Examination of the living human retina provides a unique opportunity for the direct study of nervous, vascular, and connective tissues. Many systemic disorders have retinal manifestations that are valuable for screening, diagnosis, and management of these conditions. Furthermore, retinal involvement in systemic disorders, such as diabetes mellitus, is a major cause of morbidity. Early recognition by ophthalmoscopic screening is a key factor in effective treatment. Ophthalmoscopy has the potential to be one of the most “high-yield” elements of the physical examination. Effective ophthalmoscopy requires a basic understanding of ocular structures and ophthalmoscopic techniques and recognition of abnormal findings.

OVERVIEW OF OCULAR STRUCTURES
The eye consists of a shell (cornea and sclera), lens, iris diaphragm, ciliary body, choroid, and retina. The anterior chamber is the space between the cornea and the lens, and it is filled with aqueous humor. The space between the posterior aspect of the lens and the retina is filled by vitreous gel. The choroid and the retina cover the posterior two-thirds of the sclera internally. The cornea and the lens form the focusing system of the eye, while the retina functions as the photoreceptor system, translating light to neuronal signals that are in turn transmitted to the brain via the optic nerve and visual pathways. The choroid is a layer of highly vascularized tissue that nourishes the retina and is located between the sclera and the retina. The retinal pigment epithelium (RPE) layer is a monolayer of pigmented cells that are adherent to the overlying retinal photoreceptor cells. RPE plays a major role in retinal photoreceptor metabolism.

NORMAL FUNDUS
The important areas that are visible by ophthalmoscopy include the macula, optic disc, retinal blood vessels, and retinal periphery (Fig. 40e-1).

THE MACULA
The macula is the central part of the retina and is responsible for detailed vision (acuity) and perception of color. The macula is defined clinically as the area of the retina centered on the posterior pole of the fundus, measuring about 5 disc diameters (DD) (7–8 mm) and bordered by the optic disc nasally and the temporal vascular arcades superiorly and inferiorly. Temporally, the macula extends for about 2.5 DD from its center. The fovea, in the central part of the macula, corresponds to the site of sharpest visual acuity. It is approximately 1 DD in size and appears darker in color than the surrounding area. The center of the fovea, the foveola, has a depressed pit-like configuration measuring about 350 μm.

THE OPTIC DISC
The optic disc measures about 1.5 mm and is located about 4 mm (2.5 DD) nasal to the fovea. It contains the central retinal artery and vein as they branch, a central excavation (cup), and a peripheral neural rim. Normally, the cup-to-disc ratio is less than 0.6. The cup is located temporal to the entry of the disc vessels. The normal optic disc is yellow/pink in color. It has clear and well-defined margins and is in the same plane as the retina (Fig. 40e-2). Pathologic findings include pallor (atrophy), swelling, and enlarged cupping.

THE EQUATOR AND PERIPHERAL RETINA
The equator of the fundus is clinically defined as the area that includes the internal opening of the vortex veins. The peripheral retina extends from the equator anteriorly to the ora serrata.
OPHTHALMOSCOPY

There are a number of ways to visualize the retina, including direct ophthalmoscopy, binocular indirect ophthalmoscopy, and slit-lamp biomicroscopy. Most nonophthalmologists prefer direct ophthalmoscopy, performed with a hand-held ophthalmoscope, because the technique is simple to master and the device is very portable. Ophthalmologists often use slit-lamp biomicroscopy and indirect ophthalmoscopy to obtain a more extensive view of the fundus.

DIRECT OPHTHALMOSCOPE

Direct ophthalmoscopes are simple hand-held devices that include a small light source for illumination, a viewing aperture through which the examiner looks at the retina, and a lens dial used for correction of the examiner’s and the patient’s refractive errors. A more recent design, the PanOptic ophthalmoscope, provides a wider field of view.

How to Use a Direct Ophthalmoscope

Good alignment is the key. The goal is to align the examiner’s eye with the viewing aperture of the ophthalmoscope, the patient’s pupil, and the area of interest on the retina. Both the patient and the examiner should be in a comfortable position (sitting or lying for the patient, sitting or standing for the examiner). Dilating the pupil and dimming the room lights make the examination easier. Steps for performing direct ophthalmoscopy are summarized in Table 40e-1.

