Principles and Practice of Clinical Electrophysiology of Vision

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Dominant Drusen

Michael F. Marmor

DEFINITION

Drusen, defined as small, round, discrete yellowish lesions in the posterior fundus, are common in older eyes and are thought to develop as a part of the aging process.[6, 14] "Hard" drusen, including basal laminar drusen and cuticular drusen, represent hyaline thickening of Bruch's membrane or focal thickening of the basal membrane underlying the retinal pigment epithelium (RPE) and are relatively benign. Larger, "soft" drusen that histopathologically represent small detachments of the RPE are a more serious sign of degenerative change and carry a higher risk of macular degenerative changes (atrophy or exudative degeneration). The development of drusen in aged eyes may well depend upon hereditary predisposition in addition to acquired factors, but it is rare that one can establish a positive family history (because parents and siblings are typically elderly or deceased), and judgments about electrophysiological findings would be confounded by effects of aging.

This chapter will be concerned with drusen that develop in younger individuals who do not show other stigmata of aging in the retina. These individuals, because of their age and sometimes the demonstration of a dominant family history, are considered to have a dystrophic condition involving the pigment epithelium and/or Bruch's membrane.

In his reviews of dominant drusen, Deutman[1, 2] used this designation to incorporate a number of different patterns of drusen such as Doyne's honeycomb dystrophy, Hutchinson-Tay choroiditis, guttate choroiditis, and malattia leventinese. Although these entities differ in the size, frequency, and locale of the drusen, we have no pathophysiological reason to separate them, and their clinical implications are similar. The published literature on inherited drusen describes dominant inheritance almost exclusively.[1, 6, 10] However, in modern times the vast majority of patients who are seen with extensive "premature" drusen are isolated cases in which a family history is hard to establish because relatives are asymptomatic and may be unavailable for examination. It is unknown whether or how many recessive forms exist since few pedigrees have been carefully investigated.

CLINICAL FINDINGS

Inherited drusen can vary widely in size and distribution. In some patients innumerable tiny, hard drusen are scattered throughout the macula and posterior pole and spare only the fovea (Fig 87–1). In other patients rather large and isolated drusen are found in clusters, sometimes outside the vascular arcade (Fig 87–2). Drusen nasal to the disc and beyond the arcades (Figs 87–2 and 87–3) strongly suggest inherited rather than age-related disease.[1] In general, the fovea is spared, and visual acuity is normal or only minimally reduced, although there appears to be a tendency for these eyes to develop frank macular degenerative changes at an earlier age

