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Chapter 33

The electrooculogram

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Abstract

The electrooculogram (EOG) measures the cornea-positive standing potential relative to the back of the eye. By attaching skin electrodes outside the eye near the lateral and medial canthus, the potential can be measured by having the patient move the eyes horizontally a set distance. The voltage becomes smaller in the dark, reaching its lowest potential after 8–12 min, the so-called dark trough. When the lights are turned on, the potential rises, reaching a peak by about 10 min. When the size of the light peak is compared to the dark trough, the normal ratio should be near 2:1. A light peak:dark trough ratio of less than 1.7 is considered abnormal. The origin of electrooculographic potentials is the pigment epithelium of the retina interacting with the midretina. The light rise of the potential requires both a normal pigment epithelium and normal midretinal function. The most common use of the electrooculogram is to confirm Best disease. Best disease is identified by the appearance of an egg-yellow fundus and can be confirmed by recording both an electroretinogram (ERG) and electrooculogram (EOG). The ERG will be normal and the EOG will be abnormal. The EOG is also used for tracking eye movement.

Elwin Marg described and named the electrooculogram in 1951 and Geoffrey Arden developed the first clinical application (Arden et al., 1962a). The electrooculogram measures the transepithelial potential (TEP) of the retinal pigment epithelium that exists between the cornea and Bruch's membrane at the back of the eye. The potential produces a dipole field with the cornea positive relative to the back of the eye. Although the origin of the EOG is the pigment epithelium of the retina, the light rise of the potential requires both a normal pigment epithelium and normal midretinal function. With the cornea positive, movement of the eye produces a shift of this electrical potential. By attaching skin electrodes on both sides of an eye (Fig. 33.1), the potential can be measured by having the subject move the eyes horizontally a set distance. Skin electrodes are attached near the lateral and medial canthus of each eye (Fig. 33.1). A ground electrode is attached, usually to the forehead or earlobe. The patient is in a chin rest to reduce head movement. Inside a Ganzfeld, the patient alternately fixates on small red LED lights 30 degrees apart (Fig. 33.2). See Constable et al. (2017) for recommended ISCEV International Standard EOG protocol.

PROTOCOL

The patient should be light adapted in a well-illuminated room for at least 30 min, and eyes dilated. Some programs have a brighter period of 10 min light adaptation prior to starting the test. After the electrodes are attached, the procedure is explained and the patient asked to practice several times while baseline data are recorded. The procedure is simple. The patient keeps their head still while moving the eyes back and forth, alternating between the two red LED lights (Fig. 33.2). The movement of the eyes produces a voltage swing of approximately 2–5 mV between the electrodes on each side of the eye, which is charted on graph paper or stored in a computer.

Sample 10-s periods of eye movement back and forth between LED lights placed 30 degrees apart inside a Ganzfeld in three phases (Fig. 33.3).

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Fig. 33.1. Placement of skin electrodes for recording of EOGs.

Fig. 33.2. Ganzfeld used for initiating eye movement. Size of LEDs is exaggerated.

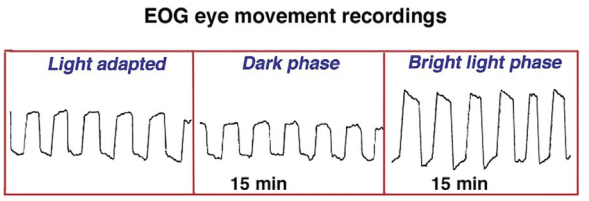

Fig. 33.3. Samples of eye movement in light adapted pre-EOG light-adaptation period, dark adaptation phase, and light-rise phase.

After light adaptation and training, the lights are turned off. About every minute, a 10-s sample of eye movement is taken as the patient looks back and forth between the two lights (Fig. 33.2). After 12–15 min in the dark, the lights are turned on and the patient again, about once a minute, moves their eyes back and forth for about 10 s. Fig. 33.3 shows segments of eye movement from 10 s samples from a normal person near the end of each phase. The chart (Fig. 33.4) graphs the change in voltage in the eye through 12–15 min of dark adaptation and up to 15 min in bright light. The voltage becomes a little smaller in the dark, reaching its lowest potential after about 8–12 min, the so-called dark trough, as previously mentioned. When the lights are turned on the potential raises (the light rise), reaching its peak in about 10 min. The light/dark ratio was originally called the Arden ratio, but is now referred to as the light peak:dark trough ratio (LP:DT ratio). When the maximum of the light peak is compared to the low amplitude in the dark trough, the normal relative size is about 2:1 or greater (Fig. 33.4). A light peak:dark trough ratio of less than 1.8 is considered abnormal for individuals less than 60 years, and a ratio of less than 1.7 for over 60 years.

