The results of the study on the efficacy of CP-45,634 in delaying cataract development in diabetic rats are depicted in Fig. 1. Within 3 weeks after the onset of diabetes, small vacuoles in the equatorial region appeared in the lens of a diabetic rat. This change was followed by a diffuse but uneven cloudiness in the anterior subcapsular region. In some cases the posterior subcapsular region was involved, but the anterior region was much more severely affected. As the cataract progressed, there was considerable disruption of the cortical fibers, leading to diffuse but marked clouding of this region. In 6 to 9 weeks a dense nuclear opacity appeared. However, the striking fact was that in diabetic rats treated with CP-45,634, none of these lens changes occurred. Even after 5 months, the early lens changes were not detected by slit-lamp examination in any of the 36 diabetic rats treated with CP-45,634.

Discussion. The AR inhibitor CP-45,634 is highly potent and effective in animals. Previously, Peterson et al.[2] found that CP-45,634 administered orally at a dose of 5 to 10 mg/kg/day to galactose-fed rats delayed lens changes so that only 10% of treated rats developed any lens opacities after 29 days on the galactose diet. At the same time untreated galactose-fed rats all developed lens opacities after 15 days on the diet. In our study with diabetic rats where we used a higher daily dose of 60 mg/kg, cataract formation appeared to be prevented. During the 5-month period no discernible lens changes were observed by slit-lamp examination of the diabetic rats treated with the AR inhibitor, whereas lens changes in the untreated diabetic rats were detected within 3 weeks after onset of diabetes. In addition, the sorbitol level in the lenses of treated diabetic rats was not significantly elevated.

In contrast to the low dose of the Pfizer inhibitor necessary to alter the course of cataract formation in diabetic rats, a much higher dose of quercitrin was used in delaying cataracts in diabetic degus.[4] In those studies quercitrin at a level of approximately 700 mg/kg was administered orally to retard the development of the nuclear opacity.[4] In the quercitrin-treated diabetic degus, lens changes in the form of vacuoles did appear, indicating that the cataractous process was not completely abolished.

The effectiveness of CP-45,634 in retarding the cataractous process in diabetic rats and the delaying of cataract formation in diabetic degus by quercitrin treatment strongly indicate that AR is involved in the initiation of diabetes cataracts. The study also suggests the possibility that AR inhibitors may be useful clinically in altering the course of human diabetes cataracts.

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Key words: diabetes cataracts, aldose reductase, sorbitol

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ERG lens with built-in Ganzfeld light source for stimulation and adaptation.

AART C. KOOIJMAN AND ALBERT DAMHOF.

A contact lens for routine electroretinography which contains a Ganzfeld light source is described. The light source consists of six light-emitting diodes and serves both as a stimulus source and a background illumination. The response characteristics with this source are comparable with those of an integrating sphere stimulator.

For clinical electroretinography generally a Ganzfeld stimulus is required. This is done to avoid indirect stimulation of a part of the retina through stray light and to obtain maximal responses.

Usually an integrating sphere is used with a xenon flash tube attached to it, and, if an adapting background is required, a second light source is also incorporated. In this report we describe an electroretinogram (ERG) contact lens with a built-in Ganzfeld light source which serves both for stimulation and for adaptation.

It proved possible to obtain identical ERGs with this light-emitting diode (LED) stimulator and an integrating sphere stimulator.

