

Physician Schedules:

SUBSPECIALTY	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY
NEURO AM	Stunkel	Stunkel *McMillan Bldg.	Van Stavern	Shepherd CL	Van Stavern
NEURO PM	Van Stavern	Van Stavern Botox Stunkel	Van Stavern	Van Stavern	Stunkel

All clinics 6th Floor COH **with the exception of Tuesday morning.**

Neuro-Ophthalmology Case Conference: 1st and 3rd Monday: 7:00 am, 7th floor McMillan (begins September)

Ophthalmology Grand Rounds: Wednesday, 5 pm, 5-6 pm.

NEURO-OPHTHALMOLOGY- AN OVERVIEW

This handout is intended to serve both as a guide for obtaining histories from neuro-ophthalmic patients, as well as a review of the neuro-ophthalmic examination. While much of this may already be familiar, the way one approaches a patient with a neuro-ophthalmic problem differs somewhat from the approach used in general ophthalmology and the examination techniques are often unfamiliar to general ophthalmologist and neurologists.

THE NEURO-OPHTHALMIC HISTORY

Evaluating patients with neuro-ophthalmic symptoms may initially seem intimidating. Neuro-ophthalmic deficits may involve complex neuro-anatomic pathways, and the differential diagnosis may be (or appear to be) quite broad. A central concept is that of localization. Once a lesion has been localized to a particular neurologic or ophthalmologic structure, one is in a far better position to generate an appropriate differential, and decide what further work-up (if any) is required. For example, the diagnostic evaluation for a patient with a lesion localizing to the retrochiasmal visual pathways would be quite different than that for a patient with retinal or optic nerve disease.

Some people find it easier to think of each neuro-ophthalmology patient as a puzzle. Although each may differ in the degree of complexity, no puzzle makes sense until all the pieces fit together appropriately. A careful history is a critical piece of the puzzle, and the neuro-ophthalmic examination should function as the natural extension of the history. If you begin the examination with some idea as to where in the visual system the problem resides, it becomes easier to focus on pertinent positive and negative findings. As a general rule of thumb, if the history doesn't match the exam, one of them (or both!) must be wrong.

Afferent Pathway Symptoms

Nature of visual symptoms

When confronting a patient with visual loss, it is important to identify the specific type of visual loss the patient is describing. “Blurred vision” is non-specific and means different things to different people, and may not necessarily indicate decreased visual acuity. Try to nail down whether the patient is actually describing decreased visual acuity (poor clarity of images), or complete loss of vision, localized visual field loss, scotoma, etc. Diplopia and oscillopsia (subjective sense that objects are moving) may be reported by patients as blurred vision, but have separate differential diagnoses. It is also critical to determine if the visual symptoms are monocular or binocular. Monocular visual loss suggests that the lesion is anterior to the optic chiasm (e.g., retina, optic nerve, cornea, etc), and helps guide the examination and any ancillary testing. In practice, patients are sometimes unable to distinguish whether one eye or both eyes are involved: since the temporal visual field is larger than the nasal, patients with homonymous visual field defects often localize vision loss to the eye with the temporal field cut. The more specific the visual symptom is, the more localizing value it has. For example, a patient describing unilateral waviness and distortion of central vision (metamorphopsia) almost certainly has a macular lesion, and the rest of the history and exam can be used to confirm that diagnosis.

Onset and duration of visual loss

The onset, duration, and tempo of visual loss provide valuable clues as to etiology, and may also determine the urgency of further evaluation. Sudden loss of vision most commonly results from a vascular or inflammatory process, whereas slowly progressive visual loss suggests a compressive, toxic/nutritional, or infiltrative process. The presence or absence of pain should be specifically addressed, since this will often distinguish vascular (painless) from inflammatory (painful) etiologies. In elderly patients with sudden loss of vision, you should always consider the possibility of a vascular event (AION, CRAO) resulting from Giant Cell Arteritis (GCA). The symptoms of GCA include headache (be sure that the headache is new or different from previous headaches), jaw claudication (specifically ask about pain with chewing), and scalp tenderness (ask about pain while washing or brushing hair). Other important GCA symptoms are fatigue,

low-grade fevers, weight loss, arthralgias, and myalgias (particularly when GCA coexists with polymyalgia rheumatica). Age is a key demographic feature when considering GCA: the highest incidence is in patients in their 70s and 80s. It is very uncommon in the 60s, rare in the 50s, and unheard of under the age of 50.

