1

# When ocular disease is mistaken for neurologic disease

Some common visual symptoms, such as blurring, double vision and flashing lights, can be produced by disorders of either the eye or the brain. Sorting out ocular disease early in the course of the evaluation is important for avoiding unnecessary and often expensive investigation, establishing a definitive diagnosis and initiating appropriate treatment. While the non-ophthalmologists cannot be expected to have the tools and refined examination skills of the ophthalmologist, there are some specific clinical findings that can help in distinguishing between eye and brain disease.

In many cases, a detailed description of the visual symptom effectively localizes the disease process. For example, visual loss due to aberration of the ocular media (e.g. cataract or corneal disease) is usually described as "blurring", while the visual loss of optic nerve dysfunction is more often experienced as "dimming" or "darkening", often with decreased color saturation (Figure 1.1). In contrast to patients with disorders of the media, those with retinal or optic nerve disease often report missing "pieces" or areas of vision. Alteration of object shape or size (metamorphopsia, micropsia or macropsia) usually indicates retinal disease and is never caused by optic neuropathy. Prominent degradation of vision in dim or bright light is also characteristic of retinal disease. Familiarity with such distinctive features of the history is particularly important for the clinician, particularly the non-ophthalmologist, because in such cases sophisticated eye examination techniques are not necessary to know that the disease process is an ocular one.

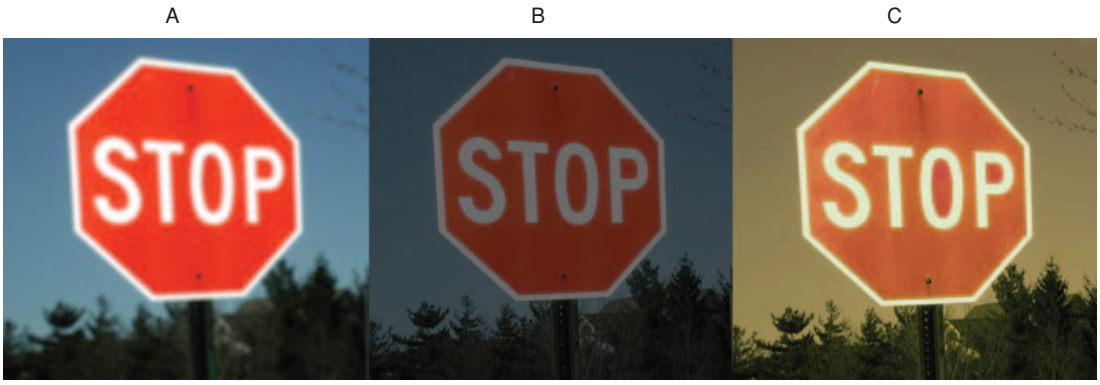


**Figure 1.1** Comparison of subjective visual abnormality in ocular vs. neurologic disease. (A) Disorders of the ocular media usually produce *blurring* of images, with loss of sharp edges. (B) Patients with optic neuropathies often describe *dimming* of images and (C) color desaturation. (Figure courtesy of Stuart Alfred.)

In some instances, the history is non-specific, and localization rests on specific examination findings and techniques. The photostress test and Amsler grid are two such examples. The *photostress test* measures the time it takes to recover central visual function, e.g. acuity following exposure to a bright light, and is very useful for distinguishing maculopathy from optic neuropathy. Recovery times are prolonged in a variety of macular disorders but are normal in optic neuropathies. *Amsler grid testing* is an objective way to assess alteration of object shape and size, a characteristic of macular disease (see Chapter 8, Sudden difficulty reading the paper). In yet other cases, a particular aspect of the eye examination that requires some experience and expertise, such as inspection of the drainage angle (gonioscopy) or visualization of the peripheral retina (scleral depression), provides the key to the correct diagnosis. While such examination techniques are beyond the purview of the non-ophthalmologist, it is crucial to know when the patient should be referred for such examination. The section that follows looks at some examples of cases in which the findings that indicate ocular disease were either subtle, absent or misinterpreted.

## Double images

**Case:** A 60-year-old seamstress sought medical attention because of a three-month history of intermittent diplopia that was most noticeable in the evening, particularly when driving. She found she could relieve her diplopia by closing her right eye. She had no head or eye pain and no recent systemic symptoms. On examination, ocular alignment was normal and eye movements in all directions were full. Refixation saccades were brisk and accurate and there was no ptosis or lid fatigability. Thyroid function tests and a magnetic resonance imaging (MRI) scan of brain and orbits were normal. Her history of intermittent diplopia that was worse at night suggested the possibility of myasthenia, and further work-up was initiated accordingly. Acetylcholine receptor antibodies were negative, electromyography (EMG) with repetitive stimulation showed no decrement, and a trial of Mestinon (pyridostigmine bromide) did not bring symptomatic relief.

