Ocular inflammation due to postoperative trauma often needs a hard-hitting, anti-inflammatory agent to quickly quiet the eye.

No other topical ophthalmic steroid hits this reaction harder than Prednefrin Forte 1.0%. Less potent measures may allow serious and/or threatening complications.

Prednefrin Forte offers more anti-inflammatory activity in a single drop than many other topical ophthalmic steroids. Even under an eye patch, the steroid component continues its prolonged therapeutic activity—that's because suspensions have been shown to maintain measurable levels of steroid for up to four hours.

Indications: Severe inflammation (non-infectious) of the eye, such as acute iritis, iridocyclitis, scleritis, episcleritis, uveitis; resistant ocular allergy and inflammation following surgery (where no infectious etiology is suspected)—particularly where unusually rapid control of the inflammation is desired.

Contraindications: PREDNEFRIN FORTE is contraindicated in acute untreated purulent infections, acute herpes simplex (dendritic keratitis), vaccinia, varicella and most other viral diseases of the cornea and conjunctiva, ocular tuberculosis and fungal diseases of the eye.

Warnings: 1. In diseases due to microorganisms, infection may be masked, enhanced or activated by the steroid. 2. Extended use of topical corticosteroids may cause increased intraocular pressure in certain individuals. It is advisable that the intraocular pressure be checked frequently. 3. In those diseases causing thinning of the cornea, perforation has been known to have occurred with the use of topical steroids. 4. Since PREDNEFRIN FORTE contains no anti-microbial, if infection is present appropriate measures must be taken to counteract the organisms involved.

5. Should be used with caution in the presence of narrow-angle glaucoma. 6. Reports in the literature indicate that posterior subcapsular lenticular opacities have been reported to occur after heavy or protracted use of topical ophthalmic corticosteroids.

Dosage: 1 to 2 drops instilled into the conjunctival sac two to four times daily. During the initial 24-48 hours the dosage may be safely increased to 2 drops every hour. The physician may choose the dosage which affords optimal therapeutic effect in each case. Care should be taken not to discontinue therapy prematurely.

Supply: 5 cc. and 10 cc. plastic dropper bottles—on prescription only.

Formula:
- prednisolone acetate (microfine suspension): 1.0%
- phenylephrine HCl: 0.12%
- methylcellulose: 0.12%
- chlorobutanol (chloral deriv.): 0.5%
- antipyrine: 0.1%
- with: boric acid, sodium citrate, sodium chloride, sodium bisulfite, EDTA, polysorbate 80, menthol, camphor, eucalyptol, phenol and purified water.

Prednefrin® Forte 1.0%
OPHTHALMIC SUSPENSION
ALLERGAN PHARMACEUTICALS/SANTA ANA, CALIFORNIA/MONTREAL, CANADA
Red-free light fundus photography

Photographic optogram

K. Mizuno, A. Majima, K. Ozawa, and H. Ito

Red-free light fundus photography has been developed to compare rhodopsin contents in the retina during light and dark adaptations by means of a filter with a wavelength of 500 nm. In order to avoid a probable artifact by the photographic procedure, half of the fundus, either upper or lower half, is irradiated after dark adaptation, and a red-free light fundus photograph is taken. This half occlusion procedure is assumed to be similar to an optogram and is able to differentiate the degree of rhodopsin contents in situ in the same picture. The new technique has also opened new vistas in determining retinal regions lacking the ability of rhodopsin synthesis in patients with night blindness. This principle is also applicable to detect minimum changes in the vascular system and nerve fibers in the retina.

