# THE ELECTRORETINOGRAM IN CHRONIC METHYL ALCOHOL POISONING IN HUMAN BEINGS

BY *A. D. Ruedemann, Jr.*, M.D.

THE PURPOSE OF THIS INVESTIGATION was to determine whether methanol poisoning produces changes in the electroretinogram which follow a consistent pattern and are of diagnostic significance.

The electroretinogram (ERG) is a graphic tracing of a mass response from the retina upon stimulation by light. The electroretinogram is of value in studying diseases of the retina and can be used as an objective measurement of retinal function. Reproducible results can be obtained using the same electroretinographic technique.

From what is known of the ERG, ganglion cells and optic nerve fibers do not contribute measurably to the response[1,2]; therefore a disease involving only those parts of the retina should be compatible with a normal ERG. Methanol poisoning is believed to be such a disease. It would follow that any changes consistently noted in the ERG in methanol poisoning are the result of pathologic changes to other parts of the retina.

The study served the additional purpose of evaluating the clinical ERG techniques to be described on a group of patients where ERG changes, if present, would be expected to be subtle.

## REVIEW OF THE LITERATURE

### THE ELECTRORETINOGRAM

It is not the purpose of this paper to review the development of knowledge concerning the parts of the ERG. Suffice it to say that from the past works of Granit,[3,4] Karpe,[5] Riggs,[6,7,8] Armington,[9,10,11] Noell,[12,13] Brown,[2] and many others there is excellent evidence that the ERG is made up of various components. These parts are engendered by changes in potential taking place in the outer layers of the

retina. From our present information the ERG may be analyzed as follows.

(1) a-WAVE (CORNEAL NEGATIVE POTENTIAL). With few exceptions investigators agree that the a-wave originates in the outermost retinal cells and depends upon the integrity of the outer region of the visual cell.[2,12] For instance, Dowling[14] has shown that in vitamin A deficiency, there is a loss of a-wave in relation to the degeneration of the outer limbs of the retina. When the total visual cell degenerates the remainder of the ERG disappears as well. Potts, *et al.*,[15] described the specific effect of sodium-l-glutamate on ganglion cells in suckling mice. The drug causes degeneration of the bipolar layer also, leaving the receptor cells intact. The ERG obtained from these animals was essentially a negative or a-wave ERG with no b-wave.

(2) b-WAVE (CORNEAL POSITIVE POTENTIAL). The b-wave depends upon the integrity of the bipolar and the visual cells.[2,12] Its smooth portion is thought to be related to scotopic activity. The "humps" on the rising b-wave are believed to represent activity from intraretinal pathways because they disappear in deep anesthesia.[16]

(3) FLICKER RESPONSE. This relates to photopic activity and measures the ability of the external retinal layers to respond to a high frequency of stimuli.[17,18,19,20,21,22,23,24]

(4) RETINAL RESPONSE. This response to red-, green-, and blue-colored light in some way indicates visual cell activity, possibly in the central retinal area.[25,26,27,28]

## THE ERG IN ACUTE METHANOL POISONING

There are several references to the eletroretinogram in acute methanol poisoning. Karpe,[29] in the discussion of another paper, noted several cases of acute methanol poisoning. In one case he observed an increased a-wave and reduced b-wave. Seven weeks later, with improvement of visual acuity; the a-wave was gone and the b-wave was normal. Five months later, with optic atrophy and diminished visual acuity, the ERG was "subnormal." He mentioned another case examined during the acute stages in which the ERG was of the negative type. This effect was evident in the work of Potts, *et al.*, on ERG in primates.[30] In their investigation of six adult rhesus monkeys in the acute stages of methyl alcohol poisoning, the authors noted a marked reduction of the b-wave and an increase in the a-wave. Histologically the only consistent finding was a cystoid degeneration of the external nuclear layer. (The authors questioned post-mortem autolysis.)

### CLINICAL, BIOCHEMICAL, AND PATHOLOGICAL ASPECTS OF METHANOL POISONING

CLINICAL. After a variable methanol imbibition, intoxication is frequently followed by visual loss. Vision is markedly reduced, the visual fields indicate loss of central vision, and there is visible retinal and papillary edema in the early stages. The late picture is generally one of damaged vision and ophthalmoscopically visible optic atrophy (Appendix 1).

PATHOLOGY. The pathology is not clear-cut, especially with reference to the rods and cones. However, there is clinico-pathologic evidence of disseminated change in the ganglion cells of the retina and brain (Appendix 2).

BIOCHEMISTRY. The biochemical changes have been studied at great length but the actual processes by which methanol damages body metabolism are not clearly indicated. The consensus seems to be that methanol or its breakdown products affects carbohydrate metabolism (Appendix 3).

## THE ELECTRORETINOGRAM

### GENERAL DESCRIPTION[31,32]

In this laboratory standard clinical electroretinography is performed by placing a contact lens with a corneal electrode on each eye of the patient, a second electrode for each eye on the midbrow area (there is less brow muscle activity there), and a third electrode on the forehead. The third electrode connects to a ground. These electrodes lead to a standard A.C. amplifier for each eye and then to a cathode ray oscilloscope. The oscilloscope sweep is synchronized with the flash of a Grass photic stimulator so that both flash and sweep are triggered simultaneously.

The light flash thus striking the retina creates a mass response of the retina which in turn creates a difference of potential between the corneal electrode and the brow electrode. The potential is noted as a complex wave response on the oscilloscope. In the conventional recording a change in potential which goes below the baseline is corneal negative (a-wave); a change in potential which goes above the baseline is corneal positive (b-wave).

### CONTACT LENS—CORNEAL ELECTRODE

The contact lens-corneal electrode (Figure 1) used is a modification of the original design by Riggs.[7] The optimum size of lens and electrode was determined by repetitive testing of normal individuals. Tears

are utilized as conducting fluid. The external portion of the electrode is insulated so as to prevent leakage of current to surrounding tissues. The electrode is placed on the limbus. Its position is constant during testing. The contact lens utilized is a standard molded scleral lens* of various sizes, for right and left eye, allowing maximum comfort and minimum lid action over short periods. The electrode is connected to the headband by a disconnect wire.

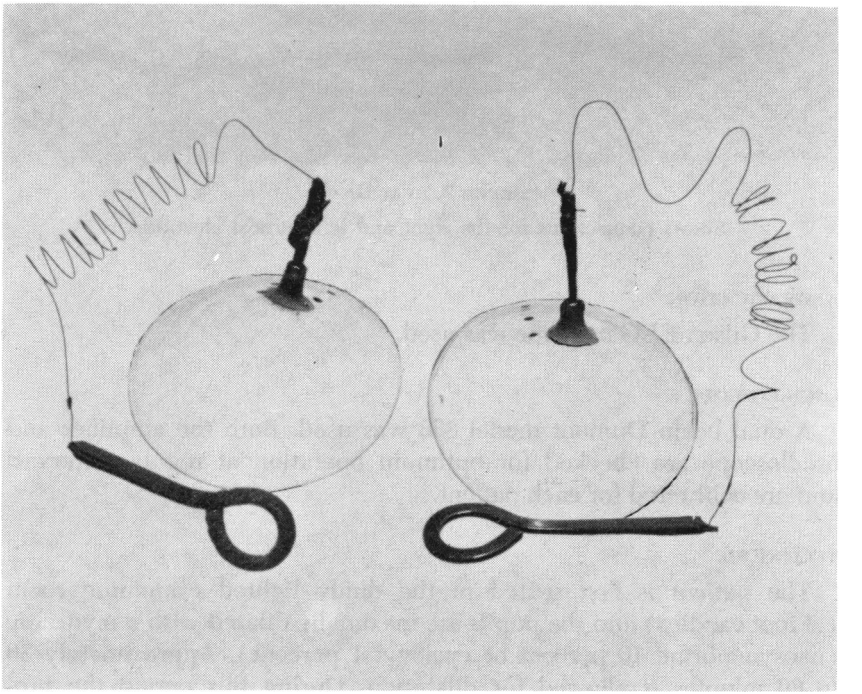


FIGURE 1. CONTACT LENS—CORNEAL ELECTRODE.

Right and left lens, molded scleral shell with connecting wires to headband.

HEADBAND

Figure 2 is a photograph of the headband. It was developed to allow minimal brow activity and low resistance between electrode and skin and optimum placement of wires in the vicinity of the eyes. The various leads from the headband are connected to a junction box which is then connected to the amplifiers.

*Jardon Laboratory, Detroit, Michigan.

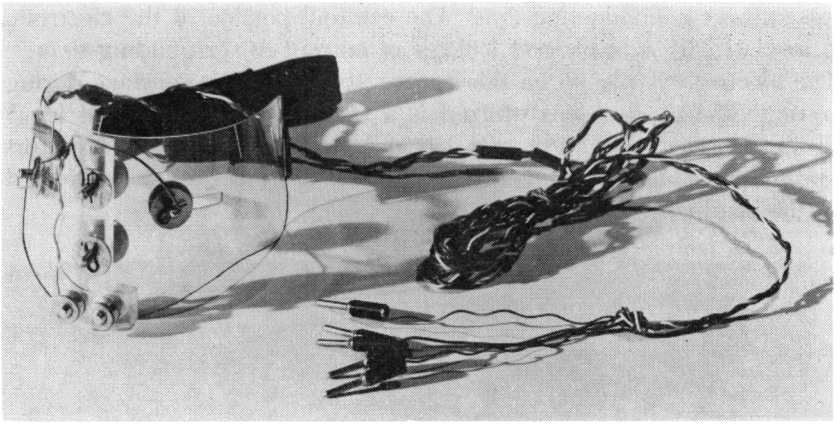


FIGURE 2. HEADBAND.
Shows connections for the right and left corneal electrode.

AMPLIFICATION

The Gilson EEG machine was used.

OSCILLOSCOPE

A dual beam Dumont model 333 was used. Both the amplifier and oscilloscope are checked for optimum operation at regular intervals and are calibrated for each patient.

TECHNIQUE

The patient is first seated in the dimly lighted examining room (.4 foot candles) and the pupils are maximally dilated with a mydriatic (neosynephrine 10 percent or cyclogyl 1 percent). Approximately 30 to 60 minutes is allowed for dilatation. During this period the procedure is explained and the patient becomes adjusted to his or her environment. When the pupils do not contract to an intermittent strong light, a local anesthetic is placed in each cul de sac and the contact lenses are inserted.

The headband (Figures 2 and 3) is then placed on the forehead, care being taken to coat the forehead properly with electrode paste. This is necessary since both the ground and indifferent electrodes are placed on the forehead as a part of the headband. All this time the patient has been comfortably seated in an easy chair.

A standard Grass photic stimulator is then placed at eye level one meter from the patient's head. A red fixation light has been constructed

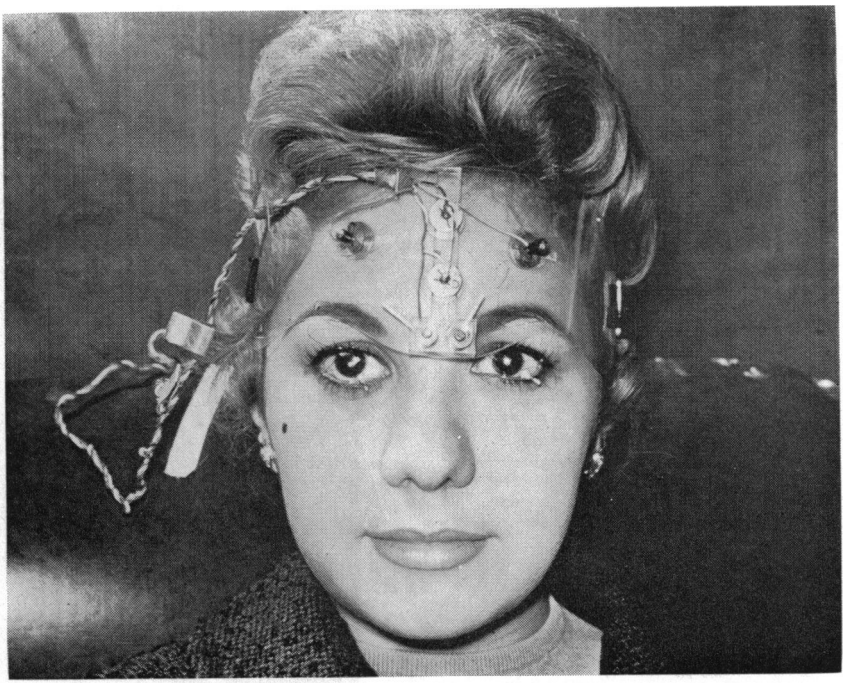


FIGURE 3. HEADBAND AND LENSES IN PLACE.

The corneal electrode may be either in the temporal or nasal palpebral fissure.

within the reflector of the stimulator. The patient is instructed to observe the fixation light at all times. If his vision is very low he is instructed to look straight ahead. (The examiner watches for this as well as to make sure that the patient keeps his eyes open.) A cathode ray oscilloscope which sweeps in synchronism with the photic stimulus records the potentials after suitable amplification. The standard sweep speed is 50 milliseconds per inch. For better resolution faster sweep speeds (10 and 25 milliseconds/inch) are used. Photographs are taken of each response or of several superimposed, utilizing Polaroid film and the camera adapted by Fairchild for the oscilloscope. Both eyes are tested simultaneously.

STIMULUS PARAMETERS

A standard Grass photic stimulator (Model #PSI) has been used since the inception of testing in this laboratory. Each patient is tested according to a routine, standard for this laboratory at the time of the test (Figure 4). The routine has remained essentially the same

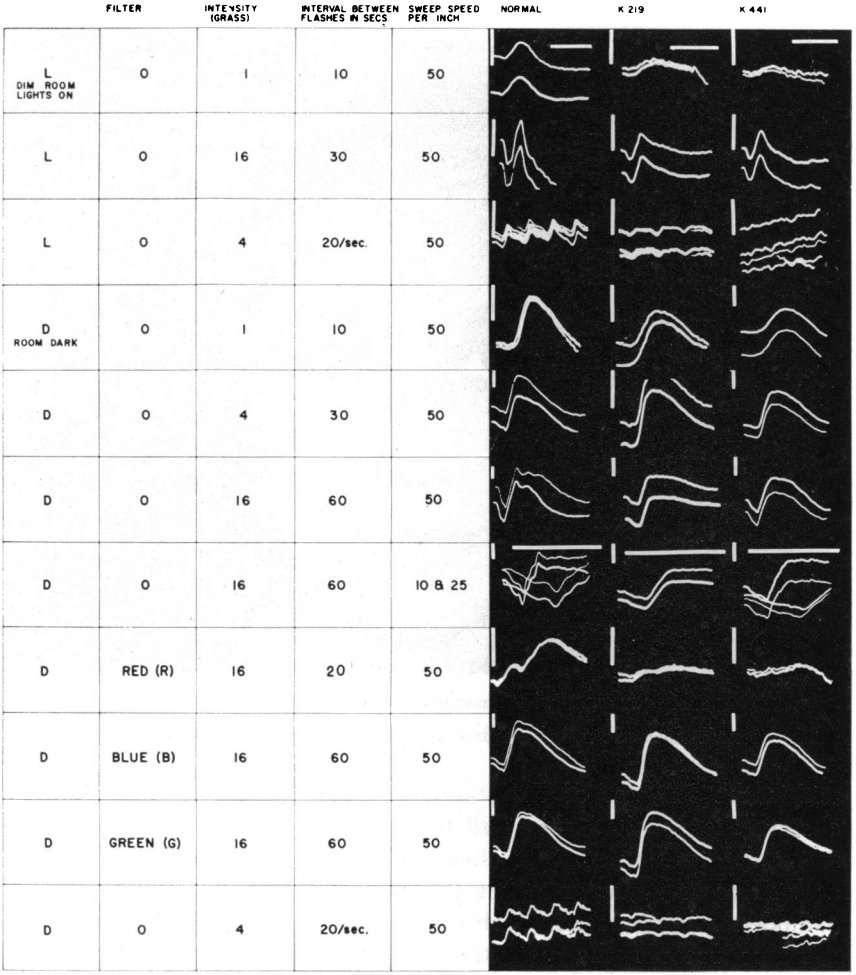



FIGURE 4. THE STANDARD TEST PROCEDURE.

Filter and intensity settings refer to the Grass photic stimulator.

over the years except for additional stimuli which have been added to gain further information. Time allowed for the test is minimized to maintain patient comfort and attention.

### SEQUENCE OF STIMULATION

In the standard procedure for this series 10 different stimuli are used at three flash intensities (1, 4, 16) as provided by the Grass

stimulator. These are given in a definite sequence and with fixed time intervals. Three different stimuli are given in a room illumination of approximately .4 foot candles. The remainder of the procedure is performed without room illumination. The first stimulus is presented after five minutes dark adaptation. Color filters (red, blue, green) are used with maximum stimulus intensity. The two flicker responses (light and dark) are elicited at intensity setting 4, at a frequency of 20 per second.

The whole test is illustrated in Figure 4.