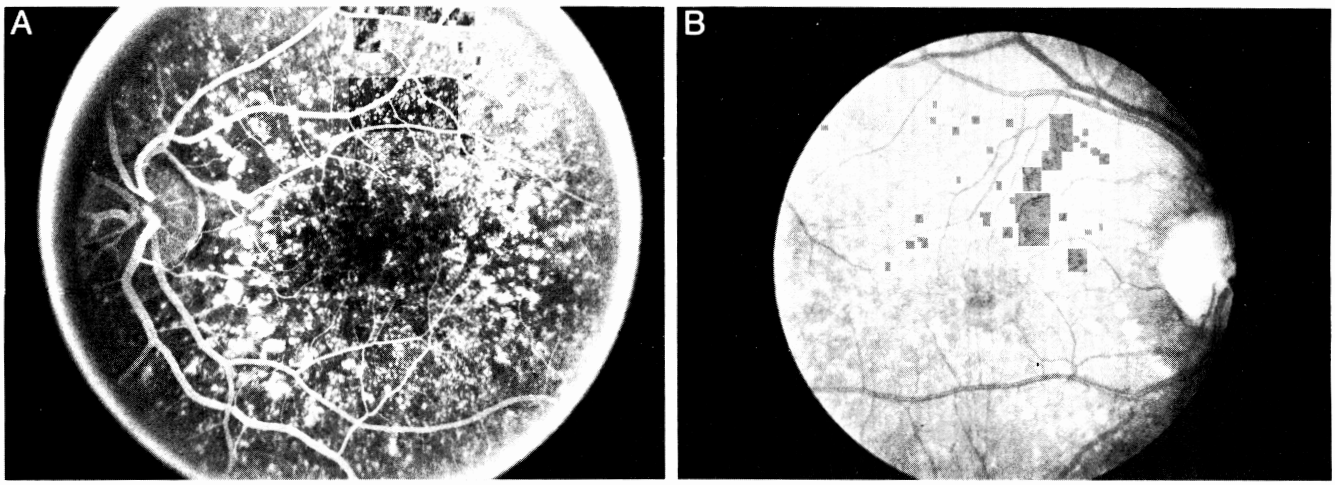

FIG 87–1.
Extensive fine posterior drusen in a 39-year-old female. Visual acuity was 20/20 in either eye, and the electro-oculogram (EOG) light/dark ratios were 2.0 OD and 2.5 OS. **A,** fluorescein angiogram of the left macula. **B,** fundus of the right macula.

than expected in the population at large.[1, 6, 10] Individuals with very extensive drusen involving the central macula are clearly at greater risk than those with peripheral drusen who may be essentially asymptomatic throughout their life. For example, eyes with exceptionally extensive cuticular drusen in the macula[7, 12] may develop a vitelliform (yolklike) degeneration (Fig 87–4) that carries a significant risk of scarring and loss of acuity. Individuals with larger drusen in the foveal zone may be at greater risk to develop degenerative changes in the RPE or a focus of subretinal neovascularization. Generally speaking, inherited drusen are relatively benign in early adulthood until or unless the fovea becomes involved; after 40 to 50 years of age foveal changes become more frequent, and the disease blends imperceptibly with age-related macular degeneration and age-related drusen, so specific causation becomes difficult to assign.

ELECTROPHYSIOLOGY AND PSYCHOPHYSICS

Changes in psychophysical parameters are minimal except acuity loss insofar as the fovea is in-

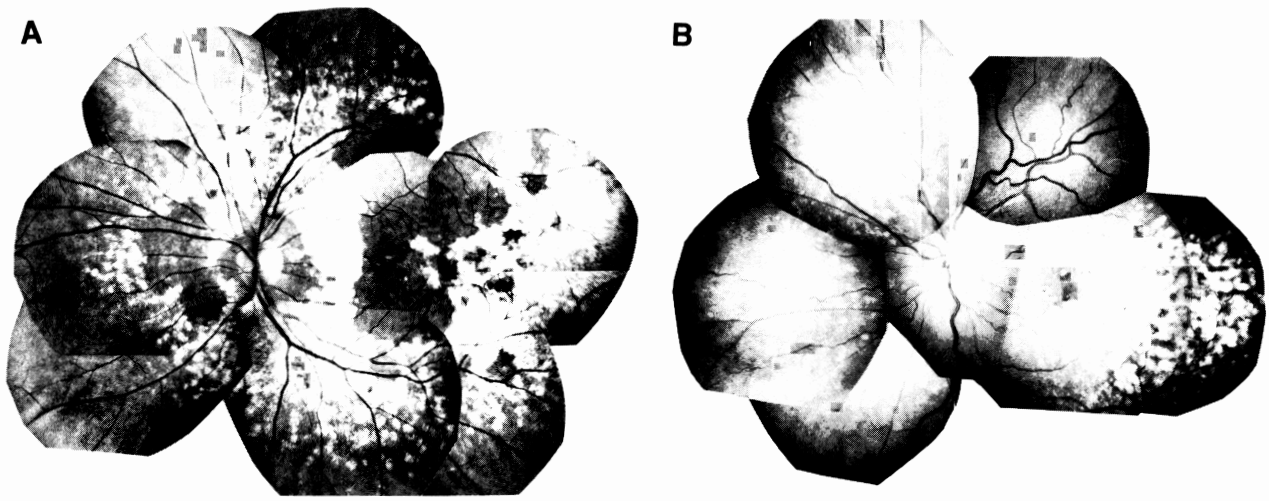

FIG 87–2.
A, large coarse drusen, both temporal and nasal to the disc, in a 44-year-old East Indian man. Visual acuity was 20/20. **B,** in a 50-year-old female, visual acuity was 20/20; EOG light/dark ratios were 2.1 OD, 2.2 OS.

