The Standing Potential of the Eye in Vascular and Degenerative Disease of the Retina

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(Received October 4, 1964)

If eye movements of a constant amplitude are made, the eye-movement potential can be employed to detect changes in the standing potential itself. This technique has been employed to study the effects of acapnia and anoxia (Fen, Galambos, Otis and Rahn, 1948) and the effects on the change of illumination (Aserinsky, 1955; Francois, Verriest and De Rouck, 1955; Ten Doesschate, G. & Ten Doesschate, J., 1956 & 1957; Kolder, 1959). It has also been employed in several pathological cases (Francois, Verriest and De Rouck, 1956 a, b).

Recently detailed descriptions are given of the changes which occur in the standing potential of the eye when retinal illumination is altered (Toyama, T., 1962; Arden & Kelsey, 1962 a, b; Arden, Barrada and Kelsey, 1962; Arden & Barrada, 1962; Horie, 1963).

The present paper deals with results obtained by this technique in some typical diseases of the fundus of the eye. In this paper the recording is called the electro-oculogram, abbreviated to EOG according to Arden and co-workers.

METHODS

The methods are almost the same as those described by Arden & Kelsey (1962). The scheme of the arrangement is shown in Figure 1. Patients are asked to look rapidly and rhythmically between two small red fixation lights (r & r') situated so that the eyes make horizontal excursions of 40°. Small chlorided silver ball electrodes are fastened to the skin near the medial and lateral canthi of either eye. Recordings are made for about 10 seconds at approximately one minute intervals.

The time constant of the pre-amplifier used is one second. The patient is seated on a deck-chair with the head supported by a cushion (R). Normal room illumination gives an intensity of about 100 lux at the eye. Recordings are made every minute for 5 minutes with the room light on, and then every minute for 15 minutes with all lights off. Finally, the lights in the viewing box are switched on and recording continues for 15 minutes. The viewing box contains two Reflector Lamps (L_1 & L_2, West Co.) with a colortemperature of 3200° Kelvin. Diffuse illumination is obtained by placing glass wool paper in front

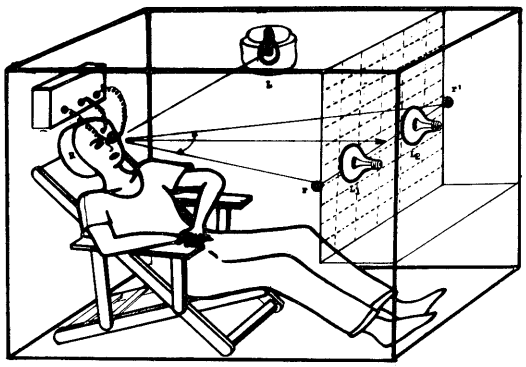

Figure 1. The scheme of the arrangement
r & r': small red lights L: normal overhead light
R: round head rest L_1 & L_2: Reflector Lamps

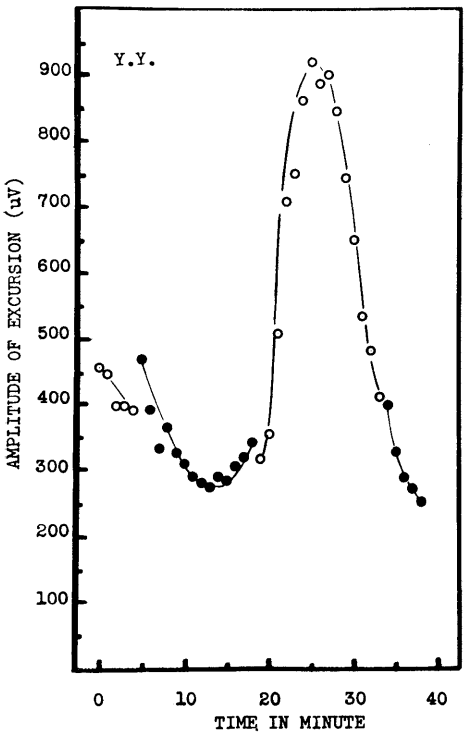

Figure 2. A typical result from normal eyes. First 5 open circles: values during prelight adaptation; solid circles: values during darkness; fifteen open circles following to solid circles: values during reillumination.

