Differential Effects of Light and Alcohol on the Electro-oculographic Responses of Patients with Age-Related Macular Disease

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Purpose. Alcohol (EtOH) affects the electro-oculogram (EOG) in ways very similar to light, although the two agents act on the RPE through different routes. Are the EOGs to light and to alcohol affected similarly in age-related macular degeneration (AMD) and age-related maculopathy (ARM)?

Methods. Standard eye movements and recording of EOGs were used. After 26 minutes of baseline recording in darkness, subjects were either exposed to 30 cd/m² light or drank 226 mg/kg alcohol (7.1% vol/vol) in water.

Results. In 17 patients with ARM and AMD (aged 67–86 years; mean, 77), the light-EOG was slowed in comparison to normal, and the voltage changes were somewhat reduced. The mean reduction in the alcohol-EOG (EtOH-EOG) was much greater. The reduction was equal in the two eyes, regardless of unioocular foveal impairment. Some EtOH-EOG loss occurred in patients with minor fundus changes and no loss of acuity, but the loss was greater in patients with “wet” or “dry” ARM and AMD. Grading of RPE changes correlated with the decrease in EtOH-EOG responsiveness, but not with light-EOG responsiveness.

Conclusions. EtOH- and light-EOGs are affected differentially. In ARM, even with minor fundus changes, patients appear to have a general abnormality in the RPE. The alcohol response abnormality is correlated to the fundus appearance, but not with age. These results provide further evidence that EtOH acts by a pathway different from that governing the action of light. These results support histologic and other evidence that in ARM there is a functional barrier between the choroid and the RPE-retina. (Invest Ophthalmol Vis Sci. 2003;44:3226–3232) DOI:10.1167/iovs.02-0998

A clinical test, the electro-oculogram (EOG), measures the increase of the standing potential of the dark-adapted eye that occurs when it is exposed to light and the subsequent decline to a trough value. The ratio of these values is an index of the normal function in the retinal pigment epithelium (RPE) that generates the voltage. The light provoking these changes is absorbed by retinal rods. Therefore, normal rods and a normal retina-RPE interface are both required for a normal EOG.1–3 For this reason, abnormality in the EOG is not in itself diagnostic of abnormality of RPE function, but it remains one of the few ways in which RPE function can be investigated physiologically in humans. Various techniques, such as fluorescein angiography and stereoscopic biomicroscopy, and developments in electoretinography permit detailed analysis of the outer retina, so that the only standard clinical use of the EOG is the diagnosis of Best’s disease. To extend the utility of the EOG, changes provoked by chemical stimuli (e.g., acetazolamide) have been investigated, but none produced a peak-to-trough waveform commensurate with the waveform produced by light,3–9 until it was shown that small doses of alcohol taken orally could evoke EOG changes nearly indistinguishable from those evoked by light.10,11 Experiments also indicate that the alcohol acts directly on the RPE and is independent of light. The characteristic peak after alcohol ingestion was absent in a study of patients with retinitis pigmentosa, although the trough remained.12 Despite deductions about how EOG voltage changes are brought about, any clinical significance of the alcohol-EOG (EtOH-EOG) depends on whether alcohol and light have differential effects in retinal disease. There are indications that this may occur in retinitis pigmentosa and other conditions12,13 and, in the current study, the same was true for age-related macular disease.