PANOPTIC OPHTHALMOSCOPE

The PanOptic ophthalmoscope is a type of direct ophthalmoscope that is designed to provide a wider view of the fundus and has slightly more magnification than the standard direct ophthalmoscope. Steps for using the PanOptic Ophthalmoscope are summarized in Table 40e-2.

Table 40e-1 Guidelines for Performing Direct Ophthalmoscopy

- Instruct the patient to remove glasses, keep the head straight, and to look steadily at a distant target straight in front. You may keep or remove your own glasses. Position your head at the same level as the patient’s head.
- Use your right eye and right hand to examine the patient’s right eye, and use your left eye and left hand to examine the patient’s left eye.
- Using the ophthalmoscope light as a pen light, briefly examine the external features of the eye, including lashes, lid margins, conjunctiva, sclera, iris, and pupil shape, size, and reactivity.
- Shine the ophthalmoscope light into the patient’s pupil at arm’s length and observe the red reflex. Note abnormalities of the red reflex such as an opacity of the media.
- Dialing up a +10 D lens in the lens wheel, while examining the eye from 10 cm, allows magnified viewing of the anterior aspect of the eye.
- Reduce the power of the lens in the wheel to zero, and move closer to the patient. Identify the optic disc by pointing the ophthalmoscope about 15° nasally or by following a blood vessel toward the apex of any branching. If the retina is out of focus, turn the lens dial either way, without moving your head. If the disc becomes clearer, keep turning until best focus is achieved; if it becomes more blurred, turn the dial the other way.
- Once you visualize the optic nerve, note its shape, size, color, margins, and the cup. Also note the presence of any venous pulsation or surrounding pigment, such as a choroidal or scleral crescent.
- Next, examine the macula. The macula is the area between the superior and inferior temporal vascular arcades, and its center is the fovea. You can examine the macula by pointing your ophthalmoscope about 15° temporal to the optic disc. Alternatively, ask the patient to look into the center of the light. Note the foveal reflex and the presence of any hemorrhage, exudate, abnormal blood vessels, scars, deposits, or other abnormalities.
- Examine the retinal blood vessels by re-identifying the optic disc and following each of the four main branches away from the disc. The veins are dark red and relatively large. The arteries are narrower and bright red.
- Ask the patient to look in the eight cardinal directions to allow you to view the peripheral fundus. In a patient with a well-dilated pupil, it is possible to visualize as far as the equator.

Table 40e-2 How to Use a PanOptic Ophthalmoscope

- Focus the ophthalmoscope: Look through the scope at an object that is at least 10 to 15 feet away. Sharpen the image of the object by using the focusing wheel. Set the aperture dial to “small” or home position.
- Turn the scope on, and adjust the light intensity to “Maximum.”
- Instruct the patient to look straight ahead. Move the ophthalmoscope close to the patient until the eyecup touches the patient’s brow. The eyecup should be compressed about half its length to optimize the view.
- Visualize the optic disc.
- Examine the fundus as described in Table 40e-1.

RETINAL SIGNS ASSOCIATED WITH SYSTEMIC DISEASES

AGE-RELATED CHANGES

Common age-related changes include diminished foveal light reflex, drusen (small yellow subretinal deposits), mild RPE atrophy, and pigment clumping.

RETINAL HEMORRHAGES

Retinal hemorrhages may take various shapes and sizes depending on their location within the retina (Figs. 40e-3 and 40e-4). Flame-shaped hemorrhages are located at the level of the superficial nerve fiber layer and represent bleeding from the inner capillary network of the retina. A white-centered hemorrhage is a superficial flame-shaped hemorrhage with an area of central whitening, often representing edema, focal necrosis, or cellular infiltration. Causes of white-centered hemorrhage include bacterial endocarditis and septicemia (Roth spots), lymphoproliferative disorders, diabetes mellitus, hypertension, anemia, and collagen vascular disorders. Dot hemorrhages are small, round, superficial hemorrhages that also originate from the superficial capillary network of the retina. They resemble microaneurysms. Blot hemorrhages are slightly larger in size, dark, and intraretinal. They represent bleeding from the deep capillary network of the retina. Subhyaloid hemorrhages are variable in shape and size and tend to be larger than other types of hemorrhages. They often have a fluid level (“boat-shaped” hemorrhage) and are located within the space between the vitreous and the retina. Subretinal hemorrhages are located deep (external) to the retina. The retinal vessels can be seen crossing over (internal to) such hemorrhages. Subretinal hemorrhages are variable in size and most commonly are caused by choroidal neovascularization (e.g., wet macular degeneration).