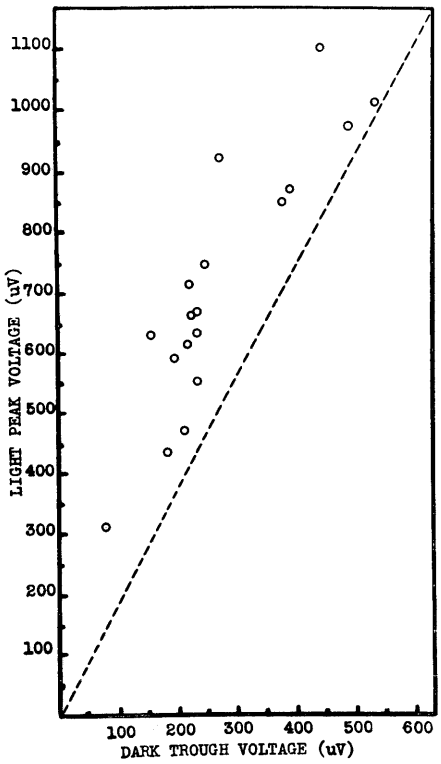

Figure 3. Relationship between light peak and dark trough potential detected from normal 18 eyes.
Ordinate: light peak voltage
Abscissa: dark trough voltage
Broken line: $\frac{\text{peak voltage}}{\text{trough voltage}} = 1.85$

of the box which provides an intensity of about 2000 lux at the eye. No mydriatic is used in these experiments (cf. Arden, Barreda and Kelsey, 1962).

The trace recorded is a series of saw-teeth; rising (or falling) rapid deflexions due to eye movements. The vertical excursion is found to vary slightly in height, so that average excursion is detected by means of a line-drawing technique.

RESULTS

1) RESULTS OBTAINED ON NORMAL SUBJECTS

The results on normal eyes were obtained with volunteers from doctors and nurses of our clinic. Their ages ranged from 22 to 42. All had normal visual acuity and no ocular or vascular diseases.

Figure 2 shows a typical result from these eyes. After prelight adaptation (first 5 open circles) the room light is turned off. The values during darkness are shown by solid circles. After a transient increase these decreases until the recordings reach a low level, after which there is a gradual increase. The lowest level of the potential has been named the "dark trough" by Arden et al. When the dark-adapted retina is reilluminated by the viewing box, the values during reillumination are shown by open circles. There is a transient decrease in potential, followed by an increase which continues for about 7 minutes. After the potential reaches a peak (named the "light peak" by Arden et al), it begins to fall.

The relationship between the light peak potential and the dark trough potential is shown in Figure 3 with normal 18 eyes from 17 subjects because with one subject his both eyes were tested. The light peak voltage is plotted along the ordinate, and the dark trough voltage along the abscissa. The broken line shows: $\frac{\text{peak voltage}}{\text{trough voltage}} = 1.85$ (Arden's normal limit)

All of the values detected from normal eyes fall in the upper area than that line, but light peak voltages vary from 3oo uV to 1100 uV, and dark trough voltages vary from 80 uV to 540 uV. The peak and the trough voltages themselves vary so widely that in an individual case they are not significant.

The dark trough, the difference between the base-value (potential in room light) and the dark trough voltage (the minimal value during dark), it is called "d" by Francois, is more than 150 uV in all the eyes but 3. Eleven out of 18 have a dark trough between 175 uV and 225 uV. These are from 20 to 66 per cent of each base-value. Since the base-value can be thought to be originally fluctated (Kolder, 1959 etc), the dark trough may depend upon the moment of lighting off: if the light is turned off when this cyclical change of bace-value reaches to its maximum, the dark trough would show also the maximal value.

The other variable we can measure is the culmination time of the light rise. It means the duration from the beginning of the reillumination to the moment when the potential reaches its maximum. Most of them are between 7 and 9 minutes but two are 6 minutes.

2) VASCULAR LESIONS

a. CLOSURE OF THE CENTRAL RETINAL ARTERY

The results obtained from the patient of complete obstruction of the central retinal artery are shown in Figure 4, in which "A" shows the intact eye, and "B" and "C" show the respective EOG of the affected eye obtained on the 4th and on the 60th day after the onset of the disease.

In "B" it is observed that the base-value is probably lower than the intact one, and there is no typical light rise or dark trough. Instead of the light rise there is a fall during reillumination.

In "C" the dark trough appears and the base-value is probably increased, but it does not reach the level of the intact side. The light rise is absent even at this stage.

By this stage the cherry red spot has disappeared and the edema has subsided with narrowed vessels.