NOMENCLATURE

The term ERG as used in this study denotes the electrical response recorded from the cornea over a period of approximately 200 milliseconds following a light flash. Its main components (Figure 5) are the a- and b-waves which vary in appearance in accordance with stimulus parameters.

The a-wave denotes the early cornea negative phase of the response. In the normal subject it is evident only with strong stimulus intensity and good resolution, as shown by records with fast sweep speeds (10

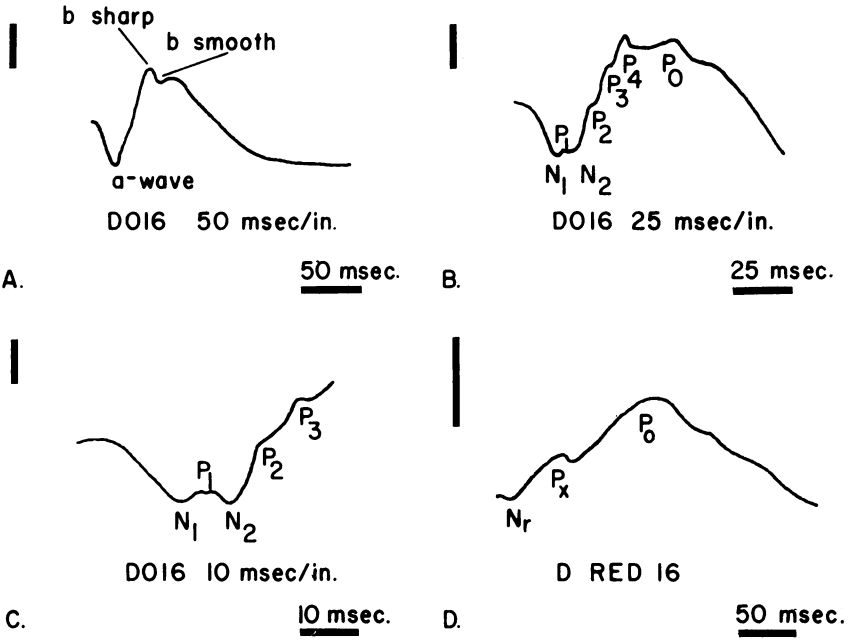



FIGURE 5. NOMENCLATURE

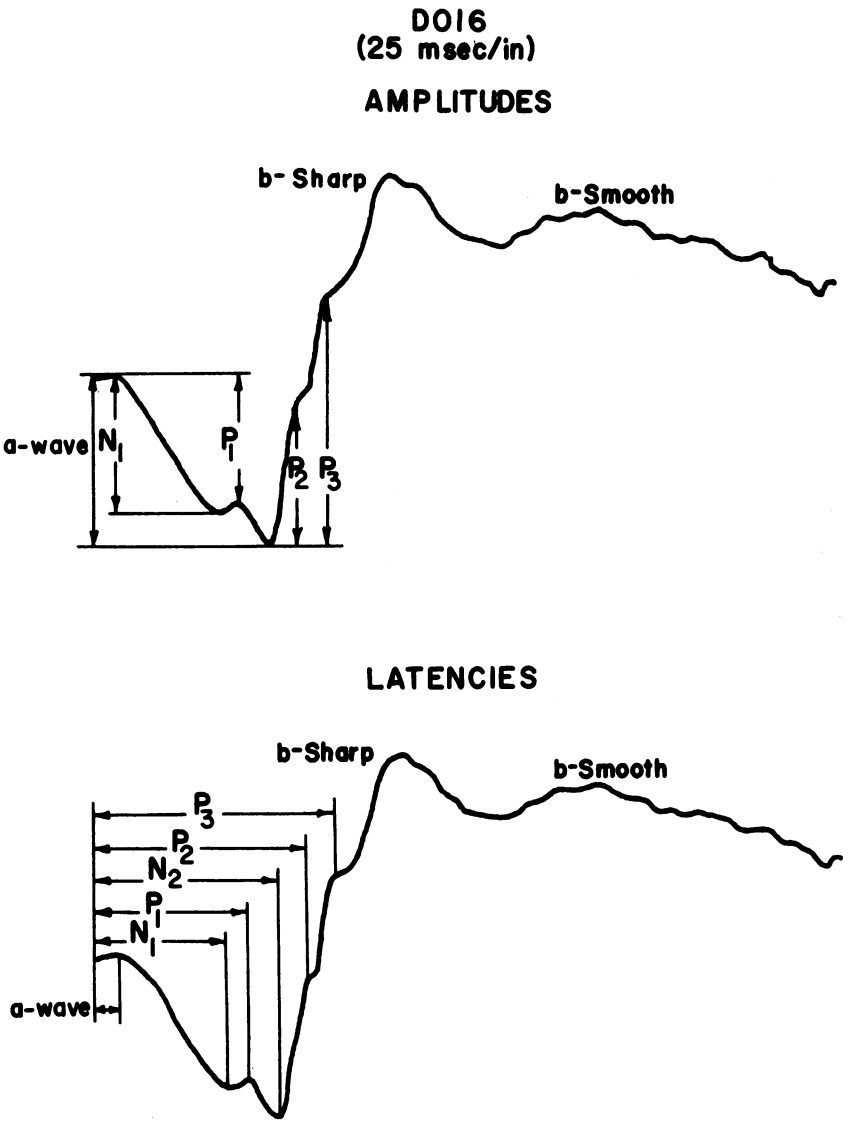



FIGURE 6. METHOD OF MEASUREMENT FOR LATENCIES, PEAK TIMES, AND AMPLITUDES.

and 25 milliseconds/inch), the a-wave from maximal stimulus has two "negative" peaks designated $n_1$ and $n_2$. Interposed is a small "positive hump" called $p_1$. The b-wave denotes the cornea positive phase of the response. It is evident for all stimuli but varies in ampli-

tude and form according to the intensity of the stimulus, the color, and the retinal adaptation. For strong intensity stimuli, one can distinguish a sharp ($p_4$) and a smooth peak ($p_0$). A series of "humps" are noted on the rising phase of the b-wave with good resolution of the record. The sharp peak of the b-wave is the last of these "humps." These "humps" are denoted $p_2$, $p_3$, and $p_4$ (b-sharp).

The ERG has a particular form in response to red light stimulus. A small a-wave is followed by a b-wave consisting of two parts, an early peak ($p_x$) and a late peak ($p_0$). The early part corresponds to the x-wave ordinarily described in the literature and usually ascribed to cone activity. This peak is missing in protanopes and monochromats. The late peak is missing in congenital stationary night blindness.

### MEASUREMENTS OF AMPLITUDES AND LATENCIES

Each component of each stimulus response (Figure 6) is measured by ruler and recorded on special procedure forms (enclosure). Amplitudes are recorded in microvolts; latencies and peak times are recorded in milliseconds.

### NORMAL CASES

The electroretinographic data refer to normal cases. From the inception of testing, under standard conditions, it was found that repetitive stimuli, at the same examination or at different examination times, generally gave similar results. Age, sex, and race appear to have no substantial effect on our ERGs. It was also found that the two eyes of a normal patient have essentially similar ERGs. The electroretinographic data from one eye of 55 patients with normal eye examinations have been utilized to establish a mean and standard deviation of what will be hereafter designated as the normal group.

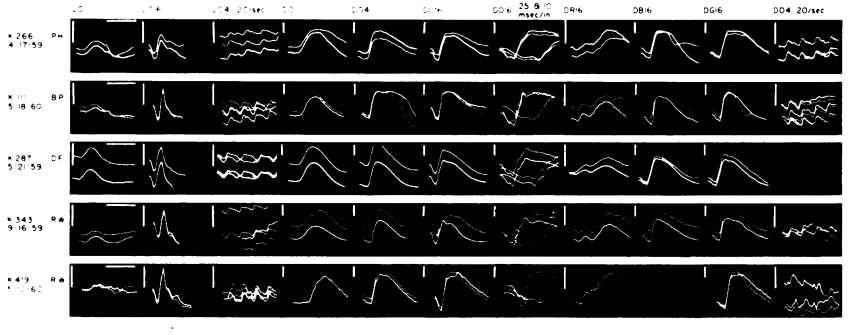


FIGURE 7. SERIES OF NORMAL ERGS (RANDOM SELECTION).

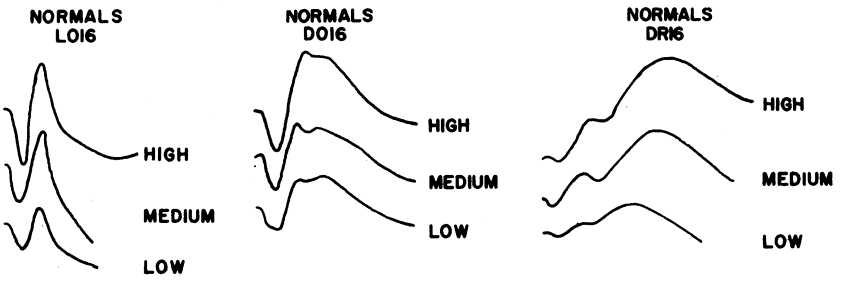



FIGURE 8. SUPERIMPOSED TRACINGS FOR LOW, MEDIUM, AND HIGH NORMAL RANGE FOR LO16, DO16, DR16.

A series of ERGs, selected at random from the normal series, are included in Figure 7. The similarity in recordings taken from these normal individuals is readily discernible. In Figure 8 superimposed tracings from the low, medium and high normal range of three different standard stimuli (LO16, DO16, DR16) are included to point out the variation in the normal response.

## CLINICAL MATERIAL ON WHICH PRESENT STUDY IS BASED

The study includes 14 patients. Pertinent clinical data are listed in Table 1. Many of these patients were chronic users of methanol and had severe visual loss for from several days to seven years prior to admission.[33,34] The 14 patients studied were tested after hospitalization for several days. No case was evaluated by ERG before, or on admission. All were admitted with the chief complaint of severe visual loss. In no case was accurate estimation of symptoms available, or was any accurate estimation of intake obtained.

In the majority of the cases, the patient had visual symptoms which varied from spots before the eyes, to misty vision, to no light perception, in one or both eyes. Several of the patients showed some improvement in vision for a short period but the vision gradually diminished to rather low levels. Practically every patient had diminished pupillary response to light. This characteristic finding is notable even in the more acute cases.

Ophthalmoscopically, practically all of the patients demonstrated temporal pallor or optic atrophy. In the more acute phases there was edema of the retina with hyperemia of the disc and choroid. The retinal arteries appeared angiospastic and often there was venous dilatation. Edema of the macular area with loss of the foveal reflex was also observed.

The visual fields in those cases which could be tested indicated poor central fixation. In some of the late cases the visual field was reduced to 5 degrees from fixation. However, fixation was so poor as to preclude accurate testing. In one case (J. L., K75) there is a marked difference in the visual acuity of the right and left eyes (right eye–count fingers 6 feet, left eye–20/20–3). The ERG indicated this difference in that the right eye had smaller amplitude than the left. Visual fields performed at a later date confirmed the ERG findings.

All of the cases were treated with alkali (nabicarbonate or lactate, B12, high vitamin intake, high fluid intake, rest, steroids, and other adjuvant means. Alcohol therepy was instituted in two cases. It was stopped in one case because of acute exacerbation of delirium tremens (J.L., K75).

### ELECTRORETINOGRAPHIC RESULTS

The ERG tracings obtained from the patients in this series of cases are all assembled in Figures 9, 10, 11, 12. The original tracings were used to measure peak times, amplitudes, and latencies as described in the section on the ERG. The measurements are all listed in Tables 2B–10B of Appendix 4.

A mean and standard deviation for both normal and methyl alcohol groups has been calculated for each type of stimulus listed in each table (see Tables 2A–10A). The significance of the difference between the means of the normal group and the group affected by methyl alcohol was evaluated by the t-test for each type of stimulus. The P-values corresponding to the computed t's are given in Table 11.

### ANALYSIS OF ERG RESULTS

Results for each stimulus will be discussed according to the sequence presented in Figure 5. The 14 patients suffering from methyl alcohol poisoning are first considered as one group and subsequently some individual cases are discussed.

LO1 (Column 1,* Figures 9, 10, 11, 12). The normal response to this stimulus consists of a b-wave of low amplitude.

*Latency.* The mean b-wave latency of the methyl alcohol group is not significantly increased ($P = .15$). The a-wave latency is not included because it is so difficult to measure.

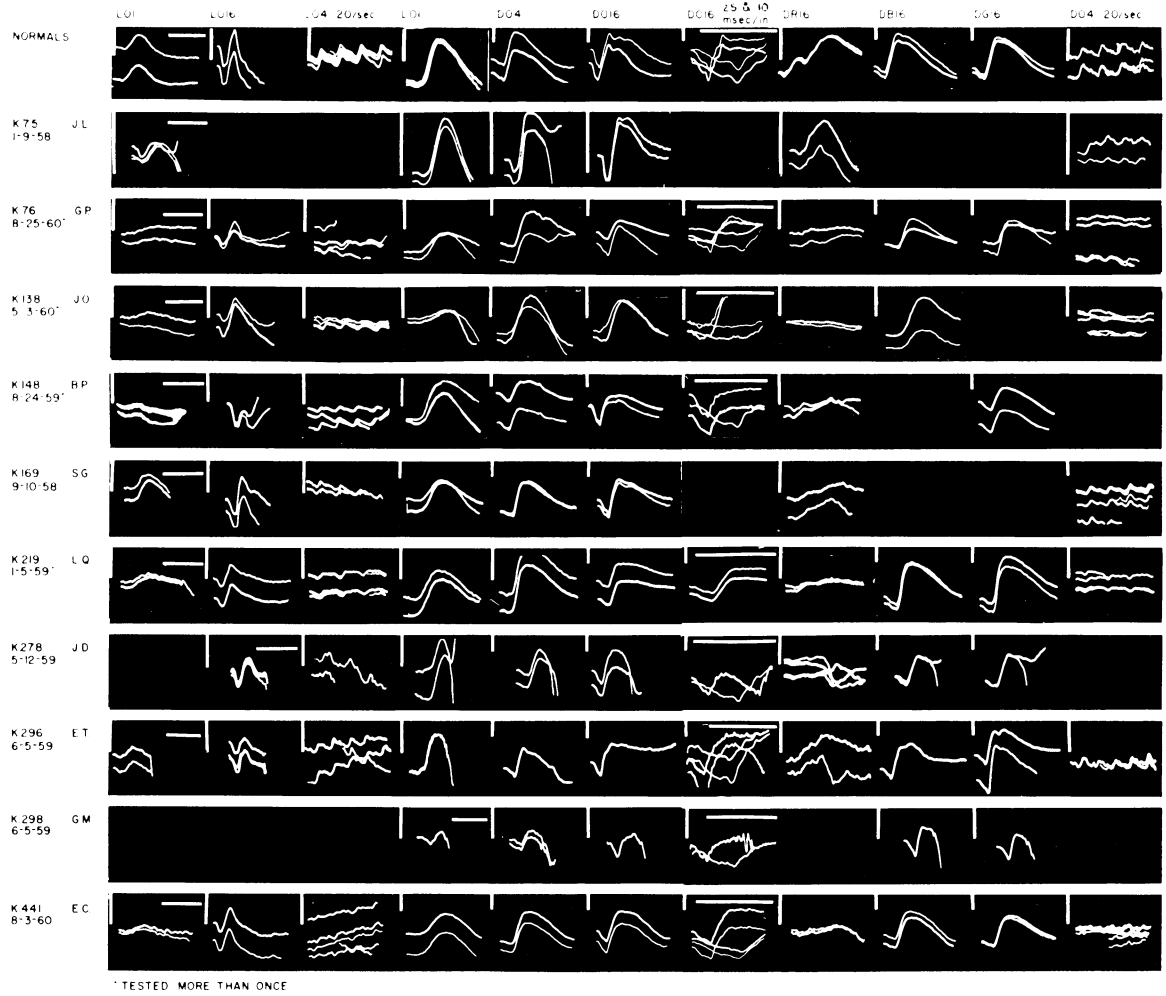
*The horizontal white bar in this column represents 50 milliseconds. The vertical white bar signifies 200 microvolts. For each column with a higher intensity stimulus the 200 microvolt bar may have different lengths depending upon the factor required at the oscilloscope to get the entire tracing on the screen.