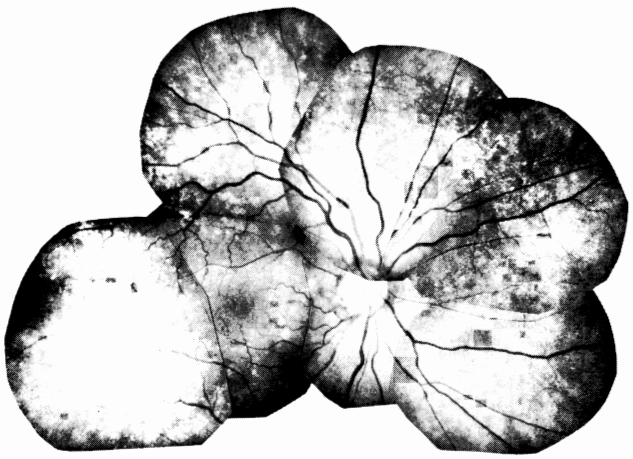

FIG 87–3.
Fine drusen, nasal as well as temporal to the disc, in a 61-year-old Mexican-American female. Visual acuity was 20/20.

volved, and the degree of metamorphopsia, contrast sensitivity loss, central scotoma, and color dysfunction is proportional to the extent of macular degeneration. There are no changes that are specific to drusen, and in general drusen that are widely scattered cause no detectable changes in any of these parameters. In fact, careful focal threshold perimetry has shown no difference in retinal sensitivity over comparable retinal areas with and without drusen.[16] Some individual cases with severe drusen have been reported to have psychophysical abnormalities, but these appear to be exceptions rather than the rule. Krill and Klien[11] noted that some patients with drusen had dark adaptation defects, and this caused them to make comparisons between the "fleck" retina caused by drusen and that caused by other conditions such as fundus flavimaculatus or fundus albipunctatus. These patients were over 50 years old, however, and sensitivity changes may have been conditioned by age or other degenerative changes. In my own experience and that of others,[1] dark adaptation abnormalities with drusen are unusual (Fig 87–5). The term "fleck retina" should be avoided insofar as these various disease entities can be distinguished clearly on clinical and pathophysiological grounds.

Documentation of electrophysiological changes in inherited drusen has been surprisingly minimal.[1, 5] The disease appears to involve the RPE primarily,

