CHAPTER 15

Diseases of the Vitreous and Vitreoretinal Interface

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Highlights

- Posterior vitreous detachment occurs commonly with age and can be associated with vitreous hemorrhage or retinal tears.
- There are 3 recognized categories of vitreomacular traction disease: vitreomacular adhesion, vitreomacular traction syndrome, and macular hole.
- Phenotypically similar to retinopathy of prematurity, familial exudative vitreoretinopathy is characterized by failure of the temporal retina to vascularize in an individual born at full term with normal respiratory status.

Posterior Vitreous Detachment

The vitreous is a transparent gel composed mainly of water, collagen, and hyaluronan (hyaluronic acid) that is attached to the basal lamina of the lens, optic nerve, and retina, and fills the vitreous cavity of the eye. A posterior vitreous detachment (PVD) is the separation of the posterior cortical gel from the retinal surface, including its adhesions at the optic nerve head (the area of Martegiani), macula, and blood vessels. At its base, the vitreous remains firmly attached to the retina. Because of this firm attachment, the basal cortical vitreous collagen cannot be peeled off the retina; instead, the vitreous must be "shaved" during vitrectomy, instead of being removed.

With increasing age, the vitreous gel undergoes both liquefaction (synchysis) and collapse (syneresis). The viscous hyaluronan accumulates in lacunae, which are surrounded by displaced collagen fibers. The gel can then contract. With this contraction, the posterior cortical gel detaches toward the firmly attached vitreous base. Clinical studies typically reveal a low occurrence of PVD in patients younger than 50 years. Autopsy studies demonstrate PVD in less than 10% of patients younger than 50 years but in 63% of those older than 70 years. The prevalence of PVD is increased in conditions such as aphakia, pseudophakia with open posterior capsule, inflammatory disease, trauma, vitreous

hemorrhage, and axial myopia. Localized regions of the posterior cortical gel can separate slowly, over the course of many years, with few if any symptoms, compared with the more acute, symptomatic event. Common symptoms of an acute PVD include the appreciation of floaters that can take many forms or of a cloud that can follow eye movement.

The diagnosis of PVD is often made with indirect ophthalmoscopy or slit-lamp biomicroscopy, with which the posterior vitreous face may be observed a few millimeters in front of the retinal surface. In eyes with a PVD, a translucent ring of fibroglial tissue (the "Weiss" or "Vogt" ring) (Fig 15-1) is frequently torn loose from the surface of the optic nerve head, and its observation helps the clinician make the diagnosis. Although a shallow detachment of the posterior cortical gel may be difficult or impossible to observe with biomicroscopy, this type of detachment may be revealed on contact B-scan ultrasonography as a thin, hyperreflective line bounding the posterior vitreous. Optical coherence tomography (OCT) has shown that PVDs often start as a localized detachment of the vitreous over the perifovea, called a *posterior perifoveal vitreous detachment,* later spreading anteriorly to involve larger areas.

Persistent focal attachment of the vitreous to the retina can cause a number of pathologic conditions. Vitreous contraction as well as traction caused by ocular saccades may lead to breaks, particularly at the posterior edge of the vitreous base. Persistent attachment to the macula may lead to vitreomacular traction syndrome (Fig 15-2). Focal attachment to the foveola can induce foveal cavitation and macular hole formation. Remnants of the vitreous often remain on the internal limiting membrane (ILM) after a posterior vitreous "detachment." For this reason, some authorities state that a presumed PVD often is actually posterior vitreoschisis that is internal or external to the layer of hyalocytes. These vitreous remnants may have a role in epiretinal membrane or macular hole formation and can contribute to traction detachments in patients with pathologic myopia and to macular edema in patients with diabetes. Plaques of these adherent remnants of cortical vitreous can often be highlighted during vitreous surgery by applying triamcinolone (Fig 15-3).

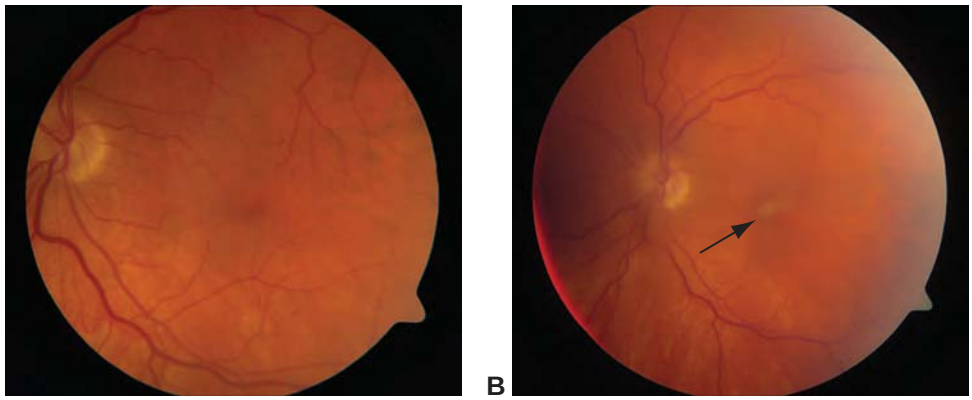

Figure 15-1 Posterior vitreous detachment. Color fundus photographs show attached vitreous **(A)** and an acute Weiss ring over the fovea with obscuration *(arrow)* occurring several days later **(B).** *(Courtesy of Stephen J. Kim, MD.)*

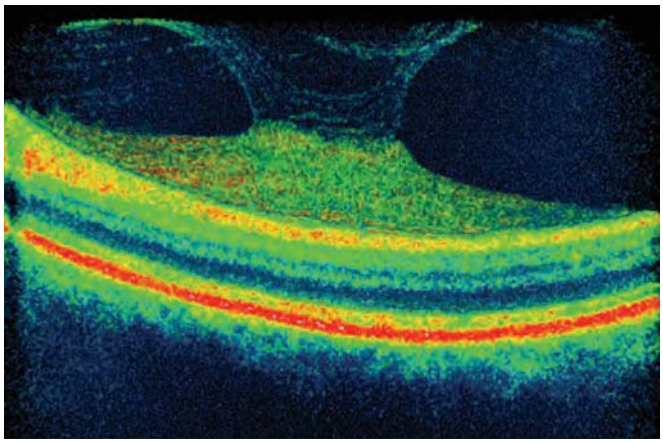

Figure 15-2 A 3-dimensional rendering of spectral-domain optical coherence tomography (SD-OCT) imaging of vitreomacular traction syndrome. The cone of vitreous is attached to and elevates the central fovea. *(Courtesy of Richard F. Spaide, MD.)*

Gishti O, van den Nieuwenhof R, Verhoekx J, van Overdam K. Symptoms related to posterior vitreous detachment and the risk of developing retinal tears: a systematic review. *Acta Ophthalmol.* 2019;97(4):347–352.

Epiretinal Membranes

An epiretinal membrane (ERM) is a transparent, avascular, fibrocellular membrane on the inner retinal surface that adheres to and covers the ILM of the retina. Proliferation of glia, retinal pigment epithelium (RPE), or hyalocytes at the vitreoretinal interface, especially at the posterior pole, results in ERM formation.

ERMs are relatively common; at autopsy, they are discovered in 2% of persons older than 50 years and in 20% older than 75 years. Both sexes are equally affected. Bilaterality occurs in approximately 10%–20% of cases, and severity is usually asymmetric. Detachment or separation of the posterior vitreous is present in almost all eyes with idiopathic ERMs and may be a requisite for ERM development. Schisis of the posterior vitreous may leave variable portions of the posterior cortical vitreous attached to the macula, allowing glial cells from the retina to proliferate along the retinal surface and hyalocytes to proliferate on posterior cortical vitreous remnants on the retinal surface. Secondary ERMs occur regardless of age or sex in association with abnormal vitreoretinal adhesions, occult retinal tears, and areas of inflammation, as well as following retinal detachment or retinal bleeding.