The EOG is a mass response to which all the RPE contributes. Thus, no increase in light-EOG occurs if less than a 30° solid angle of retina is illuminated.14–17 Small retinal lesions do not affect it, in common with the Ganzfeld ERG. Similarly, any retinal condition localized entirely to the macula produces a normal EOG and Ganzfeld ERG.18,19 Most elderly people, there are signs of aging, and one of these is the formation of small drusen (smaller than 65 μM). In early age-related maculopathy (ARM) there are additional signs of minor structural changes in the RPE and Bruch’s membrane. These are scattered larger drusen with indistinct borders (soft drusen) and some change in subretinal pigment. Even before such drusen are visible, deposits may occur between Bruch’s membrane and the choroid (basal laminar and basal linear deposits).20–24 At this stage, there are no symptoms of visual disturbance but experimental investigations of dark adaptation and color vision show minor losses.25–30 In a proportion of the elderly, the number of drusen increase and may become confluent, and basal laminar and linear deposits may thicken. The individual has a considerable risk of development of further changes to both RPE and retina, which can evolve in two directions. Either the RPE and retina become thinner, leading to atrophy and loss of visual function (geographic atrophy), or the RPE and retina become edematous, with possible RPE detachment and new vessel growth forward from the choroid, leading to leakage, local bleeding, and scarring (disciform degeneration). In these later stages the patient is often said to have AMD. The current study was concerned with the earlier stages at which vision is still well preserved and the abnormal fundus appearance seems localized to the posterior pole. Nevertheless, we show that in such patients the EtOH-EOG seems to be abnormal, and argue that this implies a widespread change in the RPE. In patients with very large degenerative lesions at the posterior pole, a small decrease in EOG potential in the dark has been reported,31 but there have been only a few conflicting accounts32–36 of the standard EOG.
in ARM. There is massive evidence about the dependence of the standard ERG and EOG to the area of stimulation (which is why Ganzfeld stimulation is necessary in clinical tests). There is less evidence that the EOG–ERG must be evoked by the RPE as a whole. However, the similarity between alcohol- and light-induced responsiveness and the fact that in retinitis pigmentosa, the EOG–ERG–positive peak is absent, even when the central visual field is preserved, makes this assumption very probable. It seems certain that alcohol reaches the entire retina, RPE and choroid. Thus, it is likely that the abnormalities described herein imply a generalized change in RPE function despite the localization of the ophthalmoscopic changes to the macula. This has implications both for the way alcohol affects the RPE and the pathogenesis of ARM.

**Methods**

**Normal Subjects**

Thirteen normal subjects participated: spouses of the patients, the authors, and their friends and relations. The inclusion criteria for the normal subjects were no systemic or eye condition, normal fundi, and normal corrected visual acuity. They also had normal color vision, which was not the case in any of our patients (manuscript in preparation). Therefore, although it was impossible to prove that in a group of elderly people the eyes have no aging changes, there was a great difference between the eyes of the normal control subjects and the patients in color vision and fundus appearance. It was not possible to recruit very old normal subjects, but some were in the age range of our patients. However, we found (as described later) no correlation between age and the normal EOG, and if any of the normal subjects had very early ARM, then the difference between them and the patients was even more significant.

**Persons with ARM**

Seventeen subjects constituted the ARM group. Three of the persons volunteering as normal subjects were shown on examination to have abnormal tritan color vision; a few had drusen, larger than 100 μm; and some irregularities of pigmentation that indicate early fundus changes in ARM. Two of these persons also had EOG responses below normal limits. All three were included in the ARM group. Fourteen more patients with various stages of ARM were recruited from meetings of the Macular Disease Society. All had been investigated in eye departments in the United Kingdom and had been given firm diagnoses of ARM. All were re-examined. Visual acuity and color vision were recorded. All had relatively good vision in one eye, but, in the other, there had been a relatively rapid loss of visual acuity (assessed in some cases with metamorphopsia) that had lead to a central scotoma of variable size and density. We excluded all patients with other systemic or eye diseases, although all with ARM had mild cataracts. Copies of clinical records were obtained. Fundi were photographed to determine the nature of the degeneration. In some cases, fluorescein angiographic results were available. Because of difficulties in some patients with full dilation of the pupils, and the presence of media that were not completely transparent, the method of photography described did not produce adequate results in all cases; therefore, to maintain consistency, we compromised and took 45° views, enlarged them to ×40, and used the grid and definitions and scoring procedures laid out in Bird et al. 27 to grade the tranparencies. In brief, three circles define annuli 0 to 1, 1 to 3, and 3 to 6 mm distant from the fovea. Each are divided into quadrants. The number and size of drusen in each quadrant are identified relative to standard opaque discs made for this purpose. Drusen of <63 μm are ignored. Different types of drusen are identified by coding, and the relative area covered by drusen in each subfield is estimated (<10%, <25%, <50%, ≥ 50%). Hyper- and hypopigmentation are scored separately, as is the presence of features suggesting geographic atrophy, or neovascular changes including hard exudates, detachment of RPE or neuroretina, the presence of hemorrhages in various planes, and the presence of scarring. In each of these cases, the involvement of the central region within the smallest circle (that is essentially foveal lesions) are separately noted. By far the most prominent feature in patients without disciform lesions (Table 1) were large areas of drusen, often confluent. For these the scoring was similar in each eye, and these were the results used in ranking the severity of the condition within the group studied. Histories were obtained to determine the duration of the (unilateral) loss of vision. Details of the patients are given in Table 1. It can be seen that the severity of the fundus photograph changes varied from the minimal to very severe, and both “wet” and “dry” forms of ARM are represented. All patients gave informed consent and the project conformed to the Declaration of Helsinki.