CLINICAL APPLICATION

Retinal diseases producing an abnormal EOG usually also have an abnormal ERG. The ERG is the better test for analysis of scotopic and photopic measures, so EOGs are rarely also recorded. Early there was promise that the EOG would be useful following the effects of high-dosage treatment with antimalarials such as chloroquine and Plaquenil over the course of treatment (Arden et al., 1962b). However, more recent research indicates that this is questionable (Neubauer et al., 2003).

The EOG is also used to monitor eye movements in neurological disorders (Rivaud-Péchoux et al., 2000; Danchaivijitr and Kennard, 2004; Banerjee et al., 2013). The EOG may be depressed in patients with acute zonal occult outer retinopathy (AZOOR).

Best disease

The most common diagnostic use of the EOG is to confirm Best vitelliform macular dystrophy (Best1). Best disease is a rare, usually autosomal dominant, progressive macular dystrophy with vitelliform (egg yolk-like) ocular fundus in the early stages associated with loss of acuity. Franz Best described the first pedigree in 1905.

Best vitelliform macular dystrophy and variants of this disease are usually identified by the appearance of a retinal lesion resembling an egg yolk early in the disease (Figs. 33.5 and 33.6). Fig. 33.5 shows a fundus photo from a patient with Best disease during the "sunny-side-up" egg yolk stage (see Fig. 33.8 for stages). There is considerable variation in the fundus appearance in Best disease.

Patients with Best disease and some patients with adult vitelliform dystrophy have normal ERGs but abnormal light peak:dark trough ratios of near 1.5 or less (Fig. 33.7).

Vitelliform lesions represent the accumulation of lipofuscin in the macular area. Further effects of retinal pigment epithelium (RPE) dysfunction include accumulation of degenerated photoreceptor outer segments in the subretinal space. Using autofluorescence imaging

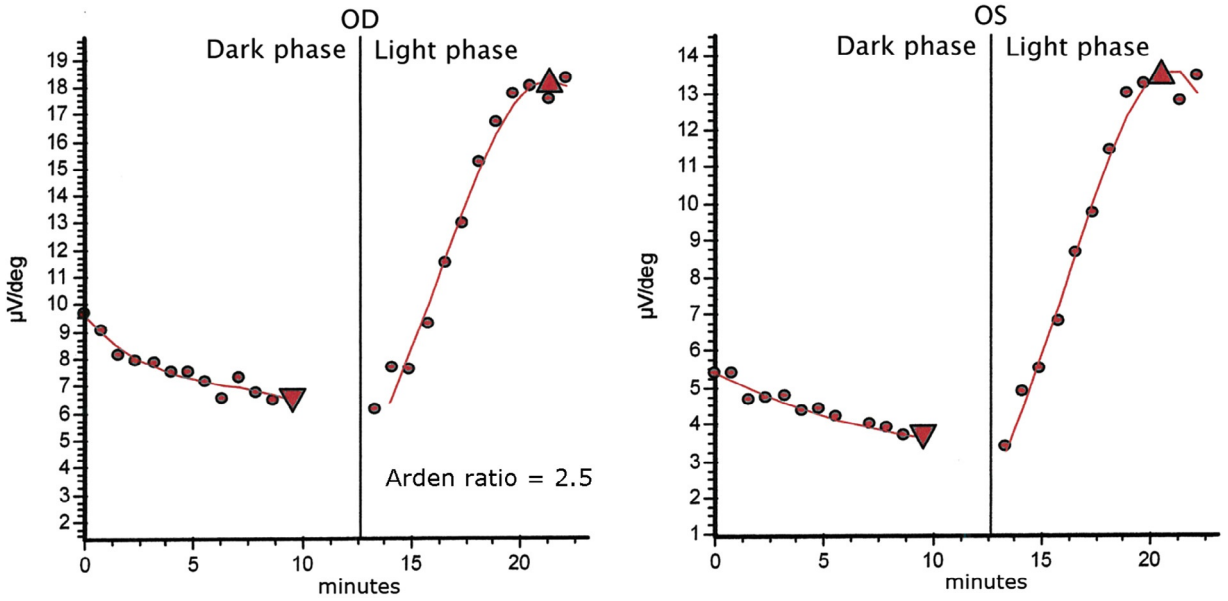

Fig. 33.4. Normal EOG progression showing light rise after dark adaptation.

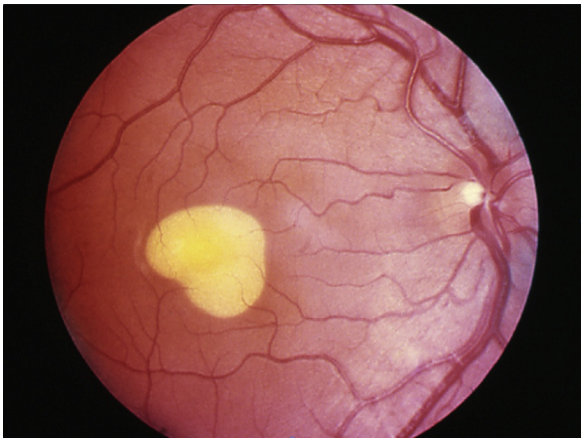

Fig. 33.5. Fundus photo of a patient with Best disease during "sunny-side-up" egg phase. All ocular fundus imaging courtesy of John A. Moran Eye Center Imaging.