The patient returned several months later reporting that her diplopia had now become constant. Her examination was unchanged.

### What important piece of historical information is still missing in this case?

The work-up so far has assumed this patient's diplopia was binocular but in fact all that we know is that it was relieved by closing her *right* eye. In order to establish that this is not monocular double vision we also need to know what happens when she closes the left eye. With her left eye closed, viewing just with the right, she described persistence of her double images.

### What maneuver might be helpful for confirming our suspicion that this patient's double vision is ocular in nature?

The *pinhole test* is useful when aberration of the ocular media or refractive error is the basis of visual disturbance, including both blurring and doubling of vision (Figure 1.2). By allowing only a small bundle of incoming light rays to enter the eye, only those that are parallel to the visual axis reach the retina. The amount of light scatter onto the retina, and thus image degradation, is therefore greatly reduced. Patients who complain of blur, halos, shadowy margins and monocular double vision will note improved image clarity or even complete resolution of symptoms when viewing through a pinhole.

This patient's diplopia was indeed relieved by pinhole. Slit-lamp examination demonstrated a developing cataract in the right eye and was otherwise normal. In retrospect, her history had been misleading. Because she reported resolution of diplopia upon covering her right eye, it was thought that she had binocular diplopia, but in reality, her diplopia was present only in the right eye. Further questioning would have revealed that diplopia

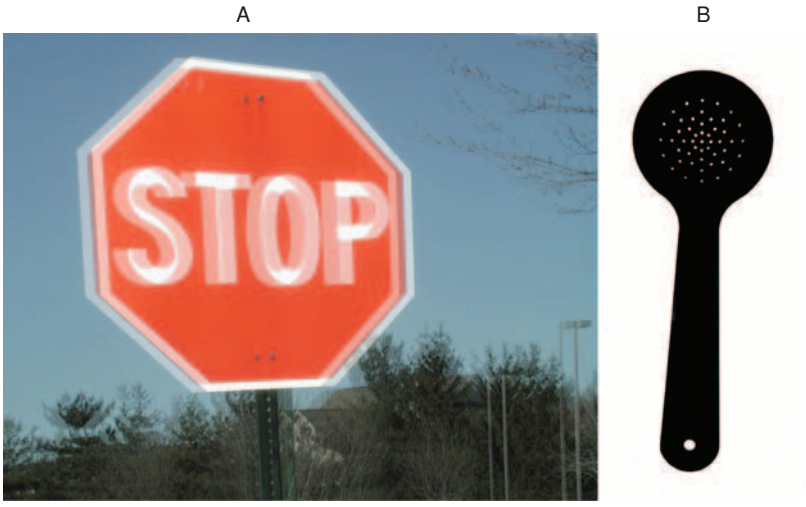


**Figure 1.2** Monocular diplopia due to aberration of the ocular media. (A) Double image is present with just one eye viewing. Note the second image has a faded appearance, sometimes termed a "ghost" image. (B) A pinhole occluder relieves diplopia due to ocular aberration.

resolved only with covering the right eye and not the left eye, clearly indicating monocular diplopia.

Her diplopia resolved completely after cataract extraction.

**Discussion:** For practical purposes, monocular diplopia or polyopia (multiple images present with just one eye viewing) is due to an aberration of the ocular media, not neurologic disease. Common causes include uncorrected refractive errors, corneal disease, cataract and macular distortion. Monocular diplopia is often less noticeable when outdoors or in a brightly lit room, because the resulting pupillary constriction induces a pinhole-like effect. Symptoms are often more noticeable in dim illumination and at nighttime, especially when driving.

Corneal surface disease related to dry eyes is an important cause of monocular diplopia. Drying of the corneal surface is a common age-related change and also occurs in a variety of other settings, including after blepharoplasty (due to increased lid height and tear evaporation), with the use of anticholinergic or antihistaminic agents (decreased tear production), contact lens wear (surface irritation), and low-humidity environments. Patients with thyroid eye disease are particularly prone to dry eyes because of lid retraction and lacrimal gland infiltration. Symptoms include burning, foreign-body sensation, blur, photosensitivity, halos around lights, and diplopia. Paradoxically, excessive watering is also a common symptom of dry eyes, caused by increased reflex tearing which produces thin, watery tears that are less effective than normal tear secretion. Symptoms related to dry eyes are often intermittent, typically made worse by prolonged viewing (e.g. reading or computer use) during which the cornea dries out from decreased blinking. Patients with parkinsonian syndromes are also prone to this condition, as a consequence of their decreased blink rate.

The one exception to the dictum that monocular diplopia indicates ocular disease is a rare neurologic condition called *cerebral polyopia*. Cerebral polyopia is a visual illusion, usually due to parietal lobe dysfunction, in which objects are seen as multiple (two or more) in each eye. In most cases, cerebral polyopia is associated with other forms of higher cortical visual disturbance, such as abnormal persistence of images and spatial distortion.