Fundus reflectometry had been initiated by Brindley and Willmer and has been in use by Weale and Rushton for some years as a method of measuring the bleaching of visual pigments which occurs when light falls on the retina. This principle has been extended by Buchanan and colleagues, and Gloster and Greaves to the study of changes in the fundus in pigmentary degenerations of the retina. After a certain modification in the apparatus with a resultant increase in sensitivity, it was possible to obtain a continuous record indicating bleaching in the fundus of the living human eye after exposure to light. Red-free light can be used to distinguish the dark-adapted retina which contains abundant rhodopsin from that which had been bleached. On the basis of this simple principle, red-free light fundus photography was developed to compare changes in the fundus which occurred during dark and light adaptation in both normal subjects and patients with night blindness and possible genetic carriers of primary retinitis pigmentosa.

Methods

Kodak Wratten filter No. 65A of wavelength 500 nm. was introduced into the light source of an Olympus fundus camera. The light source was precisely adjusted with a fluorescent plate to achieve equal brightness on the fundus picture. Kodak TR1-x 35 mm. film was used. For the enlarging photography Kodak TR1-x 6 by 6 cm. film was also used. Careful focusing was done with a red filter of wavelength 675 nm. which was placed just in front of the window of the light source of the camera, and the subject's visual axis was fixed to a certain position with the pilot lamp. The photographs during dark adaptation were taken immediately after exchanging the red filter for a blue-green one. Only the first few pictures were in general available for this purpose, although gradual fading of the background was recognized. After the removal of the blue-green filter, the eye was then illuminated with white light of about 1,200 lux. After 10 minutes of light...
adaptation, the second photograph for the bleached fundus was taken with the blue-green filter. To avoid a possible artifact of the photographic procedure, the same roll of film was always used for each subject, and printing and enlargement were done at the same time. The next attempt was made to distinguish the dark- and light-adapted fundus simultaneously; fundus photographic distinction between the two adaptations was done on the same picture. After 30 minutes of dark adaptation, either the upper or the lower half of the fundus was irradiated for 5 minutes with the maximum brightness of the light source of the camera, and the other half of the fundus was occluded by cutting off the light with a black plate at the window of the camera. Initial pictures were taken with the blue-green filter immediately after the removal of the occluding plate in the darkroom. Subsequent light adaptation and photography during this state were also done in the same manner as described before. This technique is assumed to be a photographic optogram.

Before dark adaptation the subject's pupil was dilated with 2 per cent tropicamide and during photography, fixation of the head and the eye was obtained with a tightening band and a pilot lamp, respectively. The eye position was assured by observing the fundus with the red filter on each occasion. Preliminary experiments were carried out in 9 healthy subjects whose age ranged from 17 to 46 years.

In order to support the photographic findings of the pigment bleaching differences noted on the two parts of the same retina, the dark adaptation study in these two retinal areas was done. Intensity threshold for light in two parts of the retina of 5 healthy subjects was measured with Hioki's recording adaptometer immediately after the half occlusion procedure.

Similar photographic experiments were made on 30 eyes of patients with congenital night blindness or an allied condition. All cases, except one, of fundus albi punctatus, were of primary retinitis pigmentosa and their families. Two patients with diabetic retinopathy were photographed after light adaptation with the brightness of 1,200 lux for 10 minutes.

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Fig. 1. Fundus photographs of healthy 28-year-old woman after dark (above) and light (below) adaptation. Difference of the background in brightness is apparent.

Fig. 2. Fundus photographs of 17-year-old girl. Clear bleaching phenomenon is demonstrable in irradiated lower half, whereas the background in occluded upper half of the fundus is apparently darker (above). After total irradiation fading in the background appears in the whole fundus (below).
The electroretinographic recording was done according to the standard procedure of Nagata with his contact lens as an electrode. After 15 minutes of dark adaptation, three responses to xenon lamp stimuli of 0.2, 2, and 20 joules, respectively, were recorded.

Results

Two pictures of a 28-year-old healthy woman taken after dark and light adaptations revealed that the background of the light-adapted fundus was apparently brighter and showed well-defined vessel walls and a relatively well-bordered macular appearance in comparison with those of the dark-adapted area (Fig. 1).

