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Examination of the Visual Sensory System

Despite continuous advances in neuroimaging and other new techniques, the examination of the afferent visual sensory system is still the core of the neuro-ophthalmologic examination. This chapter describes the most common subjective and objective testing parameters used in the afferent visual system examination.

Evaluation of the afferent system begins with a thorough medical history, followed by an ophthalmologic examination, including assessment of best-corrected or at least pinhole visual acuity at distance and near, color vision, visual fields, anterior segments (including the media), vitreous, intraocular pressure (IOP), and appearance of the optic discs, retinas (especially the macula), and retinal vessels. At the completion of the examination, one should have an idea as to the structure involved in the patient's visual sensory difficulties or at least have a differential diagnosis. If the diagnosis remains unclear, a number of ancillary tests are available, including ocular imaging and electrophysiologic procedures that should lead to the correct diagnosis.

History

A thorough history is one of the most important parts of the assessment, because it determines the initial strategy for differential diagnostic evaluation. For example, a patient complaining of visual loss should be asked if the loss of vision is in one or both eyes, was sudden or insidious in onset, and if the visual loss is stationary or progressing.

It also is important to ask about phosphenes and photopsias such as flashes of light or showers of sparks, distortions in vision including metamorphopsia and micropsia, and positive scotomas. A positive scotoma is one that is seen by the patient, like the purple spot that is often seen after a flash goes off, whereas a negative scotoma refers to a nonseeing area of the visual field. Metamorphopsia, micropsia, and positive scotomas most often occur in patients with maculopathies or occasionally with migraine, whereas phosphenes and photopsias may occur in patients with vitreous or generalized retinal disease, optic nerve dysfunction, or cerebral dysfunction from migraine.

Clinical Office Examination

Clinical evaluation of the afferent visual system for each eye incorporates the items described below, all of which can be performed in the office. The first goal for the neuro-ophthalmology examination is to determine if the visual loss is caused by a disorder of the ocular media (i.e., cornea, lens, vitreous), the retina, the optic nerve, the optic chiasm, the retrochiasmal pathway, or is nonorganic. The second goal is to establish a differential diagnosis. By examining various parameters of afferent visual function, the examiner frequently can determine the anatomic site of the afferent system abnormality and the most probable cause(s).

Visual Acuity

The most common measurement of visual function in a clinical setting is visual acuity. It is the primary method of assessing the integrity of the optics of the eye and the neural mechanisms subserving the fovea. Visual acuity is used to monitor central visual function in patients, is an essential part of clinical refraction procedures, and is important to the patient for reading, face recognition, and other tasks involving fine visual detail. Visual acuity is specified in terms of the

visual angle subtended by the finest spatial detail that can be identified by the observer. The physical size of an object and its distance from the observer determine its visual angle.

The most common form of reporting visual acuity is the "Snellen notation," consisting of a fraction in which the numerator is the testing distance (usually 20 ft or 6 m) and the denominator is the distance at which a "normal" observer is able to read the letter. The standard of 20/20 for "normal" vision was developed more than 100 years ago, and with today's high-contrast eye charts and better light sources, most normal persons under the age of 50 can be corrected to better than 20/20.

The measurement of visual acuity in special populations (e.g., young children and physically challenged persons) is not always possible with a standard letter chart (Fig. 1.1). For example, testing of central visual function of infants begins with an assessment of how well the infant fixes and follows the examiner's face,

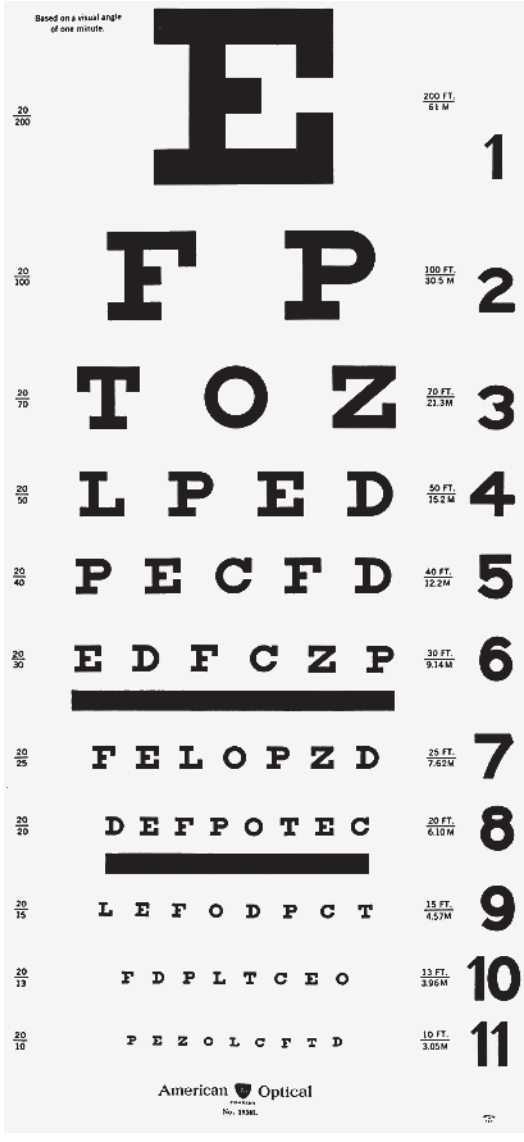


Figure 1.1 Objects used to test vision. **A:** An example of a standard eye chart for testing distance visual acuity. **B:** A "tumbling" E that can be used to assess acuity in children, illiterate individuals, and patients who are cognitively impaired. Note that the E can be turned around so that it resembles a "W" or an "M." **C:** Allen cards. These cards, designed by Dr. Henry Allen, can be used to test acuity in children and adults who have not yet learned, do not know, or, for neurologic reasons, have forgotten or cannot identify letters.

a small toy, or some other object of interest. For young children (as well as for some patients with aphasia or other neurologic disorders that affect speech), a "tumbling E cube" can be used for visual acuity testing. This cube is a white block with black E letters of different sizes on each of its sides. By rotating the cube, each of the Es can be presented in four different orientations to test the child's ability to distinguish the direction of the E, usually by indicating the direction by pointing the fingers in the same direction. The cube can be placed at various distances from the patient to make a determination of visual acuity. The "E game" also can be performed using a projected "E" acuity chart. Another test, the "HOTV" test, involves matching each test letter to one of four letters (H, O, T, or V) printed on a card held by the child. Some visual acuity tests use pictures or symbols. The most popular of the picture visual acuity tests are the Allen cards that are available as handheld picture cards or projected images. The objects include an easily identifiable birthday cake, a bird, a house, and a car (although one older card has a picture of a rotary telephone that most children have never seen!). It has been shown that visual acuity is overestimated when symbols are used instead of letters, apparently because the shape of the symbols provides extra visual information.

"Preferential-looking" techniques, ocular motor responses such as optokinetic nystagmus, and electrophysiologic measures such as the visual-evoked potential (VEP) can be used to estimate visual acuity (see section on Electrophysiologic Tests below). In addition, a number of eye charts and behavior test procedures can be used to assess visual acuity in nonverbal or physically challenged patients.

Visual acuity measurements in children present special problems, in part because the child wants to do well and please the examiner. It is therefore important for the examiner to ensure that the nontested eye is properly occluded to avoid peeking. The examiner must work quickly, may need to use more than one procedure to establish visual acuity capabilities, and should provide continuous positive feedback to the child to maintain cooperation.

In patients suspected of having nonorganic visual loss, several additional methods of assessing visual acuity may be useful. These are discussed in Chapter 24.

In normal observers, visual acuity is highest for the foveal region and decreases rapidly with increasing visual field eccentricity. In many instances, central visual field loss and reduced visual acuity appear to be closely related; however, visual acuity can also be reduced when there is generalized depression of the central visual field. In such instances, a central scotoma is not present. There also are several conditions for which the visual field may be at or near normal sensitivity, but visual acuity may be dramatically reduced. These conditions include refractive errors, corneal surface irregularities, cataract, retinal edema or serous detachment, and amblyopia.

Contrast Sensitivity

Visual acuity defines the smallest spatial detail that can be resolved for high-contrast stimuli, but it does not specify the responses of the visual system to objects of different sizes and contrasts. However, one also can assess afferent visual function by looking at the behavior of the visual system at **threshold** contrast levels.

A number of factors influence the measurement of contrast sensitivity, including background adaptation luminance, stimulus size, visual field eccentricity, pupil size, temporal characteristics, stimulus orientation, and various optical factors such as defocus, dioptric blur, diffusive blur, and astigmatism. From a neuro-ophthalmologic standpoint, measurement of contrast sensitivity can reveal subtle deficits in patients with a variety of optic neuropathies as well as in other neurologic conditions such as Alzheimer disease and Parkinson disease.

In general, assessment of contrast sensitivity is clinically useful for detecting early or subtle visual loss (especially when visual acuity is normal), making comparisons between the two eyes, and for monitoring the progression of or improvement in visual function. Assessing contrast sensitivity also may be helpful in predicting the performance for various daily tasks, such as the identification of distant objects, reading highway signs and books, recognizing faces, and mobility. Thus, it may be useful not only for revealing subtle visual deficits associated with ocular and neuro-ophthalmologic disorders but also for identifying problems that a patient is likely to encounter during daily activities.

Contrast sensitivity may be measured in several different ways. One method is the Pelli–Robson chart (Fig. 1.2), consisting of letters of a fixed size that vary in contrast. Each line consists of six letters, with the three leftmost and three rightmost letters having the same amount of contrast. The patient reads the chart in a manner similar to a standard visual acuity chart, and the minimum contrast at which the letters can be detected is recorded. This method of testing contrast sensitivity is highly reproducible and is capable of detecting disturbances in visual function that are not evident with standard visual acuity testing.

Contrast sensitivity also can be measured with low-contrast Sloan letter charts. These charts have gray letters of progressively smaller size on a white background (Fig. 1.3); each chart in the set corresponds to a different level of contrast, ranging from high (100%, about the same contrast as standard visual acuity charts) to medium (5%) to low (1.25%, 0.6%)

Figure 1.2 The Pelli–Robson contrast sensitivity chart.

contrast levels. Patients are asked to read each of the four charts at a distance of 2 m under consistent lighting while wearing their usual distance refractive correction. The charts are readily available and provide a practical, quantitative, and standardized method of visual function assessment. They have proven particularly useful in identifying subtle visual dysfunction in patients with a history of recovered optic neuritis as well as in patients with multiple sclerosis but without any other evidence of optic nerve dysfunction.

Stereoacuity

Stereoacuity requires good visual acuity in both eyes and normal cortical development. As such, stereoacuity can be helpful in establishing if a patient has visual loss from congenital amblyopia or monofixation syndrome, as well as verifying the extent of any monocular visual acuity loss. Using the Titmus or Randot Stereo tests, stereoacuity in normal observers with good binocular function and visual acuity should be at

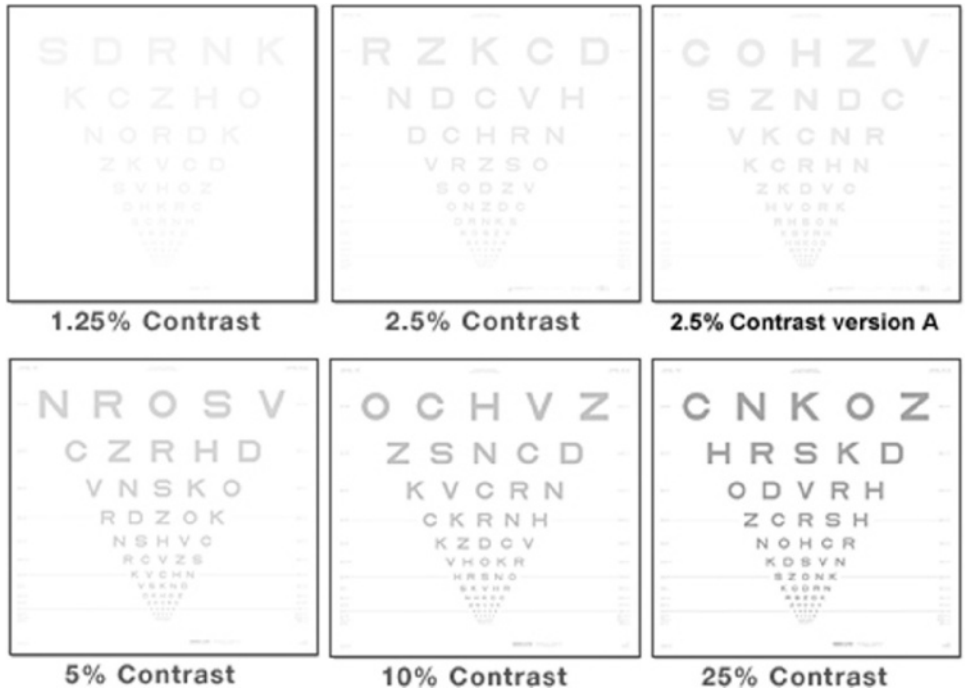


Figure 1.3 Sloan low-contrast letters. Note varying amounts of contrast.

least 40 seconds of arc or better when both eyes have 20/20 visual acuity.

Color Vision

From a clinical diagnostic standpoint, it is important to distinguish if a color vision deficiency is congenital or acquired. Congenital color vision deficits usually are easy to classify using standard clinical color vision tests because color discrimination is impaired for a specific region of the visual spectrum, and the deficits are long-standing, stable, symmetric in the two eyes, and unassociated with other visual symptoms or complaints. In patients with acquired color vision loss, however, color discrimination may be impaired throughout the visual spectrum or along a specific axis, and the deficits may be mild or severe, of sudden or insidious onset, symmetric or asymmetric, and often associated with other visual symptoms or complaints. In acquired color vision deficiencies, tritan (blue) and blue-yellow deficiencies most often are associated with diseases affecting the photoreceptors and the outer plexiform layer, whereas red-green deficiencies most often are associated with diseases affecting the optic nerve and posterior visual pathways. Some notable exceptions include glaucoma, dominant hereditary optic atrophy, and chronic papilledema, all of which may demonstrate blue-yellow deficits, and juvenile macular degenerations such as Stargardt disease and Best disease, that often produce red-green deficits. Optic neuritis produces a mixture of red-green and blue-yellow deficits, although one axis usually is more affected than the other.

A wide variety of color vision tests is available to the clinician. Because most were designed to evaluate congenital red-green color vision deficiencies, many do not permit adequate testing of blue-yellow deficits or optimum characterization of acquired color vision losses. As with any test of visual function, it is important that the testing conditions be standardized and performed in the proper manner. A particularly important factor for all clinical color vision test procedures is proper lighting, both in terms of having an adequate amount of light for the test and having a light source with the appropriate spectral distribution.

Pseudoisochromatic Plates

Pseudoisochromatic plates are the most common type of color vision tests employed in clinical practice. A number of pseudoisochromatic plate tests are available, although the Ishihara and Hardy–Rand–Rittler are the most commonly used versions (Fig. 1.4). Both tests consist of a series of plates that contain colored dots of varying size and brightness. The tests are designed so that persons with normal color vision see numbers, shapes, or letters because of grouping certain colored dots together to form a

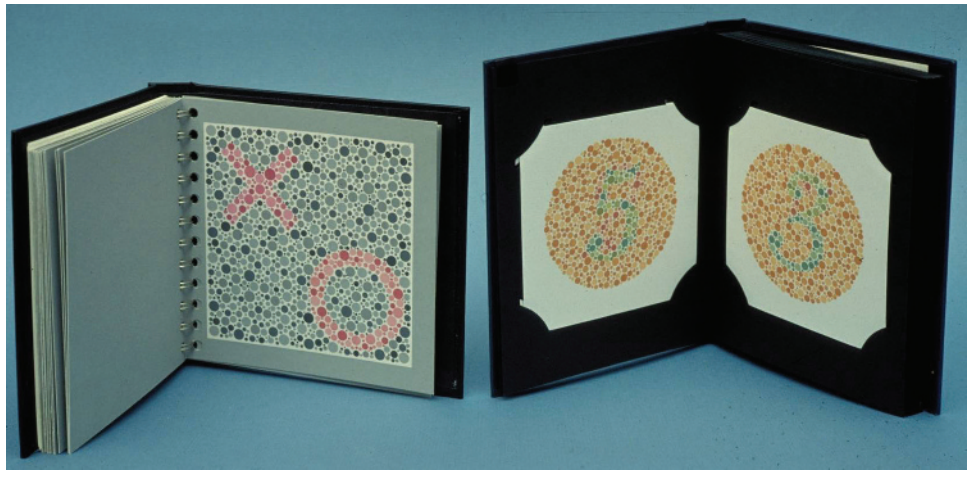


Figure 1.4 Appearance of figures on the Hardy–Rand–Rittler and Ishihara pseudoisochromatic color plates.

figure against the background of other dots. Depending on how the particular test is designed, persons with color deficiencies either are unable to see the figure because the figure dots are confused with the background dots, or see a figure different from that seen by persons with normal color vision because the figure dots and background dots are grouped together in an abnormal pattern. The variation in size and brightness of the dots is used to ensure that recognition of figures is made based on color discrimination alone; however, there is no question that contrast sensitivity plays a role in the results of the test. Nevertheless, these plates are extremely useful. Even children who are shy or don't know their colors may be able to trace the shapes of the figures they see. Other variations of pseudoisochromatic plates include winding paths of colored dots that the patient can trace. These are useful in young children, illiterates, and some neurologically ill patients who are unable to identify letters, numbers, or shapes.

Color vision testing using pseudoisochromatic plates is quick and easy to perform and, thus, can be an excellent screening procedure for distinguishing normal color vision from congenital or acquired color vision deficits.

Smartphone Applications

With the advancement in smartphone technology and the proliferation of medical software applications, physicians increasingly are incorporating smartphones into their daily practice. Several smartphone applications offer an affordable and accessible method for color vision testing; however, they may underestimate color vision loss, particularly in patients with normal contrast sensitivity.

