both studies the Mackay-Marg tonometer was demonstrated superior. The Mackay-Marg tonometer requires only a brief contact for measurement of IOP in the conscious dog with an intermittently moving eye. The pneumotonograph is more difficult to use in the conscious dog; in addition, the probe sound may distract the animal. Movement of the dog’s eye beneath the pneumotonograph probe footplate may cause corneal abrasions.

In a previous study we compared these tonometers in the normal canine eye using the same methodology. Both the Mackay-Marg and pneumotonograph tonometers were found to be highly reliable. In this study with glaucomatous globes, goodness of fit for the Mackay-Marg and pneumotonograph tonometers decreased about 10% from that of the normal canine eye. Because the Mackay-Marg and pneumotonograph tonometers evaluated in the closed and open manometric systems from 0 to 50 mm Hg exhibited r² of 0.8 or above, these tonometers provide readings 95% of the time that are accurate to within ±2.5 to 3.0 and ±2.0 to 3.0 mm Hg, respectively. The presence of corneal edema, glaucoma, and possible changes in the corneal surface may account for the differences. The statistical analyses for the glaucomatous eyes were divided into IOP from 0 to 50 mm Hg and 0 to 100 mm Hg. The upper range may have exceeded the limits of these tonometers; however, IOP in glaucomatous beagles may exceed 50 mm Hg in acute exacerbations of the disease and after water loading.

From the Division of Comparative Ophthalmology, Department of Special Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville. This work was supported in part by the National Institutes of Health grants EY01932 (Dr. Gelatt) and F32EY05392 (Dr. Barrie). Submitted for publication Aug. 27, 1980. Reprint requests: Dr. Gelatt, Department of Special Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville, Fla. 32610.

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Topical 0.5% indomethacin, 0.01% flurbiprofen, 1% prednisolone acetate, 0.1% dexamethasone, or 0.1% fluorometholone pretreatment and daily instillation did not affect the course of re-epithelialization after partial corneal epithelial denudation. However, topical 1% prednisolone acetate, 0.1% dexamethasone, and 0.1% fluorometholone—but not 0.5% indomethacin and 0.01% flurbiprofen—significantly retarded re-epithelialization after complete corneal denudation.

Recent evidence suggests that prostaglandins (PGs) are one of the mediators of certain types of experimental ocular inflammation, including the release of polymorphonuclear leukocytes (PMNs) after partial corneal denudation. Nonsteroidal anti-inflammatory drugs (NSAID) such as indomethacin, aspirin, and flurbiprofen have been used in experimental and clinical ocular inflammatory conditions. Several steroidal drugs (SAID) are also currently in clinical use as anti-inflammatory agents. Indomethacin, aspirin, and flurbiprofen inhibit the cyclooxygenase enzyme, but corticosteroids apparently block the release of arachidonic acid, the precursor of PGs, by inhibition of the phospholipase enzyme. In this report we compare the effect of anti-inflammatory agents on topical indomethacin (0.5%), flurbiprofen (0.01%), topical prednisolone acetate (1%), dexamethasone (0.1%), dexamethasone (0.1%), and flurbiprofen (0.01%) on corneal re-epithelialization.

methasone (0.1%), and fluorometholone (0.1%) on the re-epithelialization of the rabbit cornea after partial and complete epithelial denudation.

Materials and methods. New Zealand white rabbits weighing 1.5 to 2.5 kg were used throughout this experiment. Rabbits were anesthetized by intravenous injection of sodium pentobarbital (Nembutal, Abbott Laboratories, North Chicago, Ill.). After topical application of 0.5% proparacaine (Ophthaine, E. R. Squibb, Princeton, N. J.) either the entire corneal epithelium (limbus-to-limbus) or a small central area (outlined by a 6 mm trephine) was denuded by a technique previously described. The removal of the corneal epithelium was performed carefully in order to preserve as far as possible the integrity of the basement membrane. Re-epithelialization was monitored by fluorescein staining and photography.

Drug treatments. Both eyes of all animals were treated the same. Indomethacin 0.5% (total volume 50 μl, pH 7.5 to 8) was instilled topically 1/2 hr prior to partial corneal epithelial denudation and twice daily at 9 A.M. and 5 P.M. until the completion of the experiment. This dose of indomethacin has been shown to effectively inhibit the tear fluid PMN response after partial corneal denudation. Control rabbits received 50 μl of topical saline in the same manner. Similarly, eyes were treated with topical 0.01% flurbiprofen. This dose of flurbiprofen effectively inhibited the tear fluid response after partial corneal denudation.

A 50 μl dose of commercially available 1% prednisolone acetate (Allergan Pharmaceuticals, Inc., Irvine, Calif.) was administered topically 1/2 hr prior to partial corneal denudation and three times daily (9 A.M., 1 P.M., and 5 P.M.). This dose of prednisolone acetate has been shown to effectively inhibit the tear fluid PMN response after partial corneal denudation. Control animals received 50 μl of topical saline in the same manner. Similarly, eyes received 50 μl of 0.1% topical dexamethasone or 0.1% fluorometholone. These doses of dexamethasone and fluorometholone did not inhibit the tear fluid response after partial corneal denudation. As a further control, eyes received 50 μl of prednisolone vehicle (courtesy Allergan Pharmaceuticals, Inc.) 1/2 hr prior to complete corneal denudation and three times daily thereafter.