Conspicuous differences between the irradiated lower half and the occluded upper half of the fundus of a 17-year-old girl appeared by the half occlusion procedure (Fig. 2). Because the subject's visual axis was fixed to the center of the light source, this picture was distinctly separated into the two parts by the straight line that linked the disc with the macula. In the occluded upper half the background was darker and the border of the vessel walls and the macula was more indistinct than those of the irradiated lower half. The difference noted in a picture between the irradiated and occluded halves of the fundus will be referred to as the bleaching phenomenon. The bleaching phenomenon of a 19-year-old girl whose fundus was photographed on a 6 by 6 cm. film also demonstrated marked differences between the two adaptations. In addition, more typical features of the distribution of nerve fibers in the occluded upper half were noteworthy (Fig. 3). This phenomenon became less in the picture taken after the half occlusion procedure on a 46-year-old man, and the border between irradiated and occluded halves became obscure because of movement of the eye during adaptation. However, the bleaching phenomenon was still recordable, even though

Fig. 3. Fundus photography of the macular area of 19-year-old girl. Indefinite vessel walls and definite nerve fibers in occluded upper half and definite vessel walls and indefinite nerve fibers may be due to the difference in rhodopsin contents in the visual cell layer.
after complete irradiation the macular region did not show a clear border in comparison with those of young subjects (Fig. 4).

Intensity threshold for light in the irradiated part of the retina was about 4 logarithm units higher than that in the occluded part on an average of 5 healthy subjects.

When the red-free light fundus photography was conducted on patients with primary retinitis pigmentosa, it was found that the quality of the darkness in the background and distinctness of the vessel walls were much less than those obtained on healthy subjects, and it was thought that a possible difficulty in fixation was responsible for this because of occasional macular dystrophy. Therefore, only patients and their relatives with good central vision were selected for this study (Table I). Photographs of 2 patients with primary retinitis pigmentosa revealed different patterns. Although there were no changes in the area where coarse pigments were scattered, a relatively positive bleaching phenomenon could be seen around the macula of mildly advanced Case 4 (Fig. 5), coinciding with the fact that a minimum response to the light stimulus was still recordable on electroretinogram. On the contrary, it was quite clear that the picture of moderately advanced Case 18 showed no difference and no bleaching.
Table I. Nineteen patients and their relatives with retinal disease

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<th>Disease</th>
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<th>Bleaching effect</th>
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phenomenon comparable with those of healthy subjects, coinciding with the extinct electroretinographic record (Fig. 6). The red-free light fundus photograph of a patient with fundus albi punctatus of Case 30, whose electroretinogram was subnormal and slightly increased on the threshold of the dark adaptation curve, was quite interesting. It showed a large number of closely spaced, well-defined punctate lesions of equal density in the area far from the optic disc. The bleaching phenomenon could not be detected in this area, whereas it was likely positive in the region adjacent to the disc where only a few small dots were distributed (Fig. 7). The enlarged picture of the lesion showed the interesting findings that some of the dots were apparently located either on the inside or closely adjacent part of the retinal vessels (Fig. 8).

After the irradiation of the whole fundus for 10 minutes in a patient with diabetic retinopathy (Case 32) the picture showed more delicate and typical features of lesion. Little hemorrhages and even possible microaneurysms with higher magnification near the macula were demonstrable by this procedure (Figs. 9 and 10).