Farnsworth Panel D-15 Test

The Farnsworth Panel D-15 test is a color arrangement test consisting of 15 color caps that form a color circle covering the visual spectrum. A reference cap is permanently fixed in the arrangement tray; the other 15 caps are placed in a scrambled order in front of the patient. The patient's task is to select the cap that is closest in hue to the reference cap and place it next to the reference cap in the tray. The patient then is told to continue to place the caps in the tray, one at a time, so that they are arranged in an orderly transition of hue. Patients with moderate to severe protan, deutan, or tritan color vision deficits will confuse colors across the color circle, so the arrangement contains misplaced caps. On the back of each cap is a number to assist in scoring the test. On the D-15 scoring chart, the caps along the color circle are connected in a dot-to-dot fashion in the order represented in the tray, and the specific arrangement indicates the type of color deficiency. The Panel D-15 test does not indicate the degree of color deficiency, other than to separate color normals and mild anomalous trichromats from those with moderate to severe color vision deficiencies; however, a desaturated D-15 test is now available and may be more sensitive in detection of mild color vision abnormalities.

Farnsworth–Munsell 100-Hue Test

The Farnsworth–Munsell 100-Hue test permits classification of both the type of color vision deficiency and its severity. Despite its name, it consists of **85** colored caps that are arranged in roughly equal small steps around the color circle. The caps are divided into four boxes, and arrangements of caps are performed one box at a time. In each box, there are two reference caps,

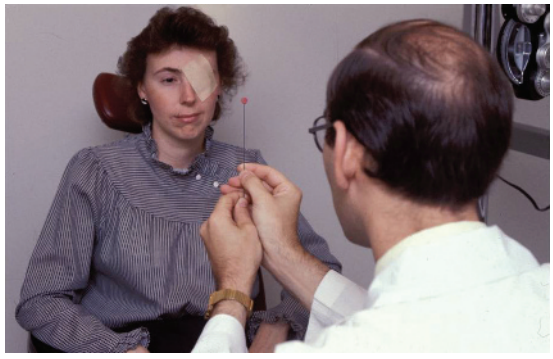


Figure 1.5 Method of testing the visual field using a red test object. This method can be used to detect a subtle central or paracentral scotoma or hemianopia.

one at each end, that are permanently attached to the box. The other caps are taken out of the box, scrambled, and placed before the patient. The patient then is told to arrange the caps so that there is an orderly transition in hue from one reference cap to another. As with the panel D-15 test, the Farnsworth–Munsell 100-Hue test is designed so that persons with congenital or acquired color deficiencies will be confused by certain caps across the color circle. The caps are numbered on the back, and scoring is determined by the arrangement of the caps in the box. Depending on the type of color deficiency, specific caps across the color circle will be confused, resulting in greater arrangement errors in those locations. In this manner, the type of color vision deficit can be classified. In addition, the severity of the color deficiency can be quantified by determining an overall error score for arrangement errors. This test rarely is used in clinical practice.

Color comparison tests, although only qualitative in nature, can provide valuable information concerning subtle visual anomalies. In general, the best color to compare is red. Using pages from the pseudoisochromatic plates, red-colored bottle caps, or other brightly colored objects, comparisons of color appearance can be very effective in detecting subtle differences between the two eyes. The brightness or saturation of the colored objects may be less in one eye, making the object's color appear dim or washed out. Similarly, comparisons within the same eye across the vertical and horizontal midline or between central vision and the mid-periphery can detect subtle differences in color appearance that are indicative of damage to the visual pathways. For example, red may appear pink, orange, or brown or the color may disappear completely (Fig. 1.5).

Visual Field Examination

Examination of the visual field is one of the fundamental parts of the afferent system evaluation. A variety of visual field test procedures can be employed, including confrontation, the Amsler grid, kinetic perimetry, and static perimetry. Each of these procedures has advantages and disadvantages.

General Principles

Perimetry and visual field testing have been clinical diagnostic test procedures for more than 150 years. Although instrumentation and testing strategies have changed dramatically over this time, the basic principle underlying conventional perimetry has remained the same. Detection sensitivity is determined for a number of locations throughout the visual field using a small target presented against a uniform background, and a loss of sensitivity at various visual field locations is a marker for identifying pathology or dysfunction of the visual pathways. The ability of perimetry to provide helpful clinical information has been responsible for its long-term use as a diagnostic procedure. Because perimetry can provide information about both the likely anatomic location and the disease process affecting the afferent visual sensory pathway, it remains a vital part of the neuro-ophthalmologic evaluation.

Perimetry and visual field testing fulfill several important diagnostic functions:

1. **Early detection of abnormalities.** Because many ocular and neurologic disorders initially are expressed as sensitivity loss in the peripheral visual field, perimetry is an important factor in identifying early signs of afferent system dysfunction. Indeed, perimetry usually is the only clinical procedure that evaluates the status of the afferent visual pathway for locations outside the macular region.
2. **Differential diagnosis.** The spatial pattern of visual field deficits and comparison of patterns of visual field loss between the two eyes also provide valuable differential diagnostic information. Not only can this information be helpful in defining the location of damage along the visual pathway, it also can assist in identifying the specific type of disease that has caused the damage.
3. **Monitoring progression and remission.** The ability to monitor a patient's visual field over time is important for verifying a working diagnosis, establishing if a condition is stable or progressive, and evaluating the effectiveness of therapeutic interventions.
4. **Revealing hidden visual loss.** Perhaps the most important role served by perimetry is the ability to detect afferent visual pathway loss that may not be apparent to the patient. Changes in central visual function typically are symptomatic. Peripheral vision loss, on the other hand, can often go unnoticed, especially if it is gradual and monocular. Paradoxically, even though a patient may be unaware

of peripheral visual field loss, it can significantly affect the performance of daily activities such as driving, orientation, and mobility.

Some form of visual field testing should be performed on all patients, regardless of their presenting visual symptoms. It is not feasible nor is it necessary to perform a long quantitative visual field examination on all patients; however, a confrontation visual field should be performed as part of a standard neuro-ophthalmologic examination. When more sensitive measurements of the visual field are needed, automated static or manual kinetic perimetry can be performed.

Manual kinetic perimetry with the Goldmann perimeter has many advantages. As the perimetric stimulus presentation is done by a human, subjects can be cajoled into performing. When the perimetrist senses patient fatigue, he/she can provide a rest break. Unlike the fixed, 6-degree spaced grid of conventional automated perimetry, perimetry using the Goldmann or a similar apparatus allows for custom test point locations along with improvisation of strategies based on coexisting findings. Specific exploration strategies can be used for individual concerns. This allows for much more accurate mapping of defect shape and can be invaluable for the topographic localization of visual field defects. However, manual perimetry is less sensitive than conventional automated perimetry and it may be more time-consuming. Its most severe limitations, though, are that replacement parts for the perimeter are increasingly difficult to find and, even more importantly, many technicians are inadequately trained (or not trained at all) in the performance of manual, kinetic perimetry.

Automated static perimetry has had a dramatic impact on improving the quality of care for patients with ocular disorders. Automatic calibration of instruments, standardized test procedures, high sensitivity and specificity, reliability checks ("catch trials"), and quantitative statistical analysis procedures are some of the many advantages of this method of perimetry. However, there also are disadvantages of automated perimetry, including prolonged test time, increased cognitive demands, patient fatigue, and lack of flexibility for evaluating difficult patient populations. We believe that there is no single method of visual field testing that is best for all circumstances and all patients. Automated perimetry is but one of many tools that the clinician can use to evaluate peripheral visual function, and the various forms of visual field testing should be regarded as **complementary** techniques, the utility and appropriateness of which are determined by the clinical circumstances and the question that is being addressed. There is no single method of data representation, analysis procedure, visual field index, or other method of evaluating visual field data that provides all of the essential clinical information. It thus is important to consider all of the available information, including reliability characteristics and the subjective clinical interpretation of the visual field. In addition, it should be kept in mind that although the test may be automated, the patient is not. It is inappropriate to begin an automated visual field test, leave a patient alone in a dark room, and expect the patient to remain alert, energetic, attentive, interested, and to maintain proper alignment and fixation throughout the test procedure. Some patients require periodic rest breaks, encouragement, and personal contact to perform visual field examinations in a reliable manner. It also is important to insure that proper test conditions, refractive characteristics, and other factors have been properly established before initiating the examination.

Specific Techniques for Testing Visual Fields

Confrontation testing. Confrontation visual fields usually are performed with the patient seated in the examination chair and the examiner seated facing the patient at a distance of 2 to 3 ft. One of the patient's eyes is occluded using the palm of the patient's hand, an occluder paddle, or a patch, and the patient is told to fixate with the uncovered eye on the examiner's opposite eye (this allows the examiner to assess stability of fixation). The basic concept is to use a small, localized target, the presence or absence of which in the visual field can be readily determined by the patient. A confrontation visual field should include an examination of each of the four visual field quadrants (superior temporal, superior nasal, inferior temporal, inferior nasal) as well as the central portion of the field and the temporal and nasal fields on either side of fixation. Most examiners test patients using finger counting to survey the visual field for any dense quadrantic defect (Fig. 1.6), although some authors recommend finger

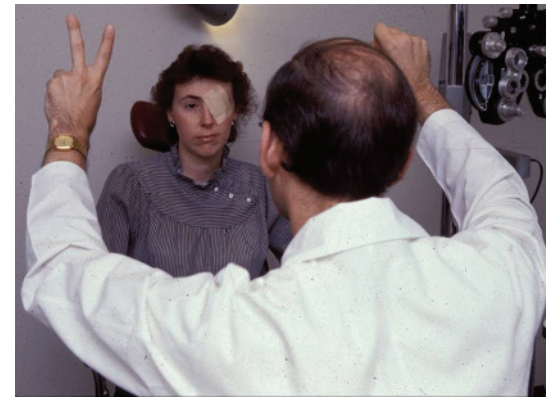


Figure 1.6 Method of testing the visual field by having the patient count fingers in the upper left, upper right, left, right, lower left, and lower right regions of each field.

wiggling instead of counting. Finger counting or wiggling then is followed by a test of the central field. One such test, as noted above, is to use a red object and compare color perception between the two eyes or between parts of the visual field in each eye (Fig. 1.5). By combining several confrontation visual field tests, about 70% of neurologic field defects can be identified, but formal perimetry usually is necessary when the patient has visual loss not explained by the results of a general ophthalmologic examination.

Confrontation visual field techniques for infants and children can be challenging (Fig. 1.7). For infants and young children, simply holding up one hand and observing whether or not the child looks at it is the best one can do. Another option is to hold both hands up on either side of the child's fixation and then wave one or wiggle a finger and see if the child looks at the moving hand/finger. For older children, finger mimicking can be used to evaluate the peripheral visual field. The child mimics the examiner by holding up the same number of fingers he/she sees.

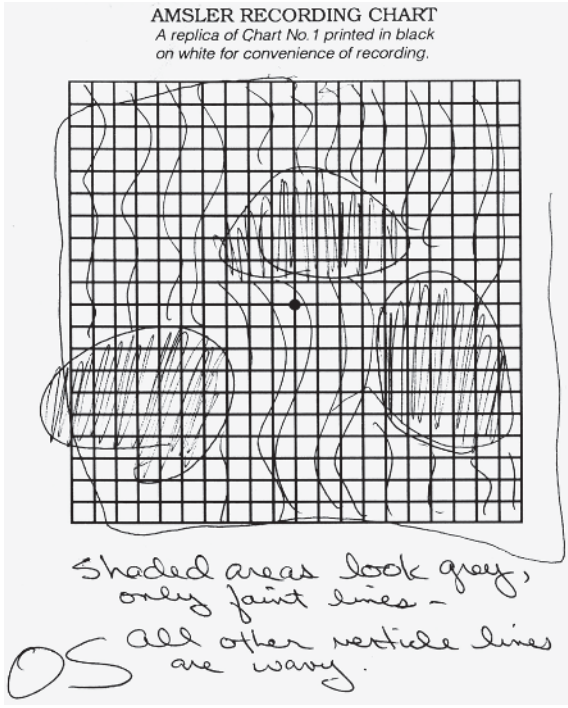
Figure 1.7 Examples of confrontation visual field testing in children. **A:** Startle response. **B:** Finger counting. **C:** Finger puppets.

In many instances, simultaneous comparison of color saturation or brightness of stimuli between hemifields or between the two eyes is useful in distinguishing subtle anomalies. When the stimuli are presented in a double simultaneous fashion to the right and left of fixation, it is possible to detect homonymous defects. Subtle deficits across the vertical midline can be detected by asking the patient to indicate which of the two test objects is clearer or brighter. In addition, double simultaneous presentation can be used to detect the phenomenon of visual extinction—the lack of awareness of an object in a seeing area of the visual field when other seeing areas of the visual field are stimulated simultaneously.

The obvious advantages of confrontation visual field testing include its simplicity, flexibility, speed of administration, and ability to be performed in any setting, including at the bedside of a hospitalized patient. The disadvantages of confrontation visual field testing include the lack of standardization, the qualitative nature of the results, and the limited ability to detect subtle deficits or to monitor progression or resolution of visual loss. Nevertheless, because it is quick and easy to perform, confrontation visual field testing should be performed on all patients, regardless of their visual complaints.

Amsler grid. The Amsler grid is a chart that is specifically designed to qualitatively analyze the disturbances of visual function that accompany the beginning and evolution of maculopathies. The charts are a series of lined and patterned grids that test the central visual field within 10 degrees of fixation when the plates are held at 1/3 of a meter from the eyes. Each square of the grid subtends 1 degree of visual angle, making the ability to define the location of small defects rather easy. The most common chart used has a black grid on a white background; however, one can also use a white grid on a black background and even a red grid on a black background.

The Amsler grid test is quick and easy to administer. The patient is instructed to look at the central dot and asked if, in fact, he/she can see it. If not, the patient may have a central scotoma, and the examiner must query the patient regarding exactly what he/she DOES see. If the patient sees the dot, the examiner asks if the patient is aware that surrounding it are numerous squares. The examiner then asks the patient if any of the squares are distorted, missing, etc. The patient is encouraged to draw directly on the grid the areas



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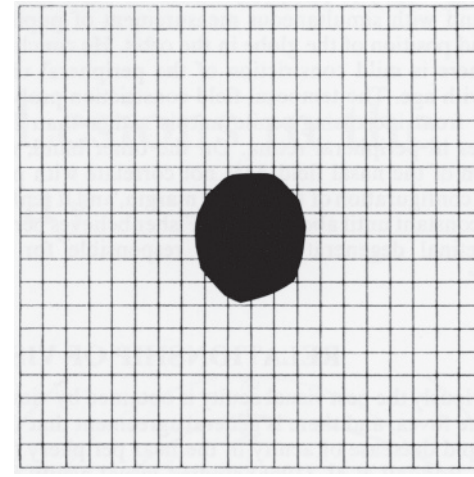


B

Figure 1.8 Amsler grid defects. **A:** Metamorphopsia and paracentral scotomas in a patient with a maculopathy. **B:** A small central scotoma in a patient with optic neuritis.

of disturbance. This testing technique is well known to ophthalmologists who routinely examine patients with known or suspected macular disease, because the Amsler grid can be used to detect metamorphopsia or identify and plot small scotomas and other visual field defects that occur with macular scars, mild macular degeneration, central serous chorioretinopathy, and related disorders. It is perhaps less well recognized that small central or paracentral scotomas that occur with optic nerve disease also can be identified with the Amsler grid (Fig. 1.8). Indeed, the grid is particularly useful for identifying small central scotomas and other subtle central visual disturbances that are difficult to detect with more sophisticated automated and manual perimeters. Its main disadvantages are related to the qualitative, subjective nature of the information derived from the test.

Static perimetry. Static perimetry uses a stationary target, the luminance of which is adjusted to vary its visibility. It most often is performed with an automated perimeter such as the Humphrey Field Analyzer or the Octopus perimeter, with the former being by far the most widely used instrument. Measurements of the increment threshold are obtained at a variety of visual field locations that usually are arranged in a grid pattern or along meridians (Fig. 1.9).

The amount of time required for static perimetry depends on several factors, including patient alertness and cooperation, the threshold strategy used, and the size of the field being tested. For example, using the Humphrey Field Analyzer, a full-threshold test usually takes about 10 to 12 minutes per eye, whereas use of the Swedish Interactive Threshold Algorithm (SITA) that employs thresholds that are 1 to 2 dB higher than the full-threshold method results in a 50% (SITA-Standard strategy) to 70% (SITA-Fast) reduction in test time (about 4 to 6 minutes for SITA-Standard and 3 to 4 minutes for SITA-Fast). The size of the target used usually is a Goldmann size III, a light stimulus with a diameter of 0.5 degrees; however, for patients with poor acuity (e.g., <20/200), a Goldmann size V stimulus with a diameter of about 2 degrees provides a more reliable and reproducible result. As far as the size of the field tested, most neuro-ophthalmologists use a 24-2 test, meaning that the central 24 degrees is tested superiorly, inferiorly, and temporally (the nasal field is tested out to 30 degrees because the developer of the program, Anders Heijl, wanted to be sure that the test would capture an early nasal step from glaucoma) (Fig. 1.9A), whereas others prefer a 30-2 test in which the entire field is tested out to 30 degrees. For patients whose history suggests one or more small central or paracentral defects, a 10-2 (i.e., 10-degree) field test is available (Fig. 1.9B).

