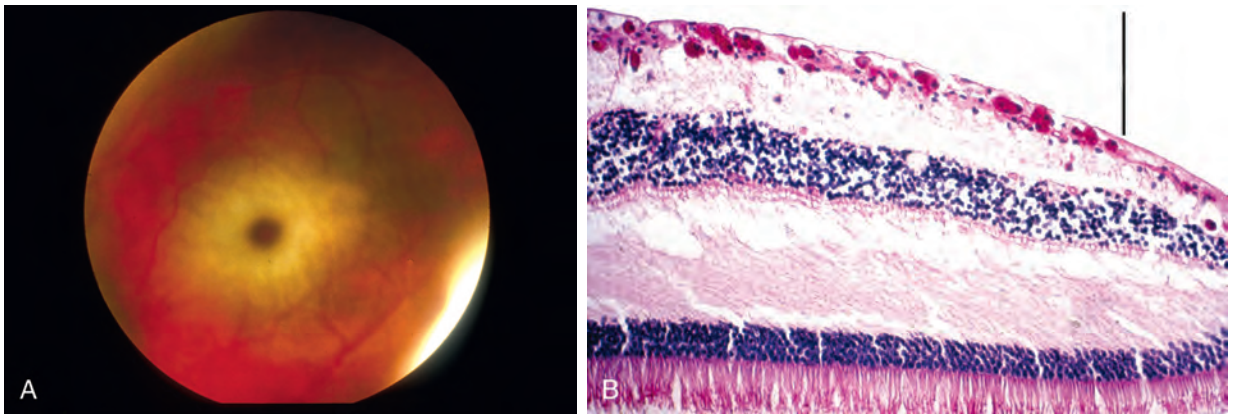

Figure 29-22 The cherry-red spot in Tay-Sachs disease. **A,** Fundus photograph of the cherry-red spot in Tay-Sachs disease. **B,** Photomicrograph of the macula in an individual with Tay-Sachs disease, stained with periodic acid–Schiff to highlight the accumulation of ganglioside material in the retinal ganglion cells. The presence of ganglion cells filled with gangliosides outside the fovea blocks the transmission of the normal orange-red color of the choroid, but absence of ganglion cells within the fovea (to the right of the *vertical bar*) permits the normal orange-red color to be visualized, accounting for the so-called cherry-red spot. (**A,** Courtesy Dr. Thomas A. Weingeist, Department of Ophthalmology and Visual Science, University of Iowa, Iowa City, Ia.; **B**, from the teaching collection of the Armed Forces Institute of Pathology.)

the injection of VEGF antagonists into the vitreous may have an important role in the treatment of this disorder. Nonischemic retinal vein occlusion may be complicated by hemorrhages, exudates, and macular edema but is seldom complicated by retinal or iris neovascularization.

Age-Related Macular Degeneration (AMD)

AMD results from damage to the macula which is required for central vision. It occurs in two forms, dry and wet that are distinguished by the presence of neoangiogeneis in the wet form and its absence in the dry form. From the name of this disorder, it is clear that advancing age is a risk factor. The cumulative incidence of age-related macular degeneration (AMD) in individuals 75 years of age and older is 8%, and with increasing longevity AMD is becoming a major health problem.

Atrophic or "dry" AMD is characterized ophthalmoscopically by diffuse or discrete deposits in the Bruch membrane (drusen) and geographic atrophy of the RPE. Loss of vision is severe in these individuals and there is currently no effective treatment for "dry" or atrophic AMD; a regenerative approach to replacing diseased RPE cells with stem cells is under investigation.

Neovascular or "wet" AMD is characterized by *choroidal neovascularization*, defined by the presence of angiogenic vessels that presumably originate from the choriocapillaris and penetrate through the Bruch membrane beneath the RPE (Fig. 29-23). This neovascular membrane may also penetrate the RPE and become situated directly beneath the neurosensory retina. The vessels in this membrane may leak, and the exuded blood may be organized by RPE cells into macular scars. Occasionally, these vessels are the source of hemorrhage, leading to the localized suffusion of blood that may be mistaken clinically for an intraocular neoplasm, or give rise to diffuse vitreous hemorrhage. Currently the mainstay of treatment for neovascular AMD is the injection of VEGF antagonists into the vitreous of the affected eye.

Choroidal neovascular membranes can develop in diverse conditions that are unrelated to age, such as pathologic myopia (Fuchs spot), following disruption of the Bruch membrane (due to trauma or other causes), or an immunologic response to systemic histoplasmosis (presumed ocular histoplasmosis syndrome).

To understand the pathogenesis of AMD it is important to appreciate the existence of a structural and functional unit composed of the retinal pigment epithelium (RPE), Bruch membrane (which contains the basement membrane of the RPE), and the innermost layer of the choroidal vasculature, the choriocapillaris. Disturbance in any component of this "unit" affects the health of the overlying photoreceptors, producing visual loss.

Nearly 71% of cases are estimated to have a genetic component. Attention is now focused on the roles of several genes, especially *CFH* (complement factor H) and other complement regulatory genes in the pathogenesis of this condition. The complement regulatory gene variants that are associated with AMD all appear to decrease

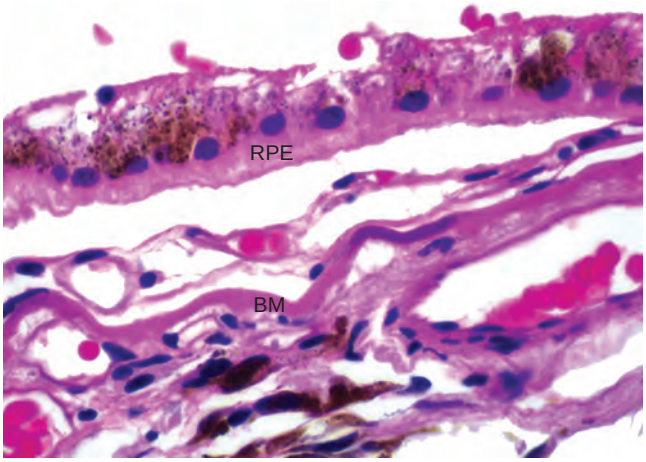

Figure 29-23 "Wet" age-related macular degeneration. A neovascular membrane is positioned between the RPE and Bruch membrane (BM). Note the blue discoloration of Bruch membrane to the right of the label, indicating focal calcification.