The ERG of the eye is shown in Figure 5. On the affected side the ERG shows the "negative"-type of response to be characteristic; that is, b-wave am-

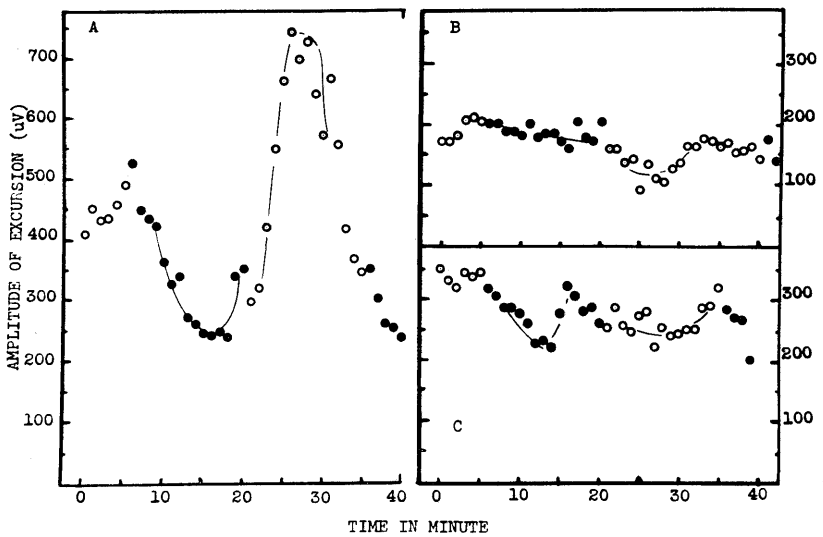

Figure 4. EOG of obstruction of central retinal artery.
A: intact side
B & C: EOGs of affected eye obtained on the 4th & on the 60th day after the onset of the disease respectively.

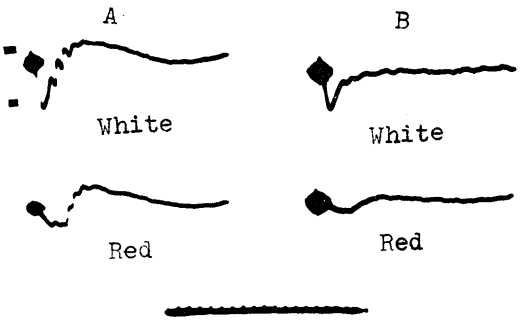

Figure 5. ERG of obstruction of central retinal artery.
A: intact side
B: affected side
The sign at the left of recording A: 500 uV
Time mark: 100 cps
These are responses to white and red light stimulus.

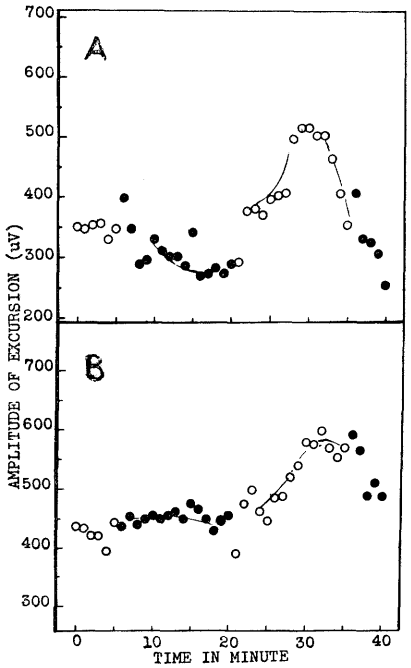

Figure 6. EOG of thrombosis of central retinal vein.
A: thrombosis of inferior temporal vein
B: occlusion of central vein

plitude is reduced, but pronounced a-wave ramains.

b. THROMBOSIS OF THE CENTRAL RETINAL VEIN

The results from two patients with central venous occlusion are given in Figure 6. "A" is from the patient with thrombosis of the inferior temporal vein, recorded about a month after the occlusion and "B" is from an occlusion of the central vein, recorded approximately 4 months after the onset. The intraocular pressure was normal in the affected eyes of these two patients at the time of examination.

In both recordings base-values were found within the normal range. In the case "B" the dark trough and the light peak were both less prominent than the normal. Similar results were obtained in the recording which was made one month prior.

The ratio of the light peak and the dark trough, of the recordings "A" and "B" are shown by the black dot *1 and *2 in Figure 16 respectively. The black dot *1 falls on the border line of the normal range, but the blackdot *2 falls in the pathological range. The difference might be expected because the affected areas are not identical.

