line pressures were determined in both eyes, a single dose of 4 per cent pilocarpine (Pilocel) was instilled into the right eye of each patient. Repeat IOP measurements were made at half-hour intervals for two hours and then hourly for two more hours. The decrease in pressure in the treated eye reached maximum levels in both groups between one and two hours, with pressure differences between the treated and untreated eye reaching significant levels at 30 minutes in the control group (p < 0.005) and 60 minutes in the EMB group (p < 0.01). Analysis of the percentage of decline in IOP revealed the two groups differed significantly only at the 30 minute reading. No attempt was made to determine a difference in the duration of the pilocarpine effect between the EMB and control groups. Blood samples were drawn prior to baseline pressure determinations. Serum analysis showed no difference in in vitro enzymatic hydrolysis of pilocarpine between the two groups (Table I).

Since this study indicates that EMB at the usual clinical dose is not effective as an inhibitor of the pilocarpine-hydrolyzing enzyme, further analysis was carried out to determine the approximate serum level at which this inhibitory effect would be observed. In addition to EMB, penicillamine, EDTA, and kanamycin were also studied. Each inhibitor was evaluated on three individuals and one pooled serum sample. The basic method of serum analysis was followed except that inhibitors were allowed to react with the serum for 30 minutes prior to the addition of pilocarpine. Total incubation time was 7 hours.

The inhibitor concentration at which 50 per cent inhibition occurred was determined from a plot of mean per cent inhibition of the enzyme against log molar concentration of the inhibitor. The concentrations of the inhibitors producing 50 per cent enzyme inhibition per 0.8 ml. of serum were: EMB, 3.07 x 10^{-2} M.; penicillamine, 2.26 x 10^{-3} M.; and EDTA, 2.11 x 10^{-3} M. (Fig. 1). Normal serum level of EMB obtained two to four hours following ingestion of the usual clinical dose of 25 mg. per kilogram is 5 µg per milliliter (1.8 x 10^{-4} M.).

The results of these present studies indicate that the pilocarpine-hydrolyzing enzyme in human serum is probably not clinically significant. There appears to be no relationship between control of clinical glaucoma with pilocarpine therapy and serum levels of the pilocarpine-hydrolyzing enzyme. In rabbits, serum enzyme levels are not altered by chronic or acute pilocarpine application, nor do pilocarpine or other glaucoma medications appear to have any effect on serum enzyme levels in patients with open-angle glaucoma. In the doses employed clinically inhibitors of the pilocarpine-hydrolyzing enzyme of serum do not increase the hypotensive action of pilocarpine.

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REFERENCES


A technique for testing visual function in the presence of opacities.

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If two small images of a coherent light source are focused in the pupil of the eye, they produce an interference pattern on the retina that is sinusoidally modulated and thus appears to the subject as a grating, with a spatial frequency that depends on the distance between the images. Because the optics of the eye are not used to form the interference pattern, this technique has been advocated as a means for estimating retinal function in patients with whom conventional methods for measuring acuity cannot be used because of opacities in the ocular media or severe optical aberrations. This technique may be of use as an aid in deciding whether retinal function is normal enough to justify surgery and whether (in Goldmann's words) not only the doctor, but also the patient, will benefit from the operation.
Fig. 1. Effect of diffusing material on visual acuity (mean data from two emmetropic observers). Triangles: interference method; circles: Maxwellian view; squares: normal optotypes. Thin opacities were simulated by placing various thicknesses of diffusing plastic close to the eye. Density is specified in terms of the amount of light that passes through the film in its original direction of travel, e.g., a density of 3.0 means that 0.1 per cent of the original light was transmitted, while the rest was scattered or absorbed by the film.

Unfortunately, the interference technique is complicated and time consuming. Its success seems, in large measure, to be due to the fact that very bright test patterns are obtained, which can be seen by the patient even after attenuation by partially opaque media. Bright retinal images can also be obtained with Maxwellian-view optics, which are much easier to use than interference patterns. The following report compares the effectiveness of normal optics, Maxwellian-view optics, and interference patterns in measuring visual acuity through opacities.

