refer to an appropriate medical specialist for diagnosis and treatment**
- B. Ophthalmologic follow-up to manage ocular complications**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.

Ocular ischemic syndrome

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Reduced blood flow to the eye (or orbit) resulting in ischemia

B. Define the relevant aspects of epidemiology of the disease

1. Any patient with a disorder resulting in poor vascular perfusion to the eye and adnexal structures
2. Usually seen in the elderly

C. List the pertinent elements of the history

1. Slowly progressive unilateral loss of vision
2. Peri-ocular, peri-orbital or facial pain, from trigeminal ischemia, iritis or elevated IOP
3. Transient visual loss often after viewing a bright light (light induced amaurosis)

D. Dilated episcleral vessels rather than ciliary flush

1. Anterior chamber low grade cell and flare
2. Iris neovascularization (a late finding)
3. Corneal edema
4. Low intraocular pressure due to ciliary body hypoperfusion or later neovascular glaucoma.
5. Asymmetric cataracts
6. Hypotensive retinopathy, "venous stasis retinopathy"
 - a. Narrowed retinal arteries
 - b. Dilated and irregular retinal veins without tortuosity
 - c. Mid-peripheral retinal hemorrhages unlike CRVO
 - d. NVD, NVE (neovascularization of the disc or elsewhere) in some
 - e. Spontaneous arterial pulsations

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Intravenous fluorescein angiography shows delayed transit time
2. Doppler duplex ultrasonography of carotid artery system, Magnetic resonance or CT angiography of carotid artery system
3. Medical evaluation for cerebral and cardiovascular disease, giant cell arteritis and vasculitis and possible invasive angiography

II. Define the risk factors

- A. Ipsilateral internal carotid artery atherosclerosis often associated with**
 - 1. Hypertension
 - 2. Diabetes mellitus
 - 3. Tobacco use
 - 4. Hyperlipidemia
- B. If normal internal carotids consider ophthalmic artery common carotid or aortic arch disease**
- C. Vasculitis and vascular disorders**
 - 1. Giant cell arteritis
 - 2. Takayasu disease
 - 3. Carotid dissection
 - 4. Radiation therapy
 - 5. other rare disorders
- D. External compression of the eye, orbit, neck**

III. List the differential diagnosis

- A. Nongranulomatous anterior uveitis**
- B. Central retinal vein occlusion**
- C. Diabetic retinopathy**

IV. Describe patient management in terms of treatment and follow-up

- A. Describe the natural history, outcome and prognosis**
 - 1. Most patients end up with poor visual acuity
 - 2. High risk of cerebrovascular events and ischemic heart disease
- B. Describe medical therapy options**
 - 1. Control of intraocular inflammation and pain
 - 2. Control of raised intraocular pressure
 - 3. Treatment of underlying vasculitis
 - 4. Antiplatelet or anticoagulation therapy
 - 5. Evaluation and management of cardiovascular and cerebrovascular comorbidities
- C. Describe surgical therapy options**
 - 1. Glaucoma surgery
 - 2. Carotid endarterectomy- to treat carotid disease but not necessarily the ocular ischemic syndrome

V. List the complications of treatment, their prevention and management

- A. Bleeding from antiplatelet or anticoagulation therapy**
- B. Cerebrovascular accident or death from carotid endarterectomy**
- C. Sudden severe intraocular pressure elevation after carotid revascularization**

VI. Describe disease-related complications

- A. Visual loss**
- B. Blind, painful eye**
- C. Cerebrovascular disease**
- D. Ischemic heart disease**

VII. Describe appropriate patient instructions

- A. Seek medical attention for increase in ocular redness, ocular pain or decline in vision**
- B. Modify systemic ischemic risk factors**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-Ophthalmology, 2013-2014.
2. Chen CS, Miller NR. Ocular ischemic syndrome: review of clinical presentations, etiology, investigation and management. *Comp Ophthalmol Update* 2007;8:17-28.
3. Mizener JB, Podhajsky P, Hayreh SS. Ocular ischemic syndrome. *Ophthalmology* 1997;104:859-864.