In patients with transient episodes of visual loss, the first question again is whether it involved one or both eyes. Inquire about duration: did the episode last for seconds, minutes, or hours? Visual loss from a transient ischemic event typically lasts 3-5 minutes, while the transient visual obscurations seen with papilledema generally last for seconds. Ask about photopsias- visual phenomena such as flashing lights, scintillations, flashing black squares- and distortions in vision such as metamorphopsia or micropsia. These phenomena may be associated with retinal disease, migraines, and epileptic seizures. Make sure to ask about symptoms associated with the visual loss, especially if these symptoms occurred at the time of the episode. Pertinent symptoms would include weakness or numbness on one side of the body, slurred speech, difficulty swallowing, word-finding problems, and imbalance. Certain retinal dystrophies may be associated with hemeralopia (“day blindness”) or nyctalopia (“night blindness”); it is often helpful to ask the patient whether they prefer to see in dim or bright light. It’s worth remembering that difficulty at night is a common symptom for many ophthalmic diseases, including cataract and refractive error- patients with true nyctalopia have profound dysfunction in dim environments, and often need to be led around or refrain from driving.

Efferent Pathway Symptoms

Diplopia may result from a large variety of disorders, and localization, both by history and examination, is particularly important. It is important to establish whether the diplopia is monocular or binocular. Monocular diplopia, except in rare circumstances, is the result of an ocular abnormality, such as refractive error or tear film insufficiency. If the diplopia is binocular, the patient should be asked if the diplopia is horizontal, vertical, or oblique; if it is particularly worse or better in one direction of gaze; and if it is different when viewing at distance or near. This may provide clues as to the offending muscle(s). For example, the history of horizontal binocular diplopia, worse at distance and worse on

left gaze immediately implicates the left lateral rectus as the weak muscle and allows you to perform the rest of the history and exam in a much more focused fashion. As a general rule, the goal of evaluating the efferent pathway is to localize to one (or more) of the following locations:

Supra-nuclear (cortical and sub-cortical)

Nuclear and inter-nuclear (3rd, 4th, 6th nerve nuclei and medial longitudinal fasciculus)

Nerve (3rd, 4th, 6th)

Neuro-muscular junction (myasthenia gravis, botulism, etc)

Extra-ocular muscle (thyroid eye disease, orbital myositis, etc)

You should ask about previous episodes of diplopia, or a history of childhood strabismus or head tilt. Many patients with a previously well-controlled phoria will decompensate later in life or after even minor head trauma. Some clues to this diagnosis include: full versions; concomitant deviation; prior history of patching or strabismus surgery; and impaired sensory testing with evidence of suppression (stereoacuity, Worth 4 dot, etc). Ask the patient if the diplopia is constant or intermittent, and if intermittent, if there is a pattern to when it occurs. For example, in myasthenia gravis, symptoms are typically absent or minimal in the morning, and worsen throughout the day, whereas with thyroid eye disease, symptoms are worse in the morning, and improve throughout the day.

Always ask about any associated ptosis or pupillary abnormalities, as this may suggest the involvement of one or more cranial nerves. It is important to ask about associated neurologic symptoms such as bulbar weakness (dysarthria, dysphagia) and proximal muscle weakness (difficulty arising from a chair, climbing stairs, brushing hair). These symptoms may be associated with myasthenia as well as certain hereditary and acquired neuromuscular diseases.

Patients with vestibular imbalance often complain of disequilibrium or unsteadiness. Oscillopsia is an illusory to-and-fro movement of the environment that may be horizontal, vertical, torsional, or a combination of these directions. Vertigo is an illusory sensation of movement of self or of the environment. These symptoms most commonly reflect a mismatch among vestibular, visual, and somatosensory inputs concerning the position or motion of the body in space. The chief concern in such patients is to identify,

by history and examination, whether the vestibular dysfunction is central (brainstem/cerebellum) or peripheral (labyrinth, vestibular nerve). Patients with central vestibular imbalance, in addition to having impaired eye movements (saccades and smooth pursuit) and central vestibular nystagmus (in most but not all cases) may report ataxia, dysarthria, dysphagia, facial numbness or weakness, or diplopia. Such symptoms, with corroborating physical findings, mandate neuroimaging and further investigation. Most cases of peripheral vestibular imbalance are benign and self-limited, and do not necessarily require neuroimaging or extensive investigations. .

Additional Medical History

The patient's medical history often provides useful information. Patients with hypertension and diabetes mellitus are more predisposed toward ischemic events than those without such risk factors. Medications, surgeries, and previous traumatic injuries may all be relevant to the presenting complaint. Certain populations, such as transplant patients and HIV patients, deserve special consideration since they are prone to a number of specific neuro-ophthalmic complications from their disease and/or treatments. Any history of malignancy also deserves special attention, particularly if it is a malignancy known to metastasize to brain (breast, lung, renal cell, etc). Another general rule of thumb: a new neuro ophthalmic deficit in a patient with a known (and recent) history of cancer should be attributed to either the cancer or its treatments until proven otherwise.