In its simplest form, a Maxwellian view system consists of a light source, a positive lens, and a test object in silhouette. The lens is placed between the light source and the observer at such a distance that an image of the source is formed in the pupil of the observer's eye. The lens then appears brightly and uniformly illuminated. The test object is placed between the source and the lens so that the observer can view it with relaxed accommodation. A diagram of the apparatus is given in Westheimer.8 In the present experiment, our source was a 100-W halogen-cycle lamp with a small tungsten filament. The light was collimated with an achromatic lens and focused in the observer's pupil by a 50 mm. focal-length objective. The test patterns were square-wave gratings and Landolt rings that were photographed on high-contrast film. A glass filter that only passed red light above 619 nm. was included in the system so that the test field had approximately the same hue as the laser interference patterns. The mean retinal illuminance was approximately 50,000 td. when no diffusing material was present.

The system for producing interference-fringe patterns has been described in detail elsewhere.9 Briefly, light from a 4 mW., He-Ne laser was split into two beams, which were focused in the observer's pupil with the same objective that was used in the Maxwellian-view system. Interference between light from the two focal images caused sine-wave interference fringes on the retina. These appeared to the observer as a vertical grating of alternate bright and dark-red bars, with the same mean brightness as the Maxwellian-view gratings.

Conventional measurements of visual acuity were made with a Rodenstock "Rodavist" optotype projector. The test objects were dark letters and Landolt rings on a white screen that had a luminance of approximately 300 cd. per square meter. Viewed with normal vision and clear media, this corresponds to a retinal illuminance of about 1,600 td.

Optical disturbances such as opacities of the cornea were simulated by observing through several thicknesses of translucent plastic film. In addition, the surface of the film is not homogeneous and presumably introduces phase distortions, which are a characteristic of cataracts.10

Visual acuity, measured with various thicknesses of plastic film immediately in front of the observer's cornea, is shown in Fig. 1. When no opaque material was present, relatively little dif-
ference was found among the results obtained with the three methods. However, visual acuity measured with conventional test objects drops rapidly when diffusing materials are placed in the optical path, whereas the same materials have little effect when acuity is measured with either interference patterns or Maxwellian-view patterns, until very dense layers of plastic are introduced. The loss in acuity as opacity is increased is similar for the interference-fringe and Maxwellian-view methods, although the former gives slightly better acuity under all conditions. The fact that optotypes gave slightly better acuity than the Maxwellian-view test patterns when no diffuser was present is probably due to the fact that at high luminance levels, Landolt-ring test objects give higher measured acuity than grating test objects. Very high acuity values for interference-fringe test objects have been reported earlier. The relative effectiveness of the interference fringes and the Maxwellian-view method were tested on a patient whose uncorrected visual acuity was reduced to O.D. 20/200; O.S. 20/100 as a result of keratitis parenchymatosa, with numerous vascular growths in the region of the optic axis. He was able to resolve interference gratings that corresponded to a visual acuity of 20/38 with either eye, and Maxwellian-view gratings that corresponded to 20/23.

Both the Maxwellian view and interference methods have a marked advantage over conventional methods when it is necessary to measure visual acuity in the presence of opacities. The relative sensitivity of the Maxwellian view and interference methods depend on the specific type of disturbance, although our results for the two methods were generally similar. We concur with Green's interpretation that one reason for the effectiveness of the interference-fringe method is that it enables one to increase the light flux that enters the eye, and thus to compensate for the light that is lost through absorption and scatter. The Maxwellian-view method also has this advantage, as well as allowing the use of red light, which is diffused less than white light by Rayleigh scatter. Both methods use a small bundle of rays entering the eye, so that if a small area of the lens is free of cataract, the light can enter as if no opacity was present. Both methods are most effective when the opacity is restricted to a thin layer, and the source image is focused at this layer.

Both methods have individual advantages and drawbacks. The laser interference system can provide extremely high levels of illumination. The retinal pattern produced with this system is not affected by the state of accommodation of the eye nor by refractive errors, as long as the system is properly adjusted and the two source images are focused at the first principal point of the eye (for practical purposes, in the apparent pupil). The interference method has the disadvantage of being large, expensive, and difficult to construct and operate. Because of the care that is needed in using this method, examinations are necessarily time consuming. Both focal images must be accurately placed in the pupil; if one is blocked, the patient will see a uniform field but no grating, which could lead to an incorrectly low estimate of retinal function. Only sine-wave test patterns can be produced, which some patients have difficulty in recognizing.