Cavernous sinus syndrome

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Neoplastic i.e. meningioma, pituitary adenoma, apoplexy, lymphoma
2. Trans neural tumor spread (from orbit, skin, sinuses)
 - a. Squamous cell carcinoma
 - b. Adenoid cystic carcinoma
3. Inflammatory
 - a. Nonspecific granulomatous (Tolosa-Hunt syndrome)
 - b. Sarcoidosis
 - c. Septic cavernous sinus thrombosis
4. Infectious
 - a. Bacterial meningitis
 - b. Herpes zoster (vasculitic)
 - c. Cavernous sinus thrombosis
5. Vascular
 - a. Cavernous carotid aneurysm
 - b. Carotid-cavernous fistula

B. Define the relevant aspects of the epidemiology of the disease

1. Meningioma is common benign tumor seen in this location, which is most frequently seen in middle aged women
2. Thrombosis
 - a. Hypercoagulable state
 - b. Infection of skull base, leptomeninges or sinuses

C. List the pertinent elements of the history

1. Double vision
2. Pain
 - a. Headache
 - b. Retrobulbar
3. Facial numbness
4. Sensory loss in Cranial Nerve (CN) V1 and, sometimes, CN V2

5. Anisocoria
6. Ptosis
7. Subjective bruit (e.g., 'swishing sound')

D. Describe pertinent clinical features

1. "Cavernous sinus syndrome"
 - a. Combination of ocular motor palsies from involvement of multiple cranial nerves in close proximity in the cavernous sinus
 - i. Oculomotor (CN III)
 - ii. Trochlear (CN IV)
 - iii. Abducens (CN VI) most commonly involved as it is not in dural wall of the cavernous sinus but rather surrounded by venous blood
 - b. Sensory loss (trigeminal CN V)
 - i. Ophthalmic division
 - ii. Maxillary division
 - iii. Mandibular division (extra-cavernous)
 - c. Sympathetic denervation (Horner syndrome)
 - i. Ptosis
 - ii. Miosis
 - d. Increased intraocular pressure from orbital venous outflow obstruction
2. Special syndromes
 - a. Primary aberrant regeneration of CN III implies slowly expanding lesion compressing the nerve
 - i. Thus by definition does not have preceding acute CN III palsy
 - ii. Sign of aberrant regeneration
 - i) Lid elevation with adduction and depression
 - ii) Miosis with elevation, adduction, or depression
 - iii) Co-contraction of superior and inferior rectus with persistent limitation of vertical gaze
 - iii. Think meningioma, aneurysm
 - b. Combination of CN VI palsy and ipsilateral Horner syndrome
3. Diagnosis carotid cavernous fistula
 - a. Increased ocular pulse pressure
 - b. May have asymmetric elevation of IOP if unilateral
 - c. Episcleral vessel prominence

- d. Chemosis
- e. Proptosis
- f. Bruit
- g. Blood in Schlemm canal

E. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Imaging
 - a. Magnetic resonance imaging (MRI)
 - b. Computerized tomography (CT)
 - c. Angiography to determine the vascular pattern of the fistula and in planning endovascular treatment options
 - i. Computerized tomographic angiography (CTA)
 - ii. Magnetic resonance angiography (MRA)
 - iii. Digital angiography if indicated

II. Define the risk factors

- A. Previous history of meningioma
- B. Closed head injury
- C. Known primary malignancy

III. List the differential diagnosis

- A. Orbital apex syndrome would show
 - 1. Optic neuropathy
 - 2. Proptosis
- B. Basilar meningitis affecting multiple cranial nerves
- C. Other causes of multiple cranial nerve palsies (brainstem syndrome, zoster, Lyme, sarcoid)

IV. Describe patient management in terms of treatment and follow-up

- A. Diplopia
 - 1. Acute
 - a. Occlusion
 - b. Prism
 - 2. Chronic
 - a. Establish stability

- b. Prism
- c. Extraocular muscle surgery

B. Neoplasia

- 1. Establish a diagnosis
 - a. Specific imaging characteristics
 - b. Biopsy
- 2. Surgical excision
- 3. Radiation therapy if appropriate
- 4. Chemotherapy if needed

C. Carotid cavernous fistula

- 1. Vascular embolization
- 2. Observation
- 3. Other forms of therapy available based on anatomic abnormality

D. Inflammatory lesions

- 1. Corticosteroids
- 2. Corticosteroid-sparing agents
- 3. Antivirals
- 4. Radiation therapy

E. Cavernous sinus thrombosis

- 1. Antibiotics
- 2. Antifungal agents
- 3. Anticoagulation

V. Complications of treatment

- A. Worsening of diplopia
- B. Optic neuropathy
- C. Ocular ischemic syndrome

VI. Describe disease-related complications

- A. Sequelae of progression of the specific etiology

VII. Describe appropriate patient instructions

- A. Immediately report worsening ocular inflammation**
- B. Report decrease in vision**
- C. Monitor change in diplopia**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Third, Fourth and Sixth Cranial Nerve Palsies, Module #8, 1996, p.2.
3. AAO, Focal Points: Orbital Cellulitis, Module #11, 1991, p. 4-5.