Figure 40e-3 Superficial flame-shaped hemorrhages, dot hemorrhages, and microaneurysms in a patient with nonproliferative diabetic retinopathy.
microaneurysms. Microaneurysms are outpouchings of the retinal capillaries, appearing as red dots (similar to dot hemorrhages) and measuring 15–50 μm. Microaneurysms have increased permeability and may bleed or leak, resulting in localized retinal hemorrhage or edema. A microaneurysm ultimately thromboses and disappears within 3–6 months. Microaneurysms may occur in any condition that causes retinal microvasculopathy (Table 40e-3).

### TABLE 40e-3 DISEASES ASSOCIATED WITH RETINAL MICROVASCULOPATHY

- Diabetes mellitus
- Systemic hypertension
- Retinal vein occlusion
- Retinal artery occlusion
- Multiple microemboli, e.g., retinopathy secondary to intravenous drug abuse, septicemia, endocarditis, Purtscher's retinopathy
- Carotid artery disease, carotid-cavernous fistula, aortic arch syndrome
- Sickle cell retinopathy
- Radiation retinopathy, head/neck irradiation
- HIV retinopathy
- Retinal vasculitis
- Anemia
- Thrombocytopenia
- Lymphoproliferative disorders
- Coagulopathy
- Hyperviscosity syndromes
- Retinopathy of prematurity

### HARD EXUDATES

Hard exudates are well-circumscribed, shiny, yellow deposits located within the retina. They arise at the margins of areas of retinal edema and indicate increased capillary permeability. Hard exudates contain lipoproteins and lipid-laden macrophages. They may clear spontaneously or following laser photoagulation, often within 6 months. Hard exudates may occur in isolation or may be scattered throughout the fundus. They may occur in a circular (circinate) pattern centered around an area of leaking microaneurysms. A macular star consists of a radiating, star-shaped pattern of hard exudates that is characteristically seen in severe systemic hypertension and in neuroretinitis associated with cat-scratch disease. Conditions associated with hard exudates include those causing retinal microvasculopathy (Table 40e-3), papilledema, neuroretinitis such as cat-scratch disease and Lyme disease, retinal vascular lesions (macroaneurysm, retinal capillary hemangioma, Coats' disease), intraocular tumors, and wet age-related macular degeneration. Drusen may be mistaken for hard exudates on ophthalmoscopy. Unlike hard exudates, drusen are nonrefractile subretinal deposits with blurred margins. They are usually seen in association with age-related macular degeneration.

### COTTON-WOOL SPOTS

Cotton-wool spots are yellow/white superficial retinal lesions with indistinct feathery borders measuring 0.25–1 DD in size (Fig. 40e-5). They represent areas of edema within the retinal nerve fiber layer due to focal ischemia. Cotton-wool spots usually resolve spontaneously within 3 months. If the underlying ischemic condition persists, new lesions can develop in different locations. Cotton-wool spots often occur in conjunction with retinal hemorrhages and microaneurysms and represent retinal microvasculopathy caused by a number of systemic conditions (Table 40e-3). They may occur in isolation in HIV retinopathy, systemic lupus erythematosus, anemia, bodily trauma, other systemic conditions (Purtscher’s/Purtscher-like retinopathy), and interferon therapy.

### RETINAL NEOVASCULARIZATION

Retinal neovascular complexes are irregular meshworks of fine blood vessels that grow in response to severe retinal ischemia or chronic inflammation (Fig. 40e-6). They may occur on or adjacent to the optic disc or elsewhere in the retina. Neovascular complexes are very
fragile and have a high risk for hemorrhaging, often causing visual loss. Diseases associated with retinal neovascularization include conditions that cause severe retinal microvasculopathy, especially diabetic and sickle cell retinopathies (Table 40e-3), intraocular tumors, intraocular inflammation (sarcoidosis, chronic uveitis), and chronic retinal detachment.