Signs and symptoms

Epiretinal proliferation is generally located in the central macula—over, surrounding, or eccentric to the fovea (Fig 15-4). The membranes usually appear as a mild sheen or glint on the retinal surface. Over time, ERMs may become more extensive, increasing retinal distortion and thickening (Activities 15-1, 15-2), which can lead to a decline in visual acuity and to image distortion. However, their rate of progression and severity vary greatly. In some cases, the ERM may become opaque, obscuring underlying retinal details. A "pseudohole" appearance

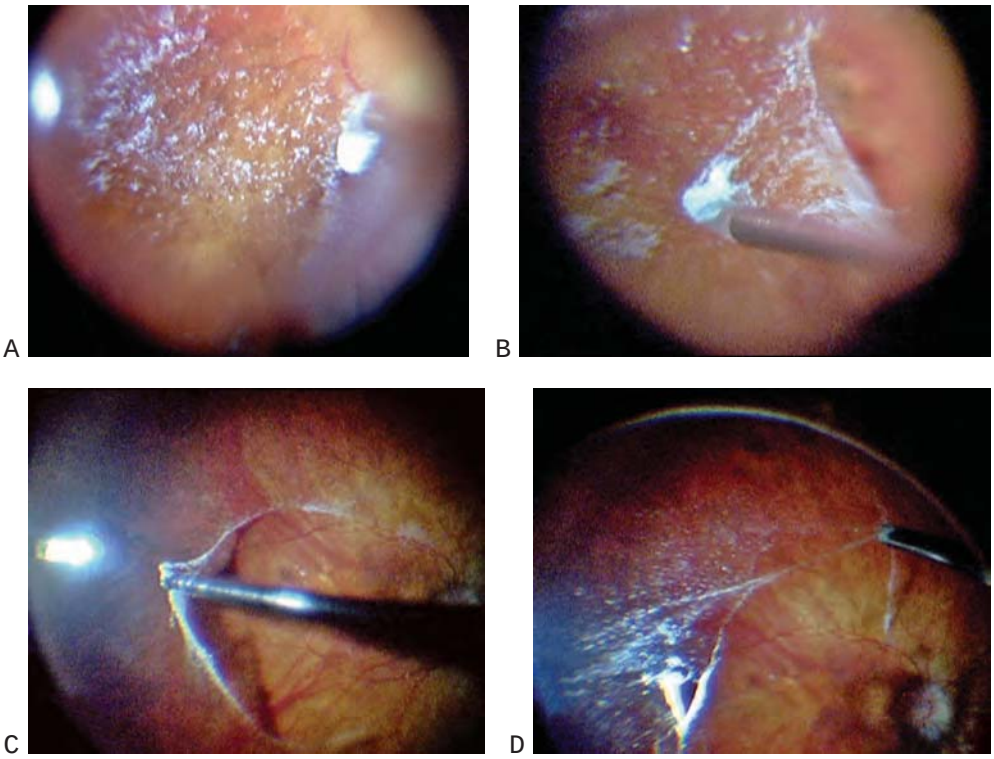

Figure 15-3 Visualization of a thin layer of adherent vitreous during vitrectomy with the use of triamcinolone. This patient appeared to have a posterior vitreous detachment (PVD) and underwent a vitrectomy. **A,** A small amount of triamcinolone was injected into the vitreous cavity; the excess was aspirated from the surface of the retina, leaving a fine distribution of triamcinolone sticking to the adherent vitreous. **B,** The vitreous membrane was elevated using a diamond-dusted silicone scraper. Note that the vitreous is difficult to see; the sheet of triamcinolone is the clue to its presence. **C,** A wide-angle viewing system then was used to visualize the elevation of the adherent vitreous, and the vitrector was set to suction only. **D,** Note the extent of the adherent vitreous sheet, which was removed with the vitrector set to cut. *(Courtesy of Richard F. Spaide, MD.)*

is produced when this preretinal membrane contracts to the edge of the clivus, steepening the gentle slope around the fovea into a cylindrical depression. Occasionally, intraretinal hemorrhages or whitened patches of superficial retina representing delayed axoplasmic flow in the nerve fiber layer and edema may be present, which can imitate a retinal vein occlusion. *Lamellar hole–associated epiretinal proliferation (LHEP)* features an avascular tissue layer of medium reflectivity that covers the premacular surface and surrounds a foveal defect without a tractional component. The cellular origin of ERMs is still under debate. Histologic examination reveals mainly RPE cells and retinal glial cells (astrocytes and Müller cells); however, myofibroblasts, fibroblasts, hyalocytes, and macrophages have also been identified.

ACTIVITY 15-1 OCT Activity: Epiretinal membrane.
Courtesy of Colin A. McCannel, MD.

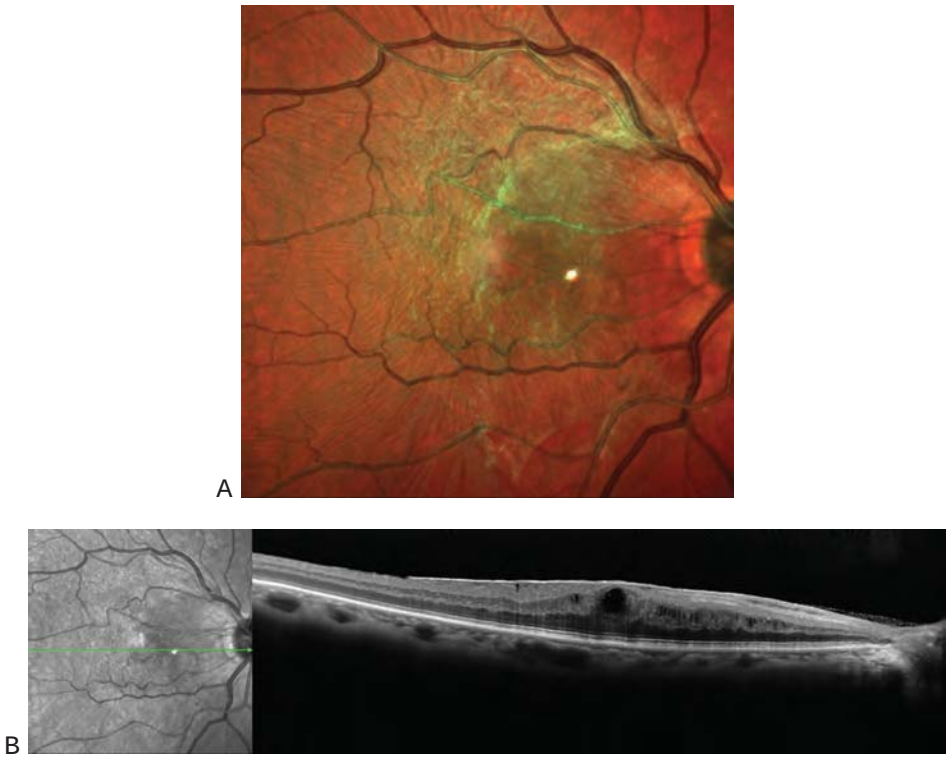

Figure 15-4 Epiretinal membrane (ERM). **A,** Multicolor fundus image obtained with the scanning laser ophthalmoscope (30° field of view) reveals an ERM in the central macula with radiating striae of the internal limiting membrane (ILM) in the superior, temporal, and inferior macula. The colors in reflectance multicolor images are not exactly true to life. **B,** OCT scan through the fovea shows increased retinal thickening and cystoid edema with a large central cyst. The ERM is distorting the retinal surface temporally, which appears as several small optical voids between the ERM and the retina. *(Courtesy of Colin A. McCannel, MD.)*

ACTIVITY 15-2 OCT Activity: Epiretinal membrane progression.
Courtesy of Colin A. McCannel, MD.