TABLE 1. SYNOPSIS OF CLINICAL OBSERVATIONS

| *Patient* | | *Duration of ingestion* | *Amount ingested* | *Initial visual acuity* | *Duration of visual symptoms on admission* | *ERG first performed (number of days after visual symptoms began)* | *Ophth. notes* | *Progress* |
|---|---|---|---|---|---|---|---|---|
| J.G. 34 | K74 C.M. | Several days | Unknown | H.M. only | 9 days | 30 days ± | Optic atrophy, O.U. | No visual improvement |
| J.L. 43 | K75 C.M. | 4 mos. | 1 can Sterno per day | VRE 20/30 VLE 20/30 | Several days | 34 days ± | Temporal pallor, R.E. | No visual improvement |
| G.P. 39 | K76 C.M. | 2 mos. | ½ can Sterno per day | H.M. only | 2 days | 41 days ± | Optic atrophy, O.U. | No visual improvement |
| J.O. 41 | K138 C.M. | On and off for years | Unknown | C.F., O.U. | Several weeks | Nearly 4 years | Atrophy already present, O.U. | No visual improvement |
| B.P. 40 | K148 C.M. | 5/1/58 to 5/3/58 | Unknown | VRE H.M. VLE N.L.P. | Several days | 16 days ± | Optic atrophy, O.U. | No visual improvement |
| S.G. 46 | K169 C.M. | 34 days and prior occasions | 4–5 cans Sterno per day | C.F. only | Several days | 7–10 days ± | Discs had temporal pallor on admission | No visual improvement |
| L.Q. 36 | K219 C.F. | 10 days | 1 pt. daily Gin, Sterno, wine | C.F. only | 5 days | 12 days ± | Retinal and papillary edema, O.U. | Optic atrophy V.A. was ?L.P. in April 1960 |

TABLE 1.—*(cont.)*

| *Patient* | | *Duration of ingestion* | *Amount ingested* | *Initial visual acuity* | *Duration of visual symptoms on admission* | *ERG first performed (number of days after visual symptoms began)* | *Ophth. notes* | *Progress* |
|---|---|---|---|---|---|---|---|---|
| J.D. 44 | K278 W.M. | 4 days | 7–10 cans Sterno per day | C.F., O.U. | 4 days | 12 days ± | Optic nerve pallor, O.U. | No visual improvement |
| E.T. 35 | K296 C.F. | 1 year | Unknown, at least 10 cans in past 5 days | VRE 10/80<br>VLE 10/100 | At least 2 days | 7 days ± | Retinal and papillary edema, O.U. | No visual improvement |
| G.M. 50 | K298 C.M. | 6 mos. on and off | Unknown | VRE 20/50<br>VLE 20/100 | 1–2 weeks | 14 days ± | Venous congestion and retinal edema, O.U. | No visual improvement |
| E.C. 47 | K441 C.F. | 1 year | Unknown | C.F. only | 3 days and 1 year ago | 9 days ± | 1 year previous loss of vision. Temporal pallor, O.U. | No visual improvement |
| G.V. 41 | K478 C.M. | Unknown | Unknown | VRE 20/100<br>VLE C.F.2′ | 3 weeks | 23 days ± | Temporal pallor, O.U. | No visual improvement |
| C.B. 63 | K480 W.M. | Up to 3 days prior to admission | Unknown | ?L.P., O.U. | 3 days | 20 days ± | Temporal pallor, O.U. No macular reflex | No visual improvement |
| W.W. 43 | K481 C.M. | Unknown | Unknown | VRE 20/200<br>VLE 20/200 | 7 years | 7 years ± | Optic atrophy, O.U. | No visual improvement |




* TESTED MORE THAN ONCE

TABLE 2A. a-WAVE LATENCY IN MILLISECONDS

| | *Number of eyes tested* | *Mean* | *Standard deviation* | *Standard error of mean* |
|---|---|---|---|---|
| DO16 (fast sweep speed) | | | | |
| Normal | 51 | 4.2 | .1 | .01 |
| Alcohol | 27 | 5.0 | 1.8 | .36 |

*b-wave peak time* (smooth). There is no sharp peak for the b-wave (a-wave peak time is not measured for this stimulus). The b-wave peak time of the methyl alcohol group is significantly delayed in this series ($P = <.01$).

*Amplitude.* a-wave: The mean a-wave amplitude is almost halved in the methyl alcohol group ($P = <.01$). b-wave (smooth): Qualitative observation of the tracings suffices to reveal that b-wave amplitude is reduced ($P = <.01$).

LO16 (Column 2, Figures 9, 11, 12). Characteristically, this response consists of a sharp downsweep with a slight hook at the bottom (a-wave) followed by a steeply rising b-wave with a sharp peak.

*Latency.* The a-wave latency is not measurable but b-wave ($n_2$) latency is significantly increased ($P = .02$).

*b-wave peak time* (sharp). From the figures (9-12) one may note that there is no smooth peak for LO16. The time to the peak of the b-wave is significantly increased, ($P = <.01$).

*Amplitude.* a-wave amplitude is substantially reduced ($P = <.01$); b-wave amplitude is about ⅔ normal ($P = <.01$). The peaks of both a- and b-waves are rounded.

LO4, 20/second (Column 3, Figures 9, 11, 12). The normal flicker has a sawtooth appearance. Because of the difficulty in taking accurate measurements from the tracing of this stimulus only b-wave amplitude is measured. Observation of the ERG tracings and the data (Tables 8A, 8B, and 11) reveal that the mean of the b-wave amplitude of the experimental group is about half that of the controls ($P = <.01$).

FIGURE 9. PHOTOGRAPHIC SUMMARY OF ERG TRACINGS FOR 10 PATIENTS WITH METHANOL POISONING.

The top row consists of a normal tracing for each part of the procedure. The normal tracing has been selected from the mid-range of the normal group. On each tracing is a vertical white stripe which signifies 200 microvolts. On one tracing for each case is a horizontal white stripe signifying 50 milliseconds. The measurable tracings for each part of the procedure for each case has been included. Blank spaces signify that the stimulus was not included in the procedure or the tracing was not adequate for accurate measurement.

TABLE 3A. b-WAVE LATENCY ($n_2$) IN MILLISECONDS

| | *Number of eyes tested* | *Mean* | *Standard deviation* | *Standard error of mean* |
|---|---|---|---|---|
| LO1 | | | | |
| Normal | 45 | 22.8 | 2.1 | .31 |
| Alcohol | 24 | 24.7 | 8.6 | 1.78 |
| LO16 | | | | |
| Normal | 27 | 21.9 | 2.0 | .34 |
| Alcohol | 22 | 23.4 | 2.7 | .60 |
| DO1 | | | | |
| Normal | 50 | 39.5 | 3.9 | .51 |
| Alcohol | 27 | 40.6 | 11.0 | 2.16 |
| DO4 | | | | |
| Normal | 52 | 31.1 | 1.8 | .25 |
| Alcohol | 26 | 29.9 | 4.5 | .91 |
| DO16 | | | | |
| Normal | 51 | 25.8 | 2.3 | .32 |
| Alcohol | 25 | 28.4 | 3.9 | .79 |
| DR16 | | | | |
| Normal | 45 | 25.8 | 2.3 | .34 |
| Alcohol | 25 | 27.5 | 4.8 | .97 |
| DB16 | | | | |
| Normal | 23 | 30.7 | 1.8 | .38 |
| Alcohol | 19 | 35.2 | 5.5 | 1.34 |
| DG16 | | | | |
| Normal | 23 | 32.0 | 1.6 | .34 |
| Alcohol | 20 | 35.3 | 5.5 | 1.27 |

The same statements can be made for DO4, 20/second (Column 11, Figures 9, 11, 12; Column 6, Figure 10) ($P = < .01$).

DO1 (Column 4, Figures 9, 11, 12; Column 2, Figure 10). This response usually consists of a shallow a-wave followed by a smoothly curving b-wave.

*Latency.* The time of onset for the a-wave cannot be measured accurately nor can the b-wave which possibly accounts for the lack of significance ($P = .30$). From Table 3A one notes that the standard deviation for the abnormal series is at least three times the value for the normals.

*b-wave peak time* (smooth) is somewhat delayed ($P = .04$).

*Amplitude.* In this series the a-wave is less than half normal ($P = < .01$); b-wave amplitude is reduced but less markedly ($P = < .01$).

DO4 (Column 5, Figures 9, 11, 12; Column 3, Figure 10). The increase in stimulus intensity brings out the a-wave and a sharp peak of the b-wave which is followed by a smooth peak on the downslope.

TABLE 4A. $n_1$ AND p LATENCIES, DO16, 25 MILLISECONDS/INCH

| | *Number of eyes tested* | *Mean* | *Standard deviation* | *Standard error of mean* |
|---|---|---|---|---|
| $n_1$ | | | | |
| Normal | 29 | 17.4 | 2.0 | .38 |
| Alcohol | 20 | 17.1 | 3.2 | .72 |
| $p_1$ | | | | |
| Normal | 29 | 21.5 | 2.0 | .38 |
| Alcohol | 19 | 20.6 | 4.2 | 1.34 |
| $p_2$ | | | | |
| Normal | 27 | 31.6 | 3.0 | .59 |
| Alcohol | 18 | 34.0 | 8.5 | 2.13 |
| $p_3$ | | | | |
| Normal | 28 | 36.9 | 3.0 | .58 |
| Alcohol | 18 | 41.8 | 9.7 | 2.42 |

*Latency.* Again, a-wave latency cannot be measured accurately from the tracing.

*b-wave peak time* (sharp). The first peak on the rising slope of the b-wave is called b-sharp and it is most accurately measured. DO4 and DO16 b-waves are rounded in many cases so that b-sharp peak time was only measured in 10 eyes of 28 tested. The peak time would appear significantly increased ($P = <.01$) in the 10 eyes which had a b (sharp).

*b-wave peak time* (smooth). The mean values are very close (67.1 vs. 70.3) ($P = .15$) indicating a similarity in peak times of the normal and abnormal cases. One can see from the tracings, however, that this is a difficult time to ascertain, especially in the abnormal records.

*Amplitude, a-wave.* The amplitude is reduced below the normal range in 16 out of 25 eyes tested ($P = <.01$).

*Amplitude, b-wave (sharp).* This value was significantly reduced ($P = .02$) in the eight eyes in which it could be measured. However b-sharp is typically rounded off for both DO4 and DO16 in these abnormal cases.

*Amplitude, b-wave (smooth).* This response was significantly reduced from the normals in the methanol poisoning series ($P = <.01$).


FIGURE 10. K74.

This case was not included in Figure 7 because it was recorded utilizing a fast sweep speed which is not comparable to the other records visually.

TABLE 5A. b-WAVE PEAK TIME (SHARP) IN MILLISECONDS

| | *Number of eyes tested* | *Mean* | *Standard deviation* | *Standard error of mean* |
|---|---|---|---|---|
| LO16 | | | | |
| Normal | 27 | 42.0 | 3.1 | .62 |
| Alcohol | 22 | 45.5 | 4.5 | .98 |
| DO4 | | | | |
| Normal | 26 | 53.0 | 5.3 | 1.06 |
| Alcohol | 10 | 62.9 | 7.3 | 2.43 |
| DO16 | | | | |
| Normal | 49 | 51.0 | 5.5 | .79 |
| Alcohol | 15 | 58.9 | 5.7 | 1.57 |
| DR16 | | | | |
| Normal | 49 | 50.0 | 5.5 | .79 |
| Alcohol | 24 | 56.0 | 11.0 | 2.30 |

DO16 (Columns 6 and 7, Figures 9, 11, 12; Column 4, Figure 10). The normal response to this stimulus at standard sweep speed (50 milliseconds per inch) consists of a sharp a-wave peak with a short jog just before the apex, and a sharp and smooth b-wave peak. When fast sweep speeds are used (10 and 25 milliseconds per inch) additional details of both the a-wave ($n_1$, $p_1$) and the b-wave ($p_2$, $p_3$) are noted.

*Latency and peak times.* The mean a-wave latency is slowed ($P = <.05$) as is b-wave ($n_2$) latency ($P = <.01$). The mean latencies for $n_1$, $p_1$, $p_2$ are not significantly slowed. This may mean that the latency values obtained in the methanol poisoned series are similar to the normal and there is a possible slowing of the response between $p_3$ and $p_4$ (b-wave peak time (sharp)). Such a conclusion would be borne out by the similarity of the mean values to the normal range (Table 4a) and the significant difference from the normal values noted for $n_2$ ($P = <.01$), $p_3$ ($P = <.05$) and $p_4$ $P = <.01$). However, the mean values for b-wave peak time (smooth) are not significantly different. This would indicate that the response time is within the normal range at this point and there has been a slowing of the response from $p_2$ to $p_4$.

Close scrutiny of the tracings does not permit a final conclusion on this basis. The reduction in amplitudes for all parts of the abnormal tracings prevents accurate measurement of $n_1$, $p_1$, $p_2$, $p_3$, and b-wave peak time (smooth) while the sharper break in the curve allows more exact measurement of $n_1$ and $p_4$ (when measurable). This would tend to be borne out by comparison of the standard deviations of the mean values in Tables 4A, 5A, 6A. This difficulty is also noted for LO1 and DO1 which are usually rounded in the abnormal series. (The portion of the variability which is attributable to variation in the interpretation of the records is subject to further investigation. This will be done by having records reread by several observers.)

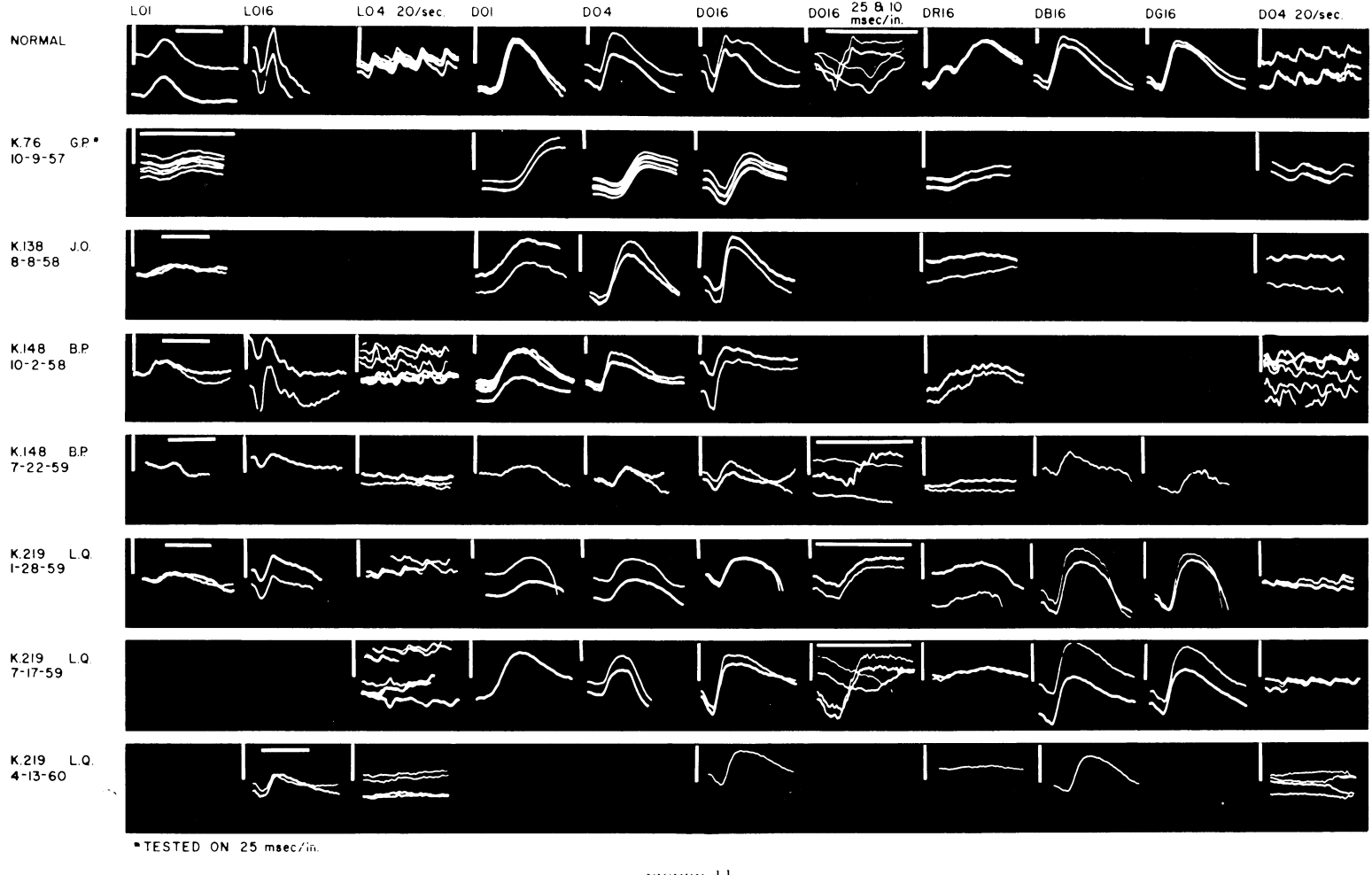



FIGURE 11.

The tracings for each case which was retested are included in this figure.