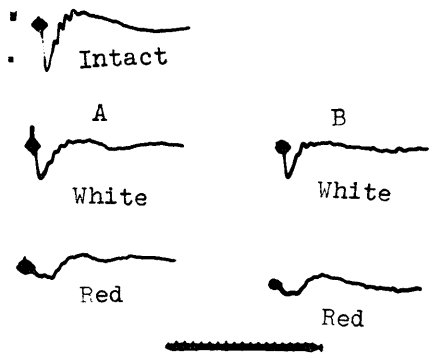

Figure 7. ERG of thrombosis of central retinal vein.
A: thrombosis of inferior temporal vein
B: occlusion of central vein
The recording at the top of the left column: response of intact side of case "A" to white light.

The ERGs of these eyes are shown in Figure 7. Both patients show "negative"- ERG; that is, small b-wave and pronounced a-wave, but these changes in the ERG are less remarkable than those of the complete obstruction of the central retinal artery, described above.

c. DIABETIC RETINOPATHY

In the case of diabetic retinopathy, stage 1 (Wagener, Dry and Wilder 1934) with a few, small, punctate hemorrhages and capillary aneurysms, there is a normal pattern of the EOG having normal base-value, deep dark trough and large light peak, though the lens had been removed (open circle *1 in Figure 16). A normal ERG was obtained in the same case.

In the case of diabetic retinopathy, early stage 2, the changes were somewhat more sevsr in the left eye than in the right showing solid, white soapy exudates in addition to punctate hemorrages. The EOG of the right eye gives the normal pattern, but the left eye shows subnormal light rise. These are illustrated by the open circles *2 and *3 in Figure 16 respectively.

The ERG of both these eyes demonstrates a little reduction in oscillatory potential amplitude (Yonemura, Aoki and Tuzuki, 1962), but the other components are within normal range.

In the case of diabetic retinopathy, late stage 2, the exudates coalesced into larger masses in addition to adove mentioned ophthalmoscopic changes. These changes were more severe in the right eye than in the left.

In Figure 8, two EOGs are shown. The top is for the right eye and the bottom, the left. In both recordings the light peaks are in the subnormal range, and it is also found that the right eye has lower base-value, less marked dark

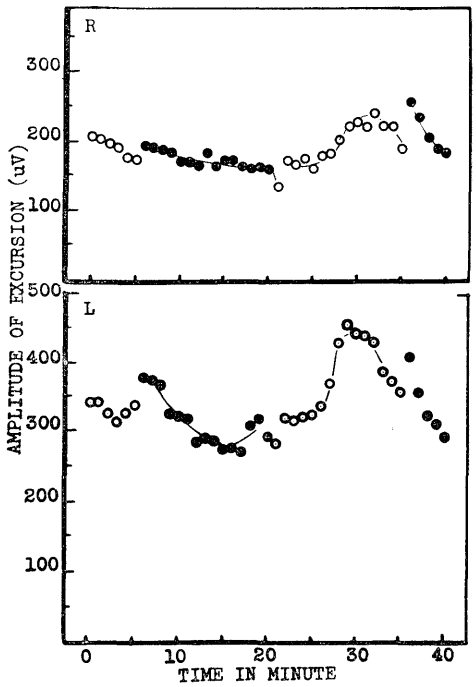

Figure 8. EOG of diabetic retinopathy, late stage2.
Recording from both eye of of same patient.
The top: right eye; the bottom: left eye

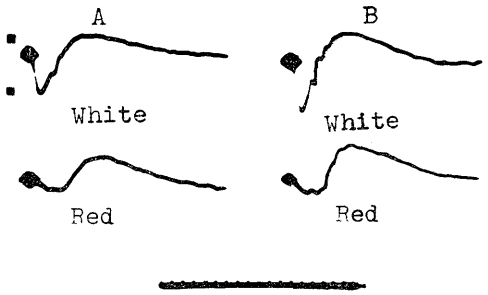

Figure 9. ERG of diabetic retinopathy.
Recording from the same patient of Figure 8.
A: right eye; B: left eye

trough and smaller delayed light peak than the left eye.

The ERGs of these eyes are shown in Figure 9. The oscillatory potentials of both ERGs are reduced in amplitude. In the right eye, furthermore, the b-wave amplitude is also depressed.