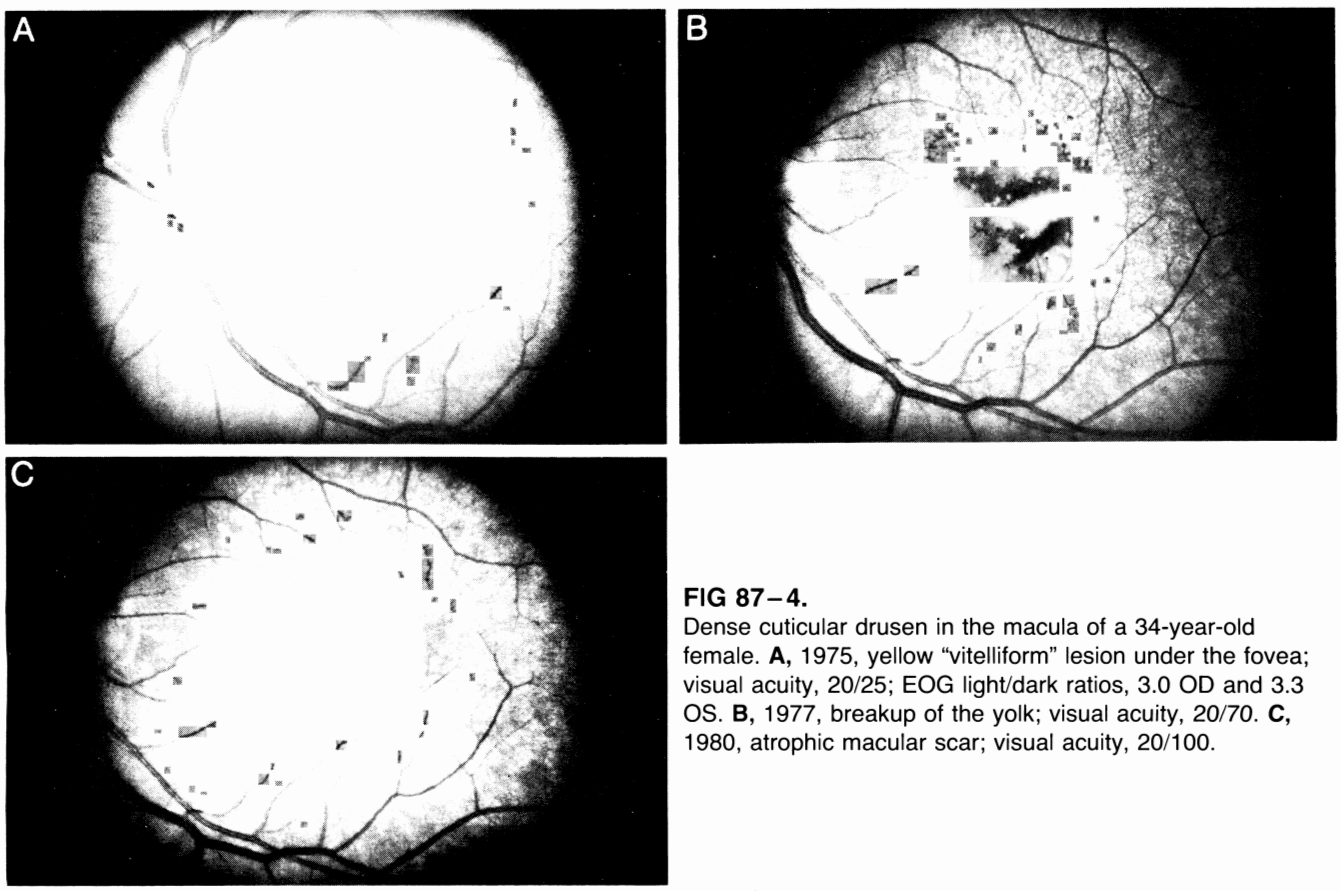

FIG 87–4.
Dense cuticular drusen in the macula of a 34-year-old female. **A,** 1975, yellow "vitelliform" lesion under the fovea; visual acuity, 20/25; EOG light/dark ratios, 3.0 OD and 3.3 OS. **B,** 1977, breakup of the yolk; visual acuity, 20/70. **C,** 1980, atrophic macular scar; visual acuity, 20/100.