Fig. 33.6. Fundus photo from another patient with Best disease.

(AF), the subretinal accumulation is seen as hyperautofluorescent, suggesting that the material is composed of retinoid fluorophores, such as photoreceptor outer segment debris.

The progression of retinal changes in Best disease per se and adult vitelliform dystrophy are similar. Fig. 33.8 shows the progression of adult vitelliform macular dystrophy (AVMD) in a 50-year-old female. During the initial stage, similar to the first optical coherence tomography (OCT) dated August 25, 2011, is when the ocular fundus may have a "sunny-side-up" egg yolk appearance. In later stages the lipofuscin disperses, resulting in a "scrambled egg" appearance with mottled pigmentation and RPE atrophy. In Best disease and in some with AVMD, the reduced light rise in the EOG is due to a dysfunction of bestrophin resulting in abnormal fluid and ion transport by the RPE. Bestrophins are a family of proteins that can function both as Cl(−) channels and as regulators of voltage-gated Ca(2+) channels. It is proposed that dysfunction of bestrophin results in abnormal fluid and ion transport in the basal RPE membrane and this results in a weakened interface between the retinal pigment epithelium and photoreceptors. Human bestrophin-1 (hBest1), located on human chromosome 11q13, was identified as the VMD2 gene

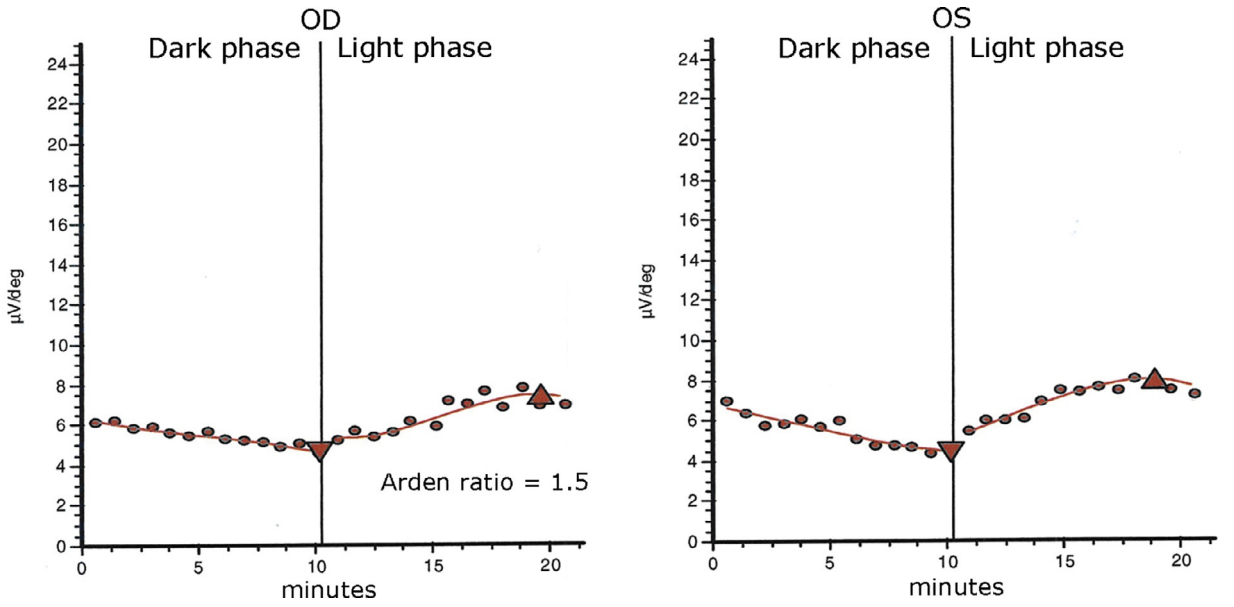

Fig. 33.7. Abnormal EOG light-rise in a patient with Best disease during dark adaptation phase.