Cerebral polyopia can be distinguished from monocular polyopia due to disorders of the ocular media by the following: (1) cerebral polyopia is always present in both eyes, (2) cerebral polyopia is *not* relieved by pinhole, and (3) cerebral polyopia is usually associated with homonymous visual field defects.

Before embarking on a neurologic evaluation for diplopia, it is important to verify that diplopia is truly binocular. If it is, the patient should note resolution of diplopia when *either* eye is covered.

**Diagnosis: Monocular diplopia due to cataract**

**Tip:** Diplopia that is present with one eye viewing and relieved by pinhole is not due to neurologic disease.

## Headache and bilateral disc edema

**Case:** A 37-year-old schoolbus driver noted rapidly progressive visual blur in both eyes. He did not have eye pain but reported intense daily headaches which had started three months previously. He was unaware of any medical problems and was taking no medications. Examination revealed visual acuity of 20/40 in each eye and bilateral optic disc edema (Figure 1.3A). Visual field testing showed central depression and paracentral scotomas in both eyes (Figure 1.3B). There was no alteration of sensorium and no focal neurologic deficits. A brain tumor was suspected and he was sent as an emergency for an MRI, which was normal. He was scheduled for a lumbar puncture, but while the procedure was pending a bedside test was performed, leading to a definitive diagnosis.

### What test was done and what was the diagnosis?

His blood pressure was checked and found to be markedly elevated at 240/170. An ophthalmic consultant performed a dilated fundus examination which revealed bilateral retinopathy in addition to disc edema. Retinal hemorrhages, cotton-wool spots and hard exudates were seen throughout the posterior poles, and macular edema was present in both eyes (Figure 1.4). A diagnosis of malignant hypertension was made and the patient was hospitalized for evaluation and initiation of treatment. Upon discharge, blood pressure control was maintained with oral medication and, at follow-up one month later, he reported resolution of headache and improvement of visual blur. Visual acuity was 20/25 in both eyes (OU) and there was marked improvement of disc edema and retinopathy.

**Discussion:** This patient with malignant hypertension presented with recent onset of headache and bilateral disc edema, suggesting the presence of increased intracranial pressure (ICP). Characteristics of the headache associated with increased ICP are non-specific and are so similar to those of increased systemic blood pressure that the distinction cannot be made based on the history. Associated symptoms such as pulsatile tinnitus or transient visual obscurations may be present in both conditions. Furthermore, both disorders can produce bilateral optic disc edema. The most important clue to the mechanism of disc edema in this case was the pattern of accompanying retinal abnormalities. Fully developed papilledema due to increased ICP may be accompanied by nerve fiber layer hemorrhages and exudates, but these vascular abnormalities are confined to the optic disc surface or the immediate peri-papillary nerve fiber layer (Figure 1.5A). The one exception is the occasional case in which hard exudates track from the swollen disc to form a partial macular star. As a general rule, the presence of retinal hemorrhages or exudates *beyond* one disc diameter from the optic nerve head indicates that a mechanism other than increased ICP underlies the disc edema (Figure 1.5B). The two main considerations in this setting are malignant hypertension and diabetes. The key feature that would have distinguished vascular disease of the eye from neurologic disease in this case was missed because a dilated fundus examination was not performed. Pharmacologic dilation is not contraindicated in a patient with disc edema who has no focal neurologic deficits and intact mental status.