Multiple cranial nerve palsies

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Skull base pathology
 - a. Neoplastic
 - i. Cavernous sinus
 - i) Meningioma
 - ii) Schwannoma
 - iii) Chordoma/chondrosarcoma
 - iv) Pituitary adenoma
 - v) Other rare primary tumor
 - vi) Metastatic
 - (i) Hematologic
 - (ii) Neurotrophic
 - (a) Squamous cell
 - (b) Adenoid cystic carcinoma
 - (iii) Direct extension
 - ii. Clivus
 - i) Meningioma
 - ii) Chordoma
 - iii) Chondrosarcoma
 - iv) Nasopharyngeal carcinoma
 - iii. Lymphoproliferative
 - i) Lymphoma
 - ii) Leukemia
 - b. Inflammatory
 - i. Nonspecific granulomatous (Tolosa-Hunt syndrome)
 - ii. Sarcoidosis
 - iii. Other rare inflammations
 - c. Infectious

- i. Meningitis including tubercular, viral and other bacterial
 - ii. Herpes zoster
 - iii. Lyme disease
 - iv. Cavernous sinus thrombosis
 - v. Fungal infection
 - i) Aspergillus
 - ii) Mucor
 - d. Vascular
 - i. Midbrain and thalamic hemorrhage
 - ii. Carotid cavernous aneurysm
 - iii. Carotid-cavernous fistula
 - iv. Venous occlusive disease
- 2. Traumatic
- 3. Miller Fisher variant Guillain-Barré
- 4. Metabolic
 - a. Wernicke
 - i. Thiamine deficiency
 - ii. Mental status change
 - iii. Autonomic instability
 - iv. Supranuclear eye movement abnormality
 - v. Nystagmus
- 5. Congenital
- 6. Multicentric infiltrative
 - a. Glioma
 - b. Metastatic disease
 - c. Carcinomatous meningitis
- 7. Demyelinating disease

B. List the pertinent elements of the history

- 1. Diplopia
- 2. Pain
- 3. Numbness
- 4. Signs or symptoms specific to the cranial nerve involved

C. Describe pertinent clinical features

1. Ocular misalignment
2. Sensory loss
3. Ptosis
4. Anisocoria
5. Unilateral or bilateral peripheral facial nerve weakness
6. Signs or symptoms specific to the cranial nerve involved

D. Describe appropriate testing and evaluation for establishing the diagnosis

1. Imaging
 - a. Magnetic resonance imaging
 - b. Computed tomography
 - c. Angiography
 - i. Digital
 - ii. Magnetic resonance angiography
 - iii. Computed tomographic angiography
2. Lumbar puncture

II. Define the risk factors

- A. Immune suppression**
- B. Prior trauma**
- C. Known intracranial or systemic malignancy**

III. List the differential diagnosis

A. Myasthenia gravis

1. No pain
2. No numbness
3. No pupillary involvement
4. Restrictive strabismus
5. Thyroid eye disease (thyroid orbitopathy)
6. Post trauma
7. Orbital inflammatory disease

B. Guillain-Barré syndrome

C. Botulism

- D. **Chronic progressive external ophthalmoplegia**
- E. **Oculopharyngeal muscular dystrophy**

IV. Describe patient management in terms of treatment and follow-up

A. Diplopia

1. Acute
 - a. Occlusion
 - b. Prism
2. Chronic
 - a. Establish stability
 - b. Prism
 - c. Extraocular muscle surgery

B. Neoplasia

1. Establish a diagnosis
 - a. Specific imaging characteristics
 - b. Biopsy
2. Surgical excision
3. Radiation therapy
 - a. Fractionated
 - b. Non-fractionated
4. Chemotherapy may be indicated

C. Carotid cavernous fistula

1. Embolization

D. Cavernous sinus thrombosis

1. Antibiotics
2. Anticoagulation may be indicated but is controversial

V. List the complications of treatment, their prevention and management

A. Persistent diplopia

B. Optic neuropathy

C. Surgical therapy may be associated with cerebrovascular accident or acquired motor, sensory or cognitive neurologic deficit

VI. Describe disease-related complications

- A. Progressive diplopia**
- B. Neurotrophic keratitis**
- C. Carotid cavernous fistula**
 - 1. Venous cortical infarction
 - 2. Optic neuropathy
 - a. Glaucoma
 - b. Venous stasis retinopathy
 - c. Optic neuropathy

VII. Describe appropriate patient instructions

- A. Call for worsening diplopia, pain**
- B. Watch for redness**
- C. Report change in vision,**
- D. New neurologic symptoms**
 - 1. Dysarthria, dysphagia, numbness , weakness, incontinence

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.