Discussion

This new technique of red-free light fundus photography is based on the principle of photographing the light reflected from the fundus of the eye; if the retina contains abundant rhodopsin it will absorb blue-green light of 500 nm. in preference to red and violet light. Hence the light
reflected from the fundus will contain less light of 500 nm, in preference to red and violet light. The decrease in the intensity of light, moreover, will give direct photographic evidence of the degree of absorption and of the degree of rhodopsin content in the retina. The identity of rhodopsin on the photographs cannot be determined from the experimental results obtained, but it would appear reasonable to assume that it was rhodopsin, because a definite bleaching phenomenon in the same picture and its fading after irradiation can be obtained in preliminary experiments in normal subjects. Apparent difference in the intensity threshold for light on two parts of the same retina may also support this opinion. It is, of course, well established by Weale\(^2\) and Rushton\(^3\) that the changes in reflection densitometry of the living fundi were due to the bleaching of a photosensitive pigment, rhodopsin, and Gloster and Greaves\(^5\) also proved that only the bleaching of rhodopsin can explain the colorimetric changes after irradiation of normal human subjects. It is, however, essentially important to confirm the relation between the difference in density recorded photographically and the biochemical estimation of rhodopsin content in animal eyes in the future.

It is also essential to avoid the probable artifacts of the photographic procedures. For this purpose a half occlusion procedure was developed and the two pictures necessary for comparison were always printed at the same time. However, it is most important to practice focusing with a red
Fig. 8. Higher magnification of Fig. 7. Small white dots are arranged on the lines of the nerve fibers. Some dots are located inside or very near part of the vessel walls.

Fig. 9. Fundus photograph of diabetic retinopathy taken after light adaptation under the brightness of 1,200 lux for 10 minutes.

filter to avoid any artificial shadow and reflection in the fundus picture. This is the only weak point of this method.

Although there is some uncertainty regarding the fundamental process of photographing, there is no doubt that the absence of the bleaching phenomenon in the patient with primary retinitis pigmentosa may be due to the lack or the absence of the ability to regenerate rhodopsin, or more reasonable morphological changes in the visual cells. On the other hand, a relatively positive bleaching phenomenon in the patient with fundus albi punctatus, one of nonprogressive congenital night blindness, suggests that the visual cell is still alive in parts and rhodopsin can be resynthesized in the outer segment of the visual cells. The differences between primary retinitis pigmentosa and fundus albi punctatus may agree with the results recorded on electroretinograms. It may be possible, from these results, to compare the degree of the capacity of rhodopsin synthesis or amount of pigments in both the normal and abnormal eyes, and further, to detect the retinal part which still has live visual cells on the retina of night-blinded patients.

It is pointless to carry speculation further at this stage, although one may reasonably hope that the observations from the red-free light fundus photography by this method may be extended as to qualitatively analyze genetic carriers of primary
retinitis pigmentosa. A profitable study could be provided by the father of a known case of primary retinitis pigmentosa. In one such case reported here, the eye of a father of a patient with primary retinitis pigmentosa gave a very weak bleaching phenomenon, in spite of a normal electroretinogram recorded and absence of any subjective complaint of night blindness or of any ophthalmoscopic changes in the fundus.

From these results, there is little doubt that the value of the red-free light fundus photography in elucidating the progress or degree of night blindness would be enhanced if it were supplemented by and correlated with the results of the electroretinogram, electrooculogram, and precise measurement of differential thresholds of brightness.

Perhaps the merit of this technique is that it is easily applicable to any type of a fundus camera, and in this way it provides realistic evidence of the status of the function of the visual cells. Furthermore, the advantage of this method is that it is also applicable to the clinical diagnosis of minimum vascular changes and nerve fibers, if the red-free light fundus photography is taken after either light or dark adaptation. The border of vessel walls becomes more definite after light adaptation because of absorption and reflection in the vessel wall and the rhodopsin layer, respectively, if irradiation is not extremely intense; moderate light adaptation is important for this purpose, because several studies showed the retina to cloud under intense stimulation by light. Conversely the nerve fibers can be more clearly photographed after dark adaptation because of enhanced contrast due to reflec-
tion and absorption of blue-green light in the nerve fiber layer and the rhodopsin layer, respectively. Therefore, it will be evident that the combined technique of monochrome reflectance fundus photography after Behrendt and Wilson and Potts and either light or dark adaptation will become a more useful routine method to find minimum retinal changes. The photographic diagnosis must become one of the most important procedures in clinical ophthalmology.

REFERENCES