Contracture of ERMs produces distortion and wrinkling of the inner surface of the retina, called *cellophane maculopathy* or *preretinal macular fibrosis*. It can range from mild to severe, with w*rinkling* or *striae* to severe *macular puckering*. Increased traction may cause shallow macular detachment, diffuse thickening, or cystic changes. Furthermore, traction on retinal vessels results in increased vascular tortuosity and straightening of the perimacular vessels. Fluorescein angiography (FA) may show staining of the optic nerve and capillary leakage in the central macula. The most common OCT findings are a highly reflective epiretinal reflective layer, loss of the normal retinal contour, and retinal thickening. Additional findings include irregularities of the inner retinal surface and cystic edema.

Treatment

When ERMs are asymptomatic and visual acuity is good, intervention is not indicated. Asymptomatic ERMs should be monitored periodically because they will often worsen, sometimes over a relatively short period, after being stable. In rare cases, an ERM may spontaneously detach from the inner retinal surface, with concomitant improvement or resolution of the retinal distortion and improvement in symptoms and vision. OCT can be used to monitor the integrity of the ellipsoid zone for progressive disruption. This metric can also provide information about prognosis, which can be useful in surgical decision-making, and about postoperative visual potential. If the patient is bothered by reduced vision or metamorphopsia, vitrectomy should be considered (see also Chapter 19). The goal of surgery is to optimize vision, reduce metamorphopsia, and restore binocularity if it was affected preoperatively.

Johnson TM, Johnson MW. Epiretinal membrane. In: Yanoff M, Duker JS. *Ophthalmology.* 4th ed. Elsevier; 2014:614–619.

Vitreomacular Traction Diseases

Vitreomacular traction (VMT) diseases include abnormalities that arise from focal or broad vitreomacular adhesions in the presence of detaching or otherwise detached posterior vitreous. The 3 recognized categories of VMT disease are vitreomacular adhesion, VMT syndrome, and macular hole. Table 15-1 summarizes a useful classification system for VMT diseases that relies on OCT findings.

Vitreomacular adhesions

Vitreomacular adhesions typically do not cause visual symptoms. They can be focal or broad and may lead to secondary traction disease, that is, VMT and macular holes.

Vitreomacular traction syndrome

In VMT syndrome, the posterior hyaloid is abnormally adherent to the macula (eg, a vitreomacular adhesion). As the vitreous detaches, the posterior hyaloid remains tethered

Table 15-1 The International Vitreomacular Traction Study Classification System for Vitreomacular Adhesion, Traction, and Macular Hole

Classification	Subclassification
Vitreomacular adhesion	Size: focal (≤1500 μm) or broad (>1500 μm) Isolated or concurrent
Vitreomacular traction	Size: focal (≤1500 μm) or broad (>1500 μm) Isolated or concurrent
Full-thickness macular hole	Size (diameter): small (≤250 μm), medium (>250–≤400 μm), or large (>400 μm) Status of vitreous: with or without vitreomacular traction Cause: primary or secondary

Modified from Duker JS, Kaiser PK, Binder S, et al. The International Vitreomacular Traction Study Group classification of vitreomacular adhesion, traction, and macular hole. *Ophthalmology.* 2013;120(12): 2611–2619. Copyright 2013, with permission from Elsevier.

at the macula, usually the fovea, causing tractional foveal distortion, cystic edema, and in severe cases, traction foveal detachment. These changes lead to metamorphopsia, decreased vision, and often vague reports about poor vision in the affected eye that are out of proportion to the measured visual acuity. VMT syndrome is differentiated clinically from typical ERM. The fundus examination is often normal. VMT syndrome is best diagnosed and differentiated from ERM with the aid of OCT, which is useful for demonstrating the vitreoretinal interface abnormalities and the tractional effects of the syndrome on foveal architecture, particularly the outer retinal layers. VMT syndrome is often progressive and is associated with a greater loss of vision compared with ERM alone. Chronic traction is generally understood to be harmful over the long term, particularly when cystic edema is present or when the patient's vision is affected. Close observation may be appropriate, as traction can spontaneously release. Spontaneous separation of the focal vitreoretinal adhesion, with resolution of all clinical features, occurs in approximately 50% of cases and less commonly when there is an associated ERM or when the adhesion is broad (Fig 15-5).

Voo I, Mavrofrides EC, Puliafito CA. Clinical applications of optical coherence tomography for the diagnosis and management of macular diseases. *Ophthalmol Clin North Am.* 2004; 17(1):21–31.

Idiopathic Macular Holes

The incidence rate of idiopathic macular holes is approximately 8 per 100,000 persons per year, and the female to male ratio is 2 to 1. Macular holes occur mostly in the sixth through eighth decades of life but can appear at a younger age in myopic eyes. Idiopathic macular holes are bilateral in approximately 10% of patients. Investigations using OCT suggest that idiopathic macular holes are caused by the same tractional forces as the forces associated with perifoveal vitreous detachment and thus are likely an early stage of age-related PVD.

The following description of the stages of macular hole formation is useful for making management decisions (Fig 15-6):

- A *stage 0,* or pre–macular, hole occurs when a PVD with persistent foveal attachment develops. Subtle loss of the foveal depression can be observed, and visual acuity is usually unaffected. Most stage 0 holes do not progress to advanced stages. This stage represents a vitreomacular adhesion.

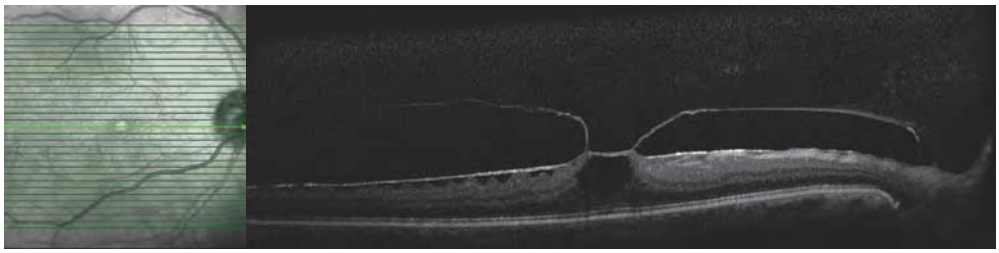

Figure 15-5 Vitreomacular traction syndrome. OCT scan of the macula through the fovea shows vitreomacular traction causing a large foveal cyst and distortion of the inner retina. An ERM is also present. *(Courtesy of Tara A. McCannel, MD, PhD.)*