RETINAL EMBOLI
Common sources of retinal emboli include carotid artery atheromatous plaque, cardiac valve and septal abnormalities, cardiac arrhythmias, atrial myxoma, bacterial endocarditis, septicemia, fungemia, and intravenous drug abuse.

Platelet emboli are yellowish in appearance and conform to the shape of the blood vessel. They usually originate from an atheromatous plaque within the carotid artery and can cause transient loss of vision (amaurosis fugax). Cholesterol emboli, otherwise termed Hollenhorst plaques, are yellow crystalline deposits that are commonly found at the bifurcations of the retinal arteries and may be associated with amaurosis fugax. Calcific emboli have a pearly white appearance, are larger than the platelet and cholesterol emboli, and tend to lodge in the larger retinal arteries in or around the optic disc. Calcific emboli often result in retinal arteriolar occlusion. Septic emboli can cause white-centered retinal hemorrhages (Roth spots), retinal microabscesses, and endogenous endophthalmitis. Fat embolism and amniotic fluid embolism are characterized by multiple small vessel occlusions, typically causing cotton-wool spots and few hemorrhages (Purtscher’s-like retinopathy). Talc embolism occurs with intravenous drug abuse and is characterized by multiple refractile deposits within the small retinal vessels. Any severe form of retinal artery embolism may result in retinal ischemia and its sequelae, including retinal neovascularization.

CHERRY RED SPOT AT THE MACULA
Cherry red spot at the macula is the term used to describe the dark red appearance of the central foveal area in comparison to the surrounding macular region (Fig. 40e-7). This appearance is most commonly due to a relative loss of transparency of the parafoveal retina resulting from ischemic cloudy swelling or storage of macromolecules within the ganglion cell layer. Diseases associated with a cherry red spot at the macula include central retinal artery occlusion, sphingolipidoses, and mucolipidoses.

RETINAL CRYSTAL DEPOSITION
Retinal crystals appear as fine, refractile, yellow-white deposits. Associated conditions include infantile cystinosis, primary hyperoxaluria, secondary oxalosis, Sjögren-Larson syndrome, intravenous drug abuse (talc retinopathy), and drugs such as tamoxifen, canthaxanthin, nitrofurantoin, methoxyflurane, and ethylene glycol. Crystals may also be seen in primary retinal diseases such as juxtafoveal telangiectasia, gyrate atrophy, and Bietti’s crystalline degeneration. Old microemboli may mimic retinal crystals.

RETINAL VASCULAR SHEATHING
Vascular sheathing appears as a yellow-white cuff surrounding a retinal artery or vein (Fig. 40e-8). Diseases associated with retinal vascular sheathing include sarcoidosis, tuberculosis, toxoplasmosis, syphilis, HIV, retinitis (cytomegalovirus, herpes zoster, and herpes simplex),
Lyme disease, cat-scratch disease, multiple sclerosis, chronic leukemia, amyloidosis, Behçet’s disease, retinal vasculitis, retinal vascular occlusion, and chronic uveitis.

**RETINAL DETACHMENT**
Retinal detachment is the separation of the retina from the underlying RPE. There are three main types: (1) serous/exudative, (2) tractional, and (3) rhegmatogenous retinal detachment.

In serous retinal detachment, the location of the subretinal fluid is position-dependent, characteristically gravitating to the lowermost part of the fundus (shifting fluid sign), and retinal breaks are absent. Diseases associated with serous/exudative retinal detachment include severe systemic hypertension, dural arteriovenous shunt, retinal vascular anomalies, hyperviscosity syndromes, papilledema, posterior uveitis, scleritis, orbital inflammation, and intraocular neoplasms such as choroidal melanoma, choroidal metastasis, lymphoma, and multiple myeloma.

Tractional retinal detachment is caused by internal traction on the retina in the absence of a retinal break. The retina in the area of detachment is immobile and concaved internally. Fibrovascular proliferation is a frequent associated finding. Conditions associated with tractional retinal detachment include vascular proliferative retinopathies such as severe proliferative diabetic retinopathy, branch retinal vein occlusion, sickle cell retinopathy, and retinopathy of prematurity. Ocular trauma, proliferative vitreoretinopathy, and intraocular inflammation are other causes of a tractional retinal detachment.