It is important to remember that the medical diagnosis that the patient self-reports should not be considered securely diagnosed without adequate documentation or verification. For example, if a patient reports a history of "stroke", "lupus", etc, a few follow-up questions should be asked to determine whether the diagnosis is secure (e.g., were they worked up for stroke, what were the symptoms, are they being seen by a rheumatologist, do they have any specific symptoms of lupus, etc.). This is particularly important when the presenting complaints may be related to the self-reported diagnosis. Family history is often pertinent, and may even suggest a diagnosis, particularly in patients with Leber's hereditary optic neuropathy, RP, and other genetic disorders.

History of alcohol use might suggest nutritional deficiency as a cause of their visual symptoms, while IV drug use raises suspicion of syphilis, HIV, cardiac disease, etc.

THE NEURO-OPHTHALMIC EXAMINATION

The key components of a clinical neuro-ophthalmic examination are discussed below. . A more detailed discussion of these examination techniques may be found in standard Ophthalmology and Neurology texts.

Visual Acuity and Refraction

Both distance and near visual acuity should be tested. A discrepancy between distance and near acuity may be due to several factors, including media opacities and accommodative insufficiency. Further, functional patients may not understand the relationship between near and distance visual acuity, and may provide inconsistent responses. A good refraction, or even the use of the pinhole, can correct optical abnormalities resulting in loss of vision, and therefore prevent an expensive and time-consuming workup. Keep in mind that visual acuity measures only a single dimension of vision, i.e., spatial resolution. Patients may have significant loss of visual function even with relatively preserved visual acuity.

Color Vision

Color vision testing is the “secret weapon” of the neuro-ophthalmologist, and often helps differentiate neurogenic from non-neurogenic visual loss. With mild optic nerve dysfunction, impaired color perception may be present when visual acuity is only minimally affected. Acquired dyschromatopsia may be seen with lesions of the optic nerve, retina, or the visual cortex. It should be noted that cerebral dyschromatopsia, typically caused by lesions at the occipital-temporal lobe junction, is rarely isolated, and often accompanied by other focal neurologic symptoms, including homonymous visual field defects.

Either the Ishihara or the HRR color plates may be used. The HRR plates are designed to test both congenital and acquired dyschromatopsia, while the Ishihara plates test only for congenital color blindness. The control plate (the first plate) does not assess color vision, but tests whether visual acuity is good enough to proceed with the rest of the test. For example, a patient with a dense cataract may have normal optic nerve function, but not be able to read the control plate due to poor visual acuity from media opacity. In such cases, color vision cannot be adequately assessed. The examiner should record the number of plates correctly identified by each eye. Remember that 9% of men and 1% of women are congenitally color blind. When color plates are unavailable, a difference in color perception between the two eyes may be identified using a colored bottle top. This technique may also be used when color plate testing is normal.

Visual Field Testing

Confrontation visual field testing is a critical part of the examination, even in patients who also receive “formal” visual field testing. All of the visual field techniques (including automated perimetry and Goldmann kinetic perimetry) are prone to error- both patient related and technician related. The confrontation VF testing can be used to confirm defects seen with automated perimetry- if the Humphrey visual field shows severe constriction but your careful confrontation fields are normal, it is much more likely that the deficits on the HVF represent artifact, not pathology. It might be better in that case to repeat the field or do Goldmann VF rather than make major diagnostic or treatment decisions based on a single field.

The field of each eye is tested individually. Ask the patient to fixate on the examiner’s nose. Ask if any parts of the face are missing; small central scotomas may be identified using this method. Have the patient compare the examiner’s eyes and upper and lower face for differences; altitudinal defects may be readily detected by this method. Have the patient then count fingers in all four quadrants. This latter technique will usually only pick up absolute scotomas, typically homonymous defects, since the target size is so large. Since 90% of the primary visual cortex subserves macular vision (central 30°), checking exclusively for large peripheral defects is often unproductive. Since red wavelengths are lost first when the visual pathways have been damaged, a small red target may detect relative visual field defects, particularly central scotomas. Formal perimetry is far more sensitive than confrontation field testing, and is required if a visual field defect is suspected.