TABLE 6A. b-WAVE PEAK TIME (SMOOTH) IN MILLISECONDS

| | *Number of eyes tested* | *Mean* | *Standard deviation* | *Standard error of mean* |
|---|---|---|---|---|
| LO1 | | | | |
| Normal | 51 | 55.6 | 5.1 | .71 |
| Alcohol | 24 | 64.2 | 11.8 | 2.46 |
| DO1 | | | | |
| Normal | 51 | 81.1 | 10.1 | 1.41 |
| Alcohol | 25 | 87.5 | 16.1 | 3.30 |
| DO4 | | | | |
| Normal | 52 | 67.1 | 9.9 | 1.37 |
| Alcohol | 25 | 70.3 | 13.7 | 2.80 |
| DO16 | | | | |
| Normal | 52 | 70.7 | 9.1 | 1.26 |
| Alcohol | 26 | 69.5 | 16.6 | 3.31 |
| DR16 | | | | |
| Normal | 44 | 113.6 | 23.8 | 3.59 |
| Alcohol | 21 | 105.7 | 32.7 | 7.31 |
| DB16 | | | | |
| Normal | 23 | 67.8 | 8.8 | 1.88 |
| Alcohol | 19 | 77.1 | 17.1 | 4.02 |
| DG16 | | | | |
| Normal | 23 | 68.8 | 7.9 | 1.68 |
| Alcohol | 20 | 75.5 | 19.3 | 4.43 |

*Amplitudes.* The mean a-wave and b-wave amplitudes in the methyl alcohol series are significantly reduced from the normal mean for all portions of the a- and b-waves ($P = <.01$). The b/a ratio in the normal group was 2.2. In the abnormal group the b/a ratio was 2.6. This indicates that the reduction of the a-wave exceeded that of the b-wave.

DR16 (Column 8, Figures 9, 11, 12; Column 5, Figure 10). The normal response to red light consists of a shallow a-wave ($n_r$) followed by a small corneal positive "hump" ($p_x$) followed by a larger corneal "hump" ($p_o$).

*Latency.* The a-wave latency cannot be accurately measured in the abnormal records. However b-wave ($n_2$) latency ($P = <.05$), b-wave peak time ($p_x$) and b-wave peak time ($p_o$) are significantly slowed from the normal mean ($P = <.01$).

*Amplitude.* The mean amplitudes for a-wave and b-wave ($p_x$ and $p_o$) in the methanol group are significantly reduced from the normal means ($P = <.01$).

DB16 (Column 9, Figures 9, 11, 12). Typically, the response to blue light is similar to DO4. DG16 is also similar to DO4. For this reason both shall be considered together.

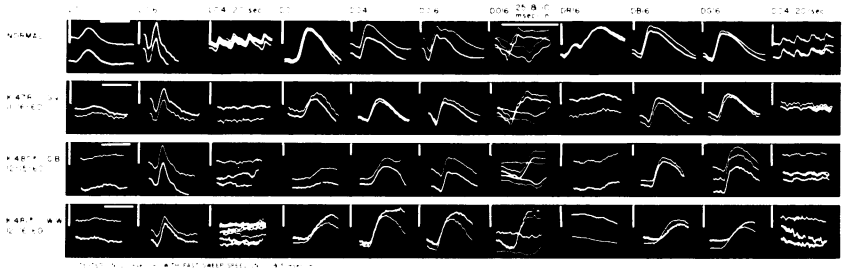


FIGURE 12.

The tracings of the last three cases are included in this figure. The last two cases were recorded utilizing portable equipment and are comparable with the other cases.

TABLE 7A. a-WAVE AMPLITUDES IN MICROVOLTS

| | *Number of eyes tested* | *Mean* | *Standard deviation* | *Standard error of mean* |
|---|---|---|---|---|
| LO1 | | | | |
| Normal | 49 | 17.0 | 6.5 | .93 |
| Alcohol | 24 | 10.7 | 8.2 | 1.71 |
| LO16 | | | | |
| Normal | 27 | 117.5 | 30.9 | 6.06 |
| Alcohol | 22 | 74.6 | 25.5 | 5.56 |
| DO1 | | | | |
| Normal | 38 | 23.6 | 8.6 | 1.40 |
| Alcohol | 25 | 10.8 | 12.8 | 2.61 |
| DO4 | | | | |
| Normal | 53 | 85.0 | 30.7 | .42 |
| Alcohol | 26 | 41.9 | 22.6 | 4.52 |
| DO16 | | | | |
| Normal | 54 | 218.0 | 50.5 | 6.87 |
| Alcohol | 24 | 136.5 | 57.0 | 11.89 |
| DR16 | | | | |
| Normal | 42 | 27.3 | 11.3 | 1.74 |
| Alcohol | 25 | 12.4 | 10.8 | 2.21 |
| DB16 | | | | |
| Normal | 23 | 124.0 | 40.9 | 8.72 |
| Alcohol | 19 | 49.2 | 11.9 | 2.80 |
| DG16 | | | | |
| Normal | 23 | 110.8 | 36.8 | 7.85 |
| Alcohol | 20 | 46.6 | 38.1 | 8.74 |

TABLE 8A. b-WAVE AMPLITUDES (SHARP) IN MICROVOLTS

| | *Number of eyes tested* | *Mean* | *Standard deviation* | *Standard error of mean* |
|---|---|---|---|---|
| LO16 | | | | |
| Normal | 27 | 223.0 | 61.4 | 12.04 |
| Alcohol | 22 | 170.0 | 45.5 | 9.93 |
| LO4, 20/second | | | | |
| Normal | 23 | 56.8 | 19.1 | 4.07 |
| Alcohol | 22 | 30.3 | 13.2 | 2.87 |
| DO4 | | | | |
| Normal | 26 | 422.0 | 89.7 | 17.94 |
| Alcohol | 8 | 367.4 | 50.9 | 19.23 |
| DO16 | | | | |
| Normal | 49 | 483.7 | 108.5 | 15.50 |
| Alcohol | 14 | 379.4 | 88.8 | 24.63 |
| DR16 | | | | |
| Normal | 51 | 79.0 | 23.5 | 3.29 |
| Alcohol | 26 | 45.1 | 24.5 | 4.90 |
| DO4, 20/second | | | | |
| Normal | 39 | 63.0 | 31.5 | 5.04 |
| Alcohol | 24 | 28.8 | 12.9 | 2.68 |

*Latency.* The b-wave latency is significantly slowed for both DB16 and DG16 ($P = <.01$). b-wave peak time (smooth) is also slowed as compared to the normal but the significance is not as marked ($P = < .05$). The standard deviations of both DB16 and DG16 series are much greater than for the normal series, indicating that in both responses b-wave (smooth) peak time may be difficult to measure (Table 6A).

*Amplitude.* Both a- and b-wave mean amplitudes are significantly reduced from the normal mean in this series ($P = <.01$).

SELECTED CASES

The ERG of several cases deserves separate comment.

J.L. (K75). The ERG performed on January 9, 1958, showed a weaker response of the right eye to both red and 20 per second flicker (Figure 9, Row 2, Columns 8 and 11; broad tracing left eye, thin tracing right eye). Visual fields performed on June 9, 1958, reveal a marked defect in the visual field of the right eye, while the visual field of the left eye appears normal. The visual acuity on that date was counts fingers at six feet right eye; 20/30–3, left eye. This patient has not been available for re-examination. (Tables 2B, 3B, 5B–9B.)

Four patients have been tested on more than one occasion.

TABLE 9A. b-WAVE AMPLITUDES (SMOOTH) IN MICROVOLTS

| | *Number of eyes tested* | *Mean* | *Standard deviation* | *Standard error of mean* |
|---|---|---|---|---|
| LO1 | | | | |
| Normal | 51 | 90.8 | 33.3 | 4.66 |
| Alcohol | 24 | 61.6 | 25.1 | 5.23 |
| DO1 | | | | |
| Normal | 51 | 368.3 | 83.5 | 11.64 |
| Alcohol | 25 | 230.0 | 75.8 | 15.47 |
| DO4 | | | | |
| Normal | 52 | 408.6 | 95.6 | 13.26 |
| Alcohol | 26 | 332.2 | 84.8 | 16.96 |
| DO16 | | | | |
| Normal | 54 | 477.6 | 101.5 | 13.81 |
| Alcohol | 25 | 353.2 | 88.6 | 18.08 |
| DR16 | | | | |
| Normal | 46 | 173.0 | 86.5 | 12.75 |
| Alcohol | 24 | 79.9 | 40.7 | 8.30 |
| DB16 | | | | |
| Normal | 23 | 441.4 | 104.2 | 22.22 |
| Alcohol | 18 | 304.7 | 118.7 | 28.80 |
| DG16 | | | | |
| Normal | 23 | 441.5 | 105.3 | 22.45 |
| Alcohol | 20 | 337.5 | 123.1 | 28.25 |

L.Q. (K219). This patient has been tested on four occasions: January 5, 1959 (Figure 9, Row 7), January 28 and July 17, 1959, and April 13, 1960 (Figure 11, Rows 6, 7, 8). The ERG was performed the first time when vision was at its lowest levels. By January 28, 1959, vision had improved to 20/400, right eye, and 20/25, left eye. The ERG had also improved. Re-examination on July 17, 1959, revealed ERG responses to be about the same as on the examination of January 28, 1959. By April 13, 1960, the ERG had shown marked reduction from the first visit and vision was down to ? light perception, right eye and left eye. There is some evidence that the patient is still using methanol.

B.P. (K148). When first seen this patient had only hand movements in the right eye; no light perception, left eye. Optic atrophy was present in both eyes. The ERG recordings are smaller from the left eye than the right eye throughout the test. On July 22, 1959, the patient was re-examined. Although the vision showed no change, the ERG showed marked reduction in all phases a little over one year after the original toxic episode. (Figure 9, Row 5; Figure 11, Row 4.)

TABLE 10A. AMPLITUDES FOR DO16, 25 MILLISECONDS/INCH

| | *Number of eyes tested* | *Mean* | *Standard deviation* | *Standard error of mean* |
|---|---|---|---|---|
| $n_1$ | | | | |
| Normal | 29 | 195.6 | 55.0 | 10.39 |
| Alcohol | 20 | 95.6 | 65.8 | 15.08 |
| $p_1$ | | | | |
| Normal | 27 | 185.8 | 55.0 | 10.79 |
| Alcohol | 19 | 94.3 | 59.0 | 13.91 |
| $n_2$ | | | | |
| Normal | 29 | 223.8 | 52.0 | 9.83 |
| Alcohol | 21 | 125.7 | 67.8 | 15.16 |
| $p_2$ | | | | |
| Normal | 27 | 201.3 | 82.0 | 16.08 |
| Alcohol | 17 | 137.7 | 81.3 | 20.32 |
| $p_3$ | | | | |
| Normal | 28 | 344.6 | 80.0 | 15.40 |
| Alcohol | 17 | 252.6 | 102.5 | 25.63 |

J.O. (K138) was examined on two occasions, August 8, 1958 (Figure 11, Row 3) and May 3, 1960 (Figure 9, Row 4). Visual loss and optic atrophy due to chronic methanol intoxication had been present since December 25, 1954. Vision was reduced to counts fingers, O.U. The ERG was subnormal on both occasions.

G.P. (K76) was examined on two occasions, October 9, 1957 (Figure 11, Row 2) and August 25, 1960 (Figure 9, Row 3). Vision was reduced to hand movements on both occasions. The ERG showed some loss of amplitudes over the three-year period.

SUMMARY OF CHANGES IN THE ERG

LATENCY. a-wave latency is measured only for DO16 (10 milliseconds/inch). In the abnormal series the mean latency is greater than the normal mean ($P = .02$). b-wave latencies were significantly greater for the high intensity stimuli LO16, DO16. The lack of reliable differences at LO1, DO1, and DO4 as compared to LO16 and DO16 is partially attributable to the sharper and more readily definable onset of the b-wave in the latter measurements. This may be confirmed by observing that the standard deviations for LO1, DO1, and DO4 are about three times as great as those for the higher intensities. Latencies $n_1$, $p_1$, $p_2$, $p_3$ are much more reliable in the given order. The explanation for this is unknown at this time.

TABLE 11. p VALUES FOR SIGNIFICANCE OF THE DIFFERENCES BETWEEN MEANS OF THE ALCOHOL POISONED GROUP AND THE NORMAL GROUP

| | LO1 | LO16 | DO1 | DO4 | DO16 | DR16 | DB16 | DG16 | LO4 DO4 20/*sec.* |
|---|---|---|---|---|---|---|---|---|---|
| a-wave latency | | | | | .02 | | | | |
| b-wave latency ($n_2$) | .15 | .02 | .30 | .10 | <.01* | .05 | <.01* | .01 | |
| $n_1$ latency | | | | | .33 | | | | |
| $p_1$ latency | | | | | .26 | | | | |
| $p_2$ latency | | | | | .14 | | | | |
| $p_3$ latency | | | | | .02 | | | | |
| b-wave peak time (sharp) | | <.01* | | <.01* | <.01* | .01 | | | |
| b-wave peak time (smooth) | <.01* | | .04 | .15 | .37 | <.01* | .02 | .01 | |
| a-wave amplitude | <.01* | <.01* | <.01* | <.01* | <.01* | <.01* | <.01* | <.01* | |
| b-wave amplitude (sharp) | | <.01* | | .02 | <.01* | <.01* | | | <.01* |
| b-wave amplitude (smooth) | <.01* | | <.01* | <.01* | <.01* | <.01* | <.01* | <.01* | |
| $n_1$ amplitude | | | | | <.01* | | | | |
| $p_1$ amplitude | | | | | <.01* | | | | |
| $n_2$ amplitude | | | | | <.01* | | | | |
| $p_2$ amplitude | | | | | <.01* | | | | |
| $p_3$ amplitude | | | | | <.01* | | | | |

p < .05 is underlined——. p <.01 is starred *.

b-WAVE PEAK TIME. In the abnormal records b-wave peak time (sharp) is difficult to measure because the peak is usually rounded. However, in those few records where measurement is possible there is a significant slowing of the b-wave peak time (sharp) from the normal series ($P = < .01$). b-wave peak time (smooth) is much more reliably measured at low intensities than high.

AMPLITUDES. Amplitudes in general more reliably differentiate the methanol poisoned group from the controls than do latencies. Mean a-wave amplitudes are significantly reduced from the normal means for all stimuli ($P = < .01$). Mean b-wave amplitudes (sharp) are significantly reduced for all stimuli ($P = < .01$) except for DO4 ($P = < .05$) which may be inaccurate due to difficult measurement. Mean b-wave amplitudes (smooth) are significantly reduced for all stimuli ($P = < .01$).

The disproportionately greater a-wave amplitude reduction compared to b-wave amplitude reduction is reflected in the b/a ratio. The b/a ratio is increased from 2.2 in the normal series to 2.6 in the methyl alcohol group.

Mean $n_1$, $p_1$, $n_2$, $p_2$, $p_3$ amplitudes are all significantly reduced from the normal means ($P = < .01$).

The ERG of patients retested over a period of time indicates that there is continued loss of electroretinographic response. The activities and ophthalmic findings of these individuals indicate continued methanol imbibition.

The ERG tracings and the measurements noted in this disease indicate that the electroretinographic response is not necessarily similar in the two eyes of a patient.

## COMMENTS

The results of this study indicate reproducible changes in the ERG of individuals poisoned by methanol. From the basic knowledge of the ERG which began with Dewar[35] there is evidence that the electroretinographic changes are not the result of damage to the ganglion cells and optic nerve. The electroretinographic findings suggest malfunction of the outer retinal layers.

### a-WAVE

There is a significant reduction in a-wave amplitude in this series of patients poisoned by methanol. Definitive studies on the origins of

various parts of the ERG by Noell, Brown, and others agree that the a-wave originates in the external retinal cells and depends upon the integrity of the outer region of the visual cell. Recent work by Dowling in vitamin A deficiency[14] corroborates this finding; there is a loss of the a-wave in relation to the degeneration of the outer limbs of the retina.

In a discussion of a paper on macular disease by Jacobson, *et al.*, Noell commented on the reduced a-wave and the b/a ratio which was noticeably increased in a case presented in the paper (a patient with a macular hole, right eye). The discussion pointed out than in animals, pathology which involves the outer limbs is associated with a-wave reduction.[28]

Noell, in the same discussion, mentioned the possibility that damage to the pigment epithelium resulted in a-wave abnormalities.

Goodman and Bornschein[36] in discussing a case of total color blindness, presented two figures which show the reduction in the a-wave and the increase in the b/a ratio. The authors concluded that the residual a-wave is a pure scotopic component. A later paper[37] was more concerned with the positive "hump" late in the a-wave which is especially notable in our normal records in which sweep speed has been changed. Their Figure IIB, page 433, shows the flattening of the a-wave in a color blind patient. The authors mention an oscillatory type response in the normal a-wave which is missing in ERGs from such patients. The a-wave in the cases of methyl alcohol poisoning and our cases of macular disease is very similar to that of the color blind patient described in the paper by Goodman and Bornschein.

### b-WAVE

The patients poisoned with methanol also showed a significant reduction in b-wave amplitude. This change may be related to the same pathology as that which causes a reduction in the a-wave. However, Potts, *et al.*,[15] found that glutamate injections in young mice caused degeneration of the inner retinal layers with associated loss of the b-wave and retention of the a-wave. There is general agreement that the outer plexiform layer and the bipolar cells participate in b-wave generation.[2,12] The possibility that loss of function can be effected through both choroidal and retinal circulation should be considered in methanol poisoning.