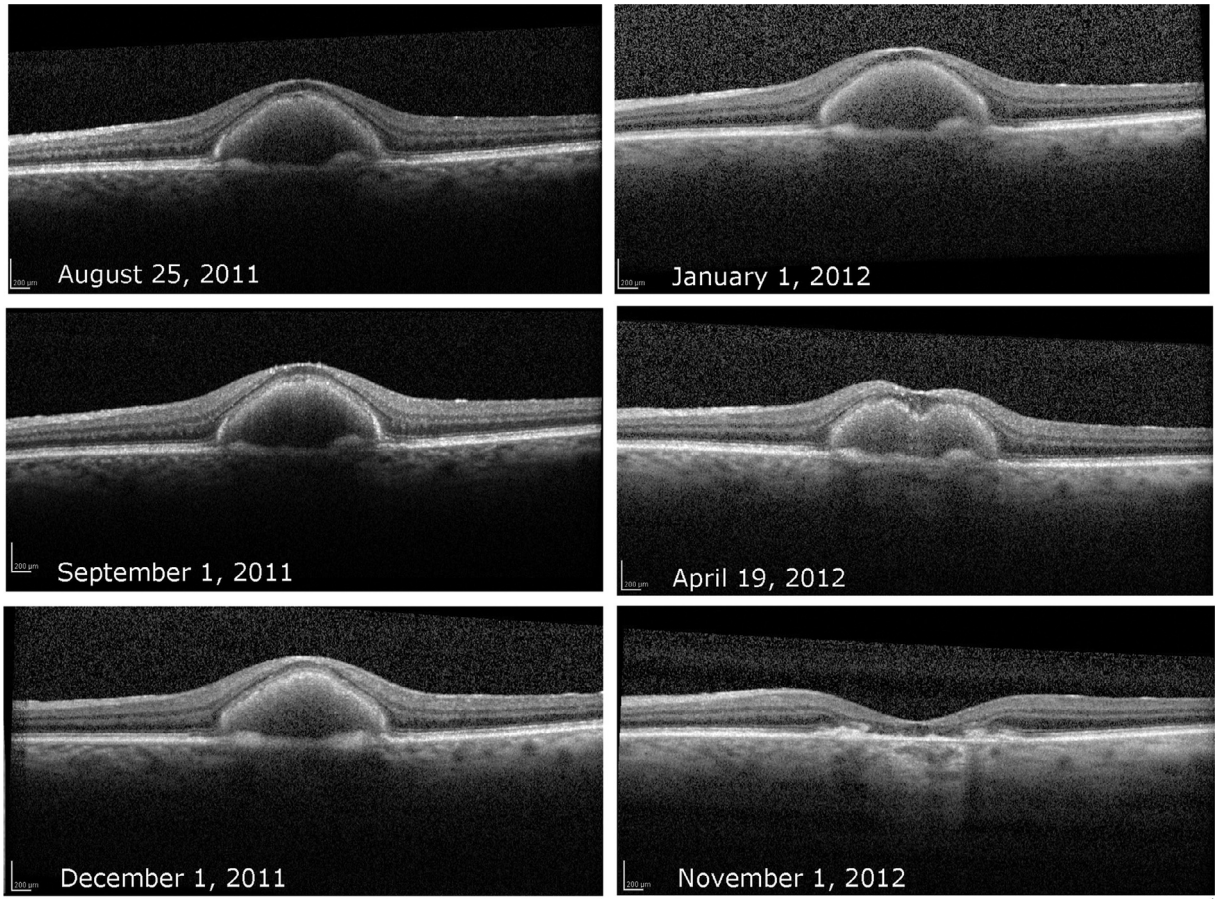

Fig. 33.8. The progression of adult vitelliform macular dystrophy (AVMD) in a 50-year-old female. Images are a series of ocular coherence tomographic (OCT) pictures. During the initial stage, similar to the first OCT dated Aug. 25, 2011 is when the ocular fundus likely had "sunny-side-up" egg yolk appearance. In later stages the lipofuscin disperses, resulting in "scrambled egg" appearance with mottled pigmentation and RPE atrophy.

responsible for the dominantly inherited juvenile-onset form, called Best vitelliform macular dystrophy. Mutations in hBest1 have also been associated with a small fraction of adult-onset vitelliform macular dystrophies (Hartzell et al., 2008). The inheritance pattern of adult-onset vitelliform macular dystrophy is uncertain. The appearance of the ocular fundus and progression of accumulation of lipofuscin within the RPE and sub-RPE space in the foveal area in AVMD can appear similar to Best disease. AVMD can be differentiated from Best disease based on clinical appearance, age of onset, and using OCT, autofluorescence imaging, and electrooculograms.

Genetic testing for Best disease is available (Best1). A study of over 100 patients demonstrated expression of Best disease and autosomal recessive bestrophinopathy is quite variable (Khan et al., 2017). Authors concluded the BEST1 mutation might be independently expressed, perhaps related to differential effects on intracellular calcium homeostasis.

The EOG will continue to be useful in tracking eye movement and research. The current common use to confirm Best disease will be less necessary as gene identification becomes more available, as well as the imaging procedures such as OCT, fluorescein angiograms, and fundus autofluorescence imaging.

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