You will encounter patients with functional, or non-organic, visual field loss. This usually manifests as severe constriction, which is itself non-specific but can reflect optic nerve, retinal, or visual cortex pathology. One clue is to double the distance at which you are testing the field: with organic VF loss, the visual field should expand (like a cone); with functional visual field loss, the VF should remain the same (like a tube- hence the term “tubular” field loss). However, it is insufficient to simply demonstrate that the visual field

loss has a functional component, since this gives no information about the true status of the visual system- a significant number of patients have combined organic and functional vision loss. The goal should be to demonstrate **normal** visual fields. One method is to do “finger-to-nose” perimetry: have the patient look at your face and then touch your fingers in the periphery, telling them that you are testing coordination (which is technically true). If they can accurately identify and touch your finger in all 4 quadrants, that proves normal or nearly normal field. Even if they don’t respond, they may make accurate saccades to the target in each quadrant, which also indicates normal or at least better than claimed visual field.

Amsler Grid testing

This test evaluates the central 20°, and is useful for detecting small central scotomas. Ask the patients if there is a break or discontinuity of the lines, or if there is any distortion. Distortion or waviness of the lines (metamorphopsia) is typically seen with macular rather than optic nerve disease.

Pupils

Pupil size should be recorded in light and darkness, with the patient fixating on a distant object. The direct response to light is recorded in each eye. Both the intensity of the stimulus and the ambient room light play an important role in the direct response. Ideally, the light is brought from below to avoid invoking a near response. The near response is evaluated by having the patient fixate on a near target (his thumb or a near card) as the examiner moves it closer.

The afferent pupillary defect (APD) is one of the most important signs in neuro-ophthalmology. The examiner has the patient fixate at distance, and then shines the light in each eye to equally bleach both retinas. The light is then swung rhythmically, holding the light on each eye for 1-2 seconds. Dilation, rather than constriction, of the affected eye as the light is swung onto it denotes an afferent pupillary defect. Since the presence of an APD is determined by comparing the light reaction of one pupil to the other, there is no such entity as a “bilateral APD”. Common sources of error include hippus (physiologic pupillary unrest), dim light source, inappropriate ambient light, and holding the light too

long on one pupil, which may cause a small APD in the eye with the longer light exposure. Any patient with a unilateral optic neuropathy, independent of etiology or duration, should have an RAPD. Failure to detect RAPD in such a patient usually means one of three things: 1) the optic nerve is not the source of the visual loss (?macula, ?refractive,? functional); 2) the process is bilateral and relatively symmetric; or, 3) it's there and you just didn't see it.

Anisocoria (unequal pupils) reflects efferent pupillary dysfunction. Remember that even transection of the optic nerve will NOT cause anisocoria: the resting pupil size will be equal, since the system is crossed. In patients with anisocoria, important components of the examination include eyelid position and motility. 20% of normals have "physiologic" anisocoria: in these patients, the anisocoria is small (< 1.0 mm), the pupillary reactions to light and near are normal, and the remainder of the examination is normal. An isolated dilated pupil indicates either tonic pupil (usually benign, especially if isolated) or pharmacologic mydriasis. It is important to also assess the near response: a tonic pupil typically has a robust but slow near response, while a pharmacologically dilated pupil will not react to near. The patient should be asked specifically about any eye drops or ointments that they may be using. **Third nerve palsies do NOT cause isolated mydriasis.** Horner's syndrome reflects sympathetic denervation to one eye, and may be a harbinger of serious neurologic or systemic conditions. The ptosis is mild, and may be missed without close inspection of the eyelids. In general, unequal pupils with normal reactivity typically represent either Horner's syndrome or physiologic anisocoria. A careful examination, with attention to upper and lower eyelid, and motility, should serve to differentiate.

Eyelid examination:

In normal individuals, the upper eyelid covers the superior 1-2 mm of iris and the lower eyelid borders the inferior aspect. The palpebral fissure usually measures 9-12 mm in normal patients. Since the lower eyelid position may vary, one may also measure the distance between the upper eyelid margin and the pupillary light reflex. This is known as the margin reflex distance, and typically measures 4-5 mm.

Levator function is useful in differentiating various etiologies of ptosis. Levator function is measured by manually neutralizing the ipsilateral brow while the patient looks downward. A ruler is placed at the eyelid margin, and the degree of eyelid elevation in mm is measured as the patient looks upward. Normal levator function exceeds 12-15 mm, and is decreased with congenital ptosis, and when ptosis is associated with myasthenia, IIIrd nerve palsy, and certain myopathies (e.g., CPEO). In contrast, levator function is normal in patients with levator dehiscence and Horner's syndrome.