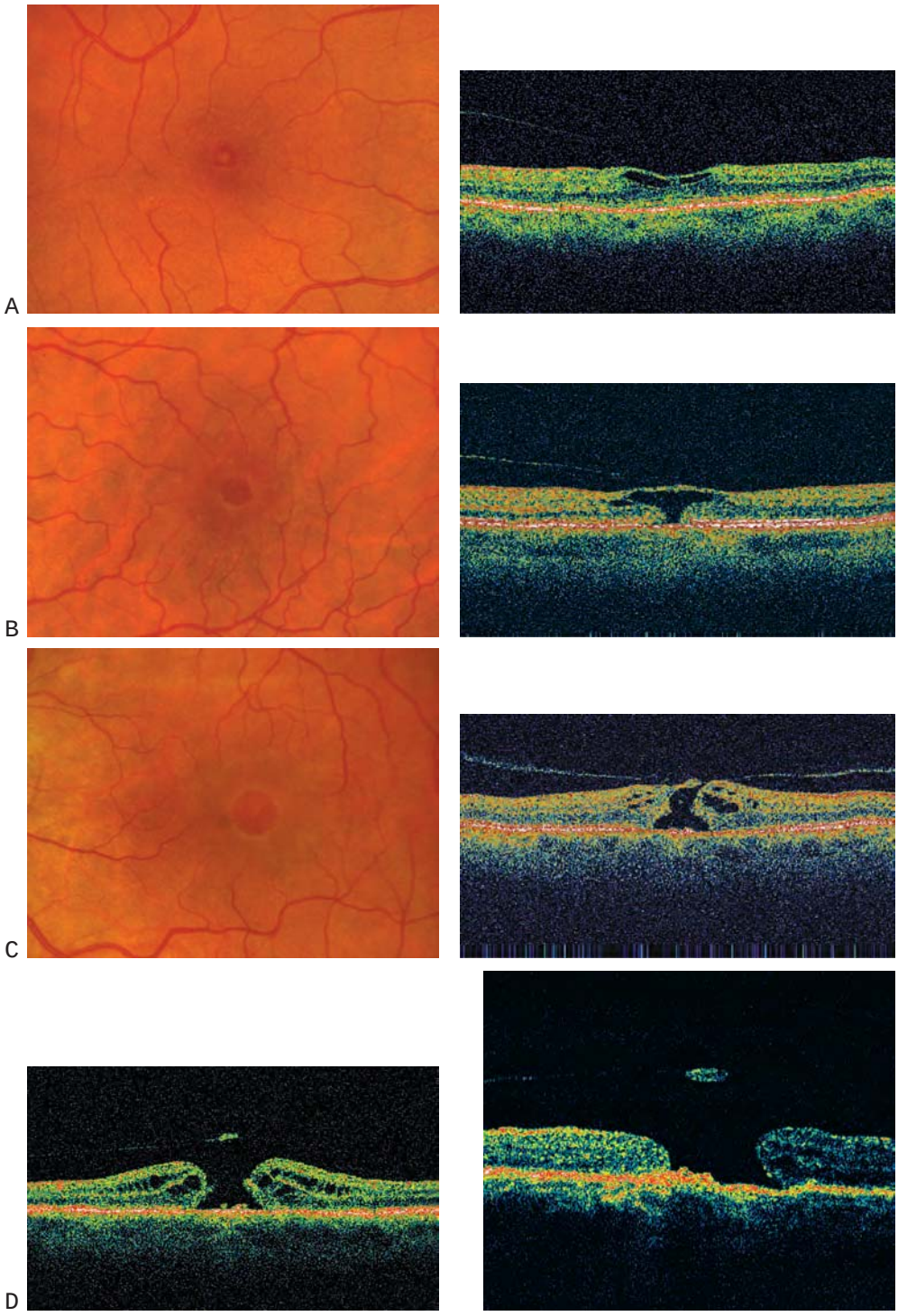

Figure 15-6 Stages of macular hole formation. **A,** Stage 1A. Color fundus photograph and corresponding OCT scan, the latter demonstrating horizontal splitting of retinal layers. **B,** Stage 1B. Fundus photograph and corresponding OCT scan. **C,** Stage 2. Fundus photograph shows a hole with a small opening in the inner layer eccentrically. Corresponding OCT scan of stage 2. **D,** Stage 3. OCT scan shows a full-thickness hole with elevation of adjacent retinal edges. **E,** Stage 4. OCT scan shows a full-thickness hole with operculum. *(Courtesy of Mark W. Johnson, MD, and Peter K. Kaiser, MD.)*

- A *stage 1* macular hole (impending macular hole) typically causes visual symptoms of metamorphopsia and central vision decline, usually to a visual acuity range of 20/25 to 20/60. The characteristic findings are either a small yellow spot (stage 1A) or a yellow ring (stage 1B) in the fovea. OCT examination reveals that a stage 1A hole is a foveal "pseudocyst," or horizontal splitting (schisis), associated with vitreous traction on the foveal center. A stage 1B hole indicates a break in the outer fovea, the margins of which constitute the yellow ring noted clinically. Spontaneous resolution of a stage 1 hole occurs in approximately 50% of cases without ERM. This stage represents VMT syndrome.
- *Stage 2* represents an early full-thickness macular hole that is less than 400 μm in diameter. As a tractional break develops in the "roof" (inner layer) of a foveal pseudocyst, foveal schisis progresses to a full-thickness dehiscence. Progression to stage 2 is accompanied by a further decline in visual acuity. OCT demonstrates the full-thickness defect and the continuing attachment of the posterior hyaloid to the foveal center. This stage represents VMT syndrome with a small- to medium-sized macular hole.
- A *stage 3* macular hole is a fully developed hole (≥400 μm in diameter), typically surrounded by a rim of thickened and detached retina. Visual acuity varies widely. The posterior hyaloid remains attached to the optic nerve head but is detached from the fovea. An operculum suspended by the posterior hyaloid may be seen overlying the hole. On OCT, this stage represents a large macular hole with no VMT (Fig 15-7, Activity 15-3).
- A *stage 4* macular hole is a fully developed hole with a complete PVD, as evidenced by the presence of a Weiss ring. On OCT, this stage represents a large macular hole with no VMT.

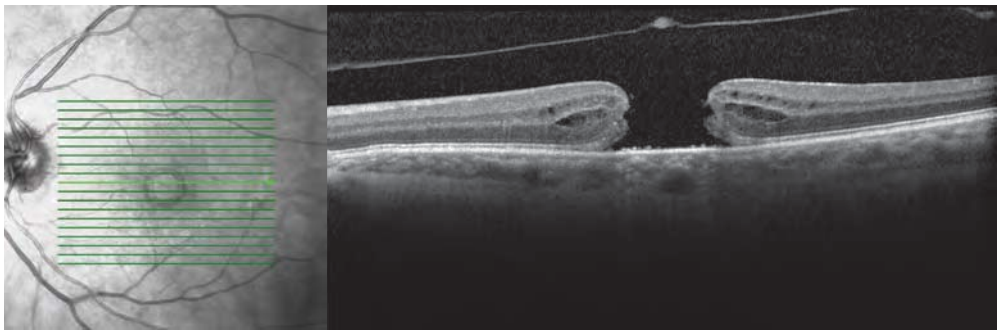

Figure 15-7 SD-OCT line cube scan of the left macula of a 62-year-old woman who had vision loss 18 months before presentation. At the time of the scan, the visual acuity of this eye was 20/40 (eccentric fixation). The infrared reflectance image *(left)* shows a hole in the central macular retina. See also Activity 15-3; scrolling through the images, a discontinuity of the retina in the central macular scans can be seen, corresponding to the macular hole. The scan through the macular hole (scan 10) shows an operculum. This operculum represents a small glial plug that helps keep the fovea together; when it is pulled away by the posterior vitreous, a macular hole is facilitated. Histologic studies indicate that the number of photoreceptors attached to the plug can vary, from none to many. The prominent posterior vitreous face can also be seen; its contour suggests that it is likely attached at the optic nerve head and peripheral macula (dome-shaped configuration), which is typical in idiopathic macular holes. *(Courtesy of Colin A. McCannel, MD.)*

ACTIVITY 15-3 OCT Activity: Stage 3 macular hole.
Courtesy of Colin A. McCannel, MD.