FLICKER

The response to a 20 per second flash was markedly reduced from the normal in the cases of methanol poisoning. Because of the high stimulus intensity employed, these responses must be considered photopic in nature. The retinal layers which produce these responses are still unknown but Noell[12] observed that the ERG of iodate poisoned rabbits which had loss of a-wave also had reduced flicker responsiveness. This would suggest that the flicker reduction is also due to visual cell damage. Iser and Goodman[38] demonstrated low flicker responses in color blindness and macular disease.

COLOR

Electroretinographic response to colored light, particularly that produced by a red filter, is notably reduced in this series of cases. The significant reduction in the response to blue and green light can not be corroborated in the literature. A number of patients, having loss of vision by central retinal disease, have been evaluated in this laboratory. The responses to blue and green light are similarly reduced. There are several papers which describe changes in the red response in both macular disease[28,39] and individuals afflicted with color blindness.[36] The changes in the ERG would appear to be the same.

One might wonder about the similarity of the ERG in methanol poisoned individuals (with ophthalmoscopically visible optic atrophy), to the ERG observed in primary optic atrophy. A number of patients with primary optic atrophy have been evaluated in this laboratory. The electroretinograms have been within normal limits. One case has been included for comparison with the methanol series (Appendix 5, Figures 13–18). Noell has found that interrupting the blood supply of the optic nerve results in degeneration of the inner retinal layers and a negative or a-wave ERG.[68]

Elsewhere in this discussion, note has been made of the electroretinographic findings in this series as compared to changes in the ERG resulting from various central retinal abnormalities, that is, macular hole and color blindness.

A series of over 50 cases, primarily involving the central visual area, has been studied in this laboratory. At least five types of central visual degeneration have been evaluated: familial juvenile central pigmentary degeneration, familial adult central pigmentary degeneration, adult disciform degeneration of the macula (Kuhnt-Junius), senile macular degeneration, and chorioretinitis involving the macular zone. Each case

was characterized by loss of central vision with a well circumscribed central scotoma (by tangent screen) and visible central retinal changes. In all of these cases, the abnormalities in the ERG are similar to those described for methanol poisoning.

It has been noted and reiterated that the ERG arises from the outer retinal layers and the electroretinographic changes in methanol poisoning are indicative of effects upon these layers. The ophthalmoscopically visible optic nerve atrophy, the pathologically evident ganglion cell damage in retina and brain are degenerative changes which cannot be detected by the ERG.

## SUMMARY

Fourteen patients whose vision was affected by methanol intoxication were evaluated by a standard electroretinographic technique. The results were compared with those obtained from a series of normal individuals subjected to similar techniques. The following aberrations from the normal ERG were noted.

(1) Within the limits of measurement, there would appear to be some increase in mean latencies and peak times over those observed in the normal group.

(2) The a- and b-wave amplitudes to all parameters of stimuli are significantly below the normal range.

(3) These changes in the ERG indicate damage to the outer retinal layers including the visual cell. The usual ERG observed in methanol poisoning is unlike that found with degeneration of the optic nerve fiber or ganglion cell layer, and is also unlike that found when damage extends to the bipolar layer.

(4) The electroretinographic changes in methanol poisoning are similar to those observed in central retinal degeneration.

(5) The results of this investigation would appear to justify the conclusion that the clinical ERG is of diagnostic significance in the evaluation of the visual loss caused by methanol poisoning.

## APPENDIXES

### I. THE CLINICAL COURSE OF THE DISEASE

There are many reports in the literature of methyl alcohol poisoning. One report is of particular interest. Wood and Buller[40] reported 54 previously published cases of methanol blindness (with or without death), 90 unpublished cases of methanol poisoning (with or without

death), 9 blinded by pulmonary or cuticular absorption, and 82 more cases (previously unpublished) of death from methanol poisoning with no history of blindness. This article was published in 1904 and at that time most authorities did not know that methanol was a poison. The report contains remarkable case records of methanol poisoning. (Among them the first recorded case: Viger, Rec. d'Ophtalmologie, page 1636, 1879). Several epidemics of methyl alcohol poisoning have been reported. One, occurring in Atlanta, Georgia, in October, 1951, involved over 300 persons, and has been well documented by at least three papers.[41-3]

Acute methyl alcohol poisoning is marked by a characteristic clinical picture:

(*a*) After a variable methanol intake (less than an ounce to more than a pint, apparently depending upon methanol concentration) the individual experiences temporary euphoria, followed by a tendency towards violence, and ending in misery, depression, and somnolence (usually sleeping off the drunk in 10 to 12 hours). The authors noted the marked variation in individual response to the drug. There are substantiated reports in the literature showing individuals who have ingested substantial quantities of methanol with no ill effects.[40,41,44] In a discussion one author noted that six Russian workers had imbibed four liters of 40 percent methanol with no symptoms.[45] O. Gayer Morgan[34] reported on methylated spirit addiction. The author noted that actually methyl alcohol is ingested routinely among society's lower elements. Usually it is mixed with red wine. Wood and Buller[40] noted a case of blindness after ingestion of two teaspoonsful of methyl alcohol. Province, Kritzler, and Calhoun[44] noted extreme variation in response. They estimated that for every patient treated in the army at least four drank a similar portion and remained unaffected.

(*b*) Usually the individual will sleep his narcosis off for 10 to 12 hours and upon awakening, drink some water and become intoxicated again.

(*c*) In those patients suffering from acute poisoning the symptoms begin 18 to 24 hours after ingestion. These symptoms commonly are: visual disturbances, headaches, appearance of shock, dizziness, nausea, and vomiting, severe abdominal pain, general malaise, marked sweating, amnesia, air hunger, peculiar alcohol smell of breath and sweat. Those patients who die usually are severely prostrated to comatose. They may demonstrate the picture of meningitis with rigidity of neck and back muscles, rigidity of abdominal musculature, hyperactive

tendon reflexes. Many are blind at death. According to the literature those patients die when[41] bradycardia is followed by opisthotonos and locked full inspiration with cessation of breathing. All are extremely acidotic and may appear in shock. However, they characteristically have good cardiovascular function, with normal pulse and blood pressure. They are cyanotic. The acidosis of methyl alcohol poisoning is often not accompanied by dyspnea but Kussmaul breathing (deep, sighing) is noted.

(*d*) In extremis, the patient may assume a position of extreme muscular spasm with severe stretching and convulsions. The abdominal muscles are tight and there may be tenderness over the pancreas which often is involved.[41,43]

## II. PATHOLOGY

No pathologic material has become available during this study.

Several authors describe changes in the ganglion cells of the retina as well as changes in the optic nerve.

Pick and Bielschowsky[46] described three cases in human beings, all of which were acute. They noted damage to cortex and putamen, spinal cord, Betz cells, and motor neurons. The retina was more severely damaged than the brain. There were no changes in the lateral geniculate body. They noted that the ganglion cells had the nucleus to one side, Nissl's bodies were gone, and the chromatin was clumped. In addition to ganglion cell change they noted a hyperchromicity of the inner nuclear layer.

Birch-Hirschfield[47] in 1901 first reported changes in retinal ganglion cells due to methanol. Monkeys undergoing chronic intoxication also showed changes in outer nuclear layer with areas free of nuclei.

Roe[48] noted the eccentric position of the nuclei of the ganglion cells in methanol poisoning in patients and generally showed changes which agreed with Pick and Nissl. However, Roe does not believe that actual ganglion cell damage occurs in the experimental animal.

Muller[49] examined a patient five hours after death and 18 hours after methanol ingestion and found in both retinae exudation from choroid and retinal vessels; also the pigment epithelium and bipolar cells were damaged.

Orthner[50,51] found the main pathologic change in the endothelium of capillaries, demonstrating edema and necrosis. The cerebral cortex and putamen were involved symmetrically. He felt localization of damage was determined by the vascular drainage system.

Fink[52] described edema of the retinal ganglion cells in two cases, and he also described disintegration of the rod and cone layer. His experimental work on rabbits and dogs also indicated degeneration of rods and cones. Menne[33] described the pathologic changes in two cases. There was marked edema and hyperemia of the optic nerve and retina, marked changes in the ganglion cells, and patchy glial cell proliferation.

A photograph taken from MacDonald[53] in Duke-Elder would indicate complete loss of the outer limbs. Again delayed fixation might produce post-mortem autolysis. MacDonald noted marked degeneration of the ganglion cell layers. (Neither Roe[48] nor McGregor[54] mention the rods and cones.)

The changes in the ganglion cells may well be secondary; however, McGregor's[54] very careful analysis would indicate no significant changes in the ganglion cells in four cases which he studied. DeSchweinitz and Friedenwald[52] also reported negative findings in animals. Potts, *et al.*,[30] noted only one monkey (out of six) which had ganglion cell changes.

From the histological observations available, it is not possible to state definitely the location of the actual lesion. There are as many authors indicating ganglion cell damage as those who do not. Some believe that rod and cone damage occurs, others believe the observed rod and cone changes to be post-mortem autolysis while still others make no mention of such damage.

### III. BIOCHEMISTRY

How does methanol cause such severe visual damage? This problem has received considerable attention over the years. To date, however, the actual process by which methanol is toxic to cells and organism is still a subject of conjecture.

The earliest American reference to methyl alcohol toxicity[40] indicates that by the old wood distillation process the wood alcohol was absolutely unpalatable. When methanol was distilled by a newer and cheaper process, it was very similar to ethanol in taste and smell. Gradually, it became widely used in tonics, extracts, liniments, and such (Jamaica ginger, lemon extract, bay rum, Columbian spirits, witch hazel, "dehorn"). Wood and Buller[40] made quite a point of the fact that many experts did not feel that methanol was toxic. The experts demonstrated their opinions in rather bizarre fashion and the details as well as some of the experts' opinions are related in their articles.

Harrop and Benedict[55] were the first to note acidosis in methanol

poisoning. This finding is peculiar to man since it is not noted in laboratory animals.[56] Lactic acid has been found in larger than normal quantities in the blood and urine in patients with methanol poisoning.[57]

Roe[57,58,59] believes that methanol inhibits oxidative processes, causing an accumulation of organic acids. The resulting acidosis is benefited by alkali. Roe believes that the poisonous effect of methanol is inhibited by ethanol which is preferentially acted upon by the oxidative enzymes. Zatman[60] also thinks that ethanol is preferentially oxidized, thereby reducing the toxicity of methanol. Kendall and Ramanathan[61] state that ethanol inhibits the oxidation of methanol to formaldehyde by alcohol dehydrogenase. The authors stated that the capacity for oxidizing methanol to formic acid exceeds capacity to oxidize formic acid which is excreted in the urine. Chew, *et al.*,[62] noted excellent visual results in the treatment of methanol poisoning with the use of alkali and ethanol.

In a fine series of papers Potts, *et al.*, [63-67,30] made an extensive study of the problem of methanol poisoning. First they considered the actual effect of methanol and its degradation products on retinal metabolism. Formaldehyde was implicated as the degradation product of methanol which poisoned glycolysis at one or both phosphorylation steps.

Potts, Gilger, and Johnson[64] then published a paper on the toxicity of methanol in mice treated with antabuse, cortisone, ethyl alcohol, glycine, and cysteine. In this article the authors noted that ethyl alcohol, given in conjunction with methanol, actually seemed to increase toxicity.

Gilger and Potts[66,67] reported that acidosis from methanol poisoning may be a response peculiar to primates. They pointed out the beneficial value of alkali therapy. The authors noted definite retinal and papillary edema which cleared last in the macular area.

Potts, *et al.*, found that formaldehyde was much more effective in poisoning the retinal metabolism than either methanol itself or formic acid. They noted that even in very low concentration its effect is rather severe. Formaldehyde affects the enzymes which convert hexose diphosphate to phosphoglyceraldehyde. Their findings indicated that the triose phosphate dehydrogenase was not affected. Formaldehyde affected oxidation and glycolysis more with glucose as a substrate than with hexose diphosphate.

A moot question is, of course, whether formaldehyde is the actual toxic agent. In any case carbohydrate metabolism is somehow affected but the actual mechanism is unknown.

IV. TABULATED RESULTS IN METHANOL POISONING CASES

TABLE 2B. a-WAVE LATENCY IN MILLISECONDS

| *Individual cases* | | | | |
|---|---|---|---|---|
| *Age* | *Tested* | *Case* | | DO16 |
| 34 | 10/9/57 | K74 | Right | 4 |
| | | | Left | 4 |
| 43 | 1/9/58 | K75 | R | 9 |
| | | | L | 9 |
| 39 | 10/9/57 | K76 | R | 4 |
| | | | L | 4 |
| | 8/25/60 | | R | 6 |
| | | | L | 6 |
| 45 | 8/8/58 | K138 | R | 4 |
| | | | L | 4 |
| | 5/3/60 | | R | 8 |
| | | | L | 6 |
| 40 | 10/2/58 | K148 | R | 4 |
| | | | L | 4 |
| | 7/22/59 | | R | 9 |
| | | | L | 8 |
| | 8/24/59 | | R | 4 |
| | | | L | 4 |
| 46 | 9/10/58 | K169 | R | 4 |
| | | | L | 4 |
| 36 | 1/5/59 | K219 | R | 7 |
| | | | L | 9 |
| | 1/28/59 | | R | 4 |
| | | | L | 4 |
| | 7/17/59 | | R | 6 |
| | | | L | 4 |
| | 4/13/60 | | R | 9 |
| | | | L | T.D. |
| 43 | 5/12/59 | K278 | R | 5 |
| | | | L | 4 |
| 35 | 6/5/59 | K296 | R | 5 |
| | | | L | 5 |
| 50 | 6/5/59 | K298 | R | 5 |
| | | | L | N.I. |
| 47 | 8/3/60 | K441 | R | 4 |
| | | | L | 4 |
| 41 | 11/16/60 | K478 | R | 3 |
| | | | L | 2 |
| 63 | 12/15/60 | K480 | R | 5 |
| | | | L | 8 |
| 43 | 12/16/60 | K481 | R | 5 |
| | | | L | 5 |

T.D.—technical difficulties; N.I.—not included in protocol.

TABLE 3B. b-WAVE LATENCY ($n_2$) IN MILLISECONDS

| *Individual cases* | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| *Age* | *Tested* | *Case* | | LO1 | LO16 | DO1 | DO4 | DO16 | DR16 | DB16 | DG16 |
| 34 | 10/9/57 | K74 | Right | 16 | N.I. | 29 | 23 | 21 | 25 | N.I. | N.I. |
| | | | Left | 16 | N.I. | 29 | 23 | 21 | 25 | N.I. | N.I. |
| 43 | 1/9/58 | K75 | R | 33 | N.I. | 33 | 28 | T.D. | 33 | N.I. | N.I. |
| | | | L | 33 | N.I. | 33 | 28 | 28 | 28 | N.I. | N.I. |
| 39 | 10/9/57 | K76 | R | 21 | N.I. | 33 | 25 | 23 | 23 | N.I. | N.I. |
| | | | L | 21 | N.I. | 35 | 25 | 23 | 23 | N.I. | N.I. |
| | 8/25/60 | | R | 34 | 22 | 47 | 37 | 30 | 30 | 34 | 34 |
| | | | L | 43 | 22 | 47 | 34 | 30 | 32 | 34 | 39 |
| 45 | 8/8/58 | K138 | R | 22 | N.I. | 43 | 34 | 34 | 34 | N.I. | N.I. |
| | | | L | 22 | N.I. | 34 | 34 | 26 | 34 | N.I. | N.I. |
| | 5/3/60 | | R | 26 | 22 | 32 | 26 | 19 | 30 | 39 | 43 |
| | | | L | 26 | 30 | 39 | 22 | 30 | 30 | 39 | 30 |
| 40 | 10/2/58 | K148 | R | 25 | 21 | 33 | 31 | 29 | 25 | N.I. | N.I. |
| | | | L | 25 | 21 | 33 | 31 | 29 | 25 | N.I. | N.I. |
| | 7/22/59 | | R | T.D. | T.D. | 45 | 37 | 29 | T.D. | 31 | 41 |
| | | | L | 33 | 21 | T.D. | 37 | 29 | 49 | T.D. | T.D. |
| | 8/24/59 | | R | 23 | 27 | 45 | 36 | 32 | 27 | 34 | 34 |
| | | | L | 36 | 27 | 50 | 36 | 32 | 27 | 36 | 36 |
| 46 | 9/10/58 | K169 | R | 16 | 25 | 33 | 29 | 29 | 26 | N.I. | N.I. |
| | | | L | 16 | 25 | 37 | 33 | 29 | 26 | N.I. | N.I. |
| 36 | 1/5/59 | K219 | R | 12 | 23 | 41 | 21 | 29 | 25 | 33 | 29 |
| | | | L | 21 | 23 | 37 | 21 | 29 | 29 | 33 | 33 |
| | 1/28/59 | | R | 30 | 24 | 26 | 34 | 30 | 30 | 34 | 30 |
| | | | L | 30 | 28 | 26 | 26 | 34 | 30 | 34 | 30 |
| | 7/17/59 | | R | T.D. | T.D. | 28 | 33 | 29 | 21 | 33 | 33 |
| | | | L | T.D. | T.D. | T.D. | 33 | 29 | 37 | 29 | 33 |
| | 4/13/60 | | R | T.D. | 32 | T.D. | T.D. | 32 | 27 | 34 | N.I. |
| | | | L | T.D. | 32 | T.D. | T.D. | 50 | T.D. | 50 | N.I. |
| 43 | 5/12/59 | K278 | R | T.D. | 21 | 41 | 29 | 27 | 29 | 29 | 29 |
| | | | L | T.D. | 21 | 37 | T.D. | 25 | 29 | 29 | 29 |
| 35 | 6/5/59 | K296 | R | 25 | 30 | 35 | 35 | T.D. | 25 | T.D. | 38 |
| | | | L | 25 | 25 | 35 | 35 | 30 | 25 | 35 | 38 |
| 50 | 6/5/59 | K298 | R | T.D. | T.D. | 40 | 33 | 33 | 19 | 35 | 35 |
| | | | L | N.I. | N.I. | N.I. | N.I. | N.I. | N.I. | N.I. | N.I. |
| 47 | 8/3/60 | K441 | R | 34 | 22 | 47 | 30 | 26 | 22 | 30 | 30 |
| | | | L | 30 | 22 | 43 | 30 | 26 | 22 | 30 | 30 |
| 41 | 11/16/60 | K478 | R | 26 | 26 | 56 | 34 | 30 | 34 | 34 | 34 |
| | | | L | 34 | 24 | 52 | 34 | 28 | 28 | 32 | 34 |
| 63 | 12/15/60 | K480 | R | 16 | 24 | 72 | 28 | 34 | 36 | 38 | 36 |
| | | | L | 16 | 26 | 72 | 36 | 32 | 38 | 38 | 36 |
| 43 | 12/16/60 | K481 | R | 44 | 20 | 36 | 32 | 32 | T.D. | 44 | 36 |
| | | | L | 44 | 20 | 48 | 36 | 36 | T.D. | 52 | 52 |

T.D.—technical difficulties; N.I.—not included in protocol.