Motility Examination:

The goal of the motility examination is to assess the integrity of the supranuclear, nuclear, and infranuclear ocular motor pathways. One should begin by taking the patient through the cardinal positions of gaze. Test both ductions (individual ocular rotations) and versions (conjugate eye movements), as the influence of binocular fusion may mask or simulate a limitation in motility. The examiner should assess the ocular rotation by recording it as a percentage of normal (e.g., 90% of normal abduction). All functional classes of eye movements should be assessed, since specific deficits in one system may help localize pathology. Saccades, or fast eye movements, are tested by having the patient look at the examiner's nose, and then at an eccentrically placed target. They may be recorded as : 1) normal; 2) hypometric if they undershoot the target; 3) hypermetric when they overshoot the target. To test the smooth pursuit system, one has the patients follow an object of regard. One must be careful not to exceed the limits of the pursuit system (40^o/sec). Abnormal pursuit appears "saccadic", as the more durable fast eye movement system must be activated to keep up with the target. The pursuit system is exquisitely vulnerable to diffuse disorders such as fever, toxins, medications, metabolic derangement, and fatigue. In patients who cannot cooperate with testing (neurologically disabled, children), the vestibular ocular reflex (VOR) may be used: the "Doll's eye maneuver". This test is based upon the fact that the vestibular nuclei connect directly with the ocular motor nuclei (III, IV, and VI). The patient's head is rotated horizontally and then vertically. Normal elevation, depression, left and right gaze suggests intact ocular motor pathways. In a patient with limited gaze (for example, upgaze limitation), normal VOR suggests a supranuclear lesion.

If ocular misalignment is discovered or suspected (e.g., binocular diplopia in the presence of apparently normal ductions and versions), quantification of the deviation may be made using the cross-cover method, the Maddox rod, or the red glass test. For the cross-cover method, one eye is covered, and the deviated eye moves to pick up fixation. The amount of deviation is measured by placing prisms over one eye. An occluder alternately covers each eye as the amount of prism is increased. When the refixation movement reverses, the deviation has been neutralized, and the amount of prism required is recorded. Base-out prism neutralizes esodeviations, while base-in prism neutralizes exodeviations (“prism apex in the direction of the deviation”). If prisms are unavailable, or no deviation is found on cross-cover testing, Maddox rod testing may uncover subtle phorias (latent deviations). The Maddox rod, and to a lesser extent the red glass, acts to dissociate fusion. By convention, the Maddox rod is held over the patient’s right eye. To evaluate a horizontal misalignment, the Maddox rod is held with the cylinders oriented horizontally. A white light is directed toward the patient, who will see a vertical red line and a single white light. The patient is then asked which side the red bar is on (relative to the white light). If the bar is to the right of the light (an **uncrossed** diplopia), this implies an esodeviation. A **crossed** diplopia (the red bar is located to the left of the white light) suggests an exodeviation. The patient is then asked to look to the right and the left, and asked if the separation of the images changes; this helps identify the dysfunctioning muscle. For example, an uncrossed diplopia that worsens with right gaze suggests weakness of the right lateral rectus muscle. To assess vertical misalignment, the cylinders are placed over the right eye with a vertical orientation, which produces a horizontal red line. If the line is located above the white light, this implies a hypodeviation, while the opposite (line below the light) suggests a hyperdeviation.

Fundoscopy:

For neurologists: Practice using your own ophthalmoscope. The direct ophthalmoscope combines a light source and a viewing system. There are many features of today’s direct ophthalmoscopes that we take for granted. First, the light source is constant because of strong rechargeable batteries. The optical systems have also improved immensely. The

light source is bright, frequently a halogen bulb, with long life and is the brightest portable light available. A rheostat control on the "on" button sets the light intensity and is helpful for extremely photophobic individuals. The best viewing of the fundus, however, requires the use of the brightest possible source tolerated

Located in the front of the ophthalmoscope head is also a set of filters. Most of the time, the examiner will use a standard illumination with no filter; this will give the brightest direct light. However, if an opacity such as a cataract is present which produces glare, try the polarized filter for an easier view. The polarized beam will also eliminate reflections from the cornea—so if you are getting a light reflex when trying to view the disc or the macula, try the polarized beam.

The red-free filter (a green light) is extremely useful. It provides a 450 nanometer (nm), short wavelength, monochromatic light which blocks long red waves. This makes surface lesions easier to see since the shorter wave length light waves reflect off the inner surface of the retina. The examiner can use this light to illuminate and "see" the transparent nerve fiber layer since the shorter wavelength reflect off the non-red inner surface of the retina. This filter is especially useful in identifying nerve fiber layer defects. The red-free filter is also good for illuminating optic nerve drusen when buried drusen are not appreciated by the standard white light.