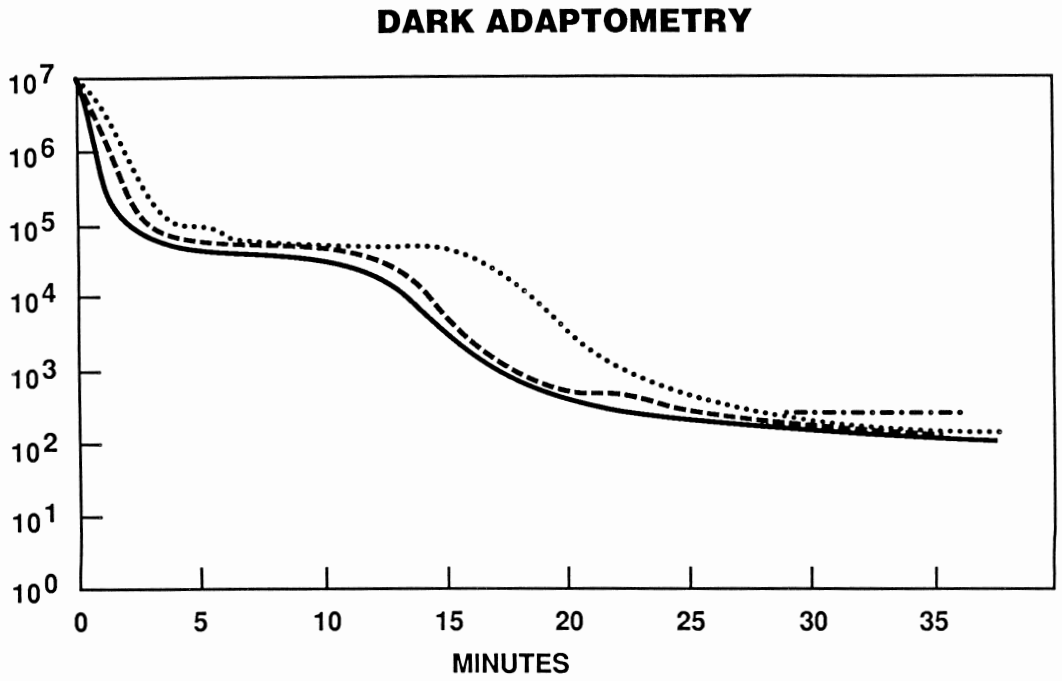

FIG 87–5.
Dark adaptation curves from four individuals with drusen. One curve (from the patient illustrated in Fig 87–4) has a delayed cone-rod break; the others are normal.