TABLE 4B. $n_1$ AND p LATENCIES, DO16, 25 MILLISECONDS/INCH

| *Individual cases* | | | | | | | |
|---|---|---|---|---|---|---|---|
| *Age* | *Tested* | *Case* | | $n_1$ | $p_1$ | $p_2$ | $p_3$ |
| 34 | 10/9/57 | K74 | Right | 14 | 16 | 25 | 31 |
| | | | Left | 14 | 16 | 25 | 31 |
| 39 | 10/9/57 | K76 | R | 16 | 19 | 27 | 35 |
| | | | L | 16 | 19 | 27 | 33 |
| | 8/25/60 | | R | 19 | 23 | 32 | 38 |
| | | | L | 21 | 23 | 34 | 40 |
| 45 | 5/3/60 | K138 | R | 16 | 24 | T.D. | T.D. |
| | | | L | 17 | 25 | T.D. | T.D. |
| 40 | 7/22/59 | K148 | R | 25 | 29 | 57 | 70 |
| | | | L | 25 | 29 | 47 | 53 |
| | 8/24/59 | | R | 18 | 22 | 28 | 35 |
| | | | L | 16 | T.D. | 31 | 42 |
| 36 | 1/5/59 | K219 | R | 18 | 25 | T.D. | T.D. |
| | | | L | 18 | T.D. | T.D. | T.D. |
| | 1/28/59 | | R | 16 | 17 | 40 | 50 |
| | | | L | 15 | 19 | 38 | 50 |
| | 7/17/59 | | R | 14 | 16 | 32 | 36 |
| | | | L | 15 | 21 | 31 | 39 |
| 43 | 5/12/59 | K278 | R | T.D. | T.D. | T.D. | T.D. |
| | | | L | 16 | 17 | 25 | 32 |
| 35 | 6/5/59 | K296 | R | T.D. | T.D. | 35 | 45 |
| | | | L | T.D. | T.D. | 30 | 43 |
| 50 | 6/5/59 | K298 | R | 17 | 20 | 28 | 32 |
| | | | L | T.D. | T.D. | T.D. | T.D. |
| 47 | 8/3/60 | K441 | R | 13 | 15 | 29 | 38 |
| | | | L | 13 | 17 | 27 | 36 |
| 41 | 11/16/60 | K478 | R | 15 | 17 | 36 | 44 |
| | | | L | 15 | 17 | 36 | 42 |
| 63 | 12/15/60 | K480 | R | 18 | 23 | T.D. | T.D. |
| | | | L | 18 | 23 | T.D. | T.D. |
| 43 | 12/16/60 | K481 | R | 19 | 20 | 38 | 41 |
| | | | L | 18 | 20 | 42 | 46 |

T.D.—technical difficulties.

TABLE 5B. b-WAVE PEAK TIME (SHARP) IN MILLISECONDS

| *Individual cases* | | | | | | | |
|---|---|---|---|---|---|---|---|
| *Age* | *Tested* | *Case* | | LO16 | DO4 | DO16 | DR16 |
| 34 | 10/9/57 | K74 | Right | N.I. | N.Sh. | N.Sh. | 37 |
| | | | Left | N.I. | N.Sh. | N.Sh. | 37 |
| 43 | 1/9/58 | K75 | R | N.I. | N.Sh. | 61 | 56 |
| | | | L | N.I. | N.Sh. | 61 | 61 |
| 42 | 8/25/60 | K76 | R | 52 | N.Sh. | N.Sh. | 60 |
| | | | L | 50 | N.Sh. | N.Sh. | 65 |
| 45 | 8/8/58 | K138 | R | N.I. | N.Sh. | N.Sh. | 47 |
| | | | L | N.I. | N.Sh. | N.Sh. | 47 |
| | 5/3/60 | | R | 47 | N.Sh. | N.Sh. | 60 |
| | | | L | 56 | N.Sh. | N.Sh. | 56 |
| 40 | 10/2/58 | K148 | R | 39 | 53 | 53 | 66 |
| | | | L | 39 | 53 | 49 | 66 |
| | 8/24/59 | | R | 45 | 63 | 59 | 54 |
| | | | L | 50 | 68 | 63 | 54 |
| 46 | 9/10/58 | K169 | R | 41 | N.Sh. | 53 | 53 |
| | | | L | 41 | N.Sh. | 53 | 53 |
| 36 | 1/5/59 | K219 | R | 41 | N.Sh. | N.Sh. | 74 |
| | | | L | 45 | N.Sh. | N.Sh. | 74 |
| | 1/28/59 | | R | 47 | N.Sh. | N.Sh. | 60 |
| | | | L | 47 | N.Sh. | N.Sh. | 60 |
| | 7/17/59 | | R | T.D. | 74 | 57 | 62 |
| | | | L | T.D. | 74 | 66 | 62 |
| | 4/13/60 | | R | 50 | T.D. | N.Sh. | 68 |
| | | | L | 59 | T.D. | T.D. | T.D. |
| 43 | 5/12/59 | K278 | R | 45 | N.Sh. | N.Sh. | 49 |
| | | | L | 45 | N.Sh. | N.Sh. | 57 |
| 35 | 6/5/59 | K296 | R | 50 | 55 | T.D. | 75 |
| | | | L | 50 | 60 | 70 | 70 |
| 50 | 6/5/59 | K298 | R | N.Sh. | N.Sh. | N.Sh. | N.Sh. |
| | | | L | N.Sh. | N.Sh. | N.Sh. | N.Sh. |
| 47 | 8/3/60 | K441 | R | 41 | 65 | 65 | 56 |
| | | | L | 43 | 65 | 65 | 56 |
| 41 | 11/16/60 | K478 | R | 52 | 65 | 56 | 39 |
| | | | L | 47 | 65 | 56 | 47 |
| 63 | 12/15/60 | K480 | R | 46 | N.Sh. | 60 | 50 |
| | | | L | 46 | N.Sh. | 58 | 50 |
| 43 | 12/16/60 | K481 | R | 42 | N.Sh. | N.Sh. | N.Sh. |
| | | | L | 44 | N.Sh. | N.Sh. | N.Sh. |

T.D.—technical difficulties; N.I.—not included in protocol; N.Sh.—no sharp measurable.

TABLE 6B. b-WAVE PEAK TIME (SMOOTH) IN MILLISECONDS

| *Individual cases* | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| *Age* | *Tested* | *Case* | | LO1 | DO1 | DO4 | DO16 | DR16 | DB16 | DG16 |
| 34 | 10/9/57 | K74 | Right | 41 | 60 | 41 | 39 | 76 | N.I. | N.I. |
| | | | Left | 41 | 55 | 41 | 39 | 76 | N.I. | N.I. |
| 43 | 1/9/58 | K75 | R | 75 | 94 | 71 | 94 | 85 | N.I. | N.I. |
| | | | L | 66 | T.D. | 75 | 85 | 99 | N.I. | N.I. |
| 39 | 10/9/57 | K76 | R | 42 | 74 | 51 | 45 | 33 | N.I. | N.I. |
| | | | L | 42 | 74 | 51 | 45 | 33 | N.I. | N.I. |
| | 8/25/60 | | R | T.D. | 108 | 73 | 60 | 129 | 73 | 69 |
| | | | L | 86 | 112 | 82 | 62 | 133 | 73 | 65 |
| 45 | 8/8/58 | K138 | R | 82 | 112 | 82 | 60 | 142 | N.I. | N.I. |
| | | | L | 73 | 112 | 82 | 60 | 142 | N.I. | N.I. |
| | 5/3/60 | | R | 50 | 100 | 82 | 69 | 116 | 90 | 86 |
| | | | L | 69 | 100 | 86 | 77 | 108 | 99 | 95 |
| 40 | 10/2/58 | K148 | R | 72 | 86 | 62 | 78 | 135 | N.I. | N.I. |
| | | | L | 72 | 94 | 62 | 78 | 135 | N.I. | N.I. |
| | 7/22/59 | | R | T.D. | 88 | 66 | 57 | N.Sm. | 57 | 74 |
| | | | L | 57 | T.D. | 66 | 52 | 78 | T.D. | T.D. |
| | 8/24/59 | | R | 50 | 104 | T.D. | 81 | 126 | 86 | 63 |
| | | | L | 54 | 99 | 85 | 81 | 126 | 86 | 68 |
| 46 | 9/10/58 | K169 | R | 62 | 82 | 66 | 82 | 107 | N.I. | N.I. |
| | | | L | 62 | 82 | 66 | 82 | 123 | N.I. | N.I. |
| 36 | 1/5/59 | K219 | R | 70 | 82 | T.D. | 57 | 103 | 66 | 66 |
| | | | L | 70 | 94 | 66 | 57 | 98 | 66 | 66 |
| | 1/28/59 | | R | 73 | 103 | 86 | 82 | 112 | 82 | 73 |
| | | | L | 73 | 95 | 86 | 69 | 112 | 82 | 82 |
| | 7/17/59 | | R | T.D. | 90 | 86 | 76 | 119 | 66 | 70 |
| | | | L | T.D. | T.D. | 86 | 82 | 119 | 66 | 74 |
| | 4/13/60 | | R | T.D. | T.D. | T.D. | 72 | 122 | 86 | N.I. |
| | | | L | T.D. | T.D. | T.D. | T.D. | T.D. | T.D. | N.I. |
| 43 | 5/12/59 | K278 | R | T.D. | 74 | 57 | 53 | T.D. | 57 | 57 |
| | | | L | T.D. | 66 | T.D. | 53 | T.D. | 57 | 57 |
| 35 | 6/5/59 | K296 | R | 60 | T.D. | 80 | T.D. | T.D. | T.D. | 80 |
| | | | L | 60 | 75 | 85 | 90 | 115 | 85 | 85 |
| 50 | 6/5/59 | K298 | R | T.D. | 71 | 66 | 66 | 71 | 71 | 56 |
| | | | L | N.I. | N.I. | N.I. | N.I. | N.I. | N.I. | N.I. |
| 47 | 8/3/60 | K441 | R | 65 | 103 | 77 | 82 | 116 | 77 | 90 |
| | | | L | 65 | 99 | 77 | 77 | 116 | 82 | 90 |
| 41 | 11/16/60 | K478 | R | 65 | 99 | 77 | 77 | 120 | 69 | 73 |
| | | | L | 69 | 99 | 77 | 77 | 120 | 69 | 69 |
| 63 | 12/15/60 | K480 | R | 80 | 82 | 88 | 78 | 144 | 72 | 80 |
| | | | L | 80 | 78 | 88 | 82 | 146 | 70 | 82 |
| 43 | 12/16/60 | K481 | R | 62 | 116 | 86 | 76 | N.Sm. | 112 | 112 |
| | | | L | 64 | 124 | 84 | 96 | N.Sm. | 120 | 138 |

T.D.—technical difficulties; N.I.—not included in protocol; N.Sm.—no smooth measurable.

TABLE 7B. a-WAVE AMPLITUDE IN MICROVOLTS

| *Individual cases* | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| *Age* | *Tested* | *Case* | | LO1 | LO16 | DO1 | DO4 | DO16 | DR16 | DB16 | DG16 |
| 34 | 10/9/57 | K74 | Right | 21 | N.I. | 23 | 85 | 216 | T.D. | N.I. | N.I. |
| | | | Left | 17 | N.I. | 22 | 78 | 204 | T.D. | N.I. | N.I. |
| 43 | 1/9/58 | K75 | R | 17 | N.I. | 11 | 25 | T.D. | 14 | N.I. | N.I. |
| | | | L | 0 | N.I. | T.D. | 41 | 76 | 38 | N.I. | N.I. |
| 39 | 10/9/57 | K76 | R | 20 | N.I. | 11 | 56 | 178 | 0 | N.I. | N.I. |
| | | | L | 20 | N.I. | 11 | 51 | 178 | 0 | N.I. | N.I. |
| | 8/25/60 | | R | 0 | 55 | 0 | 20 | 140 | 15 | 50 | 50 |
| | | | L | 0 | 49 | 0 | 32 | 74 | 11 | 32 | 32 |
| 45 | 8/8/58 | K138 | R | 11 | N.I. | 0 | 22 | 56 | 0 | N.I. | N.I. |
| | | | L | 0 | N.I. | 0 | 44 | 67 | 0 | N.I. | N.I. |
| | 5/3/60 | | R | 0 | 40 | 0 | 6 | 6 | 6 | 0 | 6 |
| | | | L | 11 | 80 | 0 | 17 | 40 | 6 | 6 | 17 |
| 40 | 10/2/58 | K148 | R | 11 | 139 | 0 | 44 | 222 | 33 | N.I. | N.I. |
| | | | L | 11 | 100 | 0 | 44 | 133 | 0 | N.I. | N.I. |
| | 7/22/59 | | R | 0 | T.D. | 11 | 21 | 42 | 0 | 37 | 32 |
| | | | L | 22 | 49 | T.D. | 32 | 54 | 0 | T.D. | T.D. |
| | 8/24/59 | | R | 28 | 139 | 11 | 106 | 247 | 28 | 176 | 106 |
| | | | L | 20 | 117 | 15 | 95 | 211 | 15 | 105 | 105 |
| 46 | 9/10/58 | K169 | R | 0 | 100 | 22 | 33 | 154 | 22 | N.I. | N.I. |
| | | | L | 0 | 100 | 22 | 56 | 178 | 17 | N.I. | N.I. |
| 36 | 1/5/59 | K219 | R | 11 | 44 | 17 | 22 | 78 | 11 | 50 | 44 |
| | | | L | 11 | 50 | 0 | 17 | 78 | 0 | 39 | 33 |
| | 1/28/59 | | R | 11 | 67 | T.D. | 22 | 111 | 0 | 89 | 78 |
| | | | L | 17 | 83 | T.D. | 22 | 44 | 0 | 56 | 61 |
| | 7/17/59 | | R | T.D. | T.D. | 0 | 11 | 92 | 11 | 42 | 32 |
| | | | L | T.D. | T.D. | T.D. | 21 | 92 | 11 | 53 | 42 |
| | 4/13/60 | | R | T.D. | 40 | 0 | 17 | 51 | 0 | 29 | N.I. |
| | | | L | T.D. | 29 | T.D. | T.D. | T.D. | T.D. | T.D. | N.I. |
| 43 | 5/12/59 | K278 | R | T.D. | 86 | 34 | 71 | 200 | 23 | 106 | 59 |
| | | | L | T.D. | 95 | 0 | T.D. | 153 | 0 | 82 | 71 |
| 35 | 6/5/59 | K296 | R | 20 | 90 | T.D. | 60 | T.D. | 15 | T.D. | 150 |
| | | | L | 15 | 60 | 0 | 60 | 150 | 15 | 100 | 100 |
| 50 | 6/5/59 | K298 | R | T.D. | T.D. | 39 | 24 | 73 | 24 | 83 | 68 |
| | | | L | T.D. | T.D. | T.D. | T.D. | T.D. | T.D. | T.D. | T.D. |
| 47 | 8/3/60 | K441 | R | 0 | 70 | 0 | 35 | 141 | 13 | 59 | 59 |
| | | | L | 0 | 57 | 0 | 35 | 129 | 17 | 47 | 47 |
| 41 | 11/16/60 | K478 | R | 0 | 63 | 34 | 71 | 153 | 17 | 94 | 82 |
| | | | L | 0 | 120 | 23 | 71 | 223 | 17 | 118 | 82 |
| 63 | 12/15/60 | K480 | R | 17 | 63 | 0 | 0 | 133 | 17 | 0 | 0 |
| | | | L | 22 | 59 | 0 | 0 | 95 | 16 | 32 | 0 |
| 43 | 12/16/60 | K481 | R | 17 | 68 | 0 | 23 | 40 | 0 | 0 | 0 |
| | | | L | 16 | 54 | 0 | 22 | 43 | 0 | 0 | 0 |

T.D.—technical difficulties; N.I.—not included in protocol; 0—flat or less than 5 microvolts.