Almost all ophthalmoscopes have a lens selection dial or lens wheel. Some offer up to 68 lenses (-30 to +38) and some only 20 or 28 (-25 to +40). These lens selections represent different powers that can be adjusted to correct for the examiner's and the patient's refraction. The red numbers are negative power, concave lenses, for near-sighted individuals or myopes, whereas the black or green numbers are positive power (convex) for far-sighted individuals with hyperopia. If the examiner is "emmetropic" (needs no glasses or is wearing a corrective contact lens or spectacle), the dial should be at zero. The "plus" lens is like a magnifying glass to make the image bigger. The larger the plus lens, though, the closer the focal point and the larger the image.

The patient should be comfortable and be sure you are comfortable too. Be sure the patient is positioned at the same height or slightly lower than you are. Align yourself with the patient—your right eye should look into their right eye and your left eye should look into their left eye. Have the patient fixate on a distant target with the unexamined

eye. Point out the target, for example, "focus on the light switch on that wall [pointing to the wall]". In our society, we have a personal space that as physicians and health care providers we are very careful not to invade. However, to see the disc you have to get close. How can you overcome this? You need to tell the patient, "In order to really look well and thoroughly into your eye, I am going to get really close to your face, is that ok?". Just telling them will warn them and give you the permission to move into their personal space and "see". Remember, the direct ophthalmoscope must be about an inch from the patient's eye for you to have the best view. Leaning over, straining, or holding your breath are obstacles to your comfort. As you dial toward zero to see the disc you must continue to get closer to the patient. Notice the distance between the patient's eye and the ophthalmoscope. This should be no further than two inches from the cornea and frequently is only 1 inch.

Look for the red reflex. Turn the lens "wheel" toward zero as you draw closer to focus the light on the disc and retina; you should be 1 inch in front of the patient's eye. The view is magnified about 14- 15 times if the examiner is emmetropic; slightly more if myopic and slightly less if hyperopic. Using the direct ophthalmoscope, the examiner has about a 10 degree view. Bring the vessels of the retina into view. The retina is normally focused within +1 to -1 lens, unless the patient or the examiner has a refractive error. Find the optic disc and the macula, and identify the central retinal artery and its branches. Since the disc is often the focal point of the examination, imagine the disc to be cut vertically into two—giving a temporal half (toward the macula) and a nasal half (away from the macula). If the patient is highly myopic and has astigmatism, the only clear view of the disc and fundus will be obtained with the patient wearing corrective refraction. Be aware of common sources of error when viewing optic discs, and try to practice as much as possible. Part of the skill in ophthalmoscopy results from viewing many normal fundi.

For Ophthalmologists and Neurologists: You should make note of the optic disc color, contour, and cup-disc ratio. The retinal vasculature should be evaluated by noting the caliber of veins and arteries in all quadrants. The macula and peripheral retina should be examined carefully, since primary retinal dystrophies may masquerade as optic

neuropathies. Remember, the optic nerve has only two responses to injury: atrophy or edema. Therefore, optic atrophy is the end result of any number of possible pathologic processes, and the exact etiology is dependent upon the history and the remainder of the examination. **Keep in mind that optic disc pallor DOES NOT always imply atrophy.** The color of the optic disc is dependent upon the surface vessels and the nerve fiber layer. Many otherwise normal optic discs may appear pale for reasons unrelated to injury: pseudophakes and myopes have whiter-appearing optic discs. Associated features such as nerve fiber layer, peripapillary vessel dropout, and gliosis are more suggestive of true atrophy. However, optic disc appearance should ALWAYS be correlated to optic nerve function: for the most part, all optic neuropathies should result in abnormalities in one or more optic nerve parameters (i.e., VA, color vision, visual field, pupillary reaction).

Optic disc swelling also results from a variety of pathologic processes, and there is no way to distinguish among them by funduscopic appearance alone. “Papilledema” means optic disc swelling secondary to elevated intracranial pressure; papilledema cannot be differentiated from other cases of optic disc swelling based on fundus appearance alone; the history and the remainder of the examination help generate the differential diagnosis. **Keep in mind that an elevated optic disc does not necessarily mean a swollen optic disc.** Many congenital optic disc anomalies (such as optic disc drusen) may cause the optic disc to appear swollen. True optic disc swelling causes obscuration of the peripapillary vessels, loss of spontaneous venous pulsations, and dilation of the vessels on the surface of the optic disc. Congenital optic disc anomalies often lack a physiologic cup, and have anomalous vascular branching (trifurcations, early branching, etc.) In some cases, orbital ultrasound and Fundus Autofluorescence Photography can help identify optic disc drusen (one of the more common causes of pseudopapilledema)- but even in those cases, it is still important to distinguish between pseudoedema and true edema: patients can have BOTH optic disc drusen and papilledema. It is important to identify pseudopapilledema, largely to spare the patient unnecessary testing (MRI, LP). that would otherwise be indicted if the optic nerves were truly swollen.