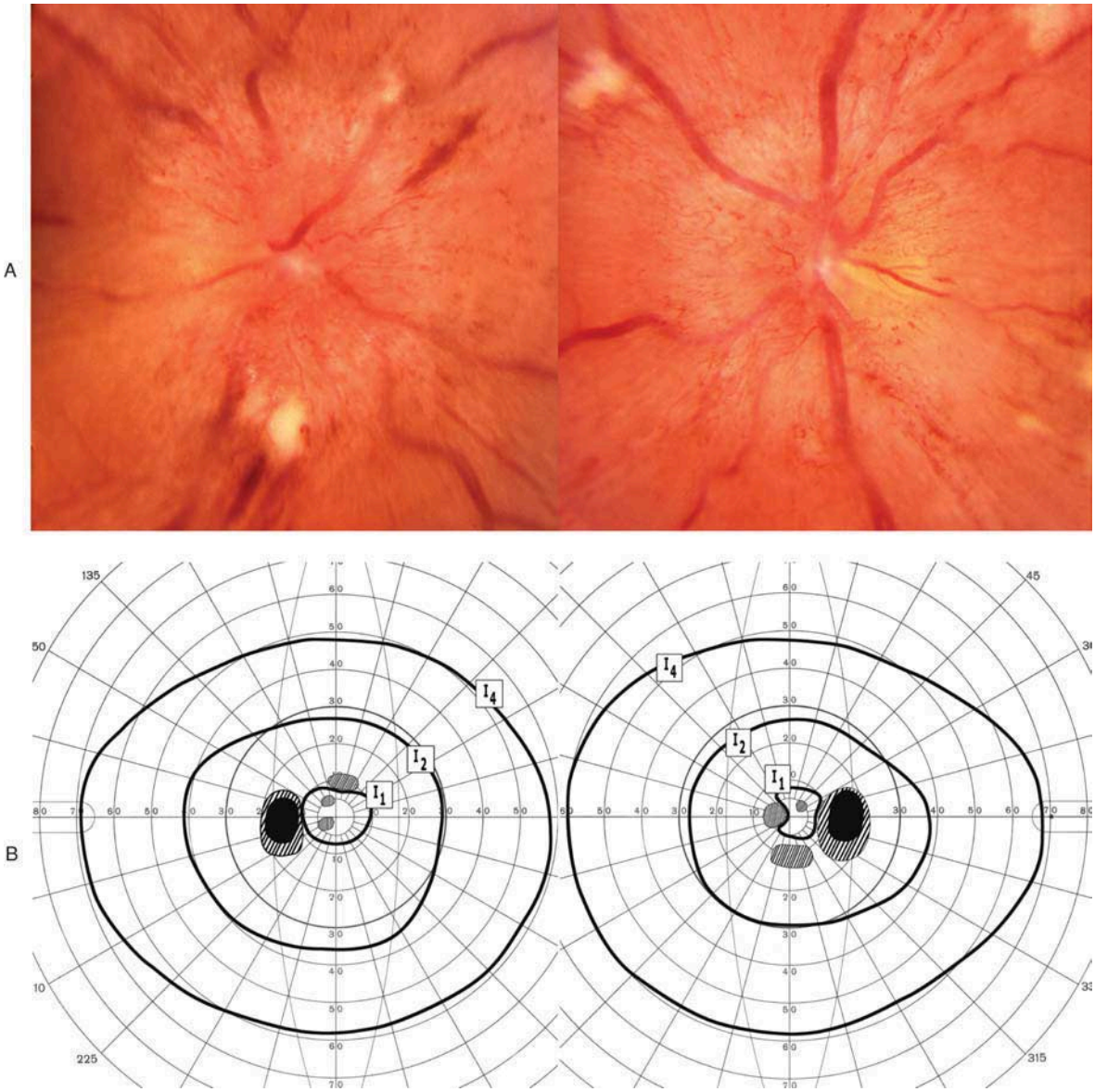


**Figure 1.3** Examination findings in a 37-year-old schoolbus driver with daily headaches. (A) Both discs are diffusely swollen and hyperemic. Several nerve fiber layer (splinter) hemorrhages and cotton-wool spots are also present. (B) Goldmann perimetry shows bilateral central depression and small paracentral scotomas. The physiologic blindspot is also enlarged in each eye.

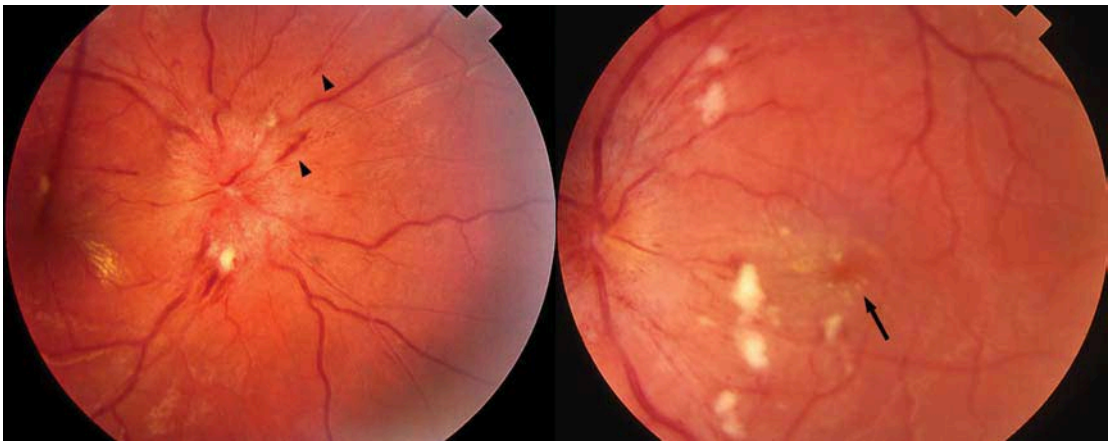

**Figure 1.4** View of the posterior pole of each eye in the above patient. In addition to the previously noted optic disc edema, it is now apparent that the vascular abnormalities are not confined to the optic discs. Nerve fiber layer hemorrhages extend along the vascular arcades (arrowheads, right eye) and there are scattered cotton-wool spots throughout the posterior pole in the left eye. Macular edema is present in both eyes and small clumps of hard exudates can be seen in the parafoveal area (arrow). The arterioles are irregular and narrowed and the veins appear mildly engorged in both eyes.