Kinetic perimetry. The Goldmann perimeter is a white hemispheric bowl of uniform luminance (31.5 asb) onto which a small bright stimulus is projected. It generally is used to perform kinetic perimetry, although static and suprathreshold static

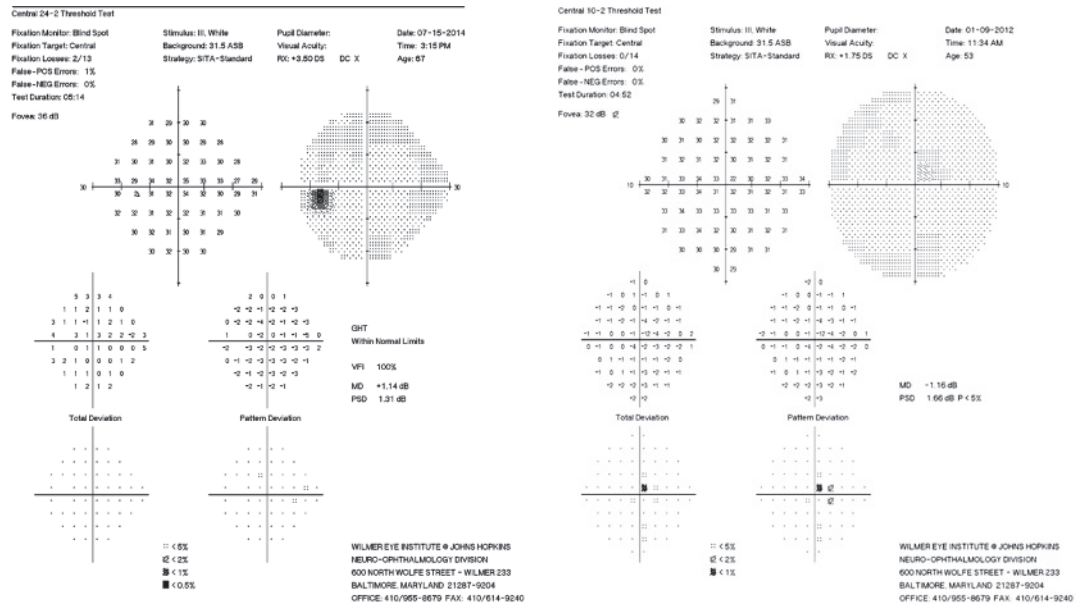


Figure 1.9 Static perimetry using a Humphrey Visual Field Analyzer. **A:** Full field using a 24-2 threshold test and SITA-Standard strategy. **B:** Tiny central scotoma in a different patient identified using a 10-2 threshold test and SITA-Standard strategy. This field defect would not have been identified using a 24-2 threshold test.

perimetry can also be tested with this perimeter. Unlike the Amsler grid and most automated perimeters, the Goldmann perimeter can be used to evaluate the entire visual field and is particularly useful when there is an extensive or a peripheral defect (Fig. 1.10). With one eye occluded, the patient fixates a small target in the center of the bowl with the uncovered eye, and the perimetrist monitors eye position by means of a telescope. A particular stimulus size and luminance are projected onto the bowl, the target is moved from the far periphery toward fixation at a constant rate of speed, typically 4 to 5 degrees/sec, and the patient is instructed to press a response button when he/she first detects the stimulus. The location of target detection is noted on a chart, and the process is repeated for different meridians around the visual field. Isopters and scotomas are plotted in a manner similar to that described for the tangent screen examination, except that both the target size and luminance can be adjusted to vary stimulus detectability. This process produces a two-dimensional representation of the hill of vision that is basically a topographical contour map of the eye's sensitivity to light. Kinetic testing (at least 1 or 2 isopters) on the Goldmann perimeter can be performed in cooperative children as young as 5 or 6 years of age.

Interpretation of Automated Visual Field Information

A large amount of visual field information is derived from perimetric testing, especially from automated perimetry. Test conditions and stimulus parameters used, indicators of patient reliability and cooperation, physiologic factors (pupil size, refractive state, visual acuity, etc.), summary statistics and visual field indices, and other items are presented in conjunction with sensitivity values for various locations in the patient's visual field. Visual field sensitivity also can be represented in many different forms (numerical values, deviations from normal, gray scale representations, probability plots, etc.). The following discussion presents a brief overview of the various types of information provided on the final printed outputs. Because of its current popularity and widespread use, this discussion and most of the examples are derived from automated static perimetry using the Humphrey machine; however, some examples of kinetic testing using the Goldmann perimeter are presented for certain clinical scenarios, especially for situations in which kinetic testing provides more information about visual field status.

Several important pieces of information that should be checked on each visual field examination are the position of the eyelids, the refractive correction used for testing, pupil size, and visual acuity. Ptosis can produce a superior visual field defect that may be minimal or significant (Fig. 1.11A). High refractive corrections (greater than 6-diopter spherical equivalent) can sometimes produce trial lens rim artifacts (Fig. 1.11B). When a patient's spherical equivalent correction for perimetric testing exceeds 6 diopters, it is advisable to use a soft contact lens correction that is appropriate for the testing distance to avoid lens rim

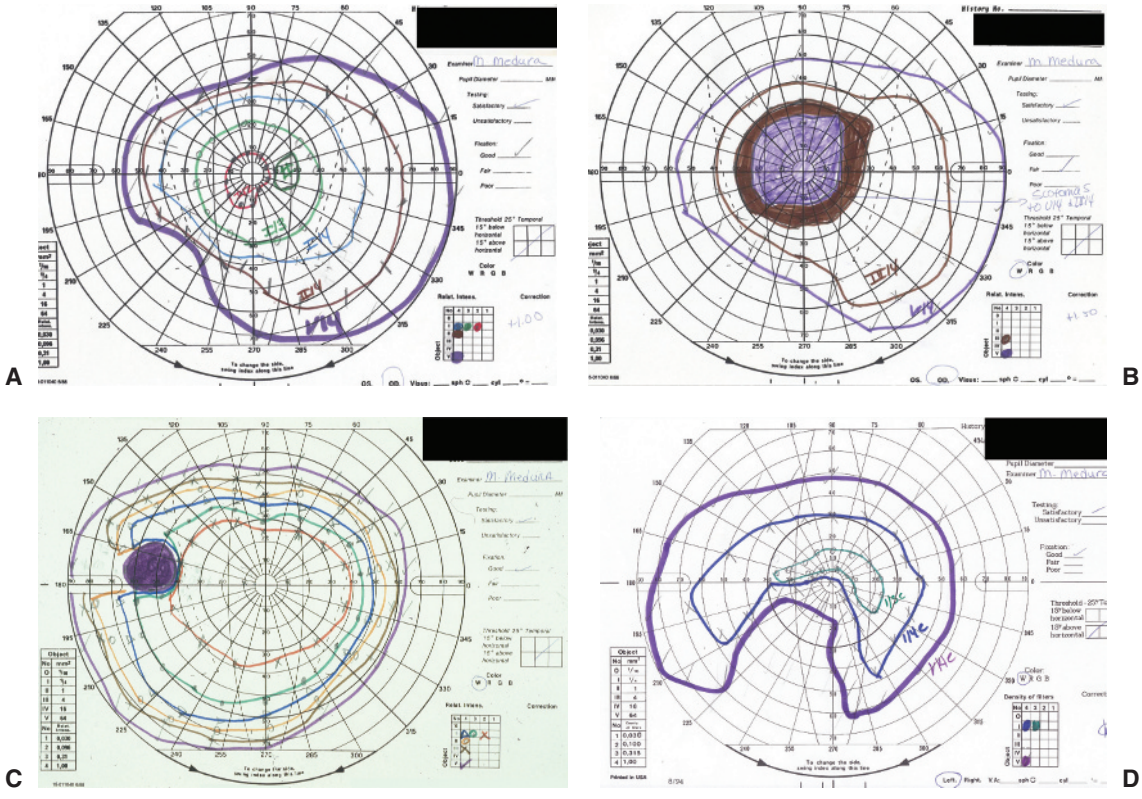


Figure 1.10 Kinetic perimetry using a Goldmann perimeter. **A:** Full visual field. **B:** Large central scotoma associated with a full peripheral field. Static perimetry using a 10-2, 24-2, or 30-2 threshold would provide no useful information as the entire field would be absent. **C:** Far peripheral scotoma. Static perimetry using a 10-2, 24-2, or 30-2 threshold would not identify this scotoma as it is too far peripherally. **D:** Partial sparing of the temporal peripheral field (the temporal crescent) in a patient with a left inferior homonymous quadrantic defect (only the field of the left eye is shown). Static perimetry would not have shown the area of spared peripheral field.

artifacts. Proper near-refractive corrections that are appropriate for the near-testing distance of the perimeter bowl and the patient's age must be used to minimize the likelihood of refraction scotomas and sensitivity reductions from blur (Fig. 1.11C). Small pupils (less than 2-mm diameter) can produce spurious test results, especially in older persons who may have early lenticular changes. If pupil size is small, the patient should be dilated to 3 mm or greater (Fig. 1.11D). Finally, the patient's visual acuity also can provide useful information when assessing generalized visual field sensitivity loss and the potential sources responsible for the loss.

Reliability indices. The quality of information obtained from perimetry and visual field testing depends on a patient's cooperation, willingness, and ability to respond in a reliable fashion and maintain a consistent response criterion. It thus is important to have an assessment of patient reliability and consistency to properly evaluate the significance of visual field information. With manual perimetry, it is possible to monitor the patient's fixation behavior directly by means of a telescopic viewer (see above). False-positive errors (responses when no stimulus is presented) and false-negative errors (failure to respond to a stimulus presented in a region previously determined to be able to detect equal or less detectable targets) can be monitored throughout the test procedure.

Automated test procedures not only have the capability of monitoring false-positive errors, false-negative errors, and fixation behavior in the same manner as described above but also can assess response fluctuation by retesting a sample of visual field locations. Also, indirect indicators of fixation accuracy (e.g., whether or not a patient responds to a target presented to the physiologic blind spot) can be monitored. An additional advantage of automated test procedures is that these **reliability indices** (false positives, false negatives, fixation losses, short-term fluctuations) can be immediately compared with those of age-adjusted normal control subjects, thereby providing an indication as to whether or not the patient's reliability parameters are within normal population characteristics (Fig. 1.12).

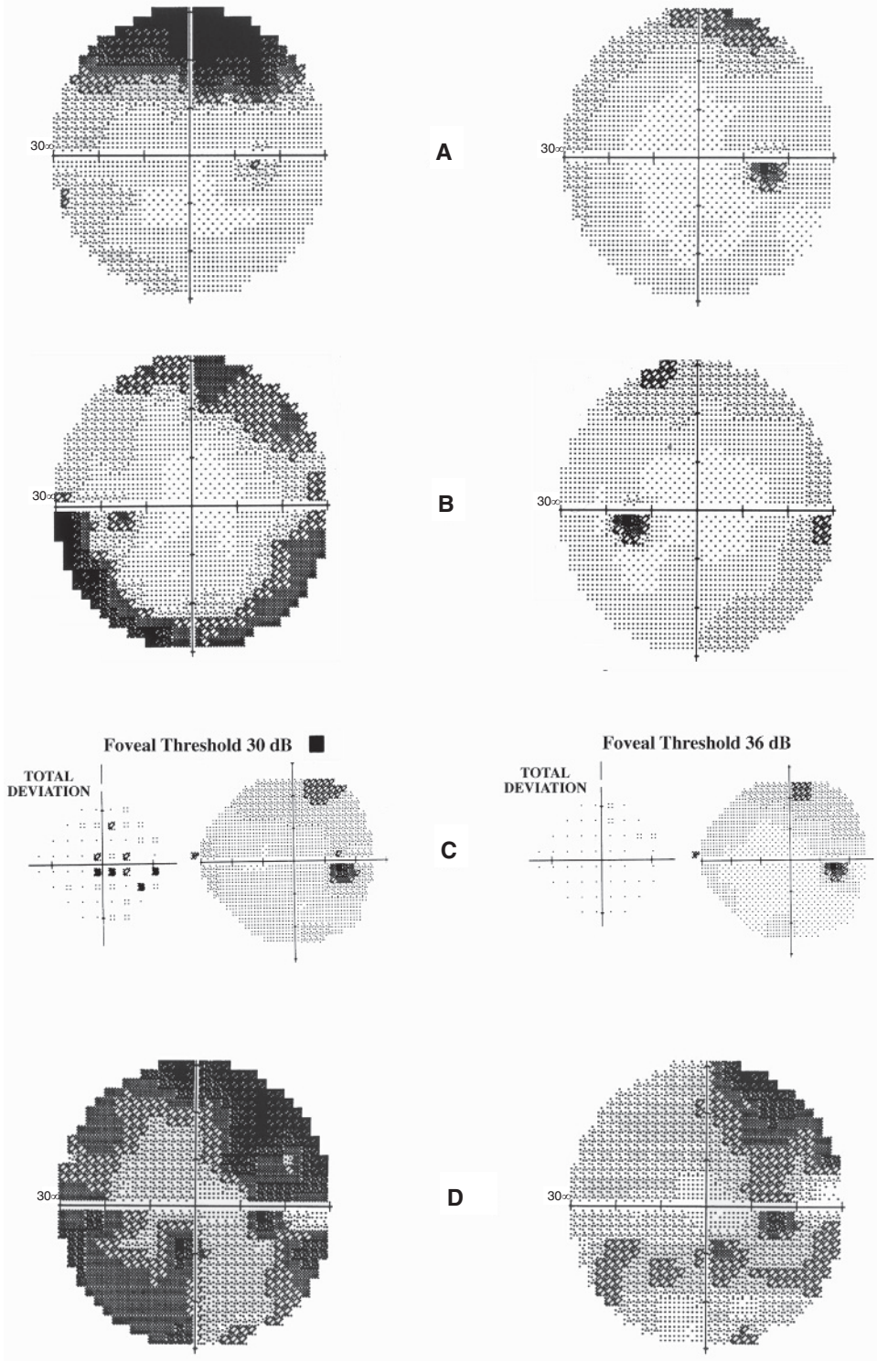


Figure 1.11 Influences on visual field test results. **A:** An example of visual field results for ptosis before (**left**) and after (**right**) taping up the upper lid and brow. **B:** Example of trial lens rim artifact (**left**) and its disappearance (**right**) after realigning the patient. **C:** Refractive error introduced by improper lens correction (**left**) and results after proper lens was employed (**right**). **D:** Visual field results obtained in the same eye with a 1-mm (**left**) and a 3-mm (**right**) pupil diameter.

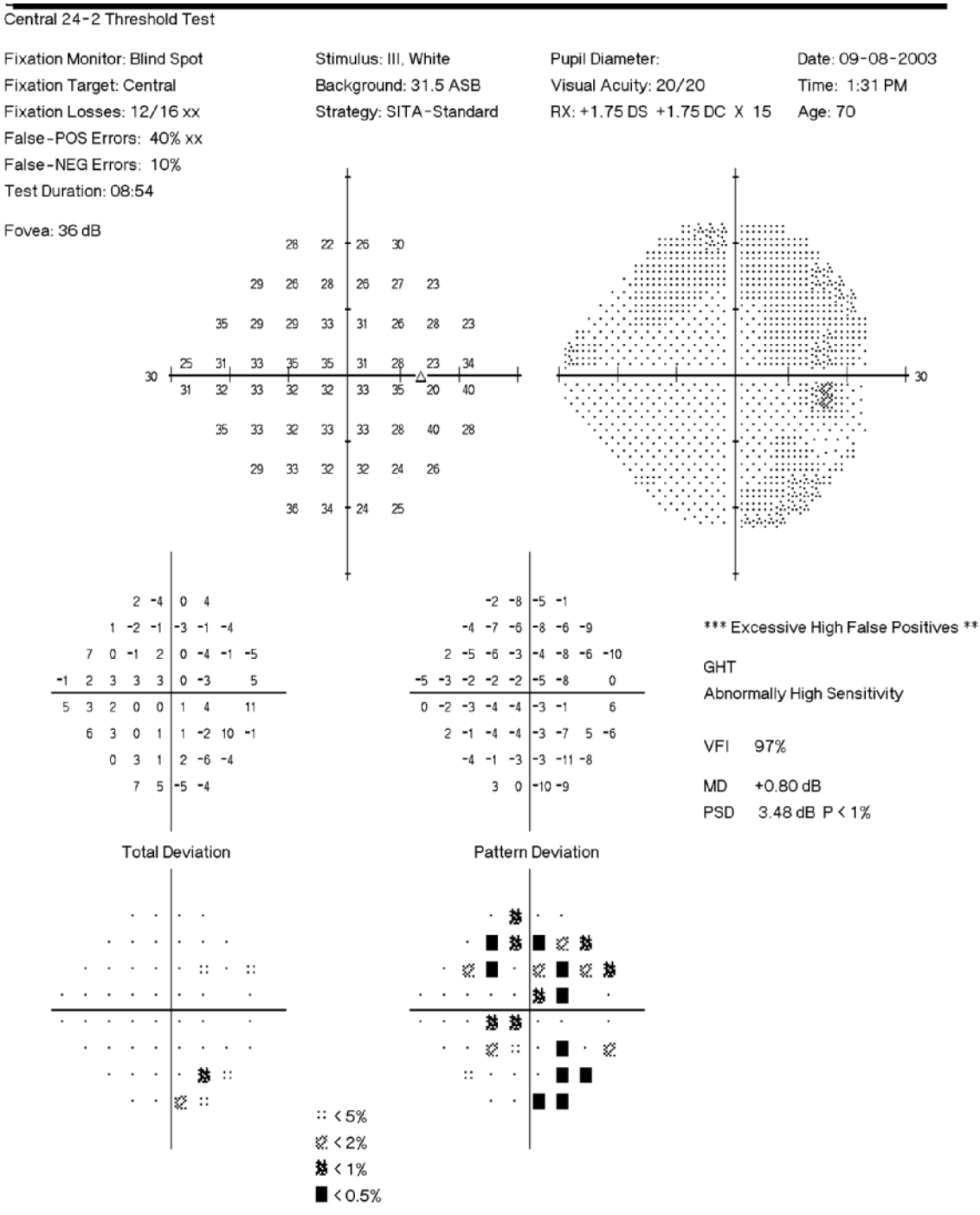


Figure 1.12 Markedly abnormal reliability indices in a patient on whom static perimetry was attempted using a Humphrey Visual Field Analyzer. Note that the patient has multiple fixation losses, false-positive responses, and false-negative responses. When faced with this issue, the physician must decide whether to repeat the field at another time in the hope that the problems were because the patient had never undergone field testing before, use a different strategy that takes less time (e.g., SITA-Fast instead of SITA-Standard), or abandon this technique and use another, such as confrontation testing or kinetic perimetry.