The fellow-eye risk of macular hole development depends on the vitreous attachment status. If a complete vitreous detachment is present in the fellow eye, there is little, if any, risk of macular hole development. However, if the fellow eye has stage 1A abnormalities, there is a substantial risk of progression to a full-thickness macular hole. When the fellow eye is normal and its vitreous is attached, the risk of developing a macular hole in that eye is approximately 10%, the rate of bilaterality.

Management options

Stage 1 macular holes without ERM have an approximate 50% rate of spontaneous resolution and thus are usually monitored. For stage 2 or higher macular holes, surgical intervention is indicated—specifically, pars plana vitrectomy usually performed with ILM peeling and gas tamponade. In most recent case series, the success rate of this procedure for closure and vision improvement was greater than 90% (see Chapter 19). Modifications of routine macular hole surgery are usually reserved for very large, chronic, or nonclosing holes; these include inverted ILM flaps and autologous retinal grafts composed of peripheral retina. Although these techniques may achieve anatomical hole closure, visual acuity may not improve.

Duker JS, Kaiser PK, Binder S, et al. The International Vitreomacular Traction Study Group classification of vitreomacular adhesion, traction, and macular hole. *Ophthalmology.* 2013; 120(12):2611–2619.

Developmental Abnormalities

Tunica Vasculosa Lentis

Remnants of the tunica vasculosa lentis and hyaloid artery are commonly noted and are usually not visually significant. *Mittendorf dot,* an anterior remnant, is a small, dense, and white round plaque attached to the posterior lens capsule nasally and inferiorly to its posterior pole (Fig 15-8). *Bergmeister papilla,* a prepapillary remnant, is a fibroglial tuft of tissue extending from the margin of the optic nerve head into the vitreous for a short distance. The entire hyaloid artery may persist from optic nerve head to lens as multilayered fenestrated sheaths forming the Cloquet canal.

Prepapillary Vascular Loops

Initially thought to be remnants of the hyaloid artery, prepapillary vascular loops are normal retinal vessels that have grown into Bergmeister papilla before returning to the retina (Fig 15-9). The loops typically extend less than 5 mm into the vitreous. These vessels may supply 1 or more quadrants of the retina. FA has shown that 95% of these vessels are arterial and 5% are venous. Complications associated with prepapillary vascular loops include branch retinal artery occlusion, amaurosis fugax, and vitreous hemorrhage.

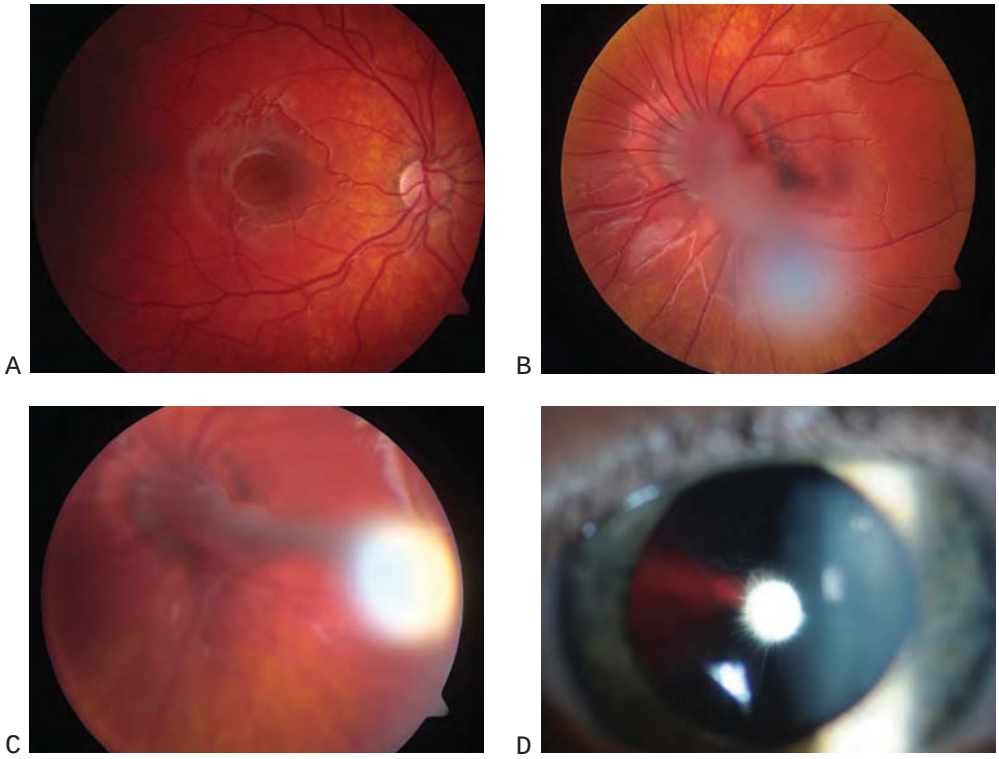

Figure 15-8 Persisting hyaloid artery. **A,** Healthy right eye. **B, C,** In the left eye, the hyaloid artery can be seen from the optic nerve head, traveling through the vitreous cavity to the lens as multilayered sheaths forming the Cloquet canal. **D,** Mittendorf dot. *(Courtesy of Stephen J. Kim, MD.)*

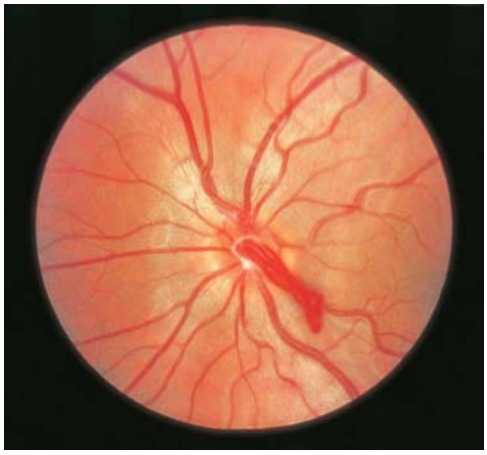

Figure 15-9 Color fundus photograph shows a prepapillary vascular loop. *(Courtesy of M. Gilbert Grand, MD.)*

Persistent Fetal Vasculature

Persistent fetal vasculature (PFV) is a congenital anomaly thought to result from failure of the primary vascular vitreous to regress. The disorder is unilateral in 90% of cases and usually has no associated systemic findings. Anterior, posterior, and combined forms of this developmental abnormality have been described. Most cases are sporadic, but PFV can occur as either an autosomal recessive (mutations in *ATOH7*) or autosomal dominant trait. In some patients with *ATOH7* mutations, the disease is bilateral and asymmetric, with the fellow eye showing a variety of changes, including avascularity. See also BCSC Section 11, *Lens and Cataract*.

Anterior persistent fetal vasculature

In anterior PFV, the hyaloid artery remains, and a white fibrovascular membrane or mass is present behind the lens. Associated findings include microphthalmos, a shallow anterior chamber, and elongated ciliary processes that are visible around the small lens. Leukocoria is often present at birth. A dehiscence of the posterior lens capsule may, in many cases, cause swelling of the lens and cataract as well as secondary angle-closure glaucoma. In addition, glaucoma may result from incomplete development of the anterior chamber angle.