Eyelid retraction

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Anatomy
 - a. Overaction or scarring of levator palpebrae or Mullers muscle or lower eyelid retractors
2. Pathophysiology
 - a. Neurogenic
 - i. Benign eyelid retraction of infancy
 - ii. Dorsal midbrain syndrome of Parinaud (Collier sign)
 - i) Associated with retraction-convergence nystagmus (simultaneous contraction of all extraocular muscles, eyes converge and retract in attempted upgaze)
 - iii. Oculogyric crisis
 - iv. Oculomotor synkinesis
 - i) Perinatal onset; Marcus Gunn jaw wink
 - ii) Aberrant regeneration oculomotor nerve (cranial nerve (CN) III)
 - b. Myogenic
 - i. Congenital
 - i) Maldevelopment of the levator palpebrae
 - ii. Thyroid eye disease (dysthyroid orbitopathy)
 - iii. Postsurgical correction of ptosis
 - c. Mechanical
 - i. Hypoglobus (pseudoretraction)
 - i) Orbital floor fracture
 - ii. Inferior rectus shortening
 - i) Blowout fracture (the upper eyelid may retract in attempted upgaze, and the lower eyelid may be mechanically retracted)
 - iii. Eyelid or orbital cicatricial changes
 - i) Metastatic breast carcinoma
 - ii) Following blepharoplasty or trauma
 - iv. Proptosis alone rarely causes eyelid retraction

B. Define the relevant aspects of epidemiology of the disease

1. Most common causes
 - a. Thyroid disease (characteristic)
 - b. Contralateral ptosis

C. List the pertinent elements of the history

1. Thyroid abnormalities
2. Diplopia
 - a. Previous CN III palsy
3. Pineal pathology
4. Previous trauma
5. Sinus disease

D. Describe pertinent clinical features

1. Normal eyelid position
 - a. 1-2mm below limbus for upper eyelid
 - b. At limbus for lower eyelid
 - c. Symmetry
2. Associated motility disturbance
3. Evidence of dorsal midbrain syndrome
 - a. Absent up gaze
 - b. Retraction convergence nystagmus
 - c. Light near dissociation
 - d. Papilledema
4. Globe position abnormalities

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Thyroid function tests
2. Magnetic resonance imaging (MRI)
 - a. Attention to the midbrain
 - b. Evidence of demyelinating disease

II. Define the risk factors

- A. Thyroid disease**
- B. Midbrain lesion**
- C. Orbital trauma or previous eyelid or orbital surgery**
- D. Epilepsy**

III. List the differential diagnosis

- A. Contralateral ptosis**
- B. Previous eyelid surgery**
- C. Orbital mass or inflammation**

IV. Describe patient management in terms of treatment and follow-up

- A. Prevention of exposure keratitis**
- B. Surgical correction of eyelid position**
- C. Surgical correction of globe position**
- D. Botox to levator**

V. List the complications of treatment, their prevention and management

- A. Induced ptosis**
- B. Worsen inferior eyelid retraction with inferior rectus surgery**

VI. Describe disease-related complications

- A. Exposure keratopathy**
- B. Decreased vision**

VII. Describe appropriate patient instructions

- A. Adequate lubrication**
 - 1. Especially at bedtime
- B. Taping if necessary**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Thyroid-Associated Orbitopathy, Module #1, 1997.
3. Bartley GB. Differential diagnosis and classification of eyelid retraction. *Ophthalmology* 1996;103:168-176.
4. AAO, Focal Points: Botulinum Toxin in Ophthalmology, Module #3, 2007.