In another case of diabetic retinopathy, stage 3 with cotton-wool patches, hemorrhages, exudates and some hypertensive changes of the vessels, the EOG shows slightly lower light rise (open circle *4 in Figure 16), though its culmination time takes 14 minutes.

It is found that the light rise of the EOG obtained from these patients is depressed in parallel with the area of involvement (especially, exudates) found by ophthalmoscopy, and with changes in the ERG.

d. HYPERTENSIVE CHANGES

Hypertensive retinopathy with exudates at the posterior pole together with hypertensive alteration of the vessels, did not remarkably change the standing potential pattern, although Arden et al have reported these to have a smaller light rise.

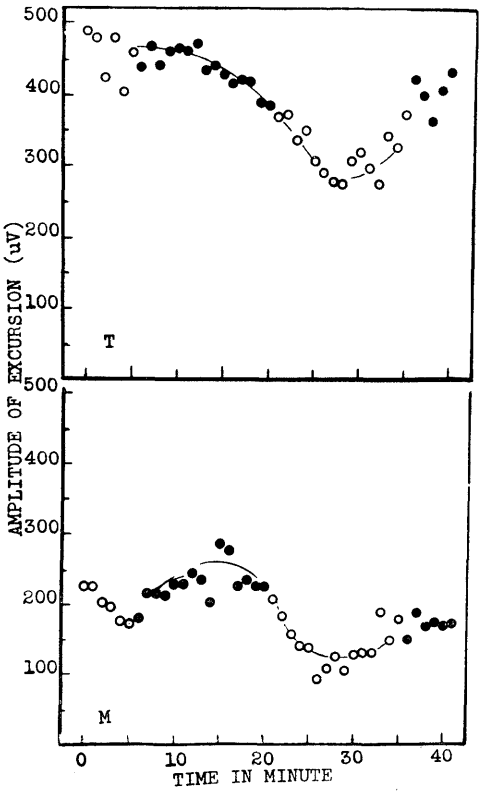

Figure 10. EOG of retinal detachment
The top: patient T
The bottom: patient M

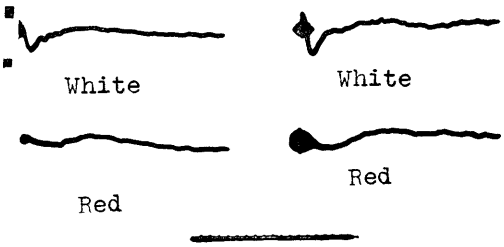

Figure 11. ERG of retinal detachment and of choroiditis
Left column: retinal detachment
(Patient T in Figure 10 with EOG)
Right column: choroiditis
(Case C in Figure 12 with EOG)

3) RETINAL DETACHMENT

Two EOGs of subtotal retinal detachment are shown in Figure 10. The most remarkable change in the EOG is found when these eyes were reilluminated, i. e. there was a fall instead of a rise. The same finding has also been reported by Arden et al.

The base-value of patient T is in normal range, and that of M in lower limit of normal range. Both EOGs show no typical trough during darkness, in M there is only gradual increase in the EOG amplitude instead of decrease to form the dark trough, and in T, there is only decrease.

The ERG of the patient T is shown in Figure 11, left column, in which there is still remaining b-wave with marked oscillatory potential. But the ERG of M is almost disappeared.

In another patient with a partial detachment, there are normal base-values, no marked dark trough and no typical light peak. The amplitude of the EOG

was almost unchanged when illumination was altered.

We have not yet been able adequately to compare the EOGs before and after surgical reposition, because our surgical procedure did not achieve complete reattachment in these patients.

4) CHOROIDITIS

The EOGs observed in choroiditis shows various types, and these are roughly divided into the following three types:

a. Normal EOG pattern

This is the type of EOG which has the base-value in normal range, marked dark trough, and normal light peak.

This type of EOG is often detected in patients whose lesions can not be found even by careful ophthalmoscopy, although vitreous opacities were present. However, the lesions may have been located near the ora serata; for example,

