trally seems to indicate that goblet cells themselves did in fact migrate, but this does not eliminate the possibility that such isolation also blocks diffusion of factors required for differentiation of central amucotic precursor cells. Thickening of the epithelium peripheral to the glue ring suggests that there was no generalized toxic reaction of the epithelium to the glue.

Similar central attrition (accompanied by peripheral thickening) in normal corneas supports the concept that centripetal cell migration occurs even across normal corneas. This observation of centripetal cell motion, coupled with those of other investigators, suggests that the pericorneal conjunctiva may play a substantial role in central corneal epithelialization even after the initial stages of wound healing. This suggests that diseases characterized by corneal epithelial abnormalities may be in part the result of conjunctival abnormalities, supporting the concept that there are pan-ocular surface diseases.

Although the fact that goblet cell appearance at the periphery initially (stage 2) is consistent with centripetal movement, the loss of goblet cells from the center first would not be expected as the result of the same phenomenon. Rather a new overriding biological transformation may be superimposed on and predominate over the continual centripetal cell migration. The stimulus for this transformation and why it occurs gradually from the center out instead of abruptly over the whole cornea are questions that remain to be answered.

The observation that healing of cornea from conjunctiva can be divided into histologically distinct stages makes this model a useful one for further studies. For example, stage 3 epithelium in which the entire cornea shows a uniform distribution of large numbers of goblet cells within a loosely adherent two- to four-cell layer epithelium, provides a simple and reliable model for the harvest of large numbers of relatively uncontaminated mucus-producing cells. Studies employing this model are currently underway in this laboratory.

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Key words: corneal re-epithelialization, conjunctiva, goblet cells, epithelial transformation, isolation of central corneal epithelium, ocular surface epithelium

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The effects of total unilateral occlusion vs. lid suture on the visual system of infant monkeys. GUNTER K. VON NOORDEN AND M. L. J. CRAWFORD.

To explore the premise that the immature primate visual system responds differently to total unilateral occlusion (no competitive abnormal binocular interaction) than it does to lid suture, one eye in two infant Macaca mulatta was completely occluded with optically opaque material. After a recovery period of 2 months, single cell responses from the striate cortex were recorded, and the lateral geniculate nuclei were examined histologically. The results show that cortical and geniculate changes are comparable in severity to those found in earlier studies after unilateral lid suture.

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It has been postulated that there is a fundamental difference between occlusion of one eye (absence of a visual stimulus) and diffusion (diffused light stimulus through sutured lids) in their effects on the development of visual functions during visual immaturity. In view of these stimulus differences, comparisons between experimental amblyopia caused by unilateral lid suture in animals and amblyopia caused by occlusion of one eye in humans have been criticized. This criticism is based on the implausible hypothesis that the diffused light entering the sutured eye constitutes a positive competitive stimulus that is different at the cortical level from the nonstimulus of complete occlusion. Thus a complete unilateral occlusion during visual immaturity is expected to merely delay visual development without affecting binocular function, since a competitive stimulus situation is said to be absent.

Because most occlusive devices used for the treatment of human amblyopia are semi-opaque, whether total occlusion exists at all in human patients is questionable, and the argument may well be artificial. Nevertheless, the possibility that the immature afferent visual system reacts differently to total vs. partial unilateral occlusion seemed worthwhile to explore, and we report herein the effects of total unilateral occlusion on cortical electrophysiology and geniculate histology of two visually immature monkeys (Macaca mulatta).

**Material and methods.** To achieve light-proof occlusion, we used a surgical technique similar to that suggested by Spiro and Kolbert. The lids of the left eye were surgically fused over a sheath of black Proplast in one infant monkey (4180) and over a black polymethylacrylate, custom-fitted scleral contact lens in another monkey (31580). Both monkeys were 3-weeks-old on the day of surgery. The eye not being tested was covered with black electrical tape. Platinum-iridium electrodes were inserted underneath the scalp near the inion and referenced to an electrode placed under the tongue. A Grass photoflash tube located at 25 cm distance from the monkey's face served as a stimulator. Thirty-two responses were averaged from each eye for various intensities.

In the terminal experiment, receptive fields of neurons from the striate cortex of both monkeys were recorded extracellularly by standard techniques. The lateral geniculate nuclei (LGNs) were processed for cell measurements from each layer by methods described in earlier publications. Matched samples of 50 cells were measured in the posterior half of each LGN layer.

**Results.** The averaged VECPs for both monkeys are shown in Figs. 1A and 1B. No VECP could be elicited through the occluded eye, indicating that the occlusion was indeed light-proof. The amplitude of the VECP recorded through the closed lids of the nonoccluded eye correlated with the intensity of the photoflash, indicating that various amounts of light entered the eye through the closed lids.

The results of the experiments are shown in Fig. 2 and are compared with previously published striate single-unit eye dominance histograms from infant monkeys (403, A-85, N-8) who were visually deprived by unilateral lid suture of the right eye at similar ages for periods ranging from 6 to 8 days followed by periods of normal visual stimulation ranging from 10 to 17 weeks. For either treatment, there is marked shift of cortical dominance in favor of the nonoccluded eye and a com-

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<th>Table 1. Summary of experiments</th>
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The chronological details of the experiment are listed in Table 1. Occlusion was maintained for 14 days in both monkeys, after which the lids were opened, the implant and contact lens removed, and both monkeys exposed