Ptosis

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Congenital
 - a. Myopathic (absent or fibrotic levator from abnormal development)
 - b. Rarely neurogenic i.e. abnormal innervation
 - i. Congenital 3rd palsy, congenital Horner
 - c. Family history in small percentage
2. Syndromic
 - a. With elevator palsy
 - b. Marcus Gunn Jaw Wink
 - i. Synkinesis between motor cranial nerve (CN) V and the levator CN III
 - ii. Elevation of the eyelid with chewing or horizontal movement of the jaw
 - iii. Associated
 - i) Ptosis
 - ii) Ocular motility disorder
 - c. Goldenhar
 - d. Blepharophimosis
3. Anatomic
 - a. Levator dehiscence, disinsertion, stretching
 - b. Mechanical
 - i. Contact lens associated
 - i) Giant papillary conjunctivitis
 - ii. Eyelid and orbit tumors as in Neurofibromatosis Hemangioma, Dermoid
 - iii. Eyelid edema from inflammation
 - c. Trauma
4. Myopathic
 - a. Mitochondrial: chronic progressive external ophthalmoplegia (CPEO)
 - b. Myotonic dystrophy
 - c. Oculopharyngeal dystrophy

- d. Corticosteroid drops
 - e. Contact lens wear
- 5. Neuropathic
 - a. Peripheral CN III dysfunction
 - b. Nuclear III disease
 - i. Bilateral ptosis typical f nuclear
 - c. Horner syndrome
 - i. Mild
 - ii. Ipsilateral miosis
 - iii. Variable ipsilateral anhidrosis
 - iv. Lower eyelid elevated
- 6. Guillain-Barré- Miller Fisher syndrome
- 7. Neuro-muscular transmission
 - a. Myasthenia gravis
 - b. Botulism

B. Define the relevant aspects of epidemiology of the disease

- 1. Common causes
 - a. Levator dehiscence in acquired adult ptosis
 - b. Congenital in childhood ptosis
 - c. CN III palsy
 - d. Myasthenia gravis
 - e. Horner syndrome

C. List the pertinent elements of the history

- 1. Noted eyelid droop ("smaller eye")
- 2. Asymmetry in eyelid position
- 3. "Heaviness" of eyelids
- 4. Variability
- 5. Change in vision, near or distance
- 6. Diplopia

D. Describe pertinent clinical features

- 1. Normal eyelid function
 - a. Palpebral fissure height

- b. Eyelid excursion as a measure of levator palpebrae superioris function (upper eyelid range with frontalis splinted)
 - c. Marginal reflex distance: upper eyelid margin to mid corneal light reflex
 - d. Eyelid crease measurements
- 2. Duration
 - a. Acquired versus congenital
 - b. Change over time
 - i. Diurnal change
 - ii. Long-term progression
- 3. Associated physical eyelid signs
 - a. Retraction of lid in downgaze i.e. congenital ptosis or aberrant 3rd nerve regeneration
 - b. Absent or elevated eyelid crease i.e. levator dehiscence
 - c. Limited upper eyelid excursion i.e. congenital ptosis causing a widening of the interpalpebral fissure in downgaze
- 4. Synkinetic movements i.e. aberrant 3rd N regeneration with lid opening with adduction or downgaze
- 5. Symmetry of lids, eye movements, pupils
- 6. Associated generalized motor findings
- 7. Chronicity i.e. from old photos

E. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Work up for myasthenia gravis
- 2. Genetic analysis
- 3. Imaging studies if indicated
- 4. Mitochondrial assessment for CPEO if clinically indicated

II. Define the risk factors

A. Family history

B. Systemic disease

- 1. Myasthenia gravis
- 2. Muscular dystrophy

III. List the differential diagnosis

A. Pseudoptosis

1. Dermatochalasis
2. Brow ptosis
3. Globe size abnormalities
4. Hypertropia
5. Eyelid retraction contralateral eye
6. Enophthalmos

B. Apraxia of eyelid opening

C. Eyelid closure

1. Aberrant regeneration of CN VII
2. Psychogenic eyelid closure

IV. Describe patient management in terms of treatment and follow-up

A. Check for dry eye

B. Recognize orbicularis weakness

C. Assess ocular motility

D. Identify systemic disease

E. Check corneal sensation

F. Measurement of upper eyelid excursion

G. Surgery

1. Levator resection/advancement
 - a. Posterior approach
 - b. Anterior approach
2. Mueller's muscle surgery
3. Frontalis suspension

V. List the complications of treatment, their prevention and management

A. Lagophthalmos

B. Exposure keratopathy or exacerbation of dry eye

C. Asymmetric eyelid position

VI. Describe disease-related complications

A. Amblyopia in infants

B. Associated diplopia

- C. Impairment of visual field
- D. Decreased central acuity

VII. Describe appropriate patient instructions

- A. Report variability or progression
- B. Report diplopia
- C. Post-surgery
 - 1. Adequate lubrication