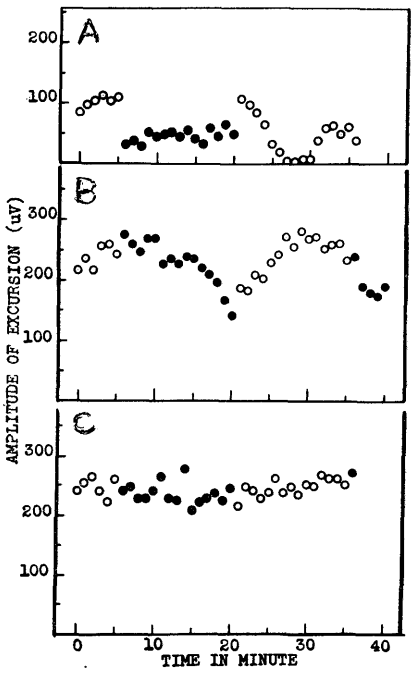

Figure 12. EOG of choroiditis
A: choroiditis attack in accordance with Behçet's syndrome
B: acute choroiditis of unknown origin (10 days after the onset)
C: subacute stage of choroiditis in accordance with Behçet's syndrome

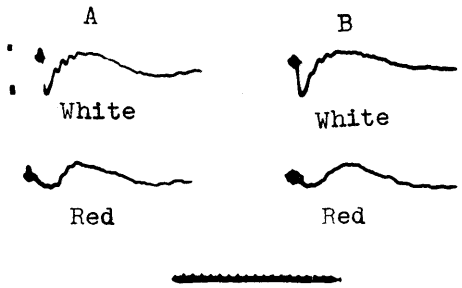

Figure 13. ERG of choroiditis
(Case B in Figure 12)
A: intact side; B: affected side

choroiditis due to leptospirosis (semisolid circle *1 in Figure 16). Also this type of EOG is more often found in cases which have been called chorioretinitis centralis (not plotted other than a case marked by semisolid circle *2 in Figure 16).

b. Abnormally small EOG in amplitude

The EOG in this type is very small in amplitude; sometimes the saw-teeth were hardly visible.

In a case of acute choroiditis of unknown origin having lesions with edema of the overlying retina, saw-teeth in the EOG were so small that they could not be measured. (The same type of EOG was recorded when choroiditis in conjunction with Behcet's syndrome occurred, Figure 12, A) After the patient had been treated with steroids for 10 days, edema of the overlying retina decreased somewhat, and the EOG increased enough in amplitude to become measurable (Figure 12, B). However, the base-value is still about a half of the other intact eye's. The amplitude of the EOG gradually decreases during darkness, but it does not form any trough for 15 minutes. It shows small light rise during re-illumination.

The ERG of this patient, however, is in striking contrast to the EOG. The ERG (Figure 13) showed normal feature with normal a- and b-wave, except slight reduction in oscillatory potential amplitude.

A similar type of the EOG was obtained from another patient suffering from subacute stage of choroiditis.

c. Flat type of EOG when illumination was altered

The EOG included in this type neither decreases in amplitude during darkness, nor increases during illumination; the amplitudes are almost constant through out the experimental process.

An EOG showing this type is found in the subacute stage of choroiditis accompanying Behcet's syndrome (Flgure 12, c). The ERG of this eye was "negative"- type which retained a pronounced a-wave followed by small b-wave without oscillatory potential (Figure 11, right column).

This type of EOG is also found in diffuse chorioretinitis and in endophthalmitis. The ERGs of these eyes are extinguished. Both electrophysiological responses are like those of pigmentary degeneration.

5) PIGMENTARY DEGENERATION OF THE RETINA

In most of the cases, the EOG remains flat when illumination is altered. The base-value is significantly lower than normal.

One of the cases is plotted in Figure 14, A. Not only is a lower base value found, but also the dark trough and the light rise disappear. The ERG of this patient is extinguished.

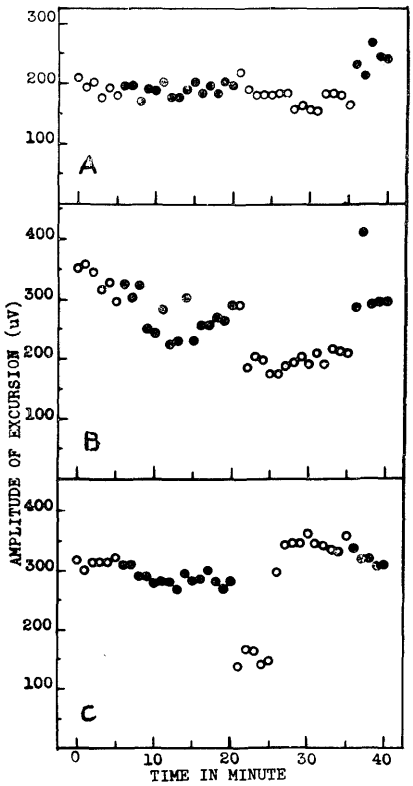

Figure 14. EOG of pigmentary degeneration

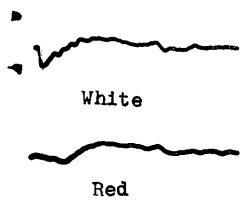

Figure 15. ERG of pigmentary degeneration (Case C in Figure 14 with EOG)