A pronounced and sudden rise in blood pressure beyond the compensatory capacity of vascular autoregulation can result in vascular leakiness and widespread end-organ dysfunction affecting the brain, heart and kidney, a condition termed *malignant hypertension*. If untreated, such systemic involvement can cause irreversible tissue damage including myocardial infarction and stroke, and thus represents a true medical emergency. Retinal changes are the earliest ophthalmic abnormality associated with accelerated hypertension (Figure 1.6). Hemorrhages can be intraretinal (described as "dot/blot") or in the nerve fiber layer (termed "flame" or "splinter" hemorrhages) and are especially prominent along the vascular arcades. Occlusion of choroidal vessels may cause areas of secondary retinal detachment that can be focal or widespread. Later these areas may appear as retinal pigment atrophy or clumping, termed Elschnig spots. Macular alterations include edema, formation of microcysts and exudates. Nerve fiber layer infarcts appear as "cotton-wool spots" on the optic disc or the retina. Exudation in the retina may appear as punctuate white opacities (indicating focal pericapillary leakage) and hard exudates which may form a macular star figure. Malignant hypertension with disc edema and macular star formation is sometimes mistakenly diagnosed as bilateral neuroretinitis. Neuroretinitis rarely affects both eyes simultaneously and does not cause the more widespread retinal abnormalities found in malignant hypertension. In any patient thought to have bilateral acute neuroretinitis, it is mandatory to check the blood pressure. The pathogenesis of optic disc swelling in malignant hypertension is multifactorial, sometimes occurring as part of the retinopathy (due to vascular leakiness), in some cases representing ischemia of the optic nerve head and in others reflecting increased ICP (see below). Thus, disc edema may occur in the absence of observable retinopathy, and in such cases may be easily confused with papilledema of increased ICP.

Patients with malignant hypertension sometimes develop symptoms of cerebral dysfunction such as lethargy, confusion, seizures and focal neurologic deficits due to vascular changes in the brain, termed *hypertensive encephalopathy*. Extravasation of fluid