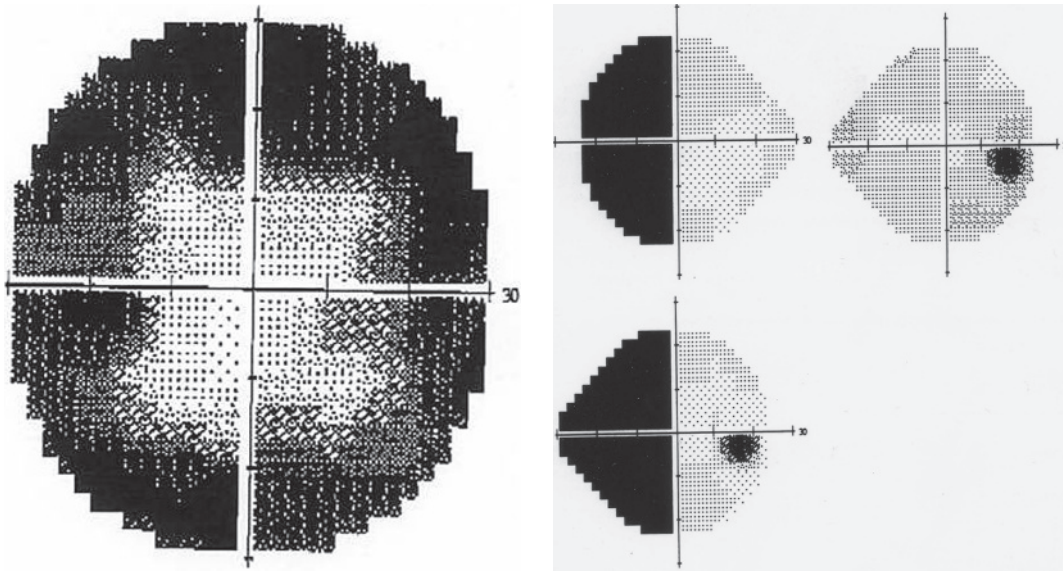


Figure 1.13 Nonorganic visual field defects. **A:** "Cloverleaf pattern." This type of constricted visual field occurs because the automated program on the Humphrey Visual Field Analyzer is designed so that four circled points are checked initially, and the testing in each quadrant proceeds outward from these points. If the patient ceases to respond after only a few points have been tested, the result is some variation of the cloverleaf visual field. **B:** A monocular nasal hemianopia is present not only when the left eye is tested but also when both eyes are tested simultaneously. If the field defect was organic, it would disappear when both eyes were tested simultaneously because the temporal field of the right eye would overlap the nasal field of the left eye (with the hemianopia).

Some of the reliability indices for automated perimetry are not always accurate indicators of a patient's true performance. For example, false-negative rates are correlated with visual field deficits, that is, there is an increase in false-negative responses with increased field loss. Thus, high false-negative rates may be more indicative of disease severity than of unreliable patient responses. Excessive fixation losses can be caused by factors such as mislocalization of the blind spot during the initial phases of testing, misalignment or head tilt of the patient midway through testing, or inattention on the part of the technician administering the visual field examination. Also, one should be careful not to consider reliability indices as a replacement for technician interaction and monitoring of patients. Some patients are uncomfortable when left alone in a darkened room during automated perimetry testing. In addition, misalignment of the patient, drowsiness, and related factors can occur during testing and go undetected if the patient is not monitored adequately. As has been emphasized above, it is important to remember that it is the test procedure that is automated, not the patient.

Although reliability indices are helpful in determining if the results of visual field testing are accurate, they are not sufficient to eliminate the possibility that a visual field defect is nonorganic in nature. Both patients and otherwise normal subjects can "fool" the automated perimeter, producing a variety of abnormal fields despite maintaining reliability indices that are within normal limits (Fig. 1.13).

Visual field indices. A distinct advantage afforded by automated perimeters is the ability to provide summary statistics, usually called **visual field indices**. The Mean Deviation (MD) on the Humphrey Field Analyzer refers to the average deviation of sensitivity at each test location from age-adjusted normal population values. The mean deviation provides an indication of the degree of generalized or widespread loss in the visual field. The Pattern Standard Deviation (PSD) on the Humphrey Field Analyzer presents a summary measure of the average deviation of individual visual field sensitivity values from the normal slope after correcting for any overall sensitivity differences, that is, the MD. It represents the degree of irregularity of visual field sensitivity about the normal slope and, therefore, indicates the amount of localized visual field loss, because scotomas produce significant departures from the normal slope of the visual field.

Probability plots. Although automated perimeters provide a general assessment of the visual field by showing increasingly dark areas correlating with decreasing sensitivity (the gray scale) (Fig. 1.14), a major advantage of automated static perimetry is that a

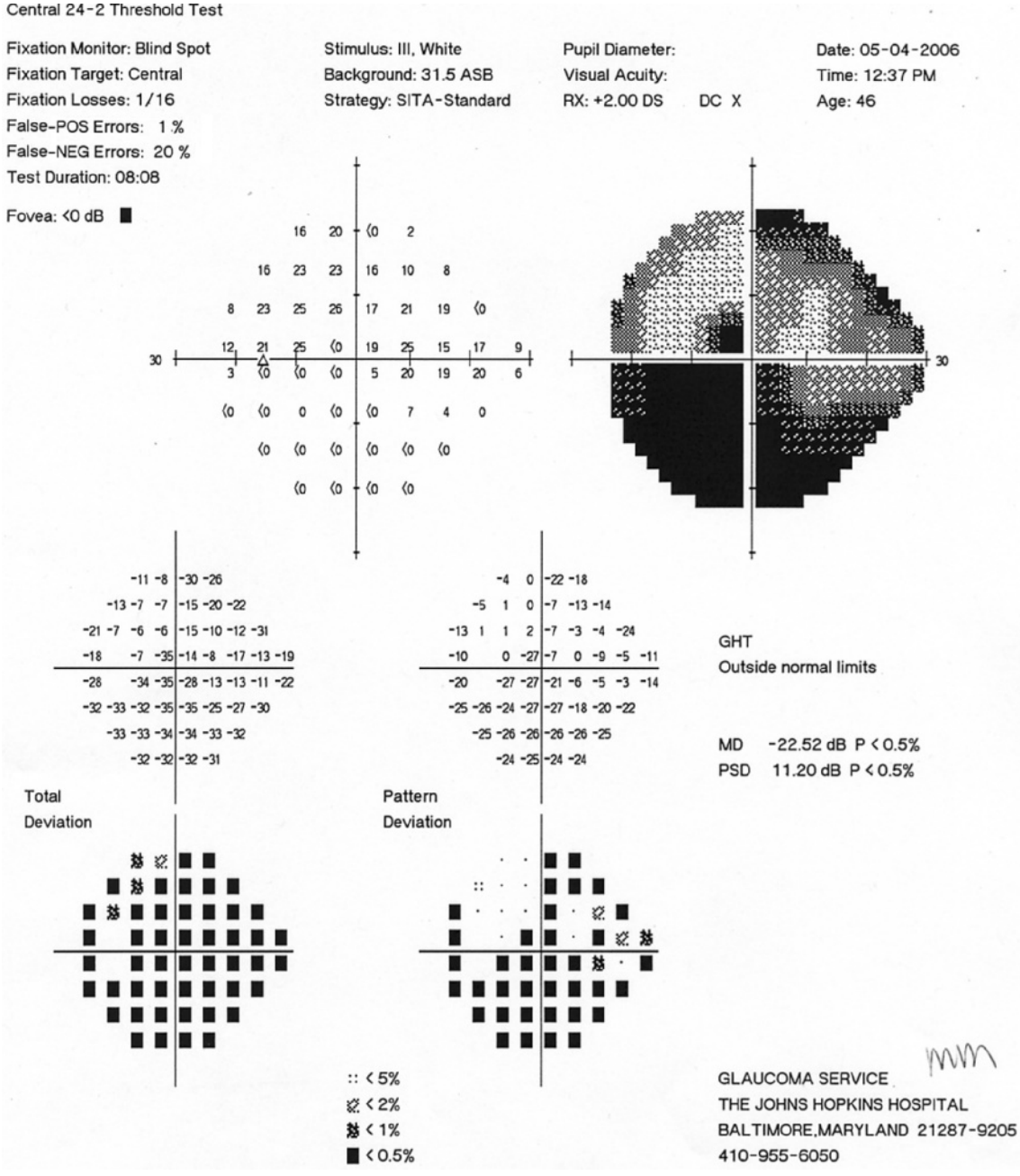


Figure 1.14 Static perimetry using a Humphrey Visual Field Analyzer. Note good correlation between the gray scale (**above right**) and the Pattern Deviation Plot (**lower right**).

patient's test results are compared with age-adjusted normal population values. Thus, it is possible to determine the amount of deviation from normal population sensitivity values on a point-by-point basis for all visual field locations tested. A useful means of expressing this information is by means of **probability plots**. The Humphrey Field Analyzer has two methods of presenting this type of information. One is called the "Total Deviation Plot" and the other is called the "Pattern Deviation Plot." For the Total Deviation Plot, each visual field location has one of a group of different symbols indicating if the sensitivity is within normal limits or is below the 5%, 2%, 1%, or 0.5% of normal limits, respectively. In other words, visual field locations or indices that have a probability corresponding to $p < 1\%$ indicate that this

value is observed less than 1% of the time in a normal population of the same age. This provides an immediate graphic representation of the locations that are abnormal and the degree to which they vary from normal levels.

The Pattern Deviation Plot is similar to the Total Deviation Plot, except that the determinations are performed after the average or overall sensitivity loss has been subtracted, thereby revealing specific locations with **localized** deviations from normal sensitivity values. The value of these representations is twofold. First, they provide an immediate indication of the locations with sensitivity loss. Second, the comparison of the Total and Pattern Deviation Plots provides a clear indication of the degree to which the loss is diffuse or localized. If the loss is predominantly diffuse, the abnormal locations will appear on the Total Deviation Plot, but all or most of these locations will be within normal limits on the Pattern Deviation Plot (Fig. 1.15A). If the deficit is predominantly localized, the Total and Pattern Deviation Plots will look almost identical (Fig. 1.15B). The degree of similarity between the Total and Pattern Deviation Plots thus gives an indication of the proportion of loss that is diffuse and localized. In some instances, the Total Deviation Plot may appear to be normal, but the Pattern Deviation Plot reveals a number of abnormal locations. This occurs when the patient's measured sensitivity is better than normal (Fig. 1.15C) or when the patient presses the response button too often ("trigger happy") (Fig. 1.15D). In general, the Pattern Deviation Plot is the most important diagram to view when assessing the results of automated field testing as it will often show subtle areas of abnormality that may not be apparent on the gray scale or may be hidden by general loss of sensitivity shown in the Total Deviation Plot.

Progression of visual field loss. The determination of whether or not a patient's visual field improves, worsens, or remains stable over time is one of the most difficult aspects of visual field interpretation. Several quantitative analysis procedures are available for evaluating visual field progression and are particularly useful in monitoring patients with glaucoma; however, none enjoys complete acceptance by the clinical neuro-ophthalmic community. Nevertheless, the use of quantitative statistical analysis procedures may be helpful in monitoring a patient's visual field status.

Several important factors should be considered when evaluating a patient's visual field status over time. First, it is necessary to examine the test conditions that were present for each visual field examination. If test strategies, target sizes, or other test conditions are different from one examination to another, it is difficult to compare the results, because the type of test procedure and the stimulus size (and characteristics) can significantly alter the appearance of the visual field. Second, it is important to determine if there are any differences in patient conditions from one visual field to another. As noted above, if there are meaningful differences in pupil size, refractive corrections, visual acuity, time of day, or other factors (e.g., upper lid taped on one occasion and not on another occasion), this can have a dramatic effect on the visual field results obtained on different visits (Fig. 1.11). Third, unless the visual field changes are dramatic, it is important to base judgments of visual field progression or stability on the basis of the entire series of visual fields that are available. It often is not possible to distinguish subtle visual field changes from long-term variation on the basis of two visual fields (e.g., comparing the current visual field to the previous visual field). In particular, patients with moderate to advanced visual field loss can sometimes exhibit considerable variations from one visual field to another. Also, factors such as fatigue and experience can produce significant differences in visual field characteristics. If it is suspected that a change in visual field loss has occurred, it is best to repeat the examination on a separate visit to confirm the suspected change. Depending on which part of the sequence and which eye is examined, any two successive visual fields can reflect apparent improvement, progression, or stability of the visual field (Fig. 1.16). As noted above, for patients with poor visual acuity (e.g., <20/200), the use of a Goldmann size V stimulus (diameter 2 degrees) instead of a Goldmann size III stimulus (diameter 0.5 degrees) provides more reliable results.

Five-Step Approach to Visual Field Interpretation

One of the common errors that occur in visual field interpretation is the lack of attention to details and specific patterns of visual field loss before obtaining a global evaluation of the visual field. To avoid this tendency, we suggest a simple five-step approach to visual field interpretation:

1. Determine if the visual field is normal or abnormal for each eye separately. Automated perimetry results provide assistance with this task, because they show both point-by-point and summary comparisons of the patient's test results with age-matched normal population values. If both eyes are normal, both in terms of statistical comparison and clinical assessment, then further evaluation is unnecessary.
2. If one or both visual fields are abnormal, examine the ancillary information to determine if proper test conditions were employed, the appropriate

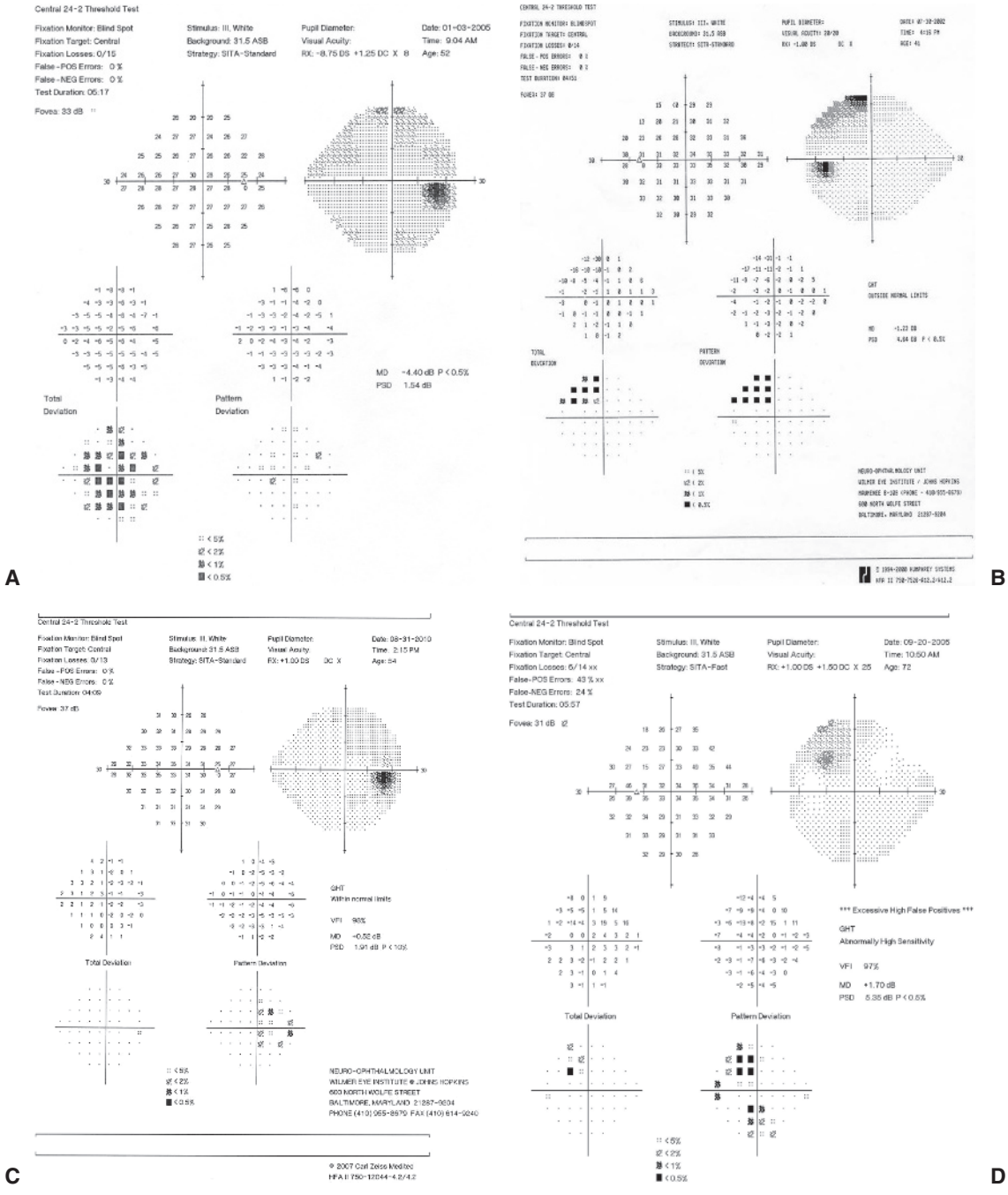


Figure 1.15 Pattern results as they are depicted on the gray scales, Total Deviation Plots, and Pattern Deviation Plots. **A:** Diffuse loss. **B:** Dense localized loss. **C:** Very mild localized loss. **D:** "Trigger happy" patient.

near correction was used, and the pupil size was sufficiently large. Also, check for patterns of field loss that are indicative of a trial lens rim artifact, a droopy upper eyelid, or other nonpathologic conditions that may account for the visual field loss. Fatigue, drowsiness, and related conditions also can produce apparent visual field loss. It is crucial that the person who performs the perimetric testing, especially with automated perimetric tests, be attentive to these factors. A surprising