The Maxwellian-view system is small, inexpensive, and relatively trouble free. Because a single entrance beam is used, alignment with the patient's pupil is easier. Any test pattern can be used, as long as it can be photographed and transilluminated. Its principal disadvantage is that the retinal image is affected by the optics and state of accommodation of the eye. While spherical errors can be corrected by adjusting the distance between the test pattern and the objective lens, severe astigmatism and other asymmetrical errors may be difficult to correct.

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REFERENCES

Visually evoked cortical responses of amblyopes to a spatially alternating stimulus. SAMUEL SOKOL AND BENJAMIN BLOOM.

Early studies of cortical activity in amblyopia consisted of presenting subjects with the diffuse flashing lights of a photostimulator and measuring electroencephalographic (EEG) activity.1 In general, EEG irregularities were found when the amblyopic eye was stimulated but not when the normal eye was stimulated. More recent results obtained with flashing stimuli and computer averaging of sensory signals evoked from the occipital cortex have been inconclusive. Some investigators report that the computer-derived signal from the amblyopic eye showed amplitude and latency irregularities2–6 while others found no difference in the cortical signals evoked by the normal and amblyopic eyes.3,7

Most recently, a checkerboard-patterned stimulus has been used to elicit visually evoked cortical potentials (VECP). While considerable attention has been given to the use of checkerboard-pattern stimuli in the study of the VECP in subjects with normal vision8 and as a technique for determining refractive errors9 there have been few reports where patterned stimuli have been used to study the VECP of amblyopes. Lombrosa, Duffy, and Robb10 report that with a patterned stimulus, 50 per cent of their subjects elicited a smaller amplitude VECP when the amblyopic eye was stimulated. The patterned stimulus used in this study, however, was a checkerboard transparent screen back illuminated with a photostimulator. Use of this type of stimulus results in a "transient" VECP containing two components: a spatial component elicited by the pattern contours and a luminance component elicited by the change in luminous flux of the photostimulator as it flashes on and off behind the transparency.11 As a result, when there is a decline in the spatially generated signals, a large luminance component is still present. The patterned stimulus used in the present study consisted of a phase reversal of the checks which results in the total luminous flux remaining nearly constant. With this type of stimulus display any contribution of luminance to the VECP is eliminated and the amplitude of the "steady state" VECP will approach zero as the ability of the visual system to resolve the spatially alternating stimulus decreases.

The spatially alternating stimulus used in the present experiment is described in detail elsewhere.12,13 Essentially, the retina is being stimulated by a pattern whose elements are changing their luminance relative to each other but whose total luminous flux remains nearly constant. Subjects sat 75 cm. from the stimulus with the aid of a chin rest. At this distance the entire checkerboard array subtended a square field of 18°. An 18° field was used to insure that subjects with eccentric fixation would still receive foveal stimulation. The total mean luminance of the stimulus was 50 ft. lamberts as measured with a S.E.I. photometer. The rate of stimulus alternation was 12 Hz.

VECP's were recorded using two electrodes located along the midline; the first electrode was 2 cm. above the inion, the second electrode was 6 cm. above the first. The ear served as a ground. Electrode leads were connected to a wide-band EEG preamplifier with low frequency cut-off at 1 Hz. and to a DC driver amplifier with high-frequency cut-off at 35 Hz. Responses were then led to an FM tape recorder and a signal averager. VECP's were recorded from 15 amblyopic subjects ranging in age from 5 to 63 years. Only two of the subjects were older than 12; one was 25 years of age, the other 63 years of age. Seven subjects had a strabismus, two subjects were anisometropic, and 6 subjects had a strabismus and anisometropia. All subjects exhibited some degree of eccentric fixation. Subject J had an unsteady nasal fixation of 5° and the remaining subjects had eccentric fixation of no greater than 1°. All of the subjects received a complete eye evaluation and those under 12 years of age were given a cycloplegic refraction. During the recording session each subject used the optical correction determined from his previous refraction.

Each eye was tested alone. The subject was instructed to fixate on a small red spot in the center of the checkerboard pattern. No mydriatics or cycloplegics were used during the recording of the VECP's. All subjects were tested with checks that subtended a visual arc of 15°. In addition, four of the subjects were tested on two separate occasions using 15° checks and one of the subjects was tested on two occasions with checks which