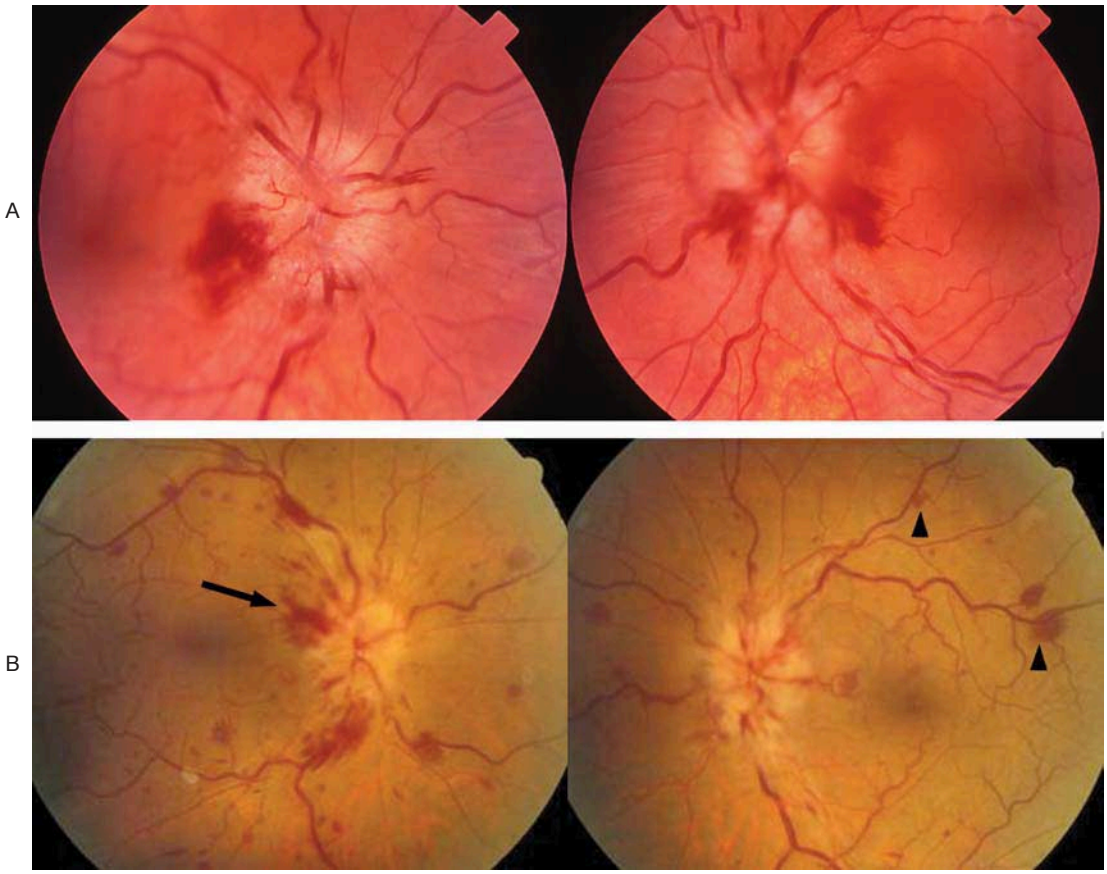


**Figure 1.5** Patterns of hemorrhage in increased intracranial pressure vs. increased systemic blood pressure. (A) In papilledema (increased intracranial pressure) nerve fiber layer hemorrhages are limited to the disc and immediate peri-papillary region. (B) In malignant systemic hypertension the disc edema and peri-papillary hemorrhages (arrow) are similar, but these superficial hemorrhages also extend into the mid-peripheral retina. In addition there are intraretinal dot and blot hemorrhages throughout the posterior pole (arrowheads).

and protein from the intravascular space into the interstitium leads to vasogenic brain edema, which causes both cerebral dysfunction and increased intracranial pressure. In such patients, both ocular and neurologic pathology may contribute to disc swelling. Visual loss may similarly be due to both retinal and occipital cortical changes. The cerebral edema in this condition has a predilection for the parietal and occipital lobes and has been termed "posterior reversible encephalopathy syndrome". This condition is best demonstrated on MR FLAIR sequences. In more severe cases, ischemic changes may also be seen on diffusion weighted images, which may progress to infarction and thus carry a more guarded prognosis. In pregnant women with acute hypertension, the same combination of clinical and radiographic findings is called the preeclampsia–eclampsia syndrome.

The clinical features and fundus findings in malignant hypertension are non-specific and may resemble several other conditions. Careful measurement of blood pressure should therefore be

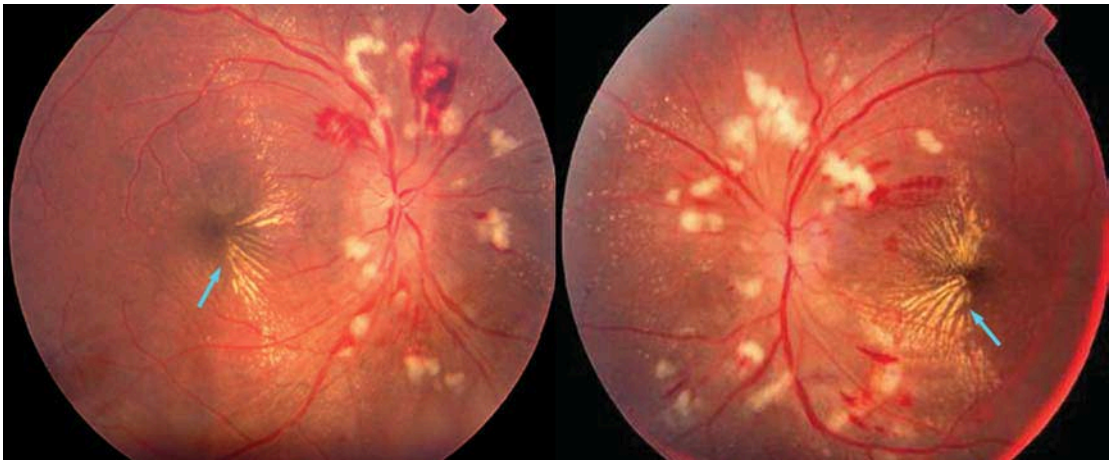

**Figure 1.6** Fundus photographs of a different patient with retinovascular changes of malignant hypertension. Cotton-wool spots are present on the disc and along the vascular arcades. Scattered retinal flame and blot hemorrhages are seen in the same distribution. Hard exudates are found temporal to the optic disc, forming a partial macular star (arrows).

included in the evaluation of any patient with unexplained bilateral optic disc edema. With timely diagnosis and treatment, the clinical manifestations of malignant hypertension are often reversible. Overly rapid lowering of blood pressure, however, may cause devastating infarction of the optic nerves and other end organs and should be discouraged.

**Diagnosis: Malignant hypertension**

**Tip:** The presence of vascular changes in the retina distinguishes the optic disc swelling of malignant hypertension from that of increased intracranial pressure.

## Chronic optic neuropathy

**Case:** A 40-year-old farmer noted blurring of vision in his left eye, of uncertain duration. He was generally healthy with no history of systemic or neurologic disease. There was a remote history of visual loss in the left eye due to trauma and he knew that vision in that eye hadn't returned to normal, but he wasn't certain if it had declined further since. Visual acuity and color vision were normal in each eye. Visual field testing was normal in the right eye but markedly abnormal in the left (Figure 1.7). Ophthalmoscopic examination showed left optic disc pallor, which prompted an MR scan of brain and orbits that was normal.