Rhegmatogenous retinal detachment is caused by the presence of a retinal break, allowing fluid from the vitreous cavity to gain access to the subretinal space. The surface of the retina is usually convex forward. Rhegmatogenous retinal detachment has a corrugated appearance, and undulates with eye movement. Causes of retinal breaks include posterior vitreous detachment, severe vitreoretinal traction, trauma, intraocular surgery, retinitis, and atrophic holes.

**OPTIC DISC SWELLING**
Optic disc swelling is abnormal elevation of the optic disc with blurring of its margins (Fig. 40e-9). The term "papilledema" is used to describe swelling of the optic disc secondary to elevation of intracranial pressure. In papilledema, the normal venous pulsation at the disc is characteristically absent. The differential diagnosis of optic disc swelling includes papilledema, anterior optic neuritis (papillitis), central retinal vein occlusion, anterior ischemic optic neuropathy, toxic optic neuropathy, hereditary optic neuropathy, neuroretinitis, diabetic papilopathy, hypertension (Fig. 40e-10), respiratory failure, carotid-cavernous fistula, optic disc nerve infiltration (glioma, lymphoma, leukemia, sarcoidosis, and granulomatous infections), ocular hypotony, chronic intraocular inflammation, optic disc drusen (pseudopapilledema), and high hypermetropia (pseudopapilledema).

**CHORIORETINAL MASS LESIONS**
Choroidal mass lesions appear thickened and may or may not be associated with increased pigmentation. Pigmented mass lesions include choroidal nevus (usually flat), choroidal malignant melanoma (Fig. 40e-11), and melanocytoma. Nonpigmented lesions include amelanotic choroidal melanoma, choroidal metastasis, retinoblastoma, capillary hemangioma, granuloma (e.g., Toxocara canis), choroidal detachment, choroidal hemorrhage, and wet age-related macular degeneration. Other rare tumors that may be visible on ophthalmoscopy include...
ostoma, astrocytoma (e.g., tuberous sclerosis), neurilemmoma, and leiomyoma.

**PIGMENTED LESIONS**
The differential diagnosis of flat pigmented lesions of the fundus is summarized in Table 40e-4. The appearance of chorioretinal scarring from old *Toxoplasma* chorioretinitis is shown in Fig. 40e-12.

### Table 40e-4  Differential Diagnosis of Flat Pigmented Lesions of the Fundus

<table>
<thead>
<tr>
<th>Bone spicule pigmentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Retinitis pigmentosa and its variants</td>
</tr>
<tr>
<td>- Pigmentary retinopathy in systemic diseases: Usher’s syndrome, abetalipoproteinemia, Refsum’s disease, Kearns-Sayre syndrome, Alström’s syndrome, Cockayne’s syndrome, Friedreich’s ataxia, mucopolysaccharidoses, paraneoplastic syndrome</td>
</tr>
<tr>
<td>- Infections: congenital rubella (salt and pepper retinopathy), congenital syphilis</td>
</tr>
<tr>
<td>- Resolved choroidal/retinal detachment</td>
</tr>
<tr>
<td>- Age-related reticular pigmented degeneration</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patchy pigmented lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Chorioretinal scars</td>
</tr>
<tr>
<td>- Infections: <em>Toxoplasma gondii</em>, <em>Toxocara canis</em>, syphilis, cytomegalovirus, herpes zoster and herpes simplex viruses, west Nile virus, histoplasmosis, parasitic infection</td>
</tr>
<tr>
<td>- Choroidal infarct: severe hypertension, sickle cell hemoglobinopathies</td>
</tr>
<tr>
<td>- Trauma, cryotherapy, laser photoocoagulation scars</td>
</tr>
<tr>
<td>- Age-related macular degeneration</td>
</tr>
<tr>
<td>- Drugs: chloroquine/hydroxychloroquine, thioridazine, chlorpromazine, desferrioxamine</td>
</tr>
<tr>
<td>- Choroidal nevus</td>
</tr>
<tr>
<td>- Congenital hypertrophy of the retinal pigment epithelium</td>
</tr>
</tbody>
</table>

**Figure 40e-12**  Chorioretinal scarring due to old *Toxoplasma* chorioretinitis. The lesion is flat and pigmented. Areas of hypopigmentation are also present.