Results. Neither 0.5% indomethacin nor 0.01% flurbiprofen pretreatment and topical application twice daily affected the course of re-epithelialization of partially denuded corneas when compared with control eyes treated with saline drops (Fig. 1). Similarly, 1% prednisolone acetate, 0.1% dexamethasone, and 0.1% fluorometholone pretreat-

Fig. 1. Rate of re-epithelialization of rabbit cornea after partial and complete corneal epithelial denudation. Control eyes (open circles) were pretreated with saline drops 1/2 hr prior to denudation and two or three times daily thereafter. Experimental eyes (closed circles) were pretreated similarly with steroidal (three times daily) or nonsteroidal agents (twice daily). Each point on the curve represents mean ± S.E.M.; n, number of eyes.
Discussion. The results indicate that NSAID did not affect corneal re-epithelialization by conjunctival epithelium, whereas SAID significantly inhibited this type of re-epithelialization by the third day. Both types of anti-inflammatory agents had no effect on re-epithelialization of partial corneal denudation, which is accomplished by the migration of adjacent corneal epithelial cells.

Ho and Elliott\(^6\) compared re-epithelialization rates after placement of partial (7 mm) corneal denudation wounds in several groups of animals treated with saline drops or 0.1% dexamethasone or vehicle. The drops were used 16 times daily and these investigators found that both steroid-treated and vehicle-treated groups had slower rates of re-epithelialization than did corneas treated with saline drops four times daily. The authors suggested that the frequent instillation of the drops and not the contents may have retarded re-epithelialization. Our results are different in that a significant retardation of re-epithelialization was evident only in the steroid-treated completely denuded corneas even though control and experimental drops were used only three times daily. Furthermore, we did not observe a significant difference in re-epithelialization in the nonsteroid-and steroid-treated partially (6 mm) denuded eyes when compared with saline-treated controls. Finally, since no significant difference was found in the rate of re-epithelialization between the vehicle- and saline-treated groups of completely denuded corneas, it would appear that steroidal inhibition of conjunctival epithelial migration is specific.

At the present time the mechanism by which steroids such as prednisolone acetate, dexamethasone, or fluorometholone retard conjunctival epithelial cell migration but not corneal epithelial migration is not clear. In contrast to the conjunctiva, the rabbit cornea does not possess a significant capacity to convert arachidonic acid (AA) to PGs. In a recent study,\(^7\) cyclooxygenase activity, as indicated by the conversion of exogenous AA to PGs, was two to three times greater in the rabbit conjunctiva than in the cornea. It is possible that corneal epithelial cell migration is not dependent on AA metabolism, thereby rendering it insensitive to the effect of NSAID and SAID. On the other hand, conjunctival epithelial cell migration may be dependent on AA release and metabolism. We are presently investigating whether the inhibitory effect of steroidal agents on conjunctival re-epithelialization is a result of the inhibition of AA release from the conjunctiva.

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From the Departments of Ophthalmology and Pharmacology, College of Physicians and Surgeons, Columbia University, New York, N. Y. This investigation was supported by U.S. Public Health Service Research Grants EY 01977, EY 02861, and EY 00457. Submitted for publication May 5, 1980. Reprint requests: Dr. B. D. Srinivasan, Columbia University, 630 W. 168th St., New York, N. Y. 10032.

Key words: re-epithelialization, cornea, conjunctiva, indomethacin, flurbiprofen, dexamethasone, prednisolone acetate, fluorometholone

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Visually evoked cortical potentials accompanying blinks. JOHN C. ARMINSTON.

Visual activity is initiated whenever there is a change in the light falling on the retinal receptors. In the present experiment, visually evoked cortical potentials, elicited by the light transients that accompany blinking, were recorded with an electrode array that minimized artifact pickup. Although these evoked potentials were roughly similar to those obtained by more conventional recording procedures, specific waveform features were observed. An ever-changing retinal stimulation is necessary for the proper maintenance of vision. The reason that steady visual scenes do not fade away is because a variety of physiologic mechanisms such as those of eye and head movement exist to continually produce fluctuations in the local stimulation of the retinal receptors.1, 2 One of these mechanisms, that of blinking,3 has received little experimental attention. Blinks briefly interrupt the light falling on the retina and thus introduce transient stimulation. This report outlines a method for recording evoked potentials that are produced as a result of blinking and describes some of their salient properties.

Methods. Most aspects of the recording situation, except for those uniquely associated with blinking, were the same as those adopted previously to record the potentials that accompany saccadic eye movement.4 A Maxwellian view stimulator presented striped patterns of light to the subject's eye. The stimulus field subtended a visual angle of 20 degrees; the stripes subtended an angle of 1 degree and had a contrast of 99%. The maximum luminance of the bright areas was 1000 trolands. Central fixation was used. There were two recording channels. One recorded the evoked potential, and the other the electro-oculogram (EOG). The latter was used to synchronize the computer with the subject's blinks.

The recording amplifiers were operated to have a "flat" response over the range of 0.2 to 55 Hz. Isolation amplifiers and "isofuses" were used in all leads to protect the subject. During amplification the physiologic potentials were recorded on magnetic tape and subsequently were played into a computer averaging system. The potentials were picked up with standard electroencephalographic electrodes of the silver cup variety. These were mounted just above and below the eye for the EOG and in the special way described below for the evoked potential.

In the analysis of the data the computer was programmed to average the response activity that followed consecutive eye blinks. To accomplish this, the EOG was used to obtain a synchronizing signal. The large blink potentials that appeared were sent to a trigger circuit, previously used to investigate saccadic eye movement.5 Its output pulse signaled the onset of a blink to the computer. The number of responses in each average depended on the frequency of blinking and was in the order of 100.

A problem that is encountered when recording these responses is that they are necessarily time-locked to the blinks that are responsible for them. Thus they may be confounded with motor artifacts.