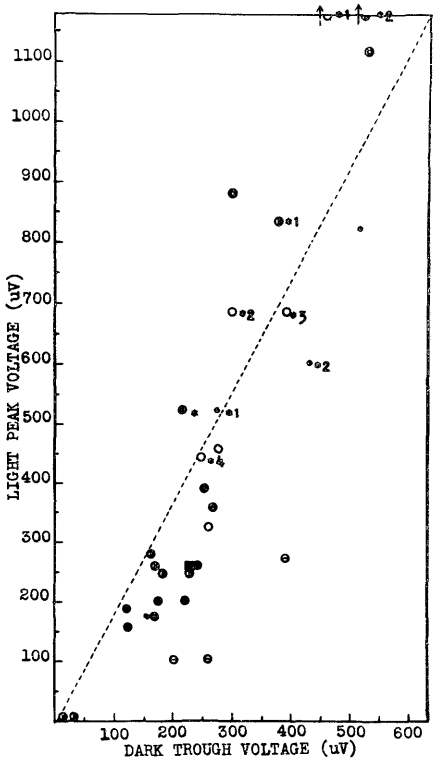

Figure 16. Relationship between light peak and dark trough potential detected from pathological conditions, as same as Figure 3 from normal subjects.
arrow sign: scale out double circle: optic neuritis, open circle: diabetic retino-pathy, solid circle: pigmentary degeneration, solid square: endophthalmitis, circle drawn about-: retinal detachment, open dot: closure of central retinal artery, black dot: thrombosis of central retinal vein, semisolid circle: choroiditis

In soma cases the EOG-amplitude decreases during reillumination instead of increases as shown in Figure 14, B. The other case, illustrated in Figure 14, C, shows a slight increase in the EOG amplitude during reillumination. The ERG of this patient (Figure 15) is subnormal in amplitude.

6) OPTIC NEURITIS

In two cases of optic neuritis the EOG showed normal pattern with marked

dark trough and normal light peak, these are shown by two double circles in Figure 16.

DISCUSSION

The relationship between the light peak and the dark trough potential in pathological conditions is shown in Figure 16. Here, the light peak voltage is plotted along the ordinate, and the dark trough voltage along the abscissa, as same as Figure 3 with normal subjects.

In most of fundus diseases except optic neuritis and some mild cases of fundus diseases described above, the values fall in the area below Arden's line.

Arden, Barrada and Kelsey (1962) have stated that the ratio: $\frac{\text{peak voltage}}{\text{trough voltage}}$ 100 does not depend upon the position of the electrodes and gives an index of the functional capacity of the pigment epithelium; in normal eyes this ratio is greater than 185 per cent.

They have suggested that the factors which one would expect to be necessary for a normal light rise are: (1) functioning rods, (2) functioning pigment epithelium, (3) contact between neural and pigment layers, and (4) adequate choroidal blood supply. And in practice, an abnormal EOG may be found in diseases where each one of these conditions is not fulfilled.

In the present experiments, the ratio of peak voltage to trough voltage is greater than Arden's normal limit in normal subjects, as illustrated in Figure 3 and smaller in pathological conditions, as illustrated in Figure 16.

From these results, it is suggested that the ratio would give an index of the functional capacity of the eye. Possidly the layers generating the light rise may be pigment epithelium as Arden has suggested.

In present experiments, the EOG of obstruction of the central retinal artery did not show any evident light peak, while its ERG showed a "negative"- type of response, i. e. the a-wave remained whereas the b-wave almost completely disapeared.

The same results of ERG with obstruction of the central retinal artery have been reported by Henkes, Karpe and Uchermann, and Krill, etc. It has been considered that the maintenance of the response is because the nutrition by the choroidal circulation of the outer layers of the retina is not necessarily compromised by central retinal arterial disease (Jacobson, 1961).

In addition, it has deen demonstrated in histological investigation of ischemic necrosis of the retina secondary to occlusion of the central retinal artery that the inner retinal layers have shrunk while the outer layers are well preserved (Perraut & Zimmerman 1959).