Anterior PFV may result in blindness in the most advanced cases. Lensectomy and removal of the fibrovascular retrolental membrane prevent angle-closure glaucoma in some cases; however, development of a secondary cataract is common. Deprivation amblyopia and refractive amblyopia are serious postoperative challenges in patients with PFV. Anterior PFV should be considered in the differential diagnosis of leukocoria.

Posterior persistent fetal vasculature

Posterior PFV may occur in association with anterior PFV or as an isolated finding. The eye may be microphthalmic, but the anterior chamber is usually normal and the lens is typically clear and without a retrolental membrane. A stalk of tissue emanates from the optic nerve head and courses toward the retrolental region, often running along the apex of a retinal fold that may extend anteriorly from the optic nerve head, usually in an inferior quadrant. The stalk fans out circumferentially toward the anterior retina. Posterior PFV should be distinguished from retinopathy of prematurity (ROP), familial exudative vitreoretinopathy, and ocular toxocariasis. Surgical repair of posterior PFV consists of lensectomy and vitrectomy, which result in formed vision in approximately 70% of cases.

Goldberg MF. Persistent fetal vasculature (PFV): an integrated interpretation of signs and symptoms associated with persistent hyperplastic primary vitreous (PHPV). LIV Edward Jackson Memorial Lecture. *Am J Ophthalmol.* 1997;124(5):587–626.

Sisk RA, Berrocal AM, Feuer WJ, Murray TG. Visual and anatomic outcomes with or without surgery in persistent fetal vasculature. *Ophthalmology.* 2010;117(11):2178–2183.

Hereditary Hyaloideoretinopathies With Optically Empty Vitreous: Wagner and Stickler Syndromes

The hallmark of the group of conditions known as *hereditary hyaloideoretinopathies* is vitreous liquefaction that results in an optically empty cavity except for a thin layer of cortical

vitreous behind the lens and threadlike, avascular membranes that run circumferentially and adhere to the retina. Fundus abnormalities include equatorial and perivascular (radial) lattice degeneration. The electroretinogram response may be subnormal.

In *Wagner syndrome,* the optically empty vitreous is accompanied by myopia, strabismus, and cataract. It is not associated with retinal detachment. The syndrome is inherited in an autosomal dominant manner, and there are no associated systemic findings.

Stickler syndrome is the most common form of hereditary hyaloideoretinopathy with associated systemic findings and is transmitted as an autosomal dominant trait (Fig 15-10). Most patients have a mutation in *COL2A1,* which encodes type II procollagen. Various mutations may produce Stickler syndrome phenotypes of differing severity. Additional ocular abnormalities include myopia, open-angle glaucoma, and cataract. Orofacial findings include midfacial flattening and the Pierre Robin malformation complex of cleft palate, micrognathia, and glossoptosis. These abnormalities may be dramatic at birth, requiring tracheostomy, or they may not be obvious at all. Generalized skeletal abnormalities include joint hyperextensibility and enlargement; arthritis, particularly of the knees; and mild spondyloepiphyseal dysplasia.

Early recognition of Stickler syndrome is important because of the high occurrence of retinal detachment. In one case series, retinal tears were associated with mutations in *COL2A1* in 91% of cases and retinal detachments in 53%. The detachments may be difficult to repair because of multiple, posterior, or large breaks and the tendency for proliferative vitreoretinopathy to develop in these cases. Patients with this condition typically have cortical vitreous condensations that are firmly adherent to the retina. For this reason, prophylactic treatment of retinal breaks should be performed (see the section Prophylactic Treatment of Retinal Breaks in Chapter 16).

Other forms of hereditary hyaloideoretinopathy associated with systemic abnormalities include Weill-Marchesani syndrome and some varieties of dwarfism.

Rose PS, Levy HP, Liberfarb RM, et al. Stickler syndrome: clinical characteristics and diagnostic criteria. *Am J Med Genet A.* 2005;138A(3):199–207.

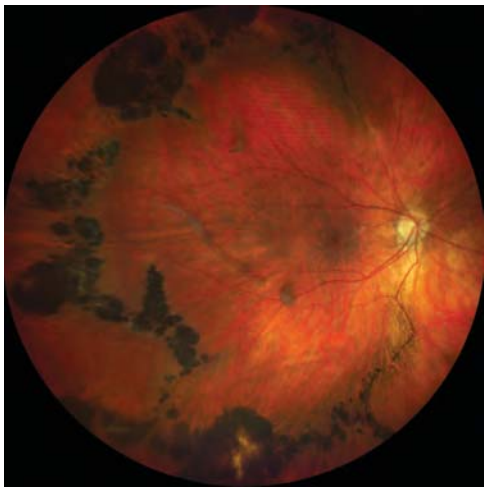

Figure 15-10 Color fundus photograph shows extensive lattice degeneration and pigmentary change in a patient with Stickler syndrome. *(Courtesy of Franco M. Recchia, MD.)*

Familial Exudative Vitreoretinopathy

Familial exudative vitreoretinopathy (FEVR) is characterized by failure of the temporal retina to vascularize and is phenotypically similar to ROP (Table 15-2). Retinal folds and peripheral fibrovascular proliferation, as well as traction and exudative retinal detachments, are often associated with FEVR (Fig 15-11). Temporal dragging of the macula may cause the patient to appear to have exotropia. Late-onset rhegmatogenous retinal detachments may occur. Generally, the earlier the disease presents, the more severe the manifestations.

The condition is frequently bilateral, although the severity of ocular involvement may be asymmetric. Unlike patients with ROP, individuals with FEVR are born full term and have normal respiratory status. In FEVR, the peripheral retinal vessels are dragged and straightened, and they end abruptly a variable distance from the ora serrata (brush border). Distinguishing FEVR from ROP is also aided by the family history and a careful examination of all family members. The only finding in some family members with FEVR may be a straightening of vessels and peripheral retinal nonperfusion. Parents and siblings of affected children may be mildly affected and asymptomatic. FA with peripheral sweeps or wide-field angiography is indispensable when examining family members. Treatment of affected family members may consist of laser therapy applied to the avascular retina, guided by FA.

FEVR is usually inherited as an autosomal dominant trait, but X-linked transmission also occurs. Several gene loci have been associated with the FEVR phenotype. A number of genetic disorders can present with the retinal characteristics of FEVR, including dyskeratosis congenita, Coats plus syndrome, facioscapulohumeral muscular dystrophy, and progressive hemifacial atrophy (Parry-Romberg syndrome). It is important to differentiate these diseases genetically.

Ranchod TM, Ho LY, Drenser KA, Capone A Jr, Trese MT. Clinical presentation of familial exudative vitreoretinopathy. *Ophthalmology.* 2011;118(10):2070–2075.