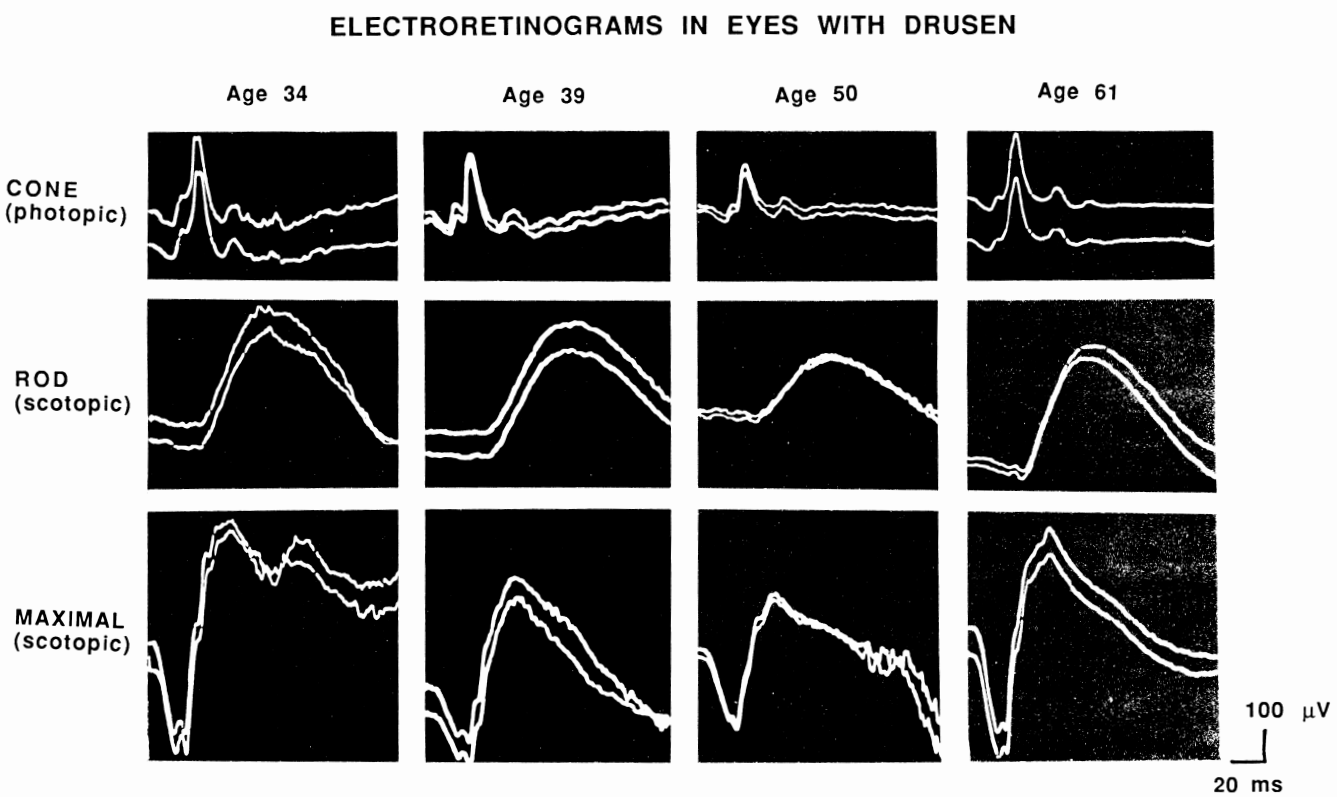

FIG 87–6.
Electroretinograms (ERGs) from four individuals with drusen (including the patients shown in Figures 87–2 to 87–4, who can be identified by age). The 50-year-old patient is a female with diffuse coarse drusen, visual acuity of 20/20, and EOG light/dark ratios of 2.1 OD and 2.2 OS.

but depression of RPE-dependent responses such as the light/dark ratio of the EOG has been noted only in rare cases[3] and some with rather severe degenerative involvement[1]; a recent survey of EOG findings by Fishman et al.[4] questioned many of those cases. Many cases with remarkably widespread drusen have been found to have normal EOGs[1, 4, 7] (see Fig 87–1, 87–4 and 87–6). Since the more severe cases sometimes have degenerative changes or involve individuals who may be subject to age-related as well as dystrophic disease, interpretation of subtle EOG changes is difficult and of questionable significance. Hess and Niemeyer[8] felt that an increase in the latency of the light peak occurred more frequently than did a depression of the light/dark ratio, but this has not been documented by others. The fast oscillation is apparently normal. Clearly, if the EOG is involved in drusen, it is not involved to a sufficient degree to serve as an early or predictive clinical test.

The ERG is typically normal in drusen (see Fig 87–6), and only a few patients with severe disease or from an isolated pedigree[11, 15] have been reported to show ERG abnormalities. These ERG changes have been a reduction to borderline or slightly subnormal levels of cone and rod b-wave amplitudes and possibly a delay in adaptation. However, as with the EOG, it is difficult to ascribe any diagnostic or pathophysiological specificity to these findings; they are clearly unusual and seem to be related to the extent of retinal damage coupled with age and other confounding factors. Rover and Bach[13] reported that in a study of seven patients with dominant drusen, the c-wave was reduced while the EOG ratio was still normal. This might indicate a physiological abnormality of the RPE but needs verification from more patients since the c-wave is notoriously variable in humans.[9]

SUMMARY

The term *inherited drusen* is used to refer to discrete drusen present in younger eyes that do not show stigmata of age-related macular degeneration. The extent of pathology varies enormously, and eyes with milder nonfoveal involvement are essentially asymptomatic, both functionally and electrophysiologically. Changes in the ERG and/or EOG are uncommon but may be occasionally found in eyes with extensive disease, usually in proportion to the degree of visible damage to the retina and RPE. There is little evidence that electrophysiological tests are either specific or diagnostic for drusen. This is somewhat surprising since one might have suspected involvement of signals that reflect RPE pathology such as the c-wave, fast oscillation, and EOG (light response). Apparently, the pathological changes that cause the development of the drusen do not significantly alter the electrical properties of the RPE cells.

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