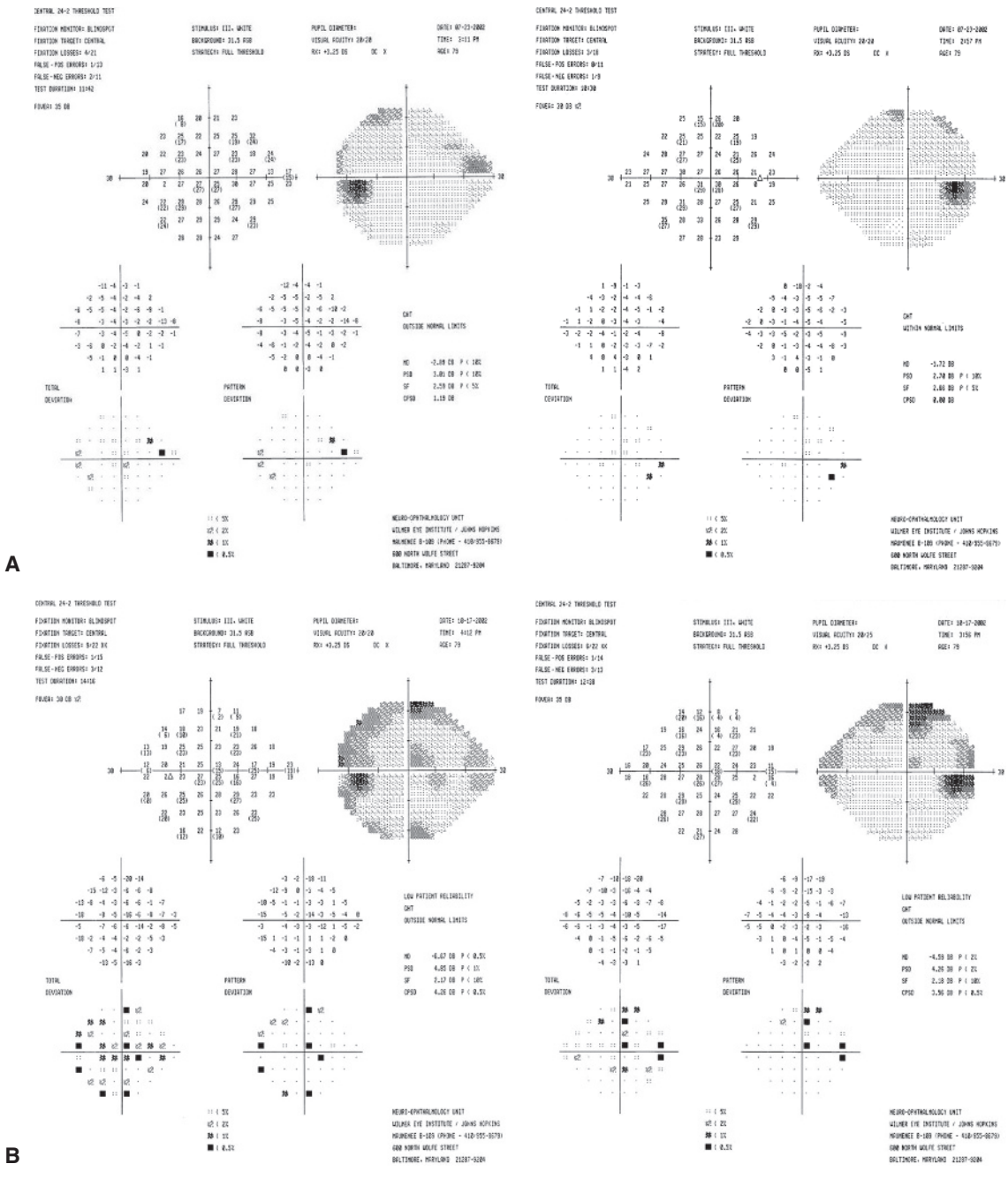
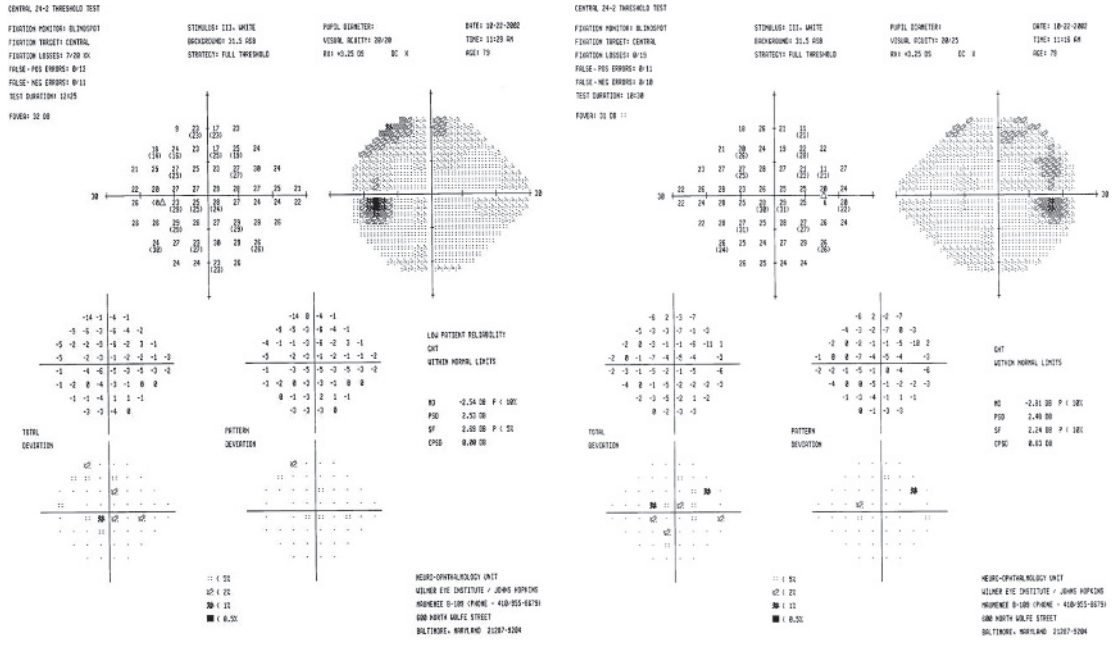


Figure 1.16 Spurious field defect in a patient with a pituitary adenoma. **A:** On 7/03/02, the patient has only some nonspecific defects in both eyes. **B:** On 10/17/02, 3 months later, the patient appears to have developed significant field defects in both eyes; however, note that the patient is 79 years old, and the fields were obtained at about 4 PM. Before we recommended treatment of the adenoma, we brought the patient back 5 days later for repeat fields. (*continued*)

number of visual field defects can be attributed to nonpathologic influences. In some instances, it may be necessary to query the technician as to the state of the patient when he/she was undergoing testing.

3 Determine if the visual field is abnormal in both eyes or in only one eye. If the field is abnormal in only one eye, the defect almost always is caused by a disorder anterior to the optic chiasm (Fig. 1.17), whereas if the fields of both eyes are abnormal, the



C

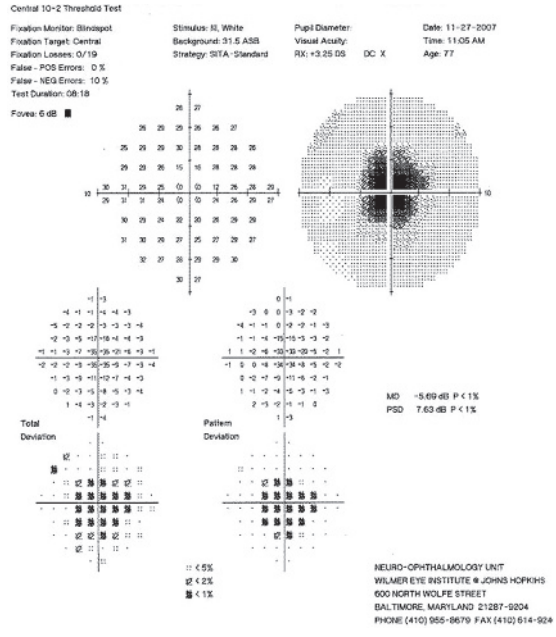
Figure 1.16 (*Continued*) **C:** Repeat fields performed earlier in the day (about 11:15 AM) on 10/22/02 show that the apparent worsening of the fields was spurious and probably related to fatigue.

deficit is at the chiasm (Fig. 1.18), posterior to the chiasm (Fig. 1.19) **or** the patient has bilateral intraocular or optic nerve disease.

4 Determine the general location of the visual field loss for each eye independently. Specifically, determine if the field loss is in the superior or inferior hemifield, the nasal or temporal hemifield, or the central portion of the field. This is especially important for the nasal and temporal hemifield assessment. If the loss is extensive, determine where the greatest amount of field loss is present. If the field loss is bitemporal and respects the vertical midline, then a chiasmal locus should be strongly suspected (Fig. 1.18). If the field loss is nasal in one eye and temporal in the other eye (i.e., homonymous), a retrochiasmal location should be suspected (Fig. 1.19). Binasal defects or a nasal deficit in only one eye should generate a suspicion of glaucoma, various nonglaucomatous optic neuropathies, or certain types of retinal disorders. A central defect in one or both eyes may indicate a macular disorder. With this simple step, a global view of visual field properties is generated, and a hierarchy of potential locations of damage along the visual pathway and probable disease entities is hypothesized.

5 Look at the specific shapes, patterns, and features of the visual field loss (Figs. 1.17 to 1.19). Does the defect respect either the horizontal or vertical meridians? What is the shape of the defect (arcuate, oval, circular, pie-shaped, irregular)? If there is field loss in both eyes, is it congruous (symmetric in the two eyes) or incongruous (more extensive visual field loss in one eye than in the other) (Fig. 1.20)? Do the edges of the defect have a steep or a gradual sloping profile? These and other specific features of the visual field should provide confirmatory information for the location of the damage determined by Step 4 or allow one to differentiate among several possible alternative locations. However, they should not be used as the initial basis for generating a hypothesis about location of damage. Attention to specific features of the visual field before getting a global view of the field from Step 4 may lead to misinterpretation of the field information.

The approach to visual field interpretation outlined above is not intended to cover all possible scenarios but, rather, is meant to guide the identification of most kinds of visual field defects and to avoid many of the common pitfalls in assessment. Once the pattern and degree of field loss has been established, a differential diagnosis needs to be determined. If there is doubt about the validity of visual field results, the test should be repeated when the patient is well rested and alert (Fig. 1.16). Pathologic visual field changes usually are replicable, whereas nonpathologic changes typically are not. If there is concern about fatigue



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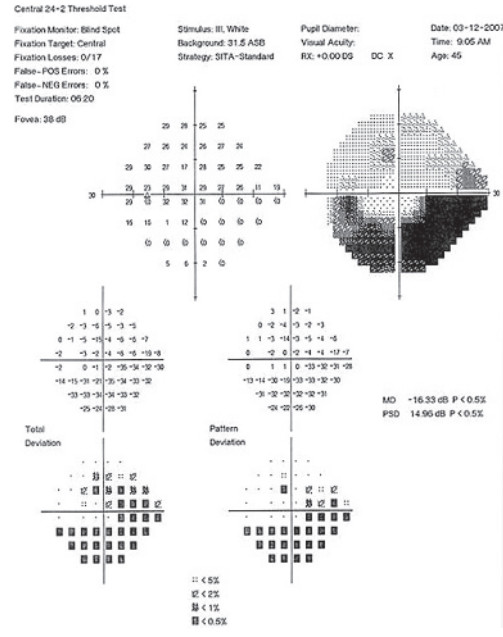

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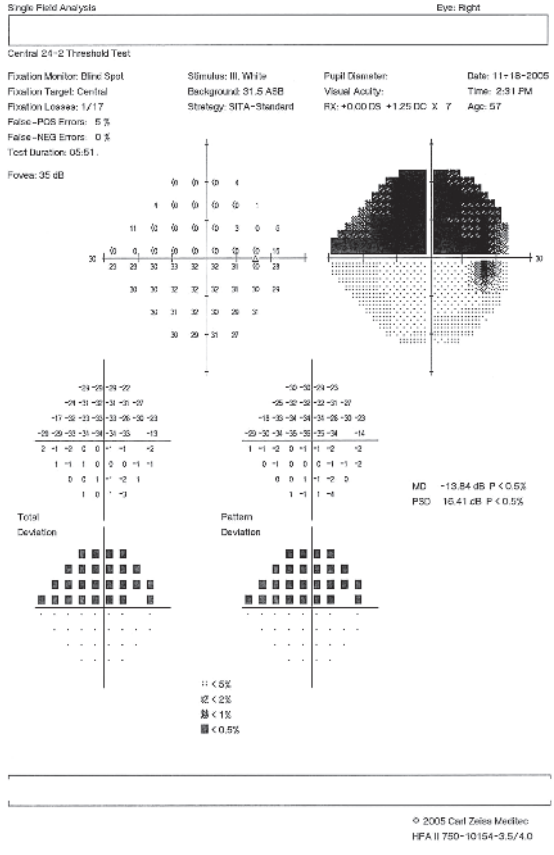


C

Figure 1.17 Examples of monocular field defects detected with a Humphrey Visual Field Analyzer. **A:** Central scotoma. **B:** Inferior arcuate defect. **C:** Superior altitudinal defect.

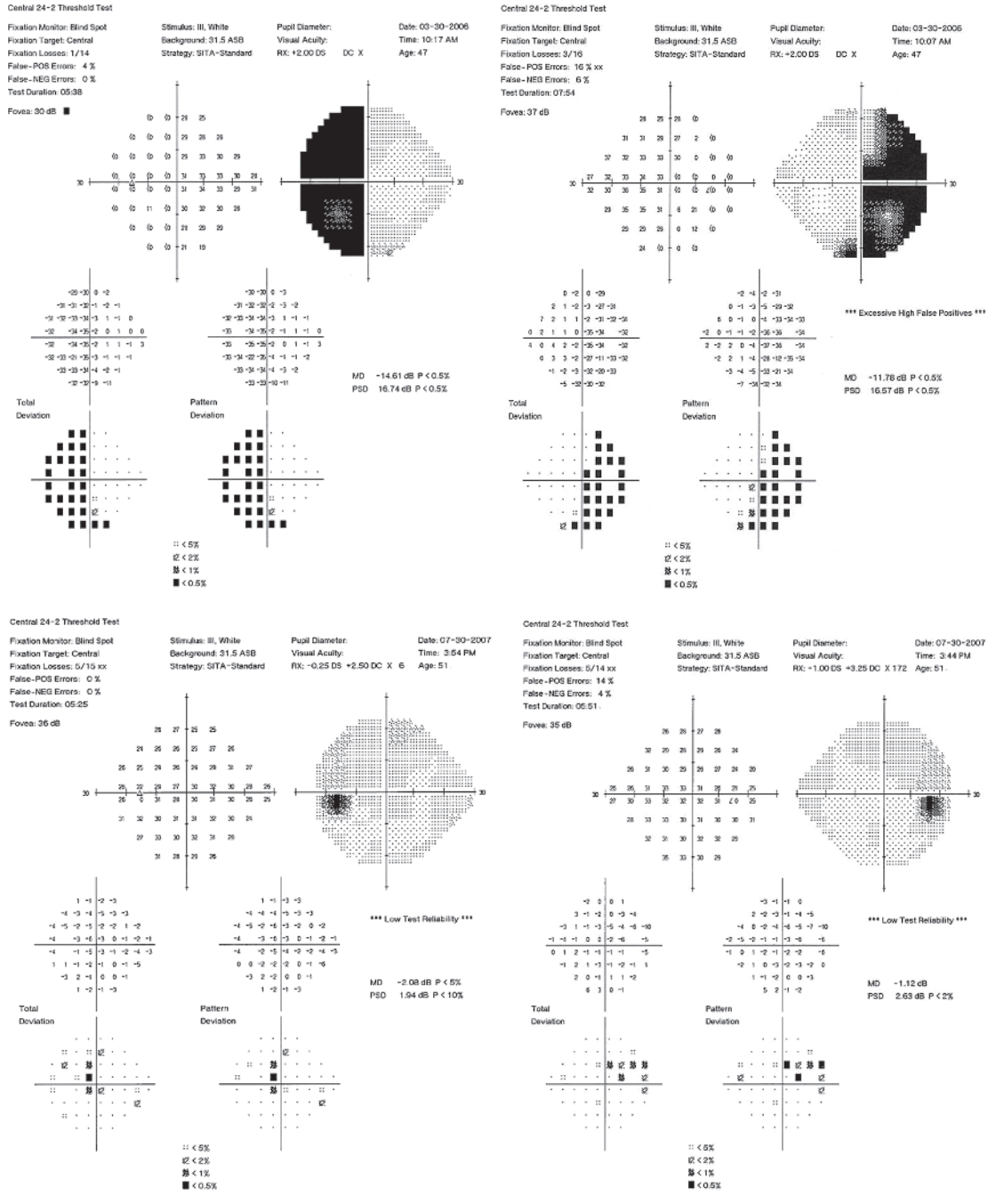


Figure 1.18 Examples of bitemporal field defects detected with a Humphrey Visual Field Analyzer. **A:** Severe bitemporal hemianopia. Note correlation between the gray scale (**above right**) and the Total (**lower left**) and Pattern (**lower right**) Deviation Plots. **B:** Very mild superior bitemporal quadrantic defect. Note that the gray scale does not clearly identify the defect, whereas it is obvious when looking at both the Total Deviation and Pattern Deviation Plots.