Methods. The design of our contact lens with

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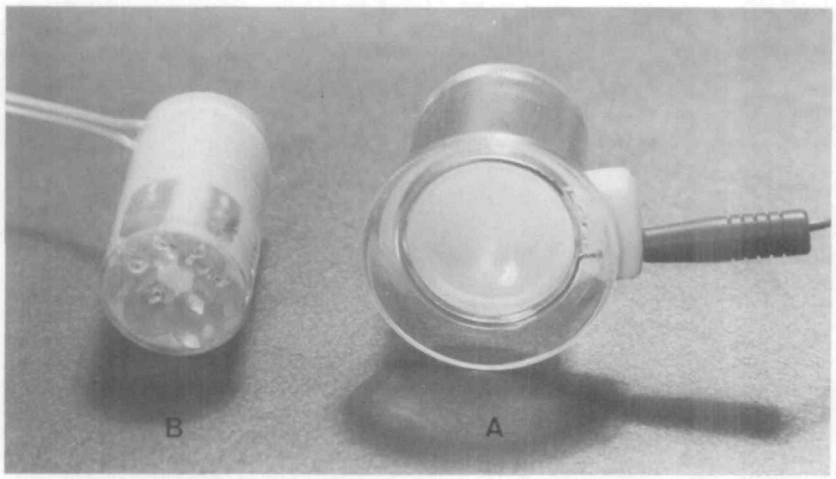

Fig. 1. Diffuse ERG lens with Ganzfeld light source. **A**, Corneal part of the scleral lens is made of diffusely translucent plastic to scatter the light emitted by the six LEDs. **B**, Six LEDs are ground off to fit them in a compact unit which can be placed on the corneal part of the contact lens. The convex frontal surfaces of the LEDs are polished concave to increase the distribution angle of the emitted light. The combination of the diffusing corneal lens with the flat LEDs gives a light distribution on the cornea which is comparable to the light distribution of light rays arising from an integrating sphere stimulator. The ERG lens contains a corneal ring electrode.

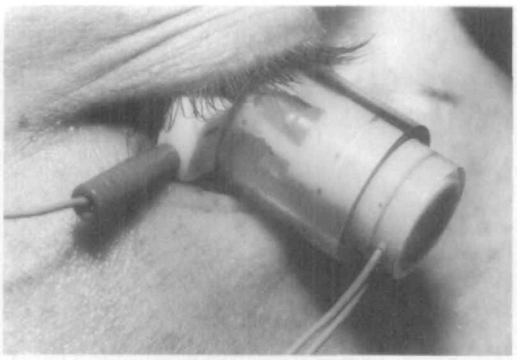

Fig. 2. Contact lens with LED unit placed on the eye.

built-in sitmulator is a modified Henkes type contact lens (Figs. 1 and 2). On the outer surface a hollow Perspex cylinder was made with a diameter of about 12 mm and a height of 15 mm. Into this hollow cylinder fits an array of six yellow-green (peak 570 nm, half-width 25 nm) LEDs (Siemens LD57C). The convex frontal surfaces are polished to a concave shape to increase the distribution angle of the emitting light and to fit closely the frontal surface of the contact lens. The corneal part of the scleral lens is made of diffusely translucent plastic and covers the whole cornea.

The combination of the LED array and the opaline corneal lens makes the distribution of the light rays which reach the cornea equal to the distribution of a Ganzfeld. The illumination energy at the cornea can be selected in steps of 0.5 log unit between 10^{-3} to 10 lux · sec by changing the stimulus flash duration (minimal 3 μsec and maximal 30 msec). This compares well with the stimulus energy range of our Ganzfeld sphere stimulator with the white xenon flash (General Electric Strobotac). In this apparatus the maximum energy is 3 lux · sec and can be reduced by neutral density filters (Agfa-Gevaert gelatin filters).

The LED stimulator can also serve as an adapting background. In that case a direct current is continuously passed through the LEDs, and the flashes are given as additional short-lasting current pulses. The maximum corneal illumination is 10 lux. With the integrating sphere the adapting background is given by incandescent lamps, and the corneal illumination is 5 lux.

The responses to both types of stimulus were measured in the same eye. The subject dark-adapted during 30 min before the start of the measurements. The pupil was dilated by 2 drops of tropicamide (0.5%). Measurements were taken in one session in the following order: (1) white flash stimulation in the dark, (2) LED flash stimulation

in the dark, (3) light adaptation by the LED light source, (4) LED flash stimulation on the adapting background, (5) light adaptation in the sphere stimulator, and (6) white flash stimulation on the adapting background. Nine subjects participated in these measurements.