EOGs were recorded in the usual fashion. 1,2,11,12 Recordings were usually performed bitemporally, because it is known that the fundus appearance of drusen in ARM (and of other manifestations in or below the RPE indicating the later evolution of the process) is roughly similar in each eye. 20-24,35 28,37-41 However, in some cases, records were made from each eye to determine whether the asymmetric symptoms and loss of visual acuity were associated with asymmetric EOG results. 1 Eye movements were 30° horizontally, approximately every 800 ms for 10 seconds, repeated at 1-minute intervals. The amplifier bandwidth was 0.3 to 100 Hz. Peak-to-peak excursions in 6 to 10 traces were averaged to obtain the measured voltage (0.6–1.0 mV in different observers). The voltage changes were amplified in the usual way and recorded by a computer-based data-acquisition system. Two horizontal cursors were available in the program used for measurement, and these were placed at the average of the peaks and troughs. Portions of the trace that contained obvious defective eye movements were not included. The difference between the cursors automatically indicated the voltage. The voltage difference was entered into a computer spreadsheet (Excel, Microsoft, Redmond, WA). Macros in the spreadsheets normalized the data, performed a simple three-point smoothing function for viewing individual records, and averaged patient data.

All patient preparation was performed in dim illumination, followed by 26 minutes of full dark adaptation. Then, either the patients ingested 226 mg/kg ethanol, diluted to 7.1% vol/vol in water, or the experimental room was illuminated to 30 cd/m², and recording continued for a further 34 minutes. Before the alcohol test, the patients fasted for more than 10 hours.

Color vision was measured with a computer graphic system that has been described previously 42-44 Flashed optotype images were displayed on a standard monitor for 100 ms each. The subject’s task was to name the letter. Thresholds were obtained by modulating the color contrast along a color confusion line, using a binary search algorithm to determine threshold. The program displayed all optotypes against an equiluminant gray background (x = 0.333, y = 0.333 in color space). The luminance was controlled to 20 cd/m². In addition, any possible luminance contribution to color recognition was masked by random dynamic luminance noise, which does not affect chromatic discriminations. 45 Both proton and tritan thresholds were tested. Two sizes of optotype were used, subtending 1.5° and 6.5° at the eye. Only the results of the latter are reported in Table 1. The mean thresholds and the standard deviations of the normal subjects had been determined previously as a function of age and were redetermined for this investigation. 47 The thresholds are expressed as a percentage of the maximum change in chromaticity along a tritan color-confusion line. The higher the percentage, the worse the color vision. The test takes approximately 1 minute per eye. The minimum displacement of color on the monitor screen is less than 1 just noticeable difference (jnd). Adjacent “caps” in the Farnsworth Munsell test are, on this basis approximately 2 jnds, but the use of large flashed optotypes and modern threshold-detecting algorithms makes any simple comparison with cap arrangement tests impossible. In particular, the changes detected with age, and the “noise” associated with aging are much less than with cap tests. In a group of elderly normal subjects (manuscript in preparation) age changes in threshold between 60 and 80 were not
significant. In the footnote to Table 1, the upper limits of the normal are shown referenced to age 80 for protan and tritan optotypes.

**RESULTS**

**Normal Subjects**

The age of this group ranged from 36 to 74 years (mean, 43). The results are shown in Figure 1. In this figure, as in all the others, the actual EOG voltages have been normalized by dividing each response by the mean of the responses occurring between the 10th and 25th minute of the experiment (to within 30 seconds of applying the stimulus; i.e., during baseline recording and before the stimulus was given at time 0). Consequently, in the prestimulus condition, the results clustered about the value of 1.0, demonstrating that a stable baseline had been achieved. After this, the patient drank alcohol diluted with water, or the lights were turned on, and the normalized values first increased and then decreased (Fig. 1).