Papilledema develops and resolves gradually. Several well-designed studies suggest that it may take up to two weeks (or longer) to manifest after an acute rise in intracranial pressure. Similarly, severe papilledema may take weeks to resolve even after intracranial pressure has normalized, placing the patient at risk for further visual loss.

NEUROIMAGING

The number of neuroimaging modalities available has expanded dramatically in the past ten years. The proper selection and interpretation of these tests is an integral part of neuro-ophthalmic practice. All of the modalities available have certain advantages and disadvantages, and it is incumbent upon the physician ordering these tests to be certain that the test selected is best suited to the patient's problem. Before deciding upon some form of imaging, one should have localized the lesion to a specific region (or regions), and have a general idea as to what processes might occur there. In this sense, diagnostic imaging should function as the natural extension of a complete neuro-ophthalmic history and examination.

With the advent of computerized tomography (CT) scans and magnetic resonance imaging (MRI) in the 1970s, it became possible to differentially image blood, water, bone, air, and soft tissues within the body. Both techniques have undergone significant advancement over the past 30 years and it is now possible to create high-resolution images of soft tissue, bone, CSF, and blood vessels in two- or three-dimensions. Despite these advances, CT and MRI remain fundamentally different imaging methods and each has distinct advantages and disadvantages.

Computerized Tomography (CT)

CT scans are obtained by passing thin beams of x-rays from an array of emitters on one side of the patient's body to detectors on the opposite side. The emitter/detector complex is mounted on a rotating gantry through which the body (or body part) is passed.

Detectors record X-ray attenuation levels along the detector array as a function of the orientation of the gantry through its 360 rotation. Fourier calculations allow image 'slices' to be constructed computationally and displayed in grayscale as a function of relative radiodensity of the tissues. Modern helical (spiral) scanners, taking advantage of advanced acquisition protocols and significant image processing power, now allow 3-dimensional volumetric images to be obtained, allowing multiple-angle viewing and variable-plane reconstructions with a minimum loss of resolution.

CT is superior to MRI in detailing bony anatomy of the orbit, skull base, and sinuses. Additionally, CT is highly sensitive for detecting acute blood and has a very short acquisition time (single images can be obtained in less than 1 second and whole scans in 30-60 seconds). CT is the imaging technique of choice in cases of trauma and when bony lesions or calcium-containing masses (meningiomas, optic nerve drusen) are suspected.

Magnetic Resonance Imaging (MRI)

The principle of magnetic resonance imaging (MRI) is significantly more complex than CT scanning but is far more versatile. MRI takes advantage of the fact that magnetic atoms (those having an odd number of electrons or protons) align their axis of spin in a magnetic field. The patient is placed within the bore of a large magnet (0.5 Tesla to 3.0 Tesla). By turning on a radiofrequency (RF) field within the magnetic field, some atoms will flip their axis of spin. When the radiofrequency field is turned off again, atoms' spin will decay ('relax') back to their original orientation, and in so doing, emit a photon of energy in the radiofrequency range. These signals (typically from hydrogen atoms) can be reconstructed into high-resolution 2- or 3- dimensional images. By varying RF pulse sequences and scanning parameters, contrast between varying types of tissue or fluid can be differentially imaged. Compared with CT, MRI provides significantly greater spatial

resolution, soft tissue differentiation, and avoids bony artifact. Some of the most common imaging sequences for MRI scanning are:

T1: Best for showing anatomy. CSF appears black, normal brain appears gray, while abnormal brain typically appears darker, owing to increased water content. Pre- and post-contrast T1 series are commonly compared to identify areas of pathology (where the blood-brain barrier has become permeable).

T2 and FLAIR: Very sensitive to water content and is good for showing pathology. Since increased water content is common for pathologic processes (tumors, edema, demyelination, and infarction) within the brain, T2 images appear brighter than normal brain in these areas, even without contrast. With T2 images, CSF appears white; whereas with FLAIR, CSF appears black and allows improved visualization of white matter disease near CSF (periventricular white matter, optic nerve, etc.).

Diffusion Weighted Imaging (DWI): A specialized form of MR imaging, DWI provides image contrast based on the molecular movement of water, which may be alerted in disease states. In standard DWI imaging, tissue in which water movement is limited (“restricted”) appears bright, as in cases of ischemic cytotoxic edema (as ion pumps fail, water enters the cell and cannot diffuse. Later as cells burst, water diffusivity actually increases above normal and the area appears darker than the surrounding brain tissue). DWI is currently used chiefly in early identification of ischemia (diffusion restriction can be detected within minutes of an ischemic stroke), but is being increasingly used to investigate tumors as well as demyelinating and inflammatory brain pathologies.