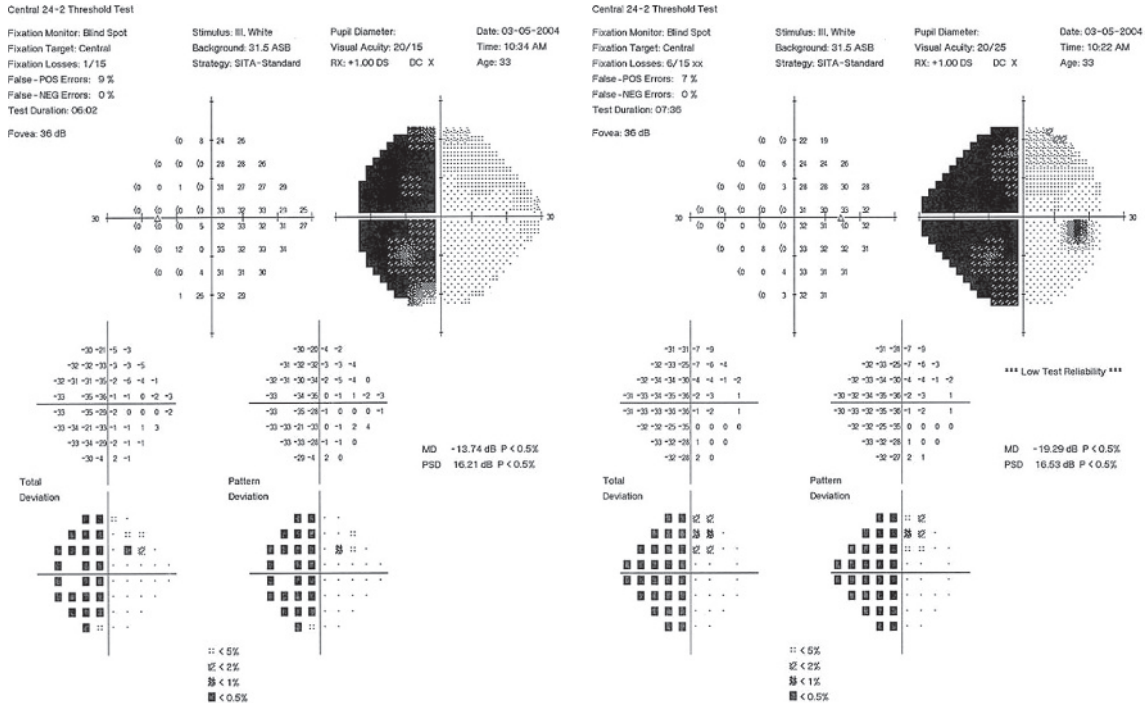
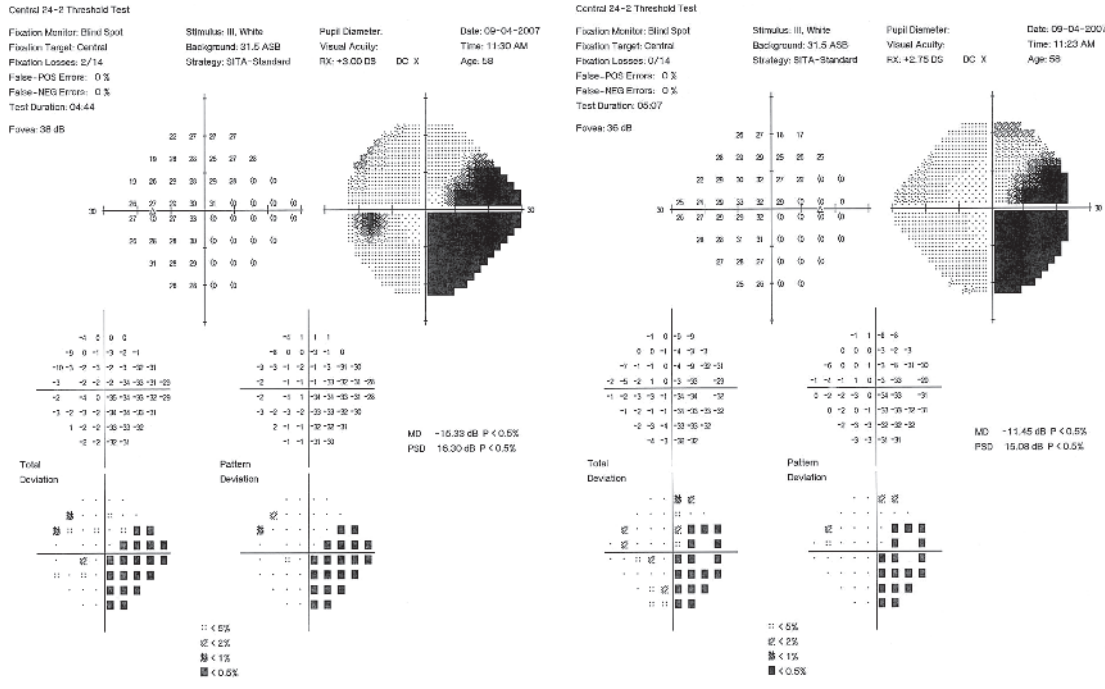


Figure 1.19 Left complete homonymous hemianopia detected with a Humphrey Visual Field Analyzer. Note correlation between the gray scale (**upper right**) and the Total (**lower left**) and Pattern (**lower right**) Deviation Plots.

affecting visual field results, a shorter test procedure should be employed.

Pupillary Examination

Examination of the pupils is an essential part of the afferent system evaluation. Pupil size for each eye should be noted, as should the magnitude and latency of the direct and consensual responses to light and near stimulation. A relative afferent pupil defect (RAPD) is the hallmark of a unilateral afferent sensory abnormality or bilateral asymmetric visual loss. The etiology usually is an optic neuropathy, but other abnormalities such as a central retinal artery occlusion, retinal detachment, or a large macular scar may be responsible (see Chapter 2). In addition, patients with complete or nearly complete homonymous hemianopias from damage to the contralateral optic tract almost always have an RAPD on the side of the hemianopia (contralateral to the lesion) due to interruption of the afferent pupillomotor fibers in the optic tract destined for the dorsal midbrain. Although it has been shown that patients with postgeniculate homonymous hemianopias may have an RAPD, presumably from transsynaptic degeneration across the lateral geniculate nucleus, it is always **subclinical** and can be identified only with pupillometry. Thus, the observation of an obvious RAPD on the side of a homonymous hemianopia unassociated with loss of acuity is indicative of damage to the contralateral optic tract. Finally, in very rare instances, a lesion of the brachium of the superior colliculus where afferent pupillomotor fibers travel to reach the Edinger–Westphal nuclei may cause an RAPD that is unassociated with ANY visual sensory disturbance. In this setting, the patient is unaware of any visual sensory disturbance, and there is no decrease in visual acuity, no color vision deficit, and no visual field defect. The presence or absence of an RAPD is one of the most crucial issues in dealing with a patient who has monocular or binocular but asymmetric visual loss because in such a setting, **an RAPD may be the only objective sign of organic and serious anterior visual pathway dysfunction.** Cataracts, refractive errors, and nonorganic visual loss NEVER cause an RAPD. Thus, an RAPD in a patient with a cataract, regardless of the cataract's density, indicates that something else (or in addition to the cataract) is responsible for the patient's decreased vision. In general, a vitreous hemorrhage, no matter how dense, does not cause an RAPD. Thus, the observation of an RAPD in a patient with a vitreous hemorrhage indicates damage to the retina, optic nerve, or both. Having said this, as some patients have been reported with very dense vitreous hemorrhages causing a flat electroretinogram (ERG) with restoration of the waveform after vitrectomy,



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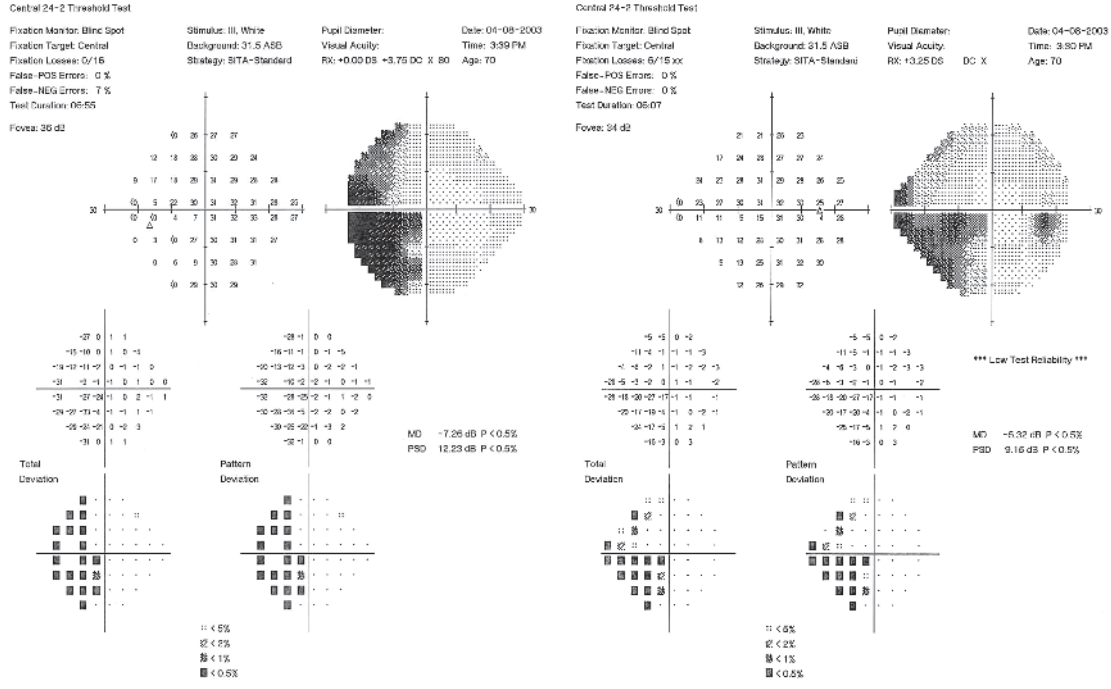


B

Figure 1.20 Congruous and incongruous homonymous field defects. **A:** Incomplete congruous right homonymous hemianopia from a left-sided occipital lobe infarct. **B:** Incomplete incongruous left homonymous hemianopia from a right-sided parietal lobe tumor.

it is conceivable that an extensive, extremely dense hemorrhage could cause an RAPD. A patient with a strabismic or anisometropic amblyopia occasionally may demonstrate an RAPD, but in such a setting, one should be concerned about some other underlying process such as an optic neuropathy. An RAPD can be quantified by placing graded neutral density filters over the normal or lesser affected eye until the RAPD no longer can be appreciated, and a subtle RAPD can be brought out by placing a 0.3 log unit neutral density filter first over one eye and then over the other while performing a swinging flashlight test (see Chapter 15).

Brightness Comparison

A comparison of brightness between a patient's eyes sometimes can identify subtle unilateral optic nerve dysfunction. The test is performed by shining a bright focused light, such as that from a transilluminator, into first one eye and telling the patient "This is a dollar's (or choose your own currency!) worth of brightness." Next, the light is shined into the contralateral eye, and the patient is asked "How much will you give me for this brightness?" The patient may answer that the brightness is the same in that eye (i.e., "one dollar"); that it is less (i.e., "50 cents"); or that it is more (i.e., "a dollar and 20 cents"). If the answer is consistent with the patient's history and other findings, it may support the diagnosis of an organic process affecting the eye in which there is decreased brightness; however, although the test can be used to corroborate other evidence of optic neuropathy, subjective brightness differences between the two eyes as an isolated finding with an otherwise normal examination usually is of no significance.

Photostress Recovery Test

The differentiation between unilateral retinal disease and retrobulbar optic neuropathy may be aided using the **photostress recovery test**. This test is based on the principle that visual pigments bleach when exposed to an intense light source, resulting in a transient state of sensitivity loss and reduced central visual acuity. Recovery of retinal sensitivity is dependent on regeneration of visual pigments that, in turn, is determined by the anatomic and physiologic apposition of the photoreceptors and retinal pigment epithelium (RPE). It is independent of neural mechanisms. Diseases that produce visual loss by damaging the photoreceptors or the adjacent RPE cause a lag in regeneration of pigment, resulting in a delay in visual recovery following light stress.

The photostress test is performed by determining best-corrected visual acuity, shielding one eye, and then telling the patient to look directly at a bright focal light source held 2 to 3 cm from the eye for about 10 seconds. The time needed to return to within one line of the best-corrected visual acuity is called the photostress recovery time (PSRT). The PSRT in normal eyes averages 27 seconds ±11 seconds. Ninety-nine percent of normal eyes have a PSRT of ≤50 seconds. In eyes with macular disease, PSRT usually is significantly prolonged, even when the retina appears to be relatively normal, whereas the PSRT is normal in eyes with optic neuropathies. The photostress test is especially useful in differentiating subtle macular disease from subtle optic neuropathies.

Cranial Nerves, External Examination, Anterior Segment Examination, and Exophthalmometry

In addition to cranial nerve II (i.e., the optic nerve), cranial nerves III, IV, V, VI, VII, VIII (and occasionally I) should be tested as part of a routine afferent visual system examination, because lesions in the orbit, cavernous sinus, suprasellar cistern, and brainstem may directly or indirectly produce afferent system dysfunction. External examination of the eye and anterior segment evaluation may suggest various causes of afferent visual loss, such as a carotid-cavernous sinus fistula or thyroid eye disease. A slit-lamp examination will establish whether or not corneal or anterior segment problems are the cause of the visual loss. It also may demonstrate iris abnormalities, such as transillumination defects characteristic of albinism or Lisch nodules seen in neurofibromatosis type 1. Tonometry should also be performed. Applanation tonometry not only will establish the IOP but also will detect any significant asymmetry of IOP and ocular pulse amplitude between the two eyes, such as occurs in patients with unilateral severe carotid artery stenosis or carotid-cavernous sinus fistula. Exophthalmometry is essential to perform in a patient with exophthalmos (proptosis) from an orbital mass, dysthyroid orbitopathy, an anteriorly draining carotid-cavernous fistula, or enophthalmos from metastatic scirrhous carcinoma or silent sinus syndrome.

Fundus Examination

A fundus examination is essential for evaluating the macula, retina, nerve fiber layer, and optic nerve. This can be performed by several methods, including direct ophthalmoscopy or indirect ophthalmoscopy with a 20-diopter handheld lens. Examination of the macula with a 78- or 90-diopter handheld lens or a corneal contact lens viewed through a slit lamp may identify the cause of visual loss as being from retinal dysfunction rather than neuro-ophthalmologic disease.

Performing a fundus examination on infants and young children can be a challenge. It is best to leave the room after performing the afferent system and motility evaluations, allowing a nurse or technician to administer dilating drops to preserve your rapport with the

child. In the case of infants, it is best to ask the parents to withhold a feeding bottle until you return to the room. Most infants will readily accept a bottle at this point and will be cooperative during a cycloplegic refraction and dilated fundus examination. The soporific effect of the cycloplegic drops also may cause them to fall asleep.

After completing the cycloplegic refraction, the physician should perform a dilated fundus examination using both a handheld direct ophthalmoscope and a 20-diopter lens in conjunction with an indirect ophthalmoscope, using a low level of illumination for both assessments. A lid speculum is not necessary for most pediatric neuro-ophthalmologic examinations because the macula and optic disc are the primary areas of interest. If a child becomes uncooperative, it may be necessary for the parents or an assistant to hold the child in a "lock-down" position (one person holding the arms outstretched over the ears with the other holding the feet) to complete the examination. This is a stressful and difficult situation for all concerned, and all rapport with the child is gone when this occurs. If it is not possible to perform an adequate dilated examination of the infant or child, it may be necessary to conduct an evaluation with the child under sedation.

Ancillary Testing

Despite taking a complete history and performing a complete examination, the physician may not be able to determine exactly what is responsible for a patient's visual symptoms. In such a setting, simple color fundus photography, fluorescein angiography, indocyanine green (ICG) angiography, and assessment of fundus autofluorescence (FAF) may be of value in detecting subtle retinal lesions (see Chapter 2). Fluorescein and ICG angiography are well-established procedures and won't be discussed in this text; however, autofluorescence is a relatively new technique and is discussed below as are the two ancillary tests most likely to be helpful in distinguishing retinal from optic nerve disease: optical coherence tomography (OCT) and electrophysiologic studies.

Ocular Imaging

Optical Coherence Tomography

OCT is a noninvasive and noncontact transpupillary imaging technique that can provide high-quality in vivo resolution (5 to 10 μm) of the retina and the optic nerve. The OCT creates a cross-sectional image using the principle of optical back-scattering of light. It can be used to measure the average thickness of the peripapillary retinal nerve fiber layer (PRNFL) as well as its thickness in various sectors, the macular volume, and the thickness of the retinal ganglion cell/inner plexiform layer (RGC/IPL). These measurements may allow differentiation between retinal and optic nerve disease (Fig. 1.21) and often can be used to provide information on stability or progression of disease (Fig. 1.22). In many cases, the thickness of the PRNFL is sufficient to diagnose permanent optic nerve

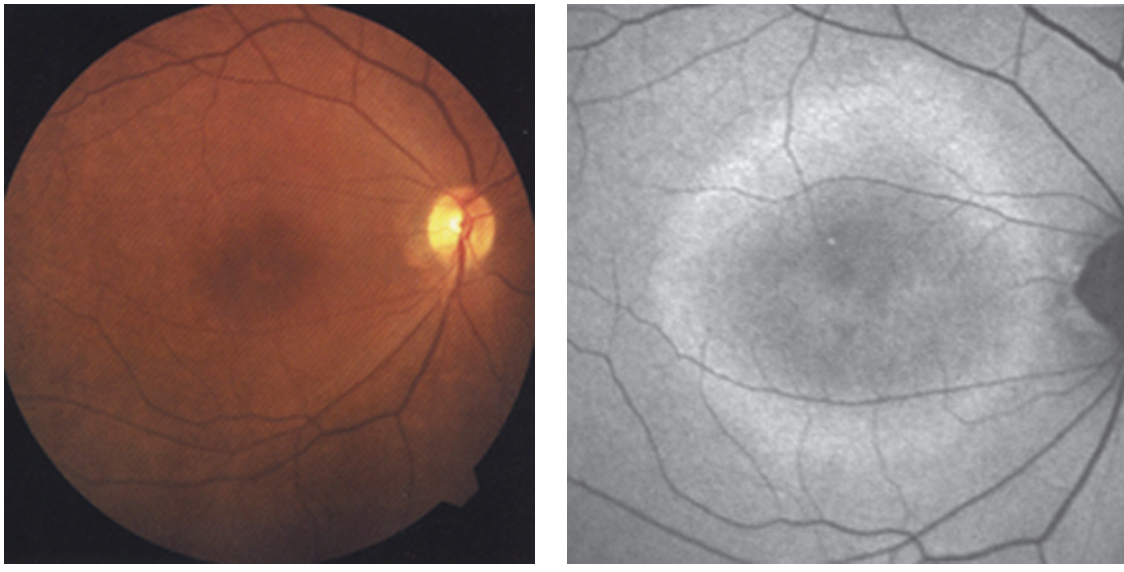


Figure 1.21 Fundus autofluorescence in a 12-year-old boy with decreased visual acuity, nonspecific central field defects, and normal pupillary reactions in both eyes. The child was thought to be malingering. **Left:** The color fundus photograph shows a slightly pale right optic disc; the macular region appears normal except for loss of the foveal reflex. **Right:** Autofluorescence shows a hyperfluorescent ring in the macula with early atrophy of the retinal pigment epithelium in the center. The patient was diagnosed as having juvenile X-linked retinoschisis.