The light intensity and the dose of alcohol used were calculated to give (from our previous knowledge of the EOG) approximately equal responses (peaks and troughs) for the two agents. Figure 1 shows how closely this result was achieved. The action of drinking alcohol caused an immediate slight transient disturbance of EOG voltage. Light and alcohol then produced the same sequence of slower voltage changes, except that there was a 3-minute delay (associated with the delay in alcohol absorption) between the light-EOG and the EtOH-EOG results. The light peak occurred after 8 to 10 minutes, and the trough occurred at 20 to 24 minutes. We found insignificantly correlations between the peak and trough voltages and age (r = 0.16 and -0.05, respectively). Because of the extreme age of some of the patients, we separated the four oldest normal subjects (mean age 67 years, range, 64–74) and plotted their results separately (Fig. 1). The responses to light were somewhat smaller than the mean in these four, and the EOG response to alcohol was insignificantly larger than in the group as a whole. The peak times were not prolonged as they were in the patients. Therefore, we consider that the normal results can be compared with those of the patients, despite the age difference. Note that the procedures, when light was used as a stimulus, differed from the International Society for Clinical Electrophysiology of Vision (ISCEV) standard. The time in the dark before light exposure was longer (to get a better baseline).

**TABLE 1. Summary of Clinical Findings in the ARM/AMD Group**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Better Eye</th>
<th>VA</th>
<th>Grade of Fundus Changea</th>
<th>Rank Order of Fundus Changes</th>
<th>Light-EOG Peak</th>
<th>Trough</th>
<th>EtOH-EOG Peak</th>
<th>Trough</th>
<th>Psychophysics, Better Eye (6.5° Letters)†</th>
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<td>DA</td>
<td>83</td>
<td>M</td>
<td>R</td>
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<td>‡</td>
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<td>0.5</td>
<td>1.27</td>
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<td>L</td>
<td>0.30</td>
<td>g</td>
<td>8</td>
<td>5</td>
<td>8</td>
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<td>‡</td>
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<td>‡</td>
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<td>1.50</td>
<td>a</td>
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<td>0.049</td>
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*a, minimal signs of ARM; b, scattered large soft drusen only; c, numerous drusen, some confluent; d, drusen, plus small disciform area (wet); e, large, old disciform scars; f, drusen, plus small area of atrophy (dry); g, large area of atrophy.
† Threshold data for color test. Higher values indicate worse vision. Normal (mean ± 2.5 SD) values at age 80 are 12.7 for tritan vision and 6.8 for protan vision.
‡ Data unreliable.
§ Data not available.

**FIGURE 1.** Light and EtOH-EOGs compared in a group of normal subjects. Separate symbols indicate mean values for the entire group. The results of the four oldest normal subjects are plotted separately, to show that there was little difference between older and younger normal subjects.
and the light intensity reduced (so EOG peak amplitudes were approximately the same in normal subjects in response to both alcohol and light). Increasing the dose of alcohol so that alcohol-EOGs were as large as the ISCEV standard for light-EOGs would have caused an unacceptable degree of inebriation.

Patients

Table 1 gives the details of the patients’ visual acuity, the ages, fundus appearances, rankings, results of a color vision test in the better eye, and the alcohol- and light-EOGs. The mean age was 76, range 63 to 89. In one case, the patient could not make reliable eye movements in the light, and the result was omitted. In two other patients, only EtOH-EOGs were recordable. In almost all cases, the smaller optotype used could not be identified in the better eye, even when the tritan color contrast was maximal.

Interocular Differences in Patients’ EOG

Figure 2 shows the mean monocular EtOH-EOGs in four patients with the greatest difference in visual acuity between the two eyes. The mean response was equal in the better and worse eyes. Similar results were obtained with light, as expected, because ARM has not been shown to affect the light-EOG. The four patients were at different stages of ARM and showed different degrees of disturbance of the EOG, but in each, the responses were the same in each eye. Therefore, in all subsequent graphs we show the average responses from both eyes (five cases), or the results are from bitemporal recordings.

Comparison of Light- and EtOH-EOG Responses in Normal Subjects and Patients

Figure 3 shows the averaged EOGs in the normal subjects and patients in response to light or alcohol. The patients’ light-EOG peaks were delayed in comparison with those of the normal subjects and were somewhat reduced.

The alcohol peaks were also delayed and greatly subnormal. The patients and normal subjects showed the same mean decrease in amplitude at the nadir of the trough, and an increase in the time to reach that minimum value. We found no significant correlation between age and any aspect of the EOG response in our patients. It is therefore likely that the differences from the normal group were caused by the pathologic processes occurring in the patients’ eyes.

Reduction in EtOH-EOG Responses

The standard errors in Figure 3 were so small that it is evident that the change in the EtOH-EOG response was much greater than was the change in response to light. This case can be made formally by comparing the ratio, R, in the two groups, where R = (response to light)/(response to alcohol).