### Having excluded compressive, inflammatory and infiltrative causes of optic neuropathy, what other mechanisms would you consider? How would you proceed?

The pattern of this patient's visual field loss indicates damage at the level of the optic disc. Specifically, the defects emerge from the physiologic blindspot and respect the horizontal meridian. Common disc-related disorders include ischemic optic neuropathy, papilledema, disc drusen and glaucoma. The next step is a critical scrutiny of the optic disc.

The right disc has a normal appearance with a 0.2 cup/disc (C/D) ratio and healthy neuroretinal rim. The left disc, however, is severely excavated with virtually no neuroretinal rim (Figure 1.8).

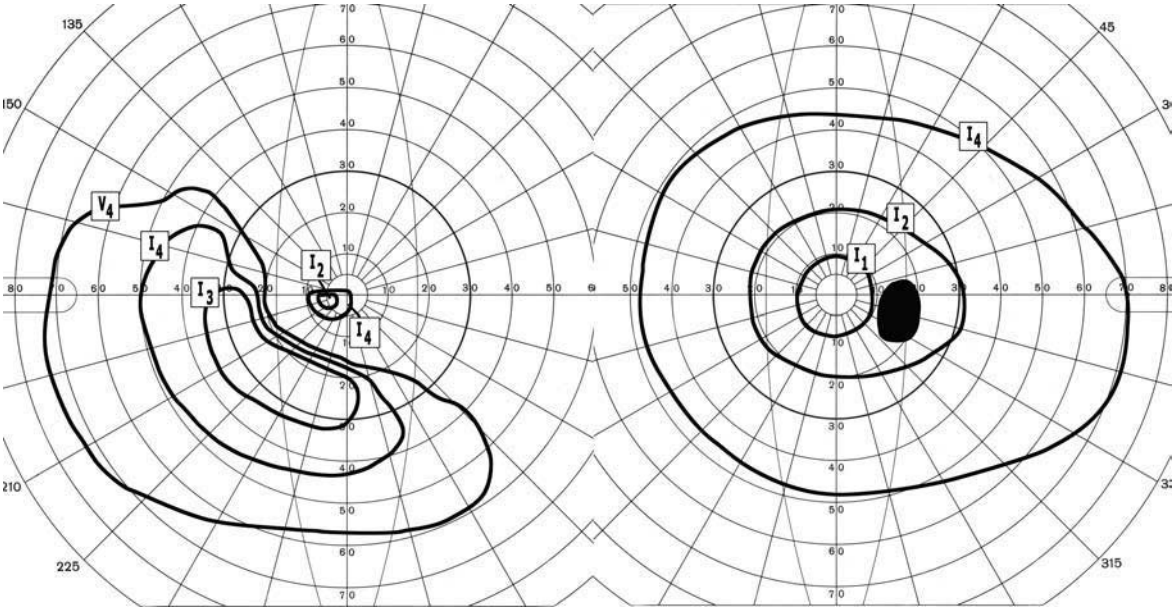


**Figure 1.7** Goldmann visual field in a 40-year-old farmer. In the left eye there is a dense superior altitudinal defect coalescing with an inferior arcuate scotoma; the field in the right eye is normal.