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Myasthenia Gravis, Module #4, 2003.
3. AAO, Focal Points: Congenital Ptosis, Module #2, 2001.
4. Siddens JD, Nesi FA. Acquired ptosis: classification and evaluation. In: Nesi FA, Lisman RD, Levine MR, eds. Smith's Ophthalmic Plastic and Reconstructive Surgery. 2nd ed. Philadelphia: Mosby; 1997:379-394.
5. Baroddy M, Holds JB, Vick VL. Advances in the diagnosis and treatment of ptosis. Curr Opin Ophthalmol 2005;16:351-5.
6. AAO, Ophthalmology Monographs 18. A Compendium of Inherited Disorders and the Eye, 2006.

Miller Fisher variant of Guillain-Barré syndrome

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Acute inflammatory demyelination of peripheral nerves
2. Preceding infection (gastrointestinal or respiratory)
 - a. *Campylobacter jejuni*
 - b. Other

B. Define the relevant aspects of the epidemiology of the disease

1. Slight increase frequency with age

C. List the pertinent elements of the history

1. Acute weakness
2. Often following viral or bacterial infection , vaccination, or gastrointestinal disturbance

D. Describe pertinent clinical features

1. Neuro-ophthalmic (C. Miller Fisher variant)
 - a. Diplopia
 - i. Single or multiple cranial nerve (CN) palsies
 - b. Ptosis
 - c. Mydriasis
2. Neurologic
 - a. Areflexia
 - b. Ataxia
 - c. Motor weakness
 - i. Bulbar muscles
 - i) Facial nerve palsy
 - ii) Dysphagia
 - ii. Ophthalmoplegia

E. Describe appropriate testing and evaluation for establishing the diagnosis

1. Auto-antibodies (e.g., GQ1b)
2. Magnetic resonance imaging (MRI)

3. LP may be indicated

II. Define the risk factors

- A. Preceding viral infection**
- B. Preceding immunization**

III. List the differential diagnosis

- A. Isolated CN palsies**
 1. Microvascular
 2. Other inflammatory conditions
 - a. Meningitis
 - b. Demyelinating
 3. Aneurysm
- B. Multiple cranial nerve palsies**
 1. Other inflammatory
 - a. Meningitis
 2. Brainstem disease
 3. Neoplastic
 4. Botulism
 5. Wernicke encephalopathy
- C. Myasthenia gravis when pupils normal**
- D. Thyroid eye disease (thyroid orbitopathy)**
- E. Carcinomatous meningitis**

IV. Describe patient management in terms of treatment and follow-up

- A. Acute**
 1. Support
 - a. Respiratory support
 - b. Urinary drainage
 - c. Stabilization of autonomic function
 2. Plasmapheresis
 3. Intravenous immunoglobulin

4. Corticosteroids - role is controversial
5. Symptomatic
 - a. Occlusion to avoid diplopia
 - b. Prism

B. Chronic

1. Rehabilitation
2. Extraocular muscle surgery when stable

V. List the complications of medical treatment, their prevention and management

- A. Fluid load intolerance to gamma globulin treatment**
- B. Complications of corticosteroid treatment**

VI. List the complications of the disease

- A. Prognosis**
 1. Majority improve
 2. Residual disabling diplopia, ataxia, facial weakness

VII. Describe appropriate patient instructions

- A. Seek medical attention for respiratory problems**
- B. Seek medical attention for swallowing problems**

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-ophthalmology, 2013-2014.
2. AAO, Focal Points: Multiple Sclerosis and Optic Neuritis, Module #12, 2003, p. 6.
3. AAO, Focal Points: Neuro-Ophthalmic Diagnoses You Don't Want to Miss, Module #9, 1999, p.13.
4. van Koningsveld R, Schmitz PI, Meche FG. Effect of methylprednisolone when added to standard treatment with intravenous immunoglobulin for Guillain-Barré syndrome: randomised trial. *Lancet* 2004;363:192-6.
5. Pritchard J, Gray IA, Idrisova ZR. A randomized controlled trial of recombinant interferon-beta 1a in Guillain-Barre syndrome. *Neurology* 2003;61:1282-4.
6. Hughes RA, van Der Meche FG. Corticosteroids for treating Guillain-Barre syndrome. *Cochrane Database Syst Rev* 2000:CD001446.
7. Hughes RA, Swan AV, van Koningsveld R, et al. Corticosteroids for Guillain-Barre syndrome. *Cochrane Database Syst Rev* 2006:CD001446.