Results. Typical examples of responses with both the LED and the sphere stimulator are shown in Fig. 3. None of the sets of responses to both stimulators of the subjects showed differences greater than those presented in this figure. The amplitudes of a and b wave and the implicit time of the b wave of the responses with the LED stimulus of nine subjects are plotted in Fig. 4. Several subjects preferred the LED stimulator above the sphere stimulator because they were frightened by the loud click with the discharge of the flash tube whereas the LED stimulator was silent.

Discussion. The LED stimulator in a light-diffusing contact lens can replace the integrating sphere stimulator for routine ERG measurements with Ganzfeld stimulation. The LEDs can produce flash stimuli in a large energy range and simultaneously can provide an adapting background. These stimulus conditions are required for the standardized ERG-measuring procedure of the Netherlands Group *Physical Methods in Ophthalmology.*[1] A single LED in a clear contact lens[2] seems less suitable for routine ERG measurements because the response characteristics are influenced by the pupil diameter and it is not possible to make a Ganzfeld adapting background. With an incandescent lamp as light source[3] it is not possible to stimulate with short flashes, and its intensity range is rather short. The yellow-green color of the LEDs is no disadvantage vs. the white xenon flash. The sensitivity of the rod system for this color is much larger than that of the cone system. Therefore it is possible (1) to measure the isolated rod response in a large stimulus energy range and (2) to use the LEDs as a very effective adapting light for rod response suppression to measure isolated cone responses. In normal as well as in protanomalous and deuteranomalous subjects the yellow-green color is able to stimulate the cone system.[4]

The control of stimulus energy and background illumination can be done electronically with the use of LEDs. This is much simpler than the hybrid control with filters and electronics in an integrating sphere stimulator. Furthermore, the construction of the contact lens with the LED stimulator is much cheaper than that of an integrating sphere-flash arrangement.

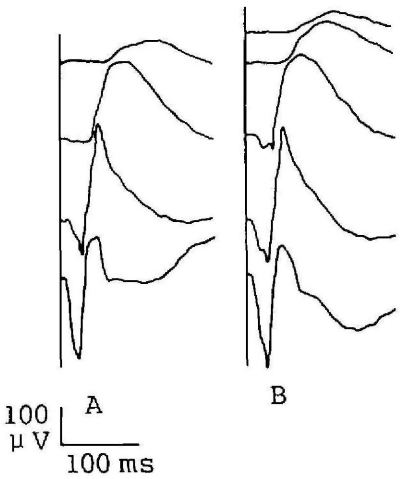

Fig. 3. Scotopic condition; dark adapted subject. **A,** ERG responses to a white flash stimulus. **B,** ERG responses to a yellow-green LED stimulus. Traces are averages of 10 responses (1 stimulus flash/sec).

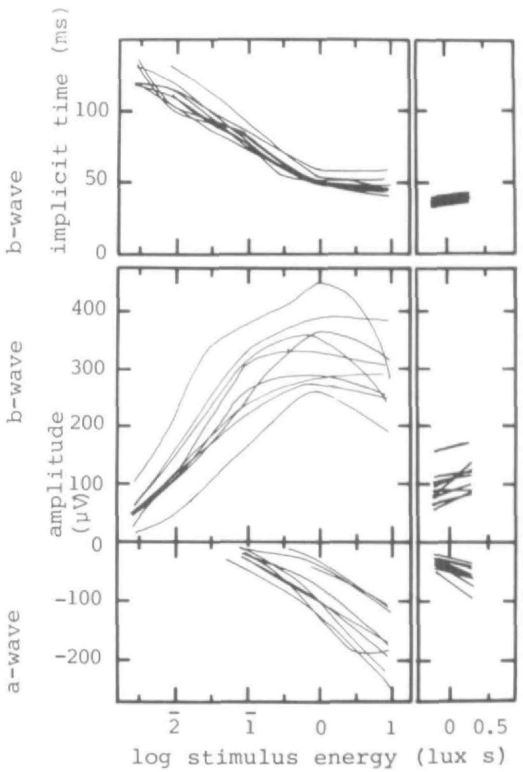

Fig. 4. Characteristics of the responses of nine subjects measured with the Ganzfeld contact lens stimulator. *Left,* scotopic condition; *right,* photopic condition.

