Hereditary macular dystrophies are a heterogeneous group of inherited rare disorders that share basic characteristics. Symmetric, bilateral, and often familial involvement of the posterior pole is typical. The most recently accepted classification is based on the primary localization of the defect within the retinal and/or choroidal layers as confirmed by clinical, histopathologic, and functional studies. Fluorescein angiography (FA) and indocyanine green angiography (ICG-A) are good methods to evaluate the morphology and the range of macular changes. Fundus autofluorescence, a noninvasive diagnostic tool, plays an important role in the differential diagnosis of retinal dystrophies. It visualizes disease-specific distribution of lipofuscin in the retinal pigment epithelium (RPE), often not (yet) visible on ophthalmoscopy and imagines well-defined areas of RPE atrophy.

Stargardt’s disease and fundus flavimaculatus

Stargardt’s macular dystrophy was originally described in 1909 by Karl Stargardt as an autosomal recessive macular dystrophy characterized by juvenile onset, rapidly progressive course, and poor visual outcome. Later, Franceschetti proposed the term fundus flavimaculatus describing fundus appearance with deep yellow fishtail or round flecks extending beyond the posterior pole to the equator. Genetic studies demonstrated that Stargardt’s disease and fundus flavimaculatus are most likely allelic autosomal recessive disorders with different features caused by the mutation of gene ABCA4 of chromosome p13 to p21 and, therefore, can be considered different types of the same hereditary disease that affects RPE and photoreceptor layer.

This dystrophy appears around the second decade with decreased central visual acuity. The retina may show early disappearance of the foveolar reflex and a granulated aspect of the RPE described as vermillion aspect, snail slime, or bronze metal appearance (Figures 18-1A to 18-1B). Another early sign of this dystrophy is the appearance of the yellowish perifoveal flecks. Flecks can be polymorphous, fusiform or pisoliform, small or large, juxtamacular or diffuse anterior to the major vascular arcades.

At later stages, a large retinal central atrophy extends into the deeper layers of the posterior pole. In fundus flavimaculatus (Figure 18-2), this can appear in patients between the second and fourth decade. The evolution is usually slowly progressive.

Histopathologic analysis demonstrates widespread accumulation of lipofuscin in RPE cells across the fundus; lipofuscin is sequestered within the interior of residual bodies (lipofuscin granules) that are membrane-bound organelles of the lysosomal compartment of the cell. Lipofuscin is autofluorescent, and the intensity of fundus autofluorescence parallels the amount and distribution of lipofuscin. In the initial stages of Stargardt’s dystrophy, the principal build-up of lipofuscin occurs in the RPE cells of the macular region, whereas later, the lipofuscin accumulation occurs also in the periphery. The intensity of autofluorescence in patients with Stargardt’s disease reaches levels that are considerably greater (3- to 4-fold higher) than in age-matched normal subjects. Autofluorescent intensity is even 2-fold higher in 20- to 29-year-old Stargardt’s patients than in 60- to 69-year-old patients with normal readings. The flecks are hyperfluorescent and may correspond to particularly high levels of lipofuscin, differentiating those areas from the atrophic hypoautofluorescent spots/areas in later stages of the disease.

The classic fluorescein angiographic staining pattern associated with Stargardt’s disease is the presence of a silent choroid. Intact RPE cells containing the lipofuscin likely absorb the excitatory blue light flashes during the angiography, leading to choroidal silence. The absence of choroidal fluorescence extends to the far periphery, and this is an important feature when trying to establish the presence of the dark choroid in cases with extensive macular atrophy. At later stages of disease, a complete atrophy of the RPE and choriocapillaris may appear, unveiling the underlying large choroidal vessel. This stage is called bull’s-eye atrophy. The flecks cause a blockage of fluorescence in the early and late phases of angiography. On the contrary, drusen are hyperfluorescent during all angiographic phases. The continual cycle of flecks formation...