Table 15-2 Features of Familial Exudative Vitreoretinopathy and Retinopathy of Prematurity

	Familial Exudative Vitreoretinopathy	Retinopathy of Prematurity
Prematurity	Absent	Present
Normal respiratory status	Present	Absent
Birth weight	Often normal	Often low
Family history	Present	Absent
Exudates	Present	Absent
Course of disease	Unpredictable	Predictable
Late stage	Reactivation common	Cicatrization common

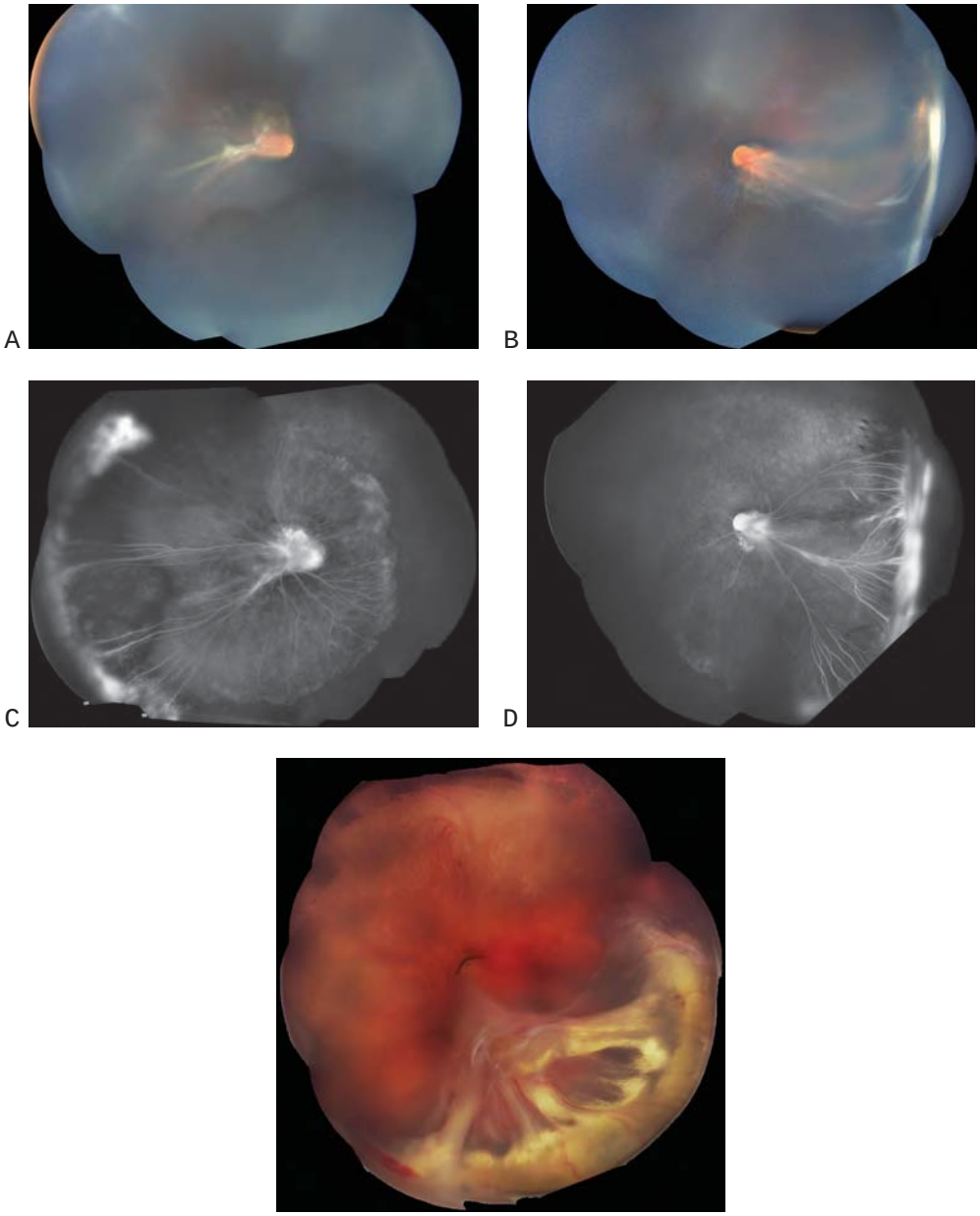

Figure 15-11 Familial exudative vitreoretinopathy (FEVR) due to the *LRP5* mutation. **A, B,** The temporal retina shows a zone of nonperfusion that is horizontally V-shaped, causing a tractional macular fold. **C, D,** Fluorescein angiography images from the same patient demonstrate dragging of the vasculature. There is evidence of leakage and avascularity. **E,** Color fundus image montage from a different patient with FEVR shows folding of the retina with massive exudation. *(Courtesy of Audina M. Berrocal, MD.)*

Vitreous Opacities

Opacities Associated With Vitreous Degeneration and Detachment

Synchysis and syneresis result in loss of the highly organized vitreous anatomy. The collagen fibers that make up the vitreous can coalesce, or tangle, producing small areas that are no longer transparent and can cast shadows. These shadows are perceived by patients as floaters, which patients may find bothersome.

Following vitreous detachment, the coalescence and tangling of vitreous collagen fibers can worsen. In addition, areas where the vitreous was attached more firmly, such as at the optic nerve, are less transparent. When these opacities move away from the retinal surface, they too can cast shadows and may be perceived as floaters.

Over time, as the vitreous continues to liquefy, the opacities may sink inferiorly and become less noticeable. Also, the brain has the capacity to learn to selectively ignore the floaters. As a result, most patients become asymptomatic or minimally symptomatic and do not require any intervention.

Asteroid Hyalosis

In asteroid hyalosis, minute white opacities composed of calcium-containing phospholipids are evenly dispersed in the otherwise normal vitreous (Fig 15-12). Clinical studies have confirmed a relationship between asteroid hyalosis and both diabetes and hypertension. The overall prevalence of asteroid hyalosis is 1 in 200 persons, most often in people older than 50 years. The condition is unilateral in 75% of cases, and significant decreases in visual acuity are rare. However, when PVD occurs, compression of the material occurs, and visual acuity may decrease. When asteroid hyalosis blocks the view of the posterior fundus

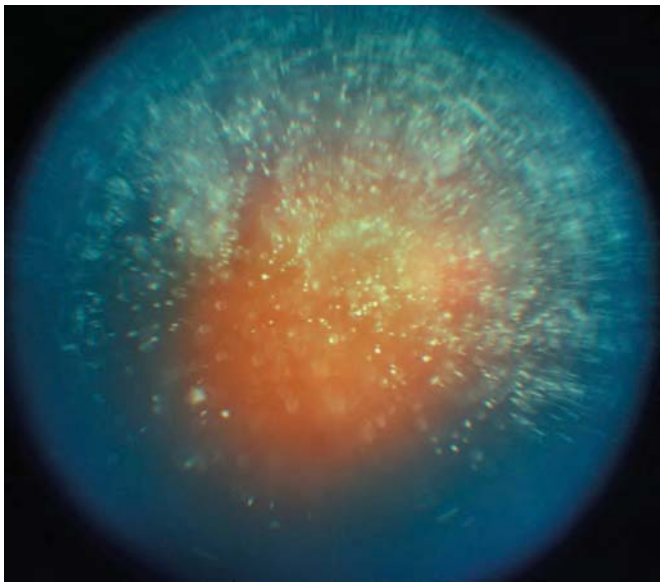

Figure 15-12 Color fundus photograph of asteroid hyalosis. *(Courtesy of Hermann D. Schubert, MD.)*

and retinal pathology is suspected, FA is usually successful in imaging the abnormalities. Occasionally, vitrectomy may be necessary to remove visually significant opacities or to facilitate treatment of underlying retinal abnormalities such as proliferative retinopathy.

Mochizuki Y, Hata Y, Kita T, et al. Anatomical findings of vitreoretinal interface in eyes with asteroid hyalosis. *Graefes Arch Clin Exp Ophthalmol.* 2009;247(9):1173–1177.

Vitreous Hemorrhage

A common cause of emergency visits to ophthalmology offices is sudden vision loss due to vitreous hemorrhage not associated with ocular trauma. In adults, the most common causes include proliferative diabetic retinopathy (see Chapter 5), PVD, central retinal vein occlusion, and retinal neovascularization from a variety of other causes (see Chapter 7, Table 7-2). Bleeding can be exacerbated by the use of systemic anticoagulants. Vitreous hemorrhage may arise from avulsion of the superficial retinal or prepapillary vessels or from rupture of retinal vessels that cross retinal tears. In cases of vitreous hemorrhage associated with an acute PVD, retinal tears are found in approximately 50%–70% of eyes; clinical retinal detachment, in 8%–12%. In children, X-linked hereditary retinoschisis and pars planitis are common causes of vitreous hemorrhage; however, trauma must always be considered in the differential diagnosis (see Chapter 17).