TABLE 8B. b-WAVE AMPLITUDE (SHARP) IN MICROVOLTS

| *Individual cases* | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *Age* | *Tested* | *Case* | | LO16 | LO4, 20/*sec.* | DO4 | DO16 | DR16 | DO4, 20/*sec.* |
| 34 | 10/9/57 | K74 | Right | N.I. | N.I. | N.Sh. | N.Sh. | 73 | 23 |
| | | | Left | N.I. | N.I. | N.Sh. | N.Sh. | 69 | 28 |
| 43 | 1/9/58 | K75 | R | N.I. | N.I. | N.Sh. | T.D. | 33 | 14 |
| | | | L | N.I. | N.I. | N.Sh. | 195 | 59 | 22 |
| 39 | 10/9/57 | K76 | R | N.I. | N.I. | N.Sh. | N.Sh. | N.Sh. | 39 |
| | | | L | N.I. | N.I. | N.Sh. | N.Sh. | N.Sh. | 39 |
| | 8/25/60 | | R | 155 | 35 | N.Sh. | N.Sh. | 45 | 25 |
| | | | L | 82 | 22 | N.Sh. | N.Sh. | 32 | 22 |
| 45 | 8/8/58 | K138 | R | N.I. | N.I. | N.Sh. | N.Sh. | 22 | 22 |
| | | | L | N.I. | N.I. | N.Sh. | N.Sh. | 22 | 27 |
| | 5/3/60 | | R | 154 | 17 | N.Sh. | N.Sh. | 23 | 17 |
| | | | L | 194 | 34 | N.Sh. | N.Sh. | 34 | 29 |
| 40 | 10/2/58 | K148 | R | 250 | 56 | 411 | 522 | 89 | 56 |
| | | | L | 111 | 33 | 255 | 300 | 100 | 44 |
| | 7/22/59 | | R | T.D. | T.D. | N.Sh. | N.Sh. | T.D. | T.D. |
| | | | L | 64 | 22 | N.Sh. | N.Sh. | T.D. | T.D. |
| | 8/24/59 | | R | 72 | 44 | 282 | 294 | 44 | 39 |
| | | | L | 71 | 46 | 232 | 305 | 51 | 41 |
| 46 | 9/10/58 | K169 | R | 200 | 28 | N.Sh. | 433 | 56 | 33 |
| | | | L | 233 | 33 | N.Sh. | 444 | 56 | 33 |
| 36 | 1/5/59 | K219 | R | 139 | 28 | N.Sh. | N.Sh. | 44 | 22 |
| | | | L | 139 | 28 | N.Sh. | N.Sh. | 33 | 22 |
| | 1/28/59 | | R | 117 | 33 | N.Sh. | N.Sh. | 50 | 28 |
| | | | L | 67 | T.D. | N.Sh. | N.Sh. | 39 | 22 |
| | 7/17/59 | | R | T.D. | 27 | 295 | 286 | 49 | 22 |
| | | | L | T.D. | 27 | 263 | 270 | 32 | 22 |
| | 4/13/60 | | R | 97 | 17 | T.D. | N.Sh. | 23 | T.D. |
| | | | L | 131 | 11 | T.D. | T.D. | T.D. | T.D. |
| 43 | 5/12/59 | K278 | R | 154 | 51 | N.Sh. | N.Sh. | 63 | T.D. |
| | | | L | 172 | 38 | N.Sh. | N.Sh. | 51 | T.D. |
| 35 | 6/5/59 | K296 | R | 120 | 40 | 390 | T.D. | 70 | 40 |
| | | | L | 80 | 45 | 320 | 420 | 75 | 50 |
| 50 | 6/5/59 | K298 | R | T.D. | T.D. | N.Sh. | N.Sh. | T.D. | T.D. |
| | | | L | T.D. | T.D. | N.Sh. | N.Sh. | T.D. | T.D. |
| 47 | 8/3/60 | K441 | R | 159 | 32 | 388 | 400 | 32 | 25 |
| | | | L | 154 | 40 | 411 | 411 | 29 | 29 |
| 41 | 11/16/60 | K478 | R | 200 | 23 | 364 | 458 | 34 | 34 |
| | | | L | 217 | 23 | 400 | 482 | 29 | 34 |
| 63 | 12/15/60 | K480 | R | 222 | 29 | N.Sh. | 344 | 29 | 29 |
| | | | L | 200 | 32 | N.Sh. | 347 | 27 | 27 |
| 43 | 12/16/60 | K481 | R | 200 | 0 | N.Sh. | N.Sh. | 0 | 0 |
| | | | L | 205 | 0 | N.Sh. | N.Sh. | 0 | 0 |

T.D.—technical difficulties; N.I.—not included in protocol; N.Sh.—no sharp measurable; 0—flat or less than 5 microvolts.

TABLE 9B. b-WAVE AMPLITUDES (SMOOTH) IN MICROVOLTS

| *Individual cases* | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| *Age* | *Tested* | *Case* | | LO1 | DO1 | DO4 | DO16 | DR16 | DB16 | DG16 |
| 34 | 10/9/57 | K74 | Right | 89 | 316 | 313 | 334 | 106 | N.I. | N.I. |
| | | | Left | 87 | 316 | 311 | 389 | 100 | N.I. | N.I. |
| 43 | 1/9/58 | K75 | R | 55 | 182 | 182 | T.D. | 74 | N.I. | N.I. |
| | | | L | 108 | T.D. | 184 | 197 | 105 | N.I. | N.I. |
| 39 | 10/9/57 | K76 | R | 50 | 239 | 369 | 411 | 67 | N.I. | N.I. |
| | | | L | 46 | 233 | 324 | 396 | 56 | N.I. | N.I. |
| | 8/25/60 | | R | T.D. | 165 | 350 | 350 | 65 | 350 | 400 |
| | | | L | 38 | 140 | 442 | 221 | 49 | 221 | 232 |
| 45 | 8/8/58 | K138 | R | 56 | 172 | 311 | 294 | 33 | N.I. | N.I. |
| | | | L | 44 | 200 | 278 | 283 | 33 | N.I. | N.I. |
| | 5/3/60 | | R | 11 | 63 | 188 | 211 | 63 | 120 | 222 |
| | | | L | 51 | 86 | 319 | 274 | 29 | 257 | 290 |
| 40 | 10/2/58 | K148 | R | 78 | 389 | 411 | 544 | 167 | N.I. | N.I. |
| | | | L | 78 | 266 | 255 | 289 | 133 | N.I. | N.I. |
| | 7/22/59 | | R | T.D. | 47 | 95 | 100 | 0 | 121 | 110 |
| | | | L | 11 | T.D. | 97 | 92 | 27 | T.D. | T.D. |
| | 8/24/59 | | R | 17 | 250 | N.Sm. | 317 | 83 | 247 | 294 |
| | | | L | 15 | 179 | 242 | 316 | 107 | 337 | 284 |
| 46 | 9/10/58 | K169 | R | 89 | 255 | 422 | 400 | 89 | N.I. | N.I. |
| | | | L | 128 | 377 | 422 | 400 | 105 | N.I. | N.I. |
| 36 | 1/5/59 | K219 | R | 61 | 189 | T.D. | 289 | 44 | 272 | 289 |
| | | | L | 67 | 233 | 305 | 289 | 50 | 289 | 300 |
| | 1/28/59 | | R | 50 | 189 | 244 | 244 | 72 | 322 | 311 |
| | | | L | 44 | 167 | 222 | 233 | 56 | 294 | 283 |
| | 7/17/59 | | R | T.D. | 205 | 274 | 286 | 76 | 284 | 284 |
| | | | L | T.D. | T.D. | 263 | 270 | 54 | 242 | 242 |
| | 4/13/60 | | R | T.D. | T.D. | T.D. | 200 | 29 | 200 | N.I. |
| | | | L | T.D. | T.D. | T.D. | T.D. | T.D. | T.D. | N.I. |
| 43 | 5/12/59 | K278 | R | T.D. | 290 | 388 | 435 | T.D. | 388 | 423 |
| | | | L | T.D. | 248 | 353 | 400 | T.D. | 364 | 423 |
| 35 | 6/5/59 | K296 | R | 65 | T.D. | 420 | T.D. | T.D. | T.D. | 520 |
| | | | L | 65 | 113 | 330 | 430 | 150 | 400 | 390 |
| 50 | 6/5/59 | K298 | R | T.D. | 68 | 78 | 112 | 112 | 155 | 136 |
| | | | L | N.I. | N.I. | N.I. | N.I. | N.I. | N.I. | N.I. |
| 47 | 8/3/60 | K441 | R | 32 | 293 | 388 | 388 | 70 | 364 | 341 |
| | | | L | 40 | 270 | 423 | 400 | 74 | 411 | 411 |
| 41 | 11/16/60 | K478 | R | 40 | 188 | 411 | 411 | 86 | 470 | 482 |
| | | | L | 29 | 171 | 423 | 482 | 74 | 470 | 458 |
| 63 | 12/15/60 | K480 | R | 51 | 211 | 400 | 333 | 103 | 433 | 488 |
| | | | L | 59 | 105 | 326 | 326 | 86 | 442 | 463 |
| 43 | 12/16/60 | K481 | R | 40 | 200 | 308 | 302 | 0 | 222 | 205 |
| | | | L | 22 | 227 | 302 | 297 | 0 | 135 | 167 |

T.D.—technical difficulties; N.I.—not included in protocol; N.Sm.—no smooth measurable; 0—flat or less than 5 microvolts.

TABLE 10B. AMPLITUDES FOR DO16, 25 MILLISECONDS/INCH

| *Individual cases* | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *Age* | *Tested* | *Case* | | $n_1$ | $p_1$ | $n_2$ | $p_2$ | $p_3$ |
| 34 | 10/9/57 | K74 | Right | 176 | 200 | 223 | 141 | 329 |
| | | | Left | 167 | 167 | 189 | 89 | 244 |
| 39 | 10/9/57 | K76 | R | 167 | 167 | 189 | 111 | 266 |
| | | | L | 144 | 155 | 167 | 111 | 244 |
| | 8/25/60 | | R | 90 | 90 | 150 | 100 | 230 |
| | | | L | 63 | 53 | 74 | 84 | 147 |
| 45 | 5/3/60 | K138 | R | 46 | 17 | 29 | T.D. | T.D. |
| | | | L | 46 | 29 | 29 | T.D. | T.D. |
| 40 | 7/22/59 | K148 | R | 16 | 16 | 37 | 32 | 53 |
| | | | L | 32 | 32 | 59 | 86 | 124 |
| | 8/24/59 | | R | 270 | 259 | 317 | 176 | 282 |
| | | | L | 158 | T.D. | 221 | 116 | 274 |
| 36 | 1/5/59 | K219 | R | 44 | 44 | 67 | T.D. | T.D. |
| | | | L | 56 | T.D. | 78 | T.D. | T.D. |
| | 1/28/59 | | R | 89 | 89 | 111 | 189 | 266 |
| | | | L | 78 | 78 | 100 | 133 | 244 |
| | 7/17/59 | | R | 82 | 65 | 92 | 82 | 194 |
| | | | L | 86 | 82 | 92 | 97 | 167 |
| 43 | 5/12/59 | K278 | R | T.D. | T.D. | T.D. | T.D. | T.D. |
| | | | L | 176 | 176 | 212 | 82 | 235 |
| 35 | 6/5/59 | K296 | R | T.D. | T.D. | T.D. | T.D. | T.D. |
| | | | L | T.D. | T.D. | 160 | 100 | 320 |
| 50 | 6/5/59 | K298 | R | 69 | 54 | 83 | 49 | 78 |
| | | | L | T.D. | T.D. | T.D. | T.D. | T.D. |
| 47 | 8/3/60 | K441 | R | 106 | 106 | 153 | 141 | 294 |
| | | | L | 106 | 106 | 153 | 71 | 235 |
| 41 | 11/16/60 | K478 | R | 129 | 129 | 223 | 306 | 435 |
| | | | L | 153 | 153 | 235 | 341 | 458 |
| 63 | 12/15/60 | K480 | R | 78 | 67 | 100 | T.D. | T.D. |
| | | | L | 74 | 63 | 116 | T.D. | T.D. |
| 43 | 12/16/60 | K481 | R | 68 | 57 | 68 | 148 | 200 |
| | | | L | 59 | 54 | 70 | 211 | 270 |

T.D.—technical difficulties.

V. OPTIC ATROPHY

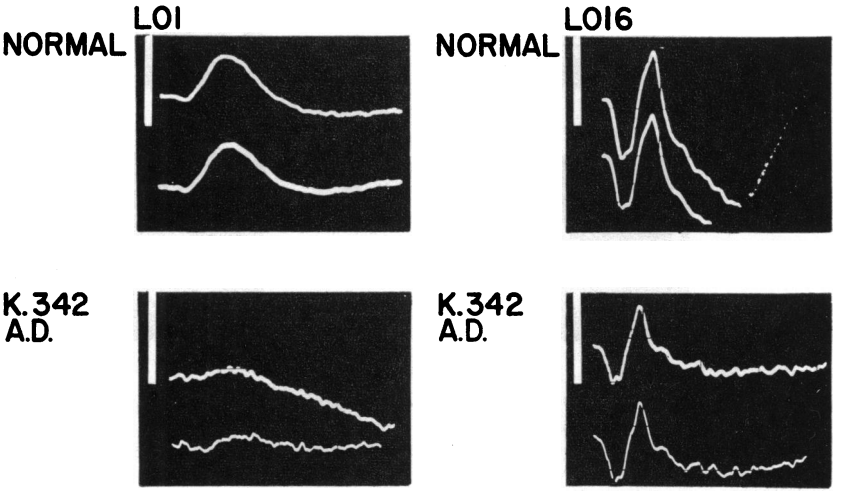



FIGURE 13.

(Upper left) Normal (LO1). The vertical stripe indicates 200 microvolts. The narrower band (above) is the response from the right eye. The broader stripe below is the left eye. Both responses are those to a low intensity stimulus in the light. (Lower left) A.D. (K342). This is a 60-year-old white male who has suffered primary optic atrophy from lues. His present vision is no light perception, both eyes, as it was at the time of testing. Although his LO1 response appears slightly reduced, the remaining stimuli will reveal an essentially normal response. (Upper right) Normal (LO16). Typical normal paired reactions to maximum stimuli in the light adapted state. (Lower right) A.D. (K342). Essentially normal response.

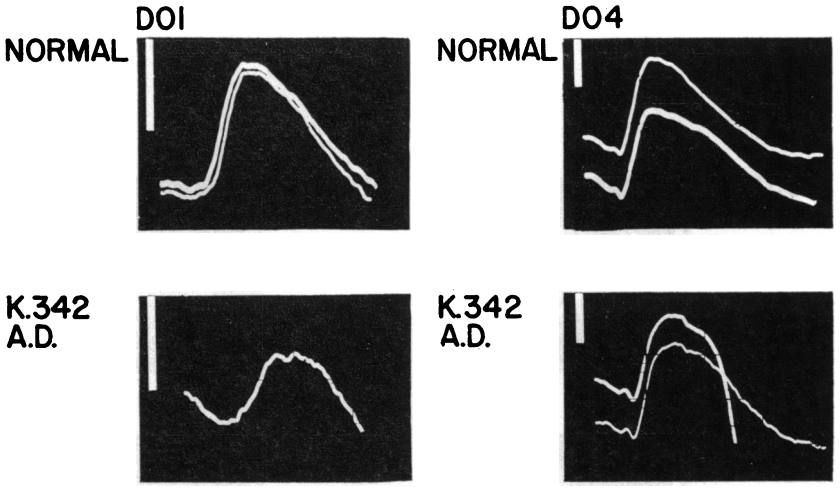



FIGURE 14.

(Upper left) Normal (DO1). After five minutes' dark adaptation a minimum intensity stimulus in the normal has this appearance. (Lower left) A.D. (K342). This response from the right eye of this blind patient is not absolutely normal but in consideration of the circumstances it is probably within normal limits. (Upper right) Normal (DO4). With a slight increase in the intensty of the stimulus the a-wave becomes more pronounced. (Lower right) A.D. (K342). The response here compares favorably with the normal. One must remember that this patient could only be faced toward the stimulus.