CT versus MRI

Because of the superiority of MRI in differentiating soft tissue and water content, MRI is superior to CT scan for intracranial disease. Because CT has superior bone imaging and is less prone to fat suppression artifact and, therefore, is generally considered superior for orbital imaging.

CT:

Advantages: Lower cost, rapid acquisition, excellent imaging of bony structures, acute blood easily identified, safe with ferromagnetic implants and indwelling electronics

Disadvantages: Poor resolution of soft tissue structures near skull base due to bony artifact, ionizing radiation exposure limits number of scans.

MRI:

Advantages: High spatial resolution, excellent grey-white differentiation, no ionizing radiation exposure, not affected by bony attenuation, able to image in any plane.

Disadvantages: Slow acquisition, may exacerbate claustrophobia, movement degrades image quality, not safe with indwelling electronics or ferromagnetic materials, poor bony imaging.

CT and MR Angiography

MRI and CT are both capable of acquiring high-resolution images of vascular structures. Both techniques, when interpreted by experienced radiologists, can be highly sensitive and specific compared with catheter angiography.

With CT angiography (CTA), iodinated contrast media is injected into a vein and using high speed CT scanning and digital tissue subtraction, high-resolution 3-dimensional reconstruction of cerebral arteries can be obtained rapidly and with minimal artifact. In many academic centers, CTA is now considered the primary imaging technique for detecting important cerebral vascular abnormalities (dissection, aneurysm, etc) in patients with normal renal function¹².

MR Angiography (MRA) can be obtained using two different techniques: contrast-enhanced (CE-MRA), and non-enhanced (NE-MRA). See picture x-8. Contrast enhanced MRA provides fast acquisition of high resolution images but depends highly on proper technique (bolus delivery and acquisition timing) and should be used with caution in patients with renal disease (see below). NE-MRA is most useful in patients with renal disease as no contrast media is required; however, this technique is more susceptible to artifact from turbulent blood flow and is less sensitive to slow moving blood (as in large aneurysmal cavities).

With all neuroimaging studies, it is critical that you either review the images personally or discuss them with your “go-to” neuroradiologist. This is most important when your suspicion is high that the MRI should show a lesion (bi-temporal hemianopia, unilateral cavernous sinus syndrome, etc). You have the advantage of knowing where the lesion MUST be, whereas the radiologist may be relying upon incomplete information. It has been said the “the job of the neuro-ophthalmologist is re-interpreting previously normal MRIs”, and there is some truth to that.

RECOMMENDED READING:

Liu G, Volpe N, Galetta G. Neuro-Ophthalmology: Diagnosis and Management. W.B. Saunders.

This is the textbook which we will provide to the rotators on the Neuro-Ophthalmology service. It is passed from one rotator to another using an honor system. All of the chapters are also available in PDF form, which we will provide. The goal would be to make it through the textbook once by the time of graduation. For the rotation, 1-2 chapters/week would be a reasonable goal, focusing on optic neuropathies (Chapter 3

and 5), Papilledema (chapter 6), Functional visual loss (chapter 11), Eye movement disorders (chapters 15-17), and Headache/facial pain (chapter 19).

The Essentials. Walsh and Hoyt's Clinical Neuro-ophthalmology, 5th ed.

Miller NR, Newman NJ. Eds.

Williams and Wilkins 1998N

This is a concise, readable primer of basic neuro-ophthalmology. I would specifically recommend chapters 4-7, 12, 14-17, as they cover most of the common disorders encountered in neuro- ophthalmology. The weak areas include the chapters on nystagmus, headache, and eyelid.

Practical Viewing of the Optic Disc, Digre K, Corbett JJ.

Butterworth-Heinemann, 2003

An excellent guide to the fundamentals of ophthalmoscopy. Written for non-ophthalmologists, this book has detailed instructions for viewing the nerve and retina, many photographs and diagrams (of both normal anatomy and pathology), and has a CD-ROM which includes several instructional videos. Highly recommended.

Neurology of Eye Movements, Zee D, Leigh J.

The true "bible" of eye movement anatomy and physiology. Much of the book is of interest to those with a special interest in eye movements and nystagmus, and might be daunting for most others. However, the last two chapters are clinical and provide detailed information on eye movement syndrome, organized anatomically. A special bonus is the CD, which has videos of many of the disorders described in the book.