In most cases of vitreous hemorrhage, the underlying cause can be determined by obtaining a history or on retinal examination. If the hemorrhage is too dense to permit indirect ophthalmoscopy or biomicroscopy, suggestive clues can be obtained from examination of the fellow eye. Diagnostic ultrasonography can be performed to detect any tractional tear (often superotemporally) and to rule out retinal detachment or tumor. Bilateral eye patching with bed rest for a few hours to several days, with the head of the bed elevated, may permit the intrahyaloid and retrohyaloid blood to settle, allowing a better view of the posterior segment. If the etiology still cannot be established, the ophthalmologist should consider frequent reexamination with repeated ultrasonography until the cause is found. Alternatively, prompt diagnostic vitrectomy in nondiabetic patients may be considered and may help prevent progression of a retinal tear to retinal detachment. Ghost cell glaucoma can result from long-standing vitreous hemorrhage.

El-Sanhouri AA, Foster RE, Petersen MR, et al. Retinal tears after posterior vitreous detachment and vitreous hemorrhage in patients on systemic anticoagulants. *Eye (Lond).* 2011;25(8):1016–1019.

Sarrafizadeh R, Hassan TS, Ruby AJ, et al. Incidence of retinal detachment and visual outcome in eyes presenting with posterior vitreous separation and dense fundus-obscuring vitreous hemorrhage. *Ophthalmology.* 2001;108(12):2273–2278.

Witmer MT, Cohen SM. Oral anticoagulation and the risk of vitreous hemorrhage and retinal tears in eyes with acute posterior vitreous detachment. *Retina.* 2013;33(3):621–626.

Pigment Granules

In a patient without uveitis, retinitis pigmentosa, or a history of surgical or accidental eye trauma, the presence of pigmented cells in the anterior vitreous ("tobacco dust"), known as a *Shafer sign,* is highly suggestive of a retinal break. See Chapter 16.

Cholesterolosis

Numerous yellow-white, gold, or multicolored cholesterol crystals are present in the vitreous and anterior chamber in cholesterolosis, also known as *synchysis scintillans.* This condition appears almost exclusively in eyes that have undergone repeated or severe accidental or surgical trauma causing large intravitreal hemorrhages. The descriptive term *synchysis scintillans* refers to the highly refractile appearance of the cholesterol-containing crystals. In contrast to eyes with asteroid hyalosis, in which the opacities are evenly distributed throughout the vitreous, eyes with cholesterolosis frequently have a PVD, which allows the crystals to settle inferiorly.

Amyloidosis

Bilateral vitreous opacification may occur as an early manifestation of the dominantly inherited form of hereditary familial amyloidosis, which is most commonly associated with a transthyretin mutation (Fig 15-13). Amyloid infiltration of the vitreous is rare in

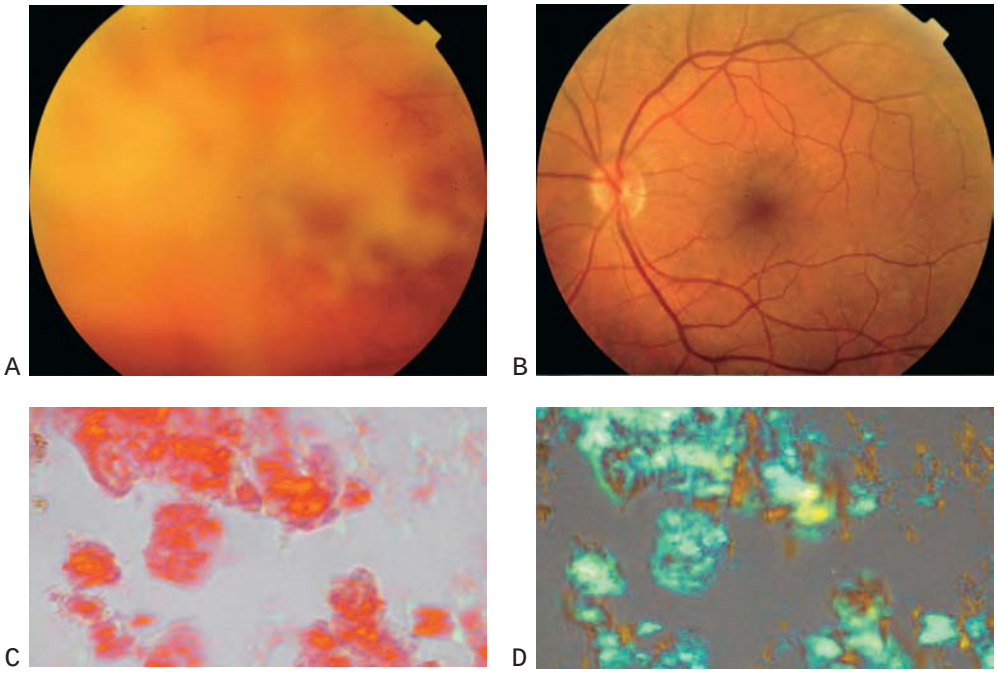

Figure 15-13 Amyloidosis. Images from a 57-year-old woman with a history of vitrectomy for floaters in the right eye. A cataract subsequently developed in the right eye and was extracted. Her vision then decreased in the left eye, which she ascribed to a cataract. **A,** Color fundus photograph of the left eye showed a dense vitreous infiltration; there was no cataract, and intraocular pressure was markedly elevated. Review of systems revealed carpal tunnel syndrome in both wrists. **B,** After vitrectomy on the left eye, there was a clear view to the posterior pole. **C,** The removed vitreous material, stained with Congo red. **D,** The material demonstrated birefringence. The patient was found to have a mutation affecting transthyretin. Glaucoma commonly develops in patients with transthyretin-related familial amyloidotic polyneuropathy. *(Courtesy of Richard F. Spaide, MD.)*

nonfamilial cases. In addition to the vitreous, amyloid may be deposited in the retinal vasculature, the choroid, and the trabecular meshwork.

Retinal findings include hemorrhages, exudates, cotton-wool spots, and peripheral neovascularization. In addition, infiltrations may be present in the orbit, extraocular muscles, eyelids, conjunctiva, cornea, and iris. Nonocular manifestations of amyloidosis include upper- and lower-extremity polyneuropathy and central nervous system abnormalities. Amyloid may be deposited in several organs, including the heart and skin, and in the gastrointestinal tract.

Initially, the extracellular vitreous opacities appear to lie adjacent to retinal vessels posteriorly; they later develop anteriorly. At first, the opacities appear granular and have wispy fringes, but as they enlarge and aggregate, the vitreous takes on a "glass wool" appearance.

The differential diagnosis of amyloidosis includes chronic (dehemoglobinized) vitreous hemorrhage, lymphoma, sarcoidosis, and Whipple disease. Vitrectomy may be indicated for vitreous opacities when symptoms warrant intervention, but recurrent opacities may develop in residual vitreous. Histologic examination of removed vitreous shows material with a fibrillar appearance and a staining reaction to Congo red, characteristic of amyloid. Birefringence and electron microscopic studies are confirmatory.

Sandgren O. Ocular amyloidosis, with special reference to the hereditary forms with vitreous involvement. *Surv Ophthalmol.* 1995;40(3):173–196.