This ratio can be measured for the mean of responses obtained during the 10 minutes preceding the stimulus (light or alcohol), when the records should be identical, and therefore the ratio should be 1.0. Therefore, it was easy to average the results of all patients and normal subjects. The standard errors of the means are shown in Figure 4.
After the provoking stimulus, the responses increased. The ratio for the next 10 minutes (allowing for the delay in alcohol absorption) should have been nearly 1.0 in normal subjects, because we had tried to achieve this result by adjusting the stimulus strength.\textsuperscript{11} For the patients with ARM, the corresponding ratio should also have been 1.0 before the stimulus, but if the ETOH-EOG response were selectively depressed, after the stimulus, the ratio would increase. Figure 4 shows that this was the case. The means and standard errors of the ratios are shown. For the prestimulus results the probability (t-test) that normal and patient data came from the same sample is 0.59 (i.e., there is no significant difference). For the poststimulus results the probability that normal and patient data came from the same sample is $P = 10^{-4}$. Figures 1, 2, 3, and 5 and Table 1 suggest that the reduction in the trough in the ETOH-EOG in patients was not as great as it was for the peak.

**Correlations between Fundus Changes and the EOG**

We graded the fundus photographs to determine the severity of RPE changes.\textsuperscript{22} Because of the technique used (see the Methods section) the results may not correspond precisely to those of other publications in which ARM has been graded, but they are internally consistent and serve to rank those with adequate fundus photographs. Figure 5 shows the mean results of the four least and four worst affected.

There appeared to be a significant loss in early ARM and an additional loss in those with more severe RPE changes. Correlations (Table 2) were found between the ETOH-EOG peak amplitude and the patient’s ranking, but not between the light-EOG peak and the ranking. However, the value of the coefficient $r$ does not reach significance at the 5% level (Mann-Whitney nonparametric test). Significant correlations were also found between visual acuity and color vision in the better eye and the ranking of fundus changes. Similarly, correlations were found (not shown in Table 2) between the EOG responses and color vision. Correlations could not be established for the “worse” eye, because color vision was unmeasurable in most cases.

**DISCUSSION**

The importance of the current experiments may lie, not in diagnosis, but rather in the light the results throw on the pathogenesis of ARM and the mechanisms of the EOG.

**Table 2. Correlation and Significance of Fundus Changes**

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<tr>
<th>Measurements</th>
<th>$r$</th>
<th>$P$</th>
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<td>ETOH peak and rank order</td>
<td>$-0.475$</td>
<td>NS</td>
</tr>
<tr>
<td>Light and rank order</td>
<td>$0.025$</td>
<td>NS</td>
</tr>
<tr>
<td>Age and rank order</td>
<td>$0.305$</td>
<td>NS</td>
</tr>
<tr>
<td>Better eye VA and rank order</td>
<td>$-0.66$</td>
<td>$P &lt; 0.01$</td>
</tr>
<tr>
<td>Tritan 6.5° vision and rank order</td>
<td>$0.63$</td>
<td>$P &lt; 0.01$</td>
</tr>
<tr>
<td>Protan 6.5° vision and rank order</td>
<td>$0.68$</td>
<td>$P &lt; 0.01$</td>
</tr>
<tr>
<td>Age and ETOH peak</td>
<td>$-0.54$</td>
<td>NS</td>
</tr>
<tr>
<td>Age and tritan threshold</td>
<td>$0.58$</td>
<td>$P &lt; 0.05 &gt; 0.02$</td>
</tr>
<tr>
<td>Age and protan threshold</td>
<td>$0.11$</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Light-EOGs in ARM**

It is known that the light-EOG is a response derived from most of the retina and is dependent on the rods. It has been shown that the number of rods decreases with age, but only by approximately 30%\textsuperscript{59} with submaximal stimuli, such as that used in the current study, when there are fewer rods and thus decreased light absorption, a small reduction in EOG peak equal to that caused by a 0.15-log unit reduction in light intensity should result. In view of the variability of the clinical EOG, it is not surprising that such a small age-related change has never been documented and that normal light-EOGs have been reported in ARM. By using a long pretest period, we were able to normalize all our results and obtain greater precision. Insofar as the peaks of the EOG response are concerned, in our normal series, there was only a small decrease between younger and older normal subjects. Therefore, the difference between the light EOGs of normal subjects and those of the patients with ARM is significant. Although the cause is obscure, from the known disease, it is likely that both retina and RPE are affected in the patients.