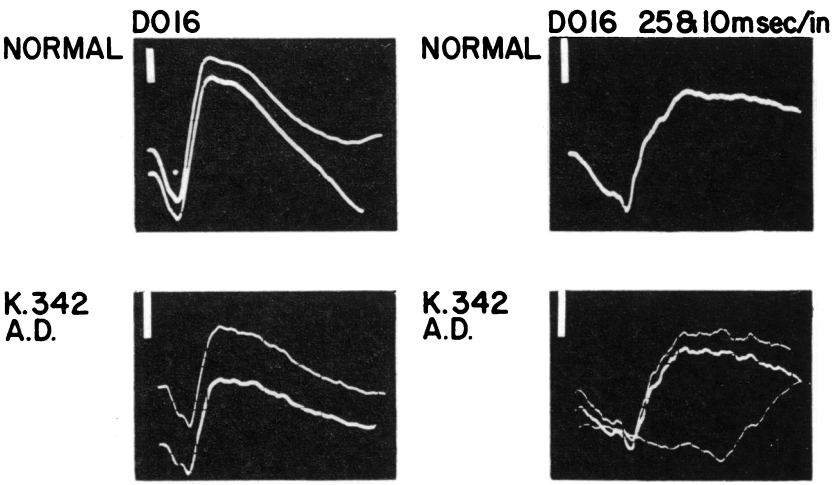



FIGURE 15.

(Upper left) Normal (DO16). Typical normal response to maximum intensity stimulus in the dark. (Lower left) A.D. (K342). The responses from both eyes are within normal limits. (Upper right) Normal (DO16). 25 millisecond sweep left eye. There is no 25 millisecond sweep right eye and the 10 millisecond sweep has not been recorded. (Lower right) A.D. (K342). The paired responses to DO16 with a 25 millisecond sweep are well within normal limits. The single sweep response (left eye) with a 10 millisecond sweep is also within normal limits.

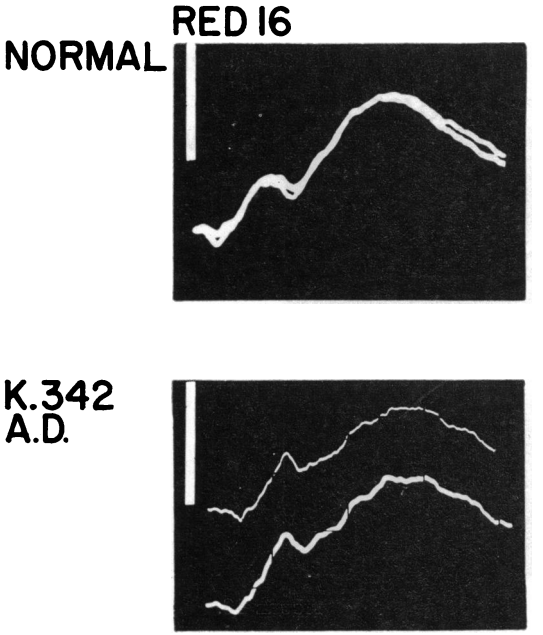



FIGURE 16.

(Upper) Normal (D red 16). The paired responses (left and right) illustrate the characteristic a-, b-wave sharp peak and slow peak. (Lower) A.D. (K342). The paired responses of the primary optic atrophy eyes are within normal limits.

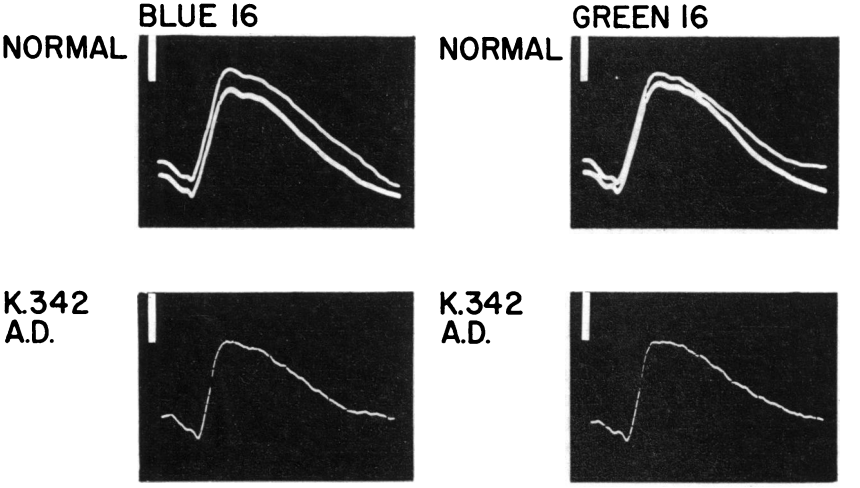



FIGURE 17.

(Upper left) Normal (D blue 16). Typical response to D blue 16. (Lower left) A.D. (K342). The responses from the right eye at similar amplification are essentially normal. (Upper right) Normal (D green 16). Very similar to D blue 16. (Lower right) A.D. (K342). The response from the right eye is within normal limits.

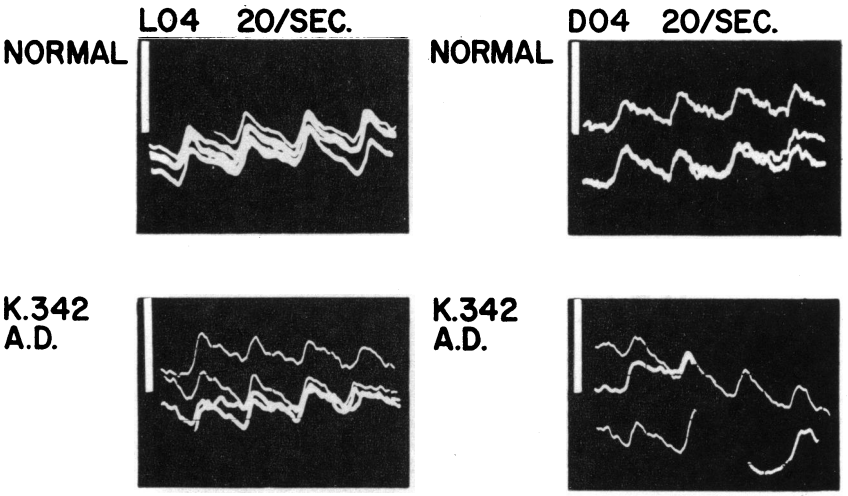



FIGURE 18.

(Upper left) Normal (LO4, 20/second flicker). (Lower left) A.D. (K342). The response is similar to the normal in every way. (Upper right) Normal (DO4, 20/second flicker). (Lower right) A.D. (K342). Similar to the normal response.

## *REFERENCES*

1. Noell, W. K., Studies on the Electrophysiology and the Metabolism of the Retina. Proj. No. 21–101–004, Report No. 1. Randolph Field, Texas, U.S.A.F. School of Aviation Medicine, October, 1953.
2. Brown, K. T., and T. N. Wiesel, Intraretinal recording in the unopened cat eye, Am. J. Ophth., 46:91, 1958.
3. Granit, R., Sensory Mechanisms of the Retina. Appendix II, Electroretinography on Man. London, Oxford University Press, 1947, p. 350.
4. ——— Receptors and Sensory Perception. The Electroretinogram. New Haven, Yale University Press, 1955, p. 151.
5. Karpe, G., Basis of clinical electroretinography, Acta Ophth., (Suppl.), 24:30, 1946.
6. Riggs, L. A., Continuous and reproducible records of the electrical activity of the human retina, Proc. Soc. Exper. Biol. & Med., 48:204–7, 1941.
7. ——— Electroretinography in cases of night blindness, Am. J. Ophth., 38:70–2, 1954.
8. Riggs, L. A., J. C. Cornsweet, and W. G. Lewis, Effects of light on electrical excitation of the human eye, psychological monograph published by the American Psychological Association, Inc., vol 71, no. 5, 1957.
9. Armington, J. C., Amplitude of response and relative spectral sensitivity of the human electroretinogram, J. Optic. Soc. America, 45:1058–64 (Dec.), 1955.
10. Armington, J. C., and F. C. Thiede, Selective adaptation of components of the human electroretinogram, J. Optic. Soc. America, 44:779–86 (Oct.), 1954.

11. Armington, J. C., and W. R. Biersdorf, Flicker and color adaptation in the human electroretinogram, J. Optic. Soc. America, 46:393–400 (June), 1956.
12. Noell, W. K., The origin of the electroretinogram, Am. J. Ophth., 38: 78–90, July (pt. 2), 1954.
13. ——— The visual cell: electrical and metabolic manifestations of its life processes; the Friedenwald Memorial Lecture, Am. J. Ophth., 48: 347–70, Nov. (pt. 2), 1959.
14. Dowling, John E., Night blindness, dark adaptation, and the electroretinogram, Am. J. Ophth., 50:875–89 (Nov.), 1960.
15. Potts, A. M., R. W. Modrell, and C. Kingsbury, Permanent fractionation of the electroretinogram by sodium glutamate, Am. J. Ophth. 50:900–7 (Nov.), 1960.
16. Noell, W. K.,Personal communication.
17. Dodt, E., and L. Wadensten, The use of flicker electroretinography in the human eye: Observations on some normal and pathological retinae, Acta Ophth., 32:165–80, 1954.
18. Henkes, H. E., Differentiation and evaluation of rod and cone system responses in the human electroretinogram, Ophthalmologica, 135:138–46 (Feb.), 1958.
19. Heck, J., The flicker electroretinogram of the human eye, Acta physiol. Scandinav., 39:158–66, 1957.
20. Dodt, E., Ergebnisse der flimmer–elektroretinographie, Experientia, 10:330, 1954.
21. Wadensten, L., The use of flicker electroretinography in the human eye, Acta Ophth., 34:311–40, 1956.
22. ——— Flimmer-elektroretinographische Untersuchungen bei Schwachsichtigkeit; Hamburger Symposium 1956, Bibl. Ophthal., 48:132–6, 1957.
23. Granit, R., Physiological basis of flicker electroretinography as applied in clinical work, Ophthalmologica, 135:327–48, 1958.
24. Goodman, G., and G. Iser, Physiologic studies with flicker electroretinography, Am. J. Ophth., 42:212–26 (Oct.), 1956.
25. Heck, J., and I. Rendahl, Components of the human electroretinogram: An analysis in normal eyes and in colour blindness. A preliminary report, Acta physiol. Scandinav., 39:167–75, 1957.
26. Rendahl, I., Clinical recording of the x-potential. A preliminary report, Acta Ophth., 35:97–103, 1957.
27. Auerbach, E., and H. M. Burian, Studies on the photopic-scotopic relationships in the human electroretinogram, Am. J. Ophth., 40: 42–59, Nov. (pt. 2), 1955.
28. Jacobson, J. H., D. Basar, A. L. Kornzweig, Spectro-differential electroretinography in macular disease, Am. J. Ophth., 42:199–205 (Oct.), 1956.
29. Karpe, G., Discussion of paper by Roe, Acta Ophth., 26:181, 1948.
30. Potts, A. M., J. Praglin, I. S. Farkas, Orbison, and Chickering, Studies on the visual toxicity of methanol. VIII. Additional observations on methanol poisoning in the primate test object, Am. J. Ophth., 40:76, 1955.
31. Ruedemann, A. D., Jr., and W. K. Noell, A contribution to the electroretinogram of retinitis pigmentosa, Am. J. Ophth., 47:564–73 (Jan.), 1959.
32. Ruedemann, A. D., Jr., The electroretinogram in hereditary visual cell degeneration, Tr. Am. Acad. Ophth., March-April, 1959, pp. 142–3.
33. Menne, Frank R., Acute methyl alcohol poisoning, Arch. Path., 26:77, 1938.
34. Morgan, O. Gayer, Four cases of methylated spirit addiction, Tr. Ophth. Soc. U. Kingdom, 72: 435–41, 1952.
35. Dewar, James, The physiological action of light, Nature, London, 15:433, 1876.

36. Goodman, G., and H. Bornschein, Comparative electroretinographic studies in congenital night blindness and total color blindness, Arch. Ophth., 58:174, 1957.
37. Bornschein, H., and G. Goodman, Studies of the a-wave in the human electroretinogram, Arch. Ophth., 58:431–7, 1957.
38. Iser, G., and G. Goodman, Clinical studies with flicker electroretinography, Am. J. Ophth., 42:227 (Oct.), 1956.
39. Ruedemann, A. D., Jr., and W. K. Noell, The electroretinogram in central retinal degeneration. In press.
40. Wood, C. A., and F. Buller, Poisoned by wood alcohol, J.A.M.A., 43:972, 1058, 1117, 1213, and 1289, 1904.
41. Bennett, I. A., F. H. Cary, G. L. Mitchell, and M. N. Cooper, A review based on experiences in an outbreak of 323 cases, Medicine, 32:431, 1953.
42. Benton, C. D., and F. P. Calhoun, The ocular effects of methyl alcohol poisoning: Report of a catastrophe involving 320 persons, Tr. Am. Acad. Ophth., 56:875–85, 1952.
43. Bennett, I. L., T. Nation, and J. F. Olley, Pancreatitis in methyl alcohol poisoning, J. Lab. Clin. Med., 40:405–9, 1952.
44. Province, W. D., R. A. Kritzler, and F. P. Calhoun, Methyl alcohol poisoning, report of cases, Bull. U.S. Army M. Dept., 5:114, 1946.
45. Aronson, Discussion of Stadelmann and Magnus-Levy. Ueber die in der Weihnachtszeit 1911 vorgekommenen Massenvergifting, Berl. klin. Wchnschr., 1:180, 1912.
46. Pick, L., and M. Bielschowsky, Ueber histologische Befunde im Auge und im Zentralnervensystem des Menschen bei akuter toedlicher Vergiftung mit Methylalkohol, Berl. klin. Wchnschr., 1:888, 1912.
47. Birch-Hirschfield, A., Contribution to knowledge of the retinal ganglion cells under physiological and pathological conditions, von Graefe's Arch. Ophth., 52:358–83, 1901.
48. Roe, O., The gangion cells of the retina in cases of methanol poisoning in humans and experimental animals, Acta Ophth., 26:169, 1948.
49. Muller, H., Histologische Untersuchung eines Auges bei akuter toedlicher Methylalkoholvergiftung, Klin. Monatsbl. Augenh., 116:135, 1950.
50. Orthner, H., Methylalkoholvergiftung mit besonders schweren Hirnveraenderungen, Arch. Path. Anat., 323:442–64, 1953.
51. Orthner, H., Methanolvergiftung, Arch. f. exper. Path. u. Pharmakol., 218: 67–9, 1953.
52. Fink, W. H., Ocular pathology of methyl aclohol poisoning, Am. J. Ophth., 26:694, 1943.
53. Duke-Elder, W. S., Textbook of Ophthalmology. St. Louis, C. V. Mosby Co., 1949, Vol. III, p. 3023, fig. 2600.
54. McGregor, I. S., Study of histopathologic changes in the retina and late changes in the visual field in acute methanol poisoning, Brit. J. Ophth., 27:523, 1943.
55. Harrop, G. A., and E. M. Benedict, Acute methyl alcohol poisoning associated with acidosis, J.A.M.A., 74: 25, 1920.
56. Haskell, C. S., S. P. Hileman, and W. R. Gardner, The significance of acidosis of methyl alcohol poisoning, Arch. Int. Med., 27:71, 1921.
57. Roe, O., Metabolism and toxicity of methanol, Pharmacol. Rev., 7:399, 1955.
58. ––– Clinical investigation of methyl alcohol poisoning with special reference to the pathogenesis and treatment of amblyopia, Acta med. Scandinav., 113:558, 1943.
59. ––– Methanol poisoning: Its clinical course, pathogenesis and treatment, Acta. med. Scandinav., 126:1–253 (Suppl. 182), 1946.

60. Zatman, L. J., The effects of ethanol on the metabolism of methanol in man, Biochem. J., 40:lxvii, 1946.
61. Kendall, L. P., and A. N. Ramanathan, Excretion of formate after methanol ingestion in man, Biochem. J., 54:424, 1953.
62. Chew, W. B., E. H. Berger, O. A. Brines, and M. J. Capron, Alkali treatment of methyl alcohol poisoning, J.A.M.A., 130:61, 1946.
63. Potts, A. M., L. V. Johnson, and D. Goodman, Studies on the visual toxicity of methanol. I. The effect of methanol and its degradation products on retinal metabolism, Am. J. Ophth., 35:107 (May), 1952.
64. Gilger, A. P., A. M. Potts, and L. V. Johnson, Studies on the visual toxicity of methanol. II. The effect of parenterally administered substances on the systemic toxicity of methyl alcohol, Am. J. Ophth., 35:113–26 (May), 1952.
65. Praglin, J., R. Spurney, and A. M. Potts, Experimental study of electroretinography; electroretinogram in experimental animals under influences of methanol and its oxidation products, Am. J. Ophth., 39:52–62 (Feb.), 1955.
66. Gilger, A. P., and A. M. Potts, Studies on the visual toxicity of methanol. V. The role of acidosis in experimental methanol poisoning, Am. J. Ophth., 39:63–86 (Feb.), 1955.
67. Potts, A. M., Studies on the visual toxicity of methanol. VI. The clinical aspects of experimental methanol poisoning treated with base, Am. J. Ophth., 39:86–92 (Feb.), 1955.
68. Noell, W. K., Personal communication.