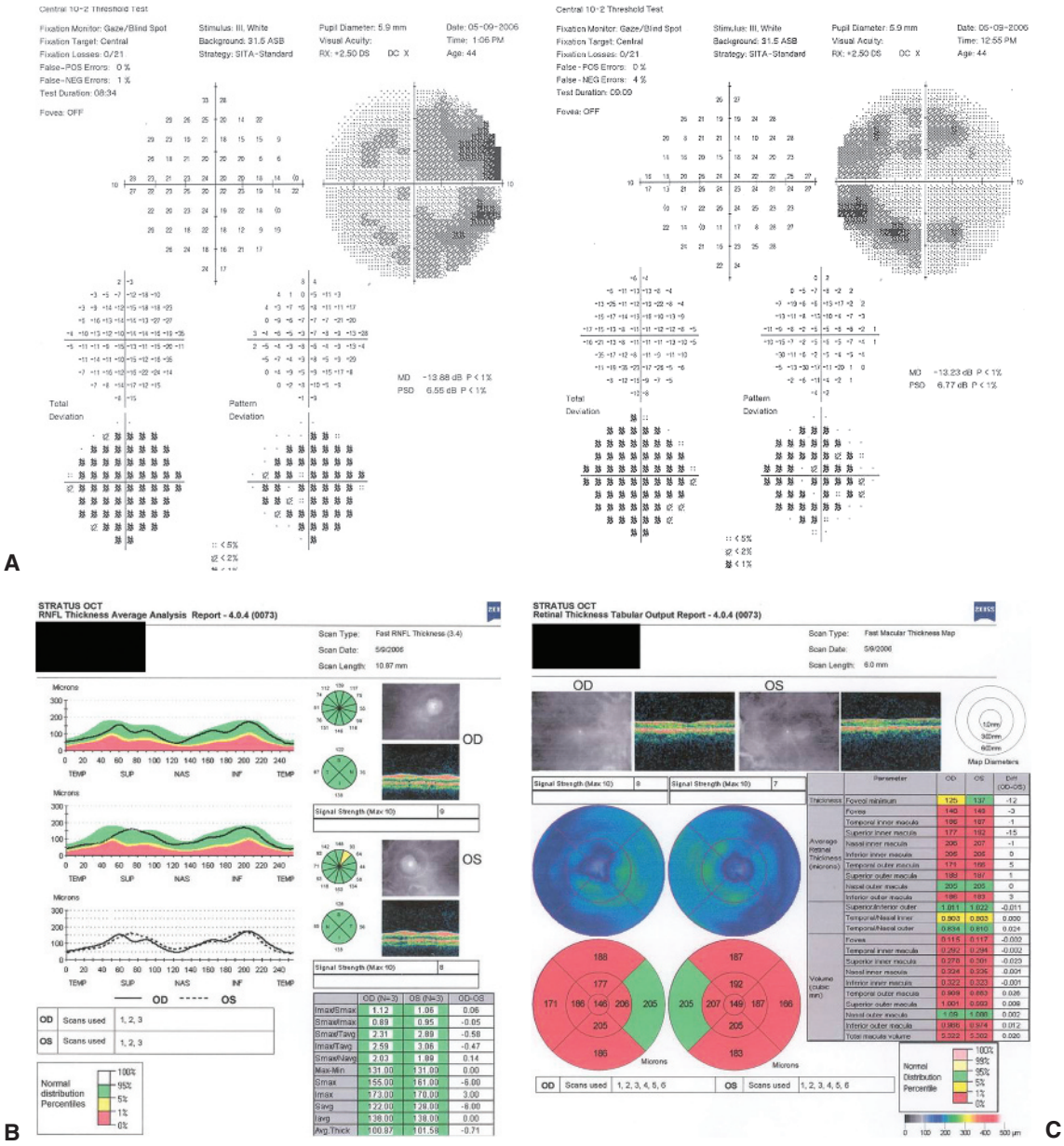


Figure 1.22 Differentiating retinal from optic nerve disease based on optical coherence tomography (OCT). The patient was a 56-year-old man with a 1-year history of progressive visual loss in both eyes. Visual acuity was 20/50 OU. The pupils were normally reactive to light stimulation and the fundi appeared normal. **A:** Visual field defects. **B:** OCT of the peripapillary retinal nerve fiber layer (PRNFL) shows no thinning in either eye, consistent with normal optic nerve function. **C:** OCT of the maculae shows marked thinning bilaterally. A diagnosis of macular dystrophy subsequently was established.

damage; however, in other cases, measurement of the thickness of the RGC/IPL provides more information regarding permanent damage and may be helpful in guiding management. For example, in patients with papilledema, measurement of RGC/IPL can identify permanent damage while the PRNFL is still swollen (Fig. 1.24). In addition, it has been shown that RGC/IPL thickness analysis is more sensitive for detecting permanent damage in patients with multiple sclerosis, even patients without a history of optic neuritis, than is assessment of PRNFL thickness because thinning of the RGC/IPL occurs before thinning of the

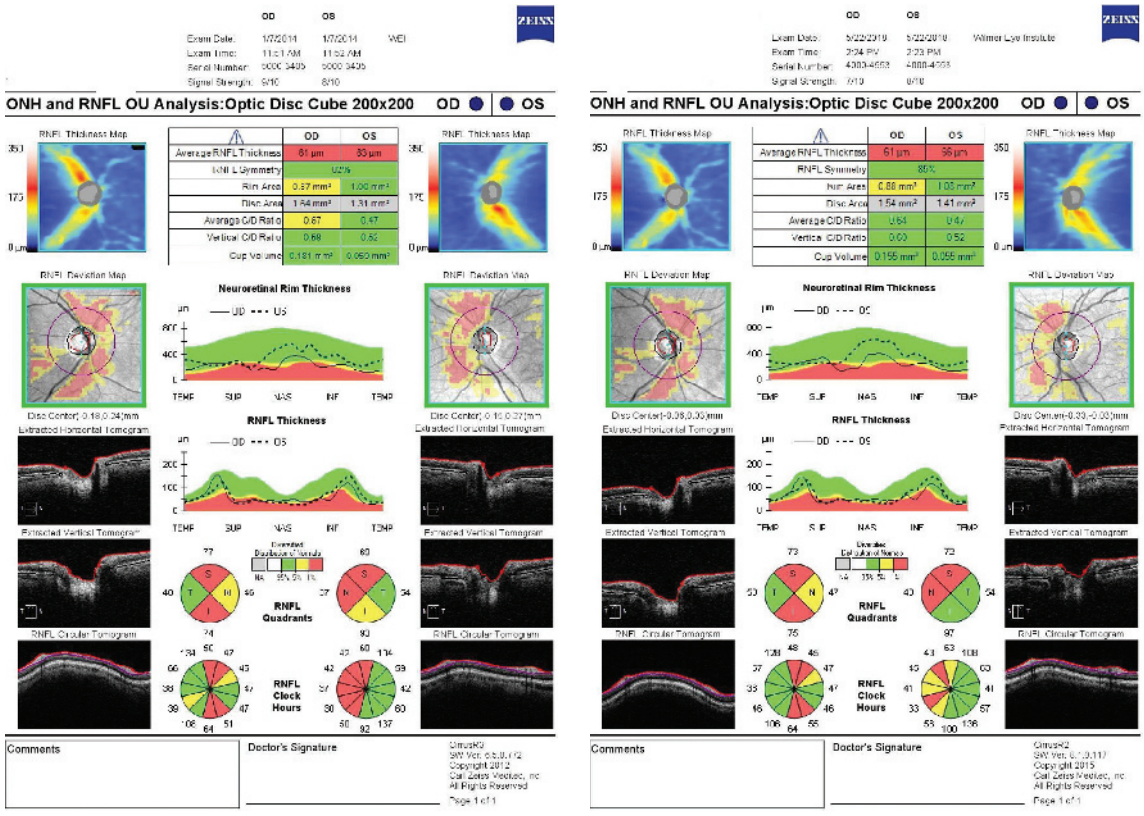


Figure 1.23 Confirming lack of progression of optic nerve damage following bilateral sequential attacks of retrobulbar optic neuritis in a patient with multiple sclerosis using optical coherence tomography (OCT). **Left:** OCT of the peripapillary retinal nerve fiber layer (PRNFL) performed in 1/14 shows bilateral thinning of the PRNFL, with average thicknesses of 61-μm OD and 63-μm OS. **Right:** OCT of the PRNFL in 5/18, 4 years later, reveals that the PRNFL measurements are unchanged, with average thickness of 61-μm OD and 66-μm OS.

PRNFL. In fact, RGC/IPL thickness correlates better with visual acuity, visual field, and magnetic resonance imaging findings than PRNFL in patients with multiple sclerosis.

Despite its contributions to diagnosis and management of neuro-ophthalmologic disorders, it is important to recognize that although OCT can be used to assess **structure,** it does not necessarily provide any information about **function.** For this, one may have to turn to electrophysiologic testing (see below). Nevertheless, in the appropriate setting, OCT can (1) provide information that can help distinguish retinal from optic nerve disease (Fig. 1.21), (2) allow objective monitoring of optic nerve axon and/or RGC damage in patients with neurologic disorders such as multiple sclerosis (Fig. 1.22), (3) provide data that can guide treatment decisions for patients with compressive and other optic neuropathies (Fig. 1.23), and (4) predict potential recovery or lack thereof after treatment. A number of OCT instruments are available to the clinician, and improvements in imaging quality continue to be forthcoming.

OCT angiography is a noninvasive means of assessing the retinal and choroidal vasculature and may be useful in differentiating among different optic neuropathies; however, its current value in neuro-ophthalmologic disorders is unclear.

Autofluorescence

FAF imaging is an in vivo imaging method for metabolic mapping of naturally or pathologically occurring fluorophores of the ocular fundus. The dominant sources are fluorophores such as A2E in lipofuscin granules that accumulate in the RPE as a by-product of the incomplete degradation of photoreceptor outer segments. Additional intrinsic fluorophores may occur with disease in the various retinal layers or the subretinal space. Minor fluorophores such as collagen and elastin in choroidal blood vessel walls may become visible in the absence or atrophy of RPE cells. Bleaching phenomena and loss of photopigment may result in increased FAF by reduced absorbance of the excitation

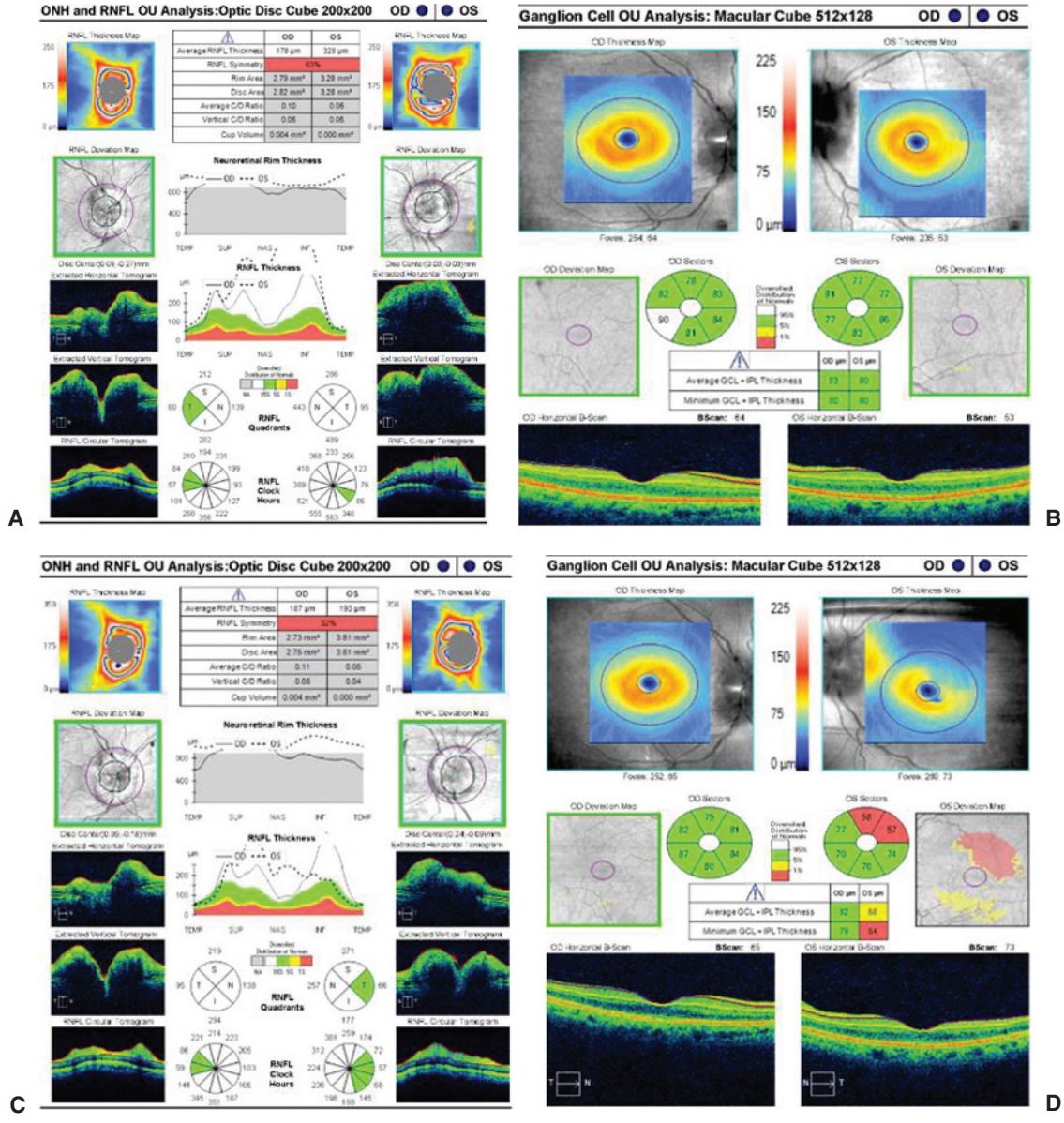


Figure 1.24 Using the retinal ganglion cell/inner plexiform layer (RGC/IPL) thickness by optical coherence tomography to assess for permanent optic nerve damage in a patient with papilledema in the setting of pseudotumor cerebri. **A:** Initial assessment of the peripapillary retinal nerve fiber layer (PRNFL) reveals marked thickening consistent with papilledema. **B:** RGC/IPL is of normal thickness. **C:** Several weeks later, repeat measurements show that the thickness is decreasing as the disc swelling resolves; however, there now is thinning of the RGC/IPL in two sectors of the retina in the left eye (**D**). This patient thus may require more aggressive treatment.

light. Finally, pathologic alterations in the inner retina at the central macula where the FAF signal usually is partially masked by luteal pigment (lutein and zeaxanthin) may result in manifest variations in FAF intensities.

FAF imaging provides information not obtainable with other imaging modalities such as standard fundus photography or fluorescein angiography. Although FAF can be assessed with a conventional fundus camera using the excitation and emission filters as applied for fluorescein angiography (but without injection of fluorescein dye), this method produces images with low contrast and high background noise. Accordingly, FAF usually is best obtained using scanning laser ophthalmoscope (SLO) technology that optimally addresses the

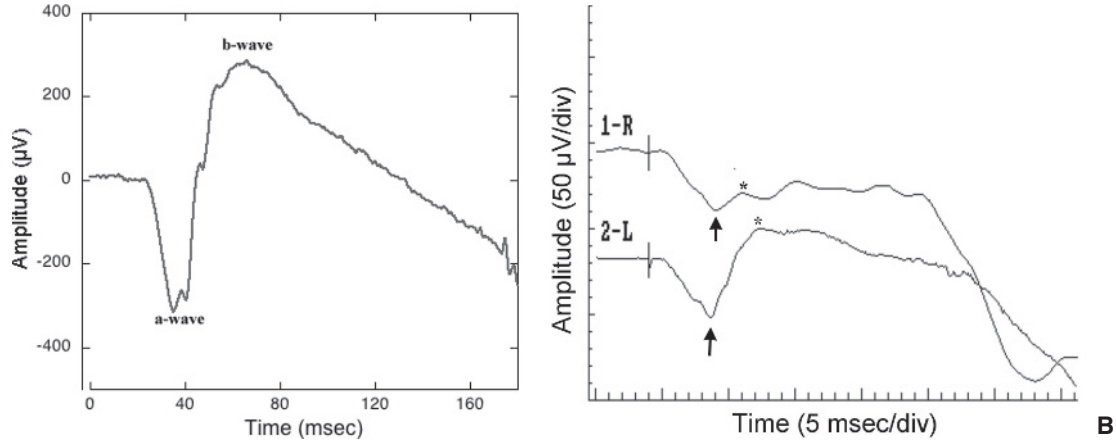


Figure 1.25 Full-field (Ganzfeld) electroretinogram (ERG). **A:** Normal ERG showing the cornea-negative a-wave and the cornea-positive b-wave. **B:** In a patient with visual loss in the right eye several years earlier associated now with optic disc pallor and some narrowing of the retinal arteries, the ERG of the left (L) eye has a normal a-wave (*arrow*) and a normal b-waves (*asterisk*); however, although the ERG of the right (R) eye has a normal a-wave (*arrow*), the b-wave amplitude is markedly diminished. This indicates that the photoreceptors are functioning but there has been damage to the inner retinal Müller and bipolar cells. These findings are consistent with a previous central retinal artery occlusion. (Both figures courtesy of Dr. Mary A. Johnson.)

limitations of the low intensity of the autofluorescence signal and the interference of the crystalline lens. The most common instruments used clinically to assess FAF are certain modified fundus cameras (e.g., Optos) and OCT machines (e.g., Heidelberg Spectralis). FAF imaging has been shown to be useful in a wide spectrum of retinal diseases (Fig. 1.24).

Electrophysiologic Testing

The physician frequently is confronted with a patient who has unexplained loss of vision and an apparently normal fundus examination. Because electrophysiologic testing often provides diagnostic clues as to the etiology of the unexplained visual loss, it should be part of the neuro-ophthalmologic examination in selected patients. Electrophysiology provides a relatively objective method for evaluating the function of the visual system from the retina to the visual cortex. Several electrodiagnostic methods can be used to evaluate the status of individual components of the afferent visual pathways, including full-field (Ganzfeld), pattern, and multifocal electroretinography and both standard and multifocal VEPs.