**ETOH-EOGs in ARM**

In our patients, there was a considerable reduction in the ETOH-EOG from the normal value. It is no surprise that the reduction is the same in better and worse eyes of the same individual, because, when fundus photographs are analyzed, the differences between the two eyes were quite small. This similarity extends to the areas of drusen (and other features scored in grading\textsuperscript{25}) in each of the retinal annuli specified in the international system even when (due to small differences in the location of lesions near the fovea\textsuperscript{41}), visual acuity has been more affected in one eye. The reduction in the ETOH-EOG cannot be directly due to changes in the intracellular mechanisms of the RPE cells, because in the same patients, the “light substance” produced by the rods can evoke a sizable EOG. (We have not analyzed the later troughs of the EOG in detail, even though we have shown that a different process produces them [Wolf JE, Arden GB, Karpik NA. ARVO Abstract 440, 2001; Wolf JE, Arden GB, ARVO Abstract 1825, 2002]. The trough deviates less from the baseline than does the peak in normal subjects, and in the patients, troughs are almost absent. We do not know whether the response of each part of the retina was uniform. If in some parts of the retina the delay in the positive peak was much longer than the delay in the retina as a whole, the arithmetic summation of delayed peak with the trough could account for the apparent absence of a clearly defined trough.) The most likely cause of the major result, that ETOH-EOG responses were smaller than light-EOG responses in patients, is that the alcohol, in some way, is unable to stimulate the RPE.

**Relation to Pathogenesis**

The common and (it is believed) major histopathologic feature in ARM is the presence of basal laminar deposit in and below...
Bruch’s membrane and the RPE.20–24,37–41 The visible manifestations of this histologic change are the drusen. The thickness of the basal laminar deposit is greater in the wet forms and thinner in cases of RPE and retinal atrophy,54,55,58,59,40–41 but these observations refer to the advanced stages of the disease, and there is a continuum20,48 between the different clinical manifestations. The change in the ETOH-EOG was also seen in those of our patients who had minimal visual or ophthalmoscopic disturbance, and the ETOH-EOG abnormality was therefore associated with the early stage of the condition, implying that there are changes to the physiology of the RPE, not only in the macula but also widespread in the periphery. This is the first demonstration of its kind. The incidence of quite widespread abnormalities in color vision in early disease also implies that retinal damage commences before the patients notice changes in vision. This subject is treated in another paper.47

In ARM, investigations into peripheral retinal functions have demonstrated both normal and abnormal25–56 results. Our experiments show a widespread and considerable loss of the response to alcohol in the RPE of these patients, which appears related to the severity of the condition. There is some evidence in this small series that the more obvious the RPE disturbance, the worse the ETOH-EOG result, suggesting that the ETOH-EOG abnormality is related to the causal sequence in this condition. The simplest hypothesis to explain our results is that alcohol acts (as suggested in our previous paper) on the basal RPE, and, in ARM, there is an obstruction to the passage of water-soluble molecules from the choroid to the RPE. Such a hypothesis has already been postulated on structural grounds20–21,38,48 and as a result of measurements on the hydraulic conductivity of Bruch’s membrane.49

This hypothesis suggests interesting lines of inquiry. If the RPE/Bruch’s changes are widespread, why is the degeneration localized? It has been suggested that this is due to the numerous rods in the perimacular region.21,26,53,59,48 The volume of shed rod fragments is so great that local accumulations of lipofuscin occur within the RPE, and there are additional local deposits (drusen) at the RPE–Bruch’s interface. These exacerbate the general defect of fluid transfer and lead to the visual disturbances.

The involvement of rods in ARM recalls a theory of the cause of diabetic retinopathy, in which the condition has been linked to the high oxygen requirements of dark-adapted rods causing the anoxia that upregulates vascular endothelial growth factor (VEGF).50 The neovascularization in disciform degeneration is also associated with increased VEGF,51 indicating local retinal anoxia. It is possible that a similar role of local obstruction to fluid transfer plays a part in some diabetic maculopathy. Laser photoocoagulation arrests the progress of diabetic retinopathy, because the oxygen requirement of the remaining rods can be met. Laser treatment of ARM has been reported to reduce the number of drusen gradually and slow down the progress of the condition,21,52–54 perhaps because, after laser treatment, the number of shed phagosomes declines, and the conductivity of Bruch’s membrane may also increase. It is possible that laser treatment early in ARM would therefore be therapeutic, and the success could be assessed by the techniques used in this study.

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References

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