8. Hughes RA, Raphael JC, Swan AV, et al. Intravenous immunoglobulin for Guillain-Barre syndrome. Cochrane Database Syst Rev 2006:CD002063.

Systemic corticosteroids in neuro-ophthalmology

I. Describe effects of corticosteroids

A. Glucocorticoid effect

1. Anti-inflammatory properties

B. Mineralocorticoid effect

1. Bone and kidney

II. List neuro-ophthalmic indications for corticosteroids

A. Giant cell arteritis

B. Neuro-ophthalmic manifestations of other autoimmune diseases and vasculitides

C. Selected cases of optic neuritis and other inflammatory/vasculitic optic neuropathies (e.g., demyelinating disease, sarcoid)

D. Idiopathic orbital inflammatory disease

E. Compressive optic neuropathies

F. Thyroid orbitopathy

G. Isolated traumatic optic neuropathy (controversial)

H. Neoplastic disease

1. Lymphoma
2. Other rapidly expanding mass lesions

I. Ophthalmoplegias

1. Myasthenia (selected cases)

III. List the contraindications

A. Invasive fungal infections

B. Untreated tuberculosis

C. Active peptic ulcer disease

IV. List the alternatives to this procedure/therapy for systemic use

A. Immunomodulatory agents

B. Radiation therapy may be indicated in certain diseases

V. Describe the instrumentation and technique

A. Oral forms, IV forms, depo forms for injection, nasal and inhaled forms available

B. Agents in common oral use

1. Prednisone
2. Dexamethasone (Decadron)

C. Agents for IV use

1. Methylprednisolone (Solu-Medrol)
2. Dexamethasone (Decadron)

VI. Describe the complications of the therapy

A. Systemic side effects

1. Short term
 - a. Hypertension
 - b. Hyperglycemia
 - c. Ulcerative perforation (in the setting of peptic ulcer disease especially if combined with nonsteroidal anti-inflammatory agents (NSAIDs))
 - d. Electrolyte disturbances
 - e. Fluid retention, congestive heart failure in susceptible patients
 - f. Increased susceptibility to infection
 - g. Sleep disturbance
 - h. Psychosis (increased incidence in elderly), emotional lability
 - i. Potentiation of fungal infection
 - j. Aseptic necrosis (rare)
2. Long term
 - a. Weight gain
 - b. Diabetes mellitus (may be a short term side effect as well)
 - c. Poor wound healing
 - d. Osteoporosis and compression fractures
 - e. Adrenal suppression: Cushing syndrome
 - f. Skin changes
 - g. Corticosteroid myopathy

- h. Fat redistribution
- i. Suppression of growth of children
- j. Aseptic necrosis (rare)

B. Ocular/orbital effects

- 1. Increased intraocular pressure (IOP) (less common with systemic corticosteroids)
- 2. Cataract formation (posterior subcapsular)

VII. List general comments on usage

A. Acute therapy (3 days or less usually needs no specific attention)

B. Alternate day therapy has much fewer side effects but not effective in certain conditions including giant cell arteritis

C. Chronic therapy

- 1. If treatment chronic, taper is necessary
- 2. When treating certain conditions (idiopathic orbital inflammatory disease), slow taper is essential to avoid recurrence

VIII. Describe the follow-up care

A. Essential to involve the patient's internist or primary care physician actively to monitor for the development of and manage corticosteroid induced side-effects including osteoporosis, hyperglycemia, hypertension and electrolyte disturbances

B. Monitor IOP and cataract status

C. Appropriate use of stress dose replacement in setting of long term corticosteroid use

IX. Describe appropriate patient instructions

A. Inform the physician of any new symptoms while on the medication

Additional Resources

- 1. AAO, Basic and Clinical Science Course. Section 1: Update on General Medicine, 2013-2014.
- 2. AAO, Basic and Clinical Science Course. Section 2: Fundamentals and Principles of Ophthalmology, 2013-2014.
- 3. Jabs DA, Rosenbaum JT, Foster ST, et. al: Guidelines for the Use of Immunosuppressive Drugs in Patients with Ocular Inflammatory Disorders: Recommendations of an Expert Panel. Am J Ophthalmol 2000;130:492-513.
- 4. AAO, Focal Points: Temporal Arteritis: Diagnosis and Management, Module #2, 1992.
- 5. AAO, Focal Points: Managing Optic Neuritis: Results of the Optic Neuritis Treatment Trial, Module

#2, 1994.