Because the obstruction of the central retinal artery affects the light rise of

the standing potential in the present studies, it is also considered that the light rise is influenced not only by the layers supplied by the choroidal arteries but also by the layers supplied by the central retinal artery.

In some cases (for example: diabetic retinopathy) the light rise of the standing potential is depressed in parallel with reduction of the oscillatory potential of the ERG. Though the origin of the oscillatory potential is still unknown, it has been considered that the oscillatory potential is closely connected with the function of the inner nuclear layer (Yonemura 1962).

Moreover, in all cases of which the b-wave of the ERG was decreased in amplitude, the light rise of the EOG was also depressed. However, in optic neuritis the EOG had normal light rise.

All this evidence suggests that the light rise of the EOG is also closely connected with the function of the inner nuclear layer.

If the light rise were generated in the pigment epithelium or receptor cells layers as Arden et al emphasized, it would have to be controlled by inner layers.

Francois, Varriest and De Rouck (1956) reported two cases of the embolism of the central retinal artery. They found that the base-value was normal in one of these, but in the other it was significantly reduced. However, in the former the dark trough deflections were barely demonstrable and the ERG was absent; but in the later there were marked deflections in the dark trough, and a subnormal ERG was present.

They concluded from these results that the base-value of the standing potential was independent of the ERG and depended merely on the presence of the photoreceptors; whereas the dark trough and the amplitude of the b-wave of the scotopic ERG were inter-dependent and expressed the intra retinal conductibility. (These suggestions are interesting when our results with choroiditis are compared with them.)

In our case, two of the ERG's which were obtained simultaneously with the EOG's ("B", 3 days and "C", 2 months after the onset) were almost the same in shape and in amplitude.

Nevertheless, the base-value of the EOG in "C" is higher than in "B", and the dark trough in "C" is deeper than in "B".

From these results, it is suggested that the base-value and the dark trough are independent of the ERG. Also, in the early stage of the disease there was marked edematous swelling of the retina, which might have acted to depress the base-value and flatten the trough.

The increased base-value and the marked trough in the later recording may indicate the recovery of the outer layers of the retina, which would suggest that the base-value and the dark trough depend on these layers.

The suggestion would be supported by the experimental works with drugs, which selectively alter the resting potential of the eye (Noell, 1953), and by

means of micro-electrode technique (Brindley, 1956, Brown & Wiesel, 1958, Tomita, Murakami & Hashimoto, 1959-60). These have suggested that the pigment epithelium generates the standing potential.

It is also interesting that in the acute stage of choroiditis, the amplitude of the EOG is of significantly small value, and becomes larger together with regression of ophthalmoscopic signs.

Since the base-values and the dark troughs as described above vary widely in individual and experimental conditions, there is some difficulty in their general clinical use.

If one can get a normal EOG from the other intact eye of the same subject simultaneously, these values become more meaningful.

It can be said that the dark trough is less marked or absent, and the base-values are statistically lower in pigmentary degeneration than in the normal.

In the patients suffering from pigmentary degeneration, there is also the question, "Which is first destroyed the EOG or the ERG?" Arden et al have reported two cases in which the EOGs showed a diminution of the light rise, but the scotopic ERGs were of fair size.

As described above (Figure 14, C & Figure 15), we have a case showing an abnormal EOG together with a subnormal ERG. The other case, a ten year old girl with an early stage of pigmentary degeneration, whose mother suffered from typical pigmentary degeneration, shows a normal EOG with normal dark trough and normal light rise (solid circle *in Figure 16), and extinguished ERG. A few pigmented areas were found by ophthalmoscopy although there was no functional disturbance.

We do not yet possess the necessary information to answer the question.

SUMMARY

The changes which occur in the standing potential of the eye when retinal illumination is altered were observed by means of the EOG technique.

A detailed description is given of some typical fundus diseases of the eye such as closure of the central retinal artery, closure of the central retinal vein, diabetic retinopathy, retinal detachment, choroiditis, and pigmentary degeneration, and results obtained by this methods were compared with the ERG.

From these observations following two suggestion are given.

1) Tho light rise of the standing potential is influenced not only by the layers supplied by the choroidal blood but also by the layers supplied by the central retinal artery. The light rise may be generated in the pigment epithelium or receptor cells layers, however, it could be also connected with the function of the inner nuclear layer.

2) The base-value and the dark trough of the standing potential depend on the outer layers of the retina.

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