The Full-Field (Ganzfeld) Electroretinogram

Full-field ERGs measure global retinal responses to a full-field flash stimulus and arise largely in the photoreceptor and inner nuclear layers of the retina. Modification of stimulus parameters and the adaptive state of the eye enable separation of the function of rod and cone systems and inner and outer retinal layers. Stimulation is provided by a Ganzfeld stimulator, an integrating sphere that provides uniform retinal illumination.

There are two main components of the ERG: an early cornea-negative a-wave and a cornea-positive b-wave (Fig. 1.25A). The photoreceptors are responsible for the generation of the leading edge of the a-wave, whereas the cellular origin of the b-wave is a combination of cells in the Müller and bipolar cell layers (Fig. 1.25B).

The rod and cone components of the ERG may be separated on the basis of their respective spectral sensitivities by altering the retinal state of adaptation or by using different flicker rates for the stimulus. ERGs often are described as having photopic (light-adapted) and scotopic (dark-adapted) responses. The wavelength, intensity, and temporal properties of the stimulus, as well as the state of retinal adaptation, are all important in separating rod and cone system contributions.

The ERG is described by the temporal characteristics and amplitudes of the recorded waveform. The temporal aspects of the waveform can be described by the latency and implicit times. Latency refers to the time between stimulus onset and response onset, whereas implicit time refers to the time needed for the response to reach maximum amplitude. Waveform amplitudes are measured from the baseline (which is usual for the a-wave) or as a peak-to-peak comparison (which is usual for the b-wave). The b/a-wave ratio can be used as an index of inner to outer retinal function.

The ERG can be affected by a number of factors. The implicit time of the waveform does not mature until 4 to 6 months of age, and the amplitude may be reduced until 1 year of age. The ERG may be greater in women than in men and may be reduced in myopes with more than 6 diopters of refractive error. There may be as much as a 13% reduction in ERG amplitude in the morning, which corresponds to the time of the maximum photoreceptor disc shedding. Systemic drugs and anesthetics may also alter the ERG. In addition, the ERG can be altered if the subject blinks, moves the eye during stimulation, or is not concentrating on the stimulus.

A full-field ERG can provide important information about a number of retinal disorders that may simulate neuro-ophthalmologic problems. These include congenital stationary night blindness, congenital achromatopsia, retinitis pigmentosa (rod–cone dystrophy), retinitis pigmentosa sine pigmento, cone–rod dystrophy, cone dystrophy, cancer-associated retinopathy (CAR), melanoma-associated retinopathy (MAR), and toxic retinopathies.

Pattern Electroretinography

The pattern electroretinogram (PERG) is the response of the retina to a centrally viewed isoluminant black and white reversing checkerboard. The transient PERG has an initial negative wave at around 35 milliseconds (N35), followed by a positive wave at approximately 50 milliseconds (P50), and a late, large negative wave at around 95 milliseconds (N95) (Fig. 1.26). The N95 component arises in the RGCs, whereas the P50, although mostly arising in the RGCs, has significant contributions from other retinal structures such as the bipolar cells. A normal P50 component depends on the integrity of the macular cones and thus acts as an objective measure of macular function. Normal persons have excellent symmetry in the waveforms between the two eyes, with amplitude ratios typically 0.8 to 0.9 in each eye. Because the N95 reflects RGC activity, the PERG can be used to determine RGC function in patients with primary RGC disease as well as optic nerve (i.e., axon) disease. This can be crucial in determining treatment windows and visual prognosis in patients with various optic neuropathies, including inflammatory (i.e., optic neuritis), ischemic, compressive, and toxic.

Multifocal Electroretinography

The human ERG recorded at the cornea in response to a full-field stimulus is a mass response generated by cells across the entire retina. Loss of half the retinal photoreceptors across the retina is associated with about a 50% reduction in ERG amplitude. Because the total cone population in the human retina is about seven million, and the number of cones in the macula is at most 440,000, the macula contains only about 7% of the total retinal cone population. Thus, a full-field ERG is unable to detect abnormalities confined to small regions of the retina, including the fovea and macula. Fortunately, it is possible to assess macular function as well as retinal function in the posterior pole using multifocal ERG (mfERG).

mfERGs typically are generated using an array of 61 or 102 hexagonal elements that subtend a total angle of 55 degrees. Each stimulus element is illuminated according to a pseudo-random binary sequence; cross-correlation techniques enable the construction of multiple responses from a single electrode. The mfERG, similar to the PERG, may be a useful complement to VEP testing (see below) but is highly dependent on accurate fixation.

Nevertheless, it can be exceptionally helpful in patients with small field defects including central or paracentral scotomas and normal-appearing fundi in whom it is unclear if the cause is retinal, due to optic nerve dysfunction, or is nonorganic (Figs. 1.27 and 1.28).

Visual-Evoked Potential

If the spontaneous occipital electroencephalogram (EEG) is recorded while brief flashes of light or an alternating black and white checkerboard pattern are

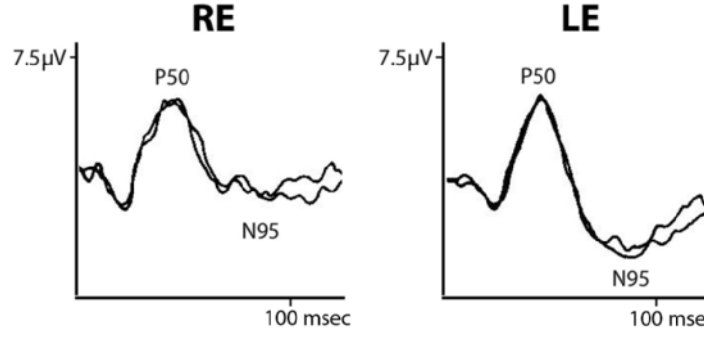


Figure 1.26 Pattern electroretinogram (PERG) in a patient with a severe demyelinating right retrobulbar neuritis. Visual acuity with the right eye was 20/200. The left eye had normal visual function. The PERG from the right eye (RE) shows a normal P50 component but significant reduction in the N95 component amplitude. The left eye findings are normal. The findings in the right eye are consistent with normal macular function (P50) but marked reduction in retinal ganglion cell function (N95) due to retrograde degeneration. (Courtesy of Dr. Graham Holder.)

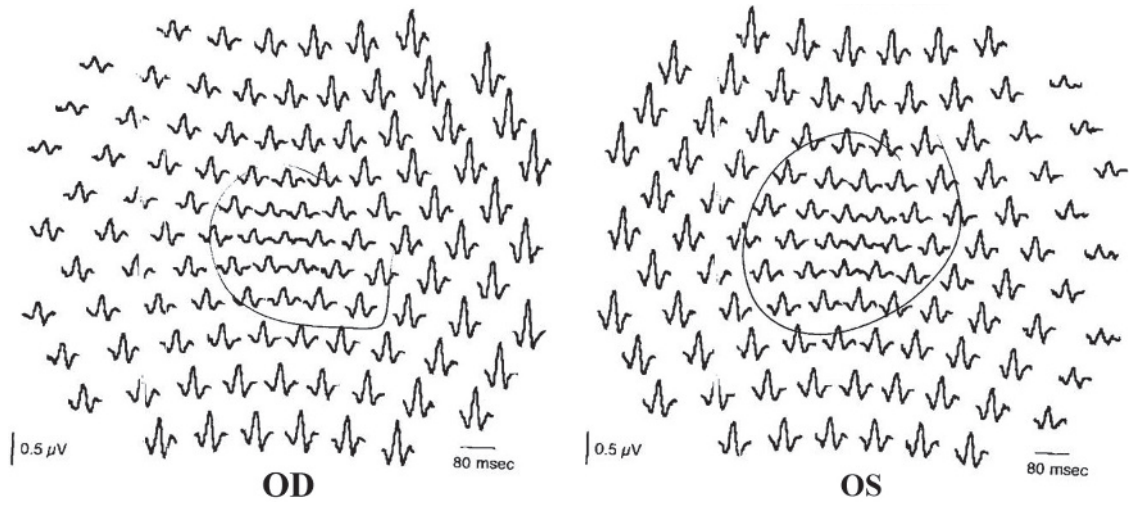


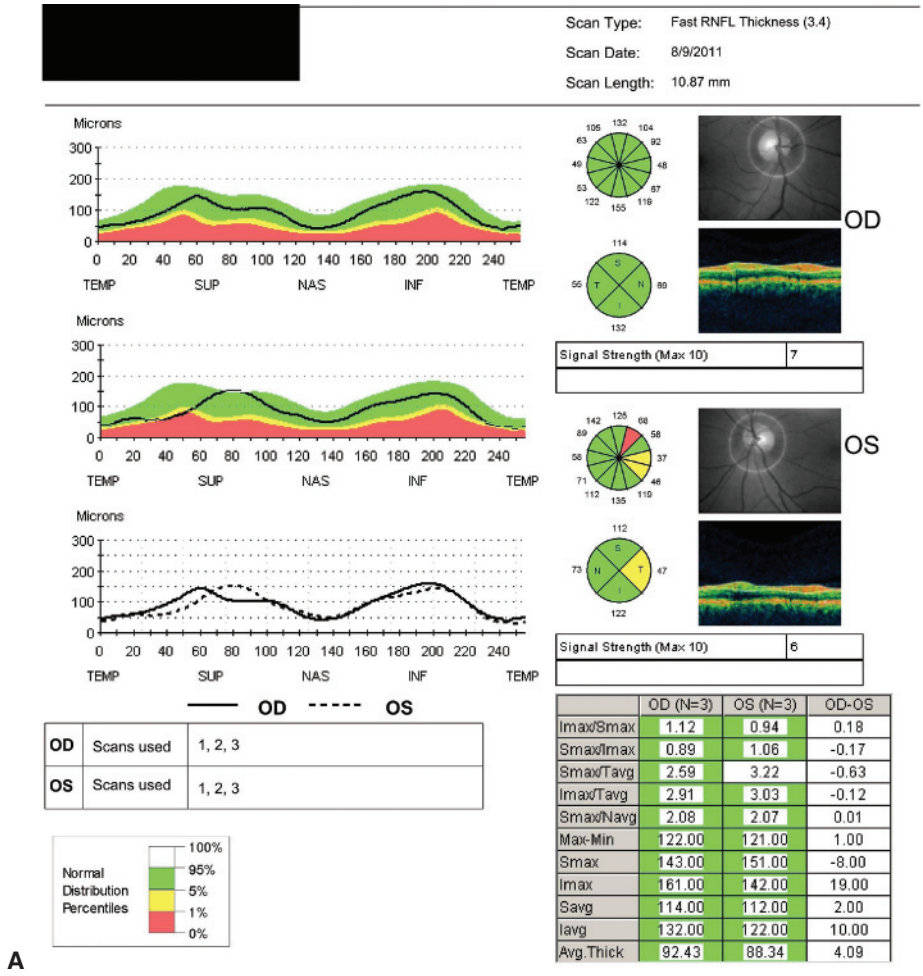
Figure 1.27 Multifocal electroretinogram (mfERG) in the patient whose optical coherence tomography is shown in Figure 1.22. The mfERG shows marked central reduction in both eyes consistent with a macular dystrophy.

presented to an eye, changes result in the occipital potential. These changes are called the VEP, visual-evoked response (VER), or visual-evoked cortical potential (VECP). The VEP thus is a gross electric potential of the visual cortex in response to visual stimulation. The VEP is limited mainly to the occipital region of the brain, with an amplitude between 1 and 20 μV. The VEP depends on the integrity of the entire visual pathway, although it remains to be determined if its components can truly be separated into anatomic correlates.

The VEP is measured by placing scalp electrodes over the occipital region (O_z) of both hemispheres, with reference electrodes attached to the ear. The patient then views the display, typically a xenon-arc photostimulator for flash VEPs and a television screen display with patterned stimuli for pattern VEPs. Recordings of the VEP may be made from either hemisphere with one or both eyes fixating. Typically, 100 to 150 stimulus presentations are generated, and time-locked signal averaging is used to extract the VEP waveform from the spontaneous EEG activity. The amplitude and latency of the waveform then are measured. A flash stimulus is used when no response is produced using a pattern stimulus. Thus, infants and patients with extremely poor acuity, dense media opacities, or poor fixation usually are tested with flash VEP. In most patients, however, a pattern stimulus is preferred for obtaining the VEP because of the greater clinical utility and more reliable waveform generated with this stimulus. A repetitive pattern of light and dark areas (checkerboards, bar gratings) are phase-reversed every 1 or 2 seconds. The pattern VEP is generated primarily from the central 5 degrees of the visual field, consistent with the anatomic correlates that the central 10 degrees of the visual field is represented by at least 50% to 60% of the posterior striate cortex and that the central 30 degrees is represented by about 80% of the cortex (see Chapter 13).

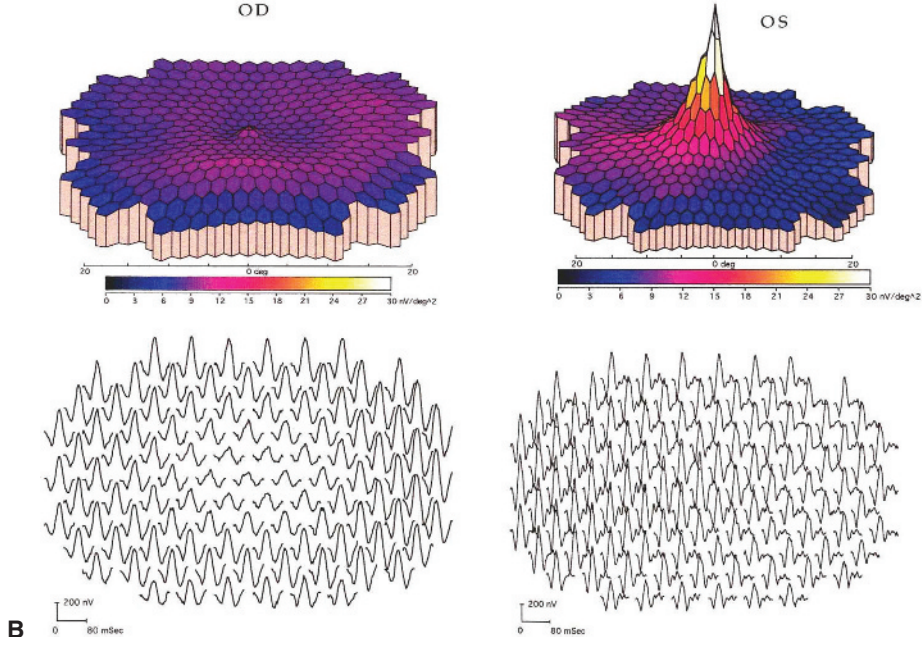
The amplitude of the pattern VEP is affected by a number of different factors. The size of the stimulus pattern can affect the amplitude of the VEP signal, as can the rate of alternation of the pattern. The VEP also varies with stimulus size and frequency, attention, mental activity, pupil size, fatigue, state of dark adaptation, color of the stimulus, and background illumination. All of these factors emphasize the importance of using standardized and optimized test conditions (including the best refractive correction) for clinical VEP testing, as well as establishing age-related normative standards for the procedures employed for each laboratory. In addition, it is crucial that the technician or physician performing the study be well trained.

Figure 1.28 Using a combination of optical coherence tomography (OCT) and multifocal electroretinogram (mfERG) to diagnose the cause of visual loss in a 47-year-old woman complaining of blurred vision in the right eye. The patient's visual acuity was 20/40 OD and 20/15 OS. There was no relative afferent pupillary defect. Visual fields showed an enlarged blind spot on the right. The fundi appeared normal. **A:** OCT of the peripapillary retinal nerve fiber layer (PRNFL) shows no thinning. Thus, there is no evidence of optic nerve disease. **B:** mfERG shows marked central reduction in cone function in the right eye. A diagnosis of acute zonal occult outer retinopathy (AZOOR) was made.



	OD (N=3)	OS (N=3)	OD-OS
Imax/Smax	1.12	0.94	0.18
Smax/Imax	0.89	1.06	-0.17
Smax/Tavg	2.59	3.22	-0.63
Imax/Tavg	2.91	3.03	-0.12
Smax/Navg	2.08	2.07	0.01
Max-Min	122.00	121.00	1.00
Smax	143.00	151.00	-8.00
Imax	161.00	142.00	19.00
Savg	114.00	112.00	2.00
Iavg	132.00	122.00	10.00
Avg.Thick	92.43	88.34	4.09

A



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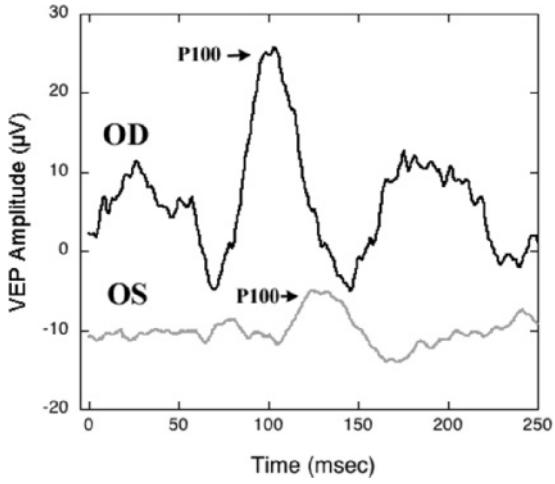

Figure 1.29 Visual-evoked potential (VEP) in a patient with a left retrobulbar optic neuritis. The VEP shows a marked reduction in amplitude and an increased latency of the P100 peak in the left eye. The P100 waveform on the right has both a normal amplitude and a normal latency. (Courtesy of Mary A. Johnson, PhD.)

Although the VEP is characterized by several waveforms, the main one used in clinical practice is the positive wave that occurs at about 100 milliseconds, called the P100 (Fig. 1.28). Both the latency and amplitude of the P100 are assessed. The latency increases in most optic neuropathies, particularly inflammatory (i.e., optic neuritis) and compressive (Fig. 1.29). Patients with ischemic optic neuropathy may show P100s that have relatively normal latencies but reduced amplitudes.

A more recent development is the use of evoked potentials to map visual field function, the **multifocal VEP**. Electrical responses to pattern reversal stimuli presented pseudorandomly to the central visual field can be extracted from occipital scalp recordings. The clinical usefulness of this test in patients with optic nerve, cerebral and nonorganic visual loss remains under investigation, and it is used mainly as a research tool.