6. AAO, Focal Points: Neuro-Ophthalmic Diagnoses You Don't Want to Miss, Module #9, 1999.
7. AAO, Focal Points: Myasthenia Gravis, Module #4, 2003.
8. AAO, Focal Points: Idiopathic Intracranial Hypertension (IIH, Pseudotumor Cerebri), Module #3, 2004.
9. AAO, Focal Points: Giant Cell Arteritis, Module #6, 2005.

Non-physiologic visual loss (NPVL)

I. Describe the approach to establishing the diagnosis

A. Describe the etiology of this disease

1. Visual complaints that have no physiologic or organic basis are due to:
 - a. Malingering, or willful exaggeration of symptoms, often when litigation involving monetary compensation, disability, or psychosocial stressors are involved
 - b. Hysteria, or a subconscious expression of nonorganic signs or symptoms (conversion reaction)
 - i. True hysteria/conversion disorder is extremely rare

B. List the pertinent elements of the history

1. Monocular diplopia
2. Unilateral or bilateral decreased vision
3. Unilateral or bilateral visual field loss
4. Onset in relationship to antecedent trauma
5. Pertinent medical history
 - a. Psychosocial stress
 - i. School
 - ii. Family/peer relationships
 - b. Secondary gain from litigation
 - i. Car accident
 - ii. Slip and fall
 - iii. Other personal injury

C. Describe pertinent clinical features

1. Monocular diplopia (may be bilateral)
2. Unilateral or bilateral decreased vision
3. Unilateral or bilateral visual field loss
 - a. Classic patterns of NPVL
 - i. Spiral fields on kinetic perimetry
 - ii. Overlapping isopters on kinetic perimetry
 - iii. Severe constriction ("tunnel fields") on kinetic or automated static perimetry and on confrontation field testing (may be non-expanding on confrontation as well)
 - iv. Cloverleaf pattern on automated static perimetry

- v. Monocular hemianopia
- vi. Generalized depression, often severe, on automated static perimetry
- 4. Pupil findings
 - a. Normal reactivity in the absence of associated ocular trauma with traumatic mydriasis or other iris pathology
 - b. Absence of an afferent pupillary defect (APD) in spite of gross asymmetry of visual fields
- 5. May have component of NPVL superimposed upon organic visual loss related to trauma

D. Describe appropriate testing and evaluation for establishing the diagnosis

- 1. Complete ophthalmologic examination including visual fields
- 2. High index of suspicion
- 3. Evaluation of monocular diplopia
 - a. Sensorimotor exam to confirm normal ocular alignment in all fields of gaze and verify monocular nature of diplopia
 - b. Rule out contributory corneal, refractive, lenticular, and retinal pathology
 - c. If monocular diplopia resolves with a pinhole, it may be due to uncorrected refractive error, lens or corneal opacity, or corneal warpage
- 4. Evaluation of monocular decreased visual acuity
 - a. Vertical prism dissociation test 2
 - b. Stereo vectograph testing
 - c. Monocular fogging at phoropter
 - d. Bottom up acuity (i.e. begin testing with 20/10 or 20/15 line)
 - e. Visual evoked potential generally not helpful as can be voluntarily suppressed
- 5. Evaluation of non-physiologic visual field loss
 - a. Observe patient performing tasks outside of stated visual field (e.g. ambulate throughout office without difficulty, shake hand beyond stated visual field, locate objects outside of stated visual field such as trashcan to throw away tissues)
 - b. Have patient look at your fingers in eccentric quadrants of field when "testing motility" after they've previously denied ability to count fingers in this region on confrontation field
 - c. Absence of an APD in face of grossly asymmetric visual fields
 - d. Normal "pink" optic nerve in setting of longstanding monocular visual loss

II. Define the risk factors

- A. Personal injury/worker's compensation litigation**
- B. Impending disability determination**

C. Psychosocial stress, anxiety, or depression

III. List the most common or critical entities in the differential diagnosis

A. Organic visual loss or superimposed organic component with non-physiologic embellishment

Additional Resources

1. AAO, Basic and Clinical Science Course. Section 5: Neuro-Ophthalmology, 2013-2014.
2. The prism dissociation test in detecting unilateral functional visual loss. Slavin MLJ Clin Neuroophthalmol. (<http://www.ncbi.nlm.nih.gov/pubmed/2141855>) 1990 Jun;10(2):127-30.