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Key words: ERG, Ganzfeld stimulator, LED light source

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The scalp topography of the human visually evoked subcortical potential.

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Stimulus and analysis parameters have been adjusted to provide optimum conditions for producing and recording the early components of flash visual evoked potentials. A visual evoked subcortical potential (VESP) of mean latency P_{23}-N_{28}-P_{34} has been recorded in 86% of subjects. The triphasic wave was maximal at an electrode position slightly posterior to the Rolandic/Sylvian fissure and topographically separate from the lid electroretinogram and the visual evoked cortical potential. Monocular stimulation shows bilateral reduction of the amplitude of the VESP, indicating that the wave is independent of the retina and optic nerve and must be arising from a postchiasmal site.

The early components, i.e., components before 50 msec latency, of the visually evoked potential in man are poorly documented because of their minute amplitude, intersubject variability, and poor repeatability under the standard experimental conditions used for eliciting the visual evoked cortical potential (VECP).[1]

Van Hasselt[2] reported an "ear-mastoid" potential of 10 msec latency which could only be recorded in a small percentage of subjects and suggested the optic nerve as its origin. Cracco and Cracco[3] described early oscillatory potentials at 100 cy/sec recorded from a wide scalp distribution of electrodes, referred to earlobe electrodes. Early in 1979 we identified a triphasic positive-negative-positive component (msec) in some subjects at latencies of positive 22 (P_{22}), negative 27 (N_{27}), and positive 35 (P_{35}).[4] Since it appeared important to delineate this component from both the scalp-recorded ERG and the VECP, we have carried out a topographic study of the scalp distribution.

Materials and method. Observations were made on 14 normal volunteer subjects (eight male and six female) ages between 19 and 38 years (mean 26 years). All had visual acuities of 6/6 or better. For this topographical study, electrodes were placed according to the International 10/20 system.[5] In the first study, an anterior-posterior series of electrodes at FP_z, F_8, T_4, T_6, and O_z and half-distance electrodes at $F_{8½}$ and $T_{4½}$ were used (Fig. 1). For the study of the transverse distribution, electrodes were placed at C_4, C_6, T_4, and T_8 and at CP_4, CP_6, $T_{4½}$, and $T_{8½}$ (Fig. 2). All recordings were made with common reference, but the choice of a relatively inactive reference site was confounded by both the ERG and VECP. Investigation of commonly used reference sites shows that the midfrontal (F_z) was affected by the ERG and both the earlobe and mastoid were highly active for the P_{22}-N_{27}-P_{35} component. Indeed it is likely that the active nature of this site[6] is probably responsible for some so-called early components of the visually evoked potential. It was found that the vertex site (C_z) was relatively inactive at the latency of the early components and had the added advantage of being equidistant from all the electrodes in the anterior-posterior chain.

This site was also used for the transverse topographic study, but since the rules of equal interelectrode distance are negated, a further reference on the anterior neck was used for comparison. The subjects were seated in a dimly lit room, and flash stimulation was delivered by a Grass PS22 photostimulator 25 cm from the eyes. Silver–silver chloride electrodes were affixed with collodion, and the resistance was maintained below 5 Kohm. A PDP8E computer was used to average the response from each of the eight channels of the electroencephalogram recorded on an Elema Schonander machine. The analysis time was 100 msec, and the bandpass of the equipment was from 66 to 700 Hz.

To maximize the signal, it was found necessary to average the response to 500 stimuli delivered at

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