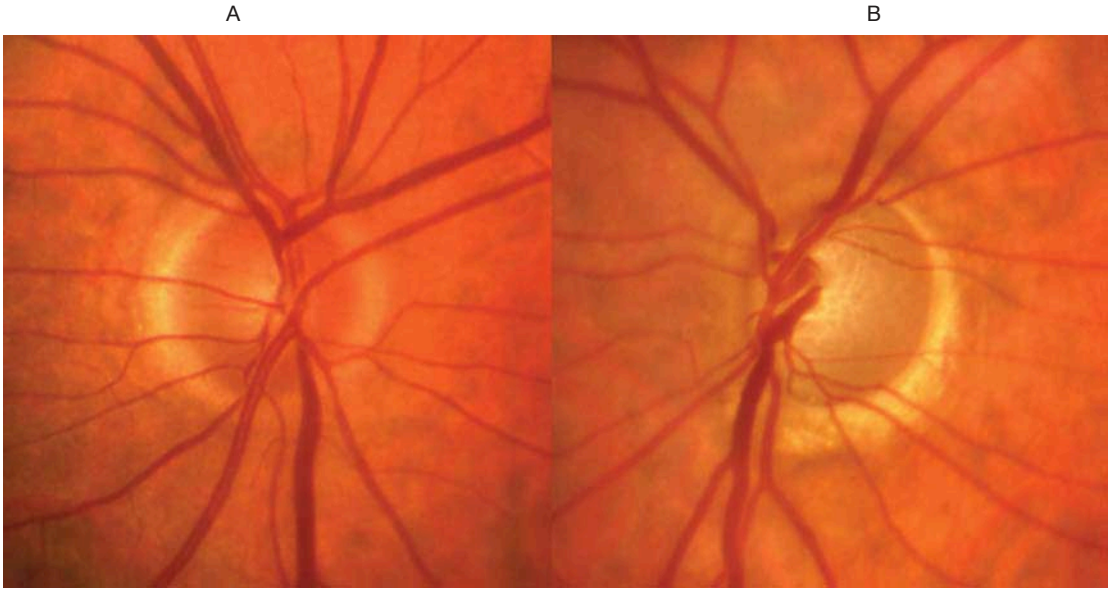


**Figure 1.8** Fundus photographs of the above patient with severe visual field loss in the left eye. (A) The right optic disc is normal. (B) The left optic disc is markedly cupped, leaving almost no neuroretinal rim. Even without a stereoscopic view, the deep saucerization can be appreciated from the curve of the retinal vessels as they emerge from the cup and cross the disc margin. The stippled appearance in the center of the disc indicates that this is the lamina cribrosa, and not neural tissue.

Its pale color is misleading. What the viewer is seeing is exposed lamina cribrosa, which, being a continuation of the sclera, is normally white. Based on this optic disc appearance, ophthalmic consultation was obtained. His intraocular pressures (IOPs) were asymmetric, measuring 13 mm OD and 26 mm OS. Gonioscopy revealed angle recession in the left eye, presumed due to his past history of eye injury. He was treated with topical medications to lower the IOP in his left eye, and subsequent serial examinations showed that his visual field defect was stable.

**Discussion:** The optic disc has a limited repertoire of expression. Processes that interfere with axonal transport cause disc swelling, whereas those that reflect axonal loss manifest as pallor and/or excavation. Acquired excavation of the optic nerve head, or disc cupping, is traditionally divided into glaucomatous and non-glaucomatous forms. The large majority of cases of disc cupping are glaucomatous in origin.

Glaucomatous optic nerve damage has a characteristic appearance. The disease has a predilection for the arcuate fibers, which produces progressive loss of the neural rim starting at the superior and inferior poles of the optic disc, and causes vertical elongation of the cup. If both eyes are equally affected, this early stage of the disease may be difficult to recognize. In other cases, asymmetry of the C/D ratio in the two eyes may be the first sign of the condition (Figure 1.9A). An interocular C/D asymmetry of 0.1 or more is found in only 10% of the normal population, and thus raises suspicion of glaucoma. Another helpful finding is the presence of a single splinter hemorrhage on the disc margin, termed a Drance hemorrhage (Figure 1.9B). While similar hemorrhages are seen in a variety of conditions that cause disc edema, in the absence of disc swelling this finding is strongly suggestive of glaucoma. Focal damage to the nerve fiber layer, appearing as a notch in the neural rim, is also characteristic of glaucomatous optic neuropathy and sometimes follows a Drance hemorrhage (Figure 1.9C).

Uncommonly, causes of optic nerve damage other than glaucoma produce optic disc excavation. These mechanisms include compression, disc infarction due to giant cell arteritis, trauma and radiation necrosis. The fundus feature that is most helpful for distinguishing glaucomatous from non-glaucomatous cupping is the status of the remaining neural rim. In glaucomatous discs, the rim generally maintains a more normal hue. Even in advanced cases of glaucoma in which nerve fiber loss is severe, the degree of disc excavation is disproportionately greater than the severity of rim pallor (Figure 1.10). In contrast, rim pallor is a prominent feature of non-glaucomatous cupping. Other fundus features may also be helpful in making this distinction. Focal thinning of the temporal retinal rim is more characteristic of non-glaucomatous damage, whereas diffuse obliteration of the neural rim and peri-papillary atrophy usually reflect glaucomatous change.

In addition to optic disc appearance, measures of optic nerve function are also important. In keeping with the predilection for superior and inferior nerve fiber bundles, field defects in glaucoma are typically arcuate, particularly affecting the superior field. Central vision is spared until late in the course of the disease. In contrast, compressive causes of acquired disc excavation are often associated with visual field loss that respects the vertical meridian. The clinical challenge in cases such as the above is to distinguish optic disc excavation from disc atrophy. Despite advances in optic disc imaging techniques such as ocular coherence tomography (OCT), careful fundus examination is usually the key to making this diagnosis.

**Diagnosis: Glaucomatous optic neuropathy**

**Tip:** Glaucoma should be included in the differential diagnosis for any patient with unexplained optic neuropathy.

## Painful mydriasis

**Case:** A 62-year-old librarian periodically noted a dull pain around her right eye when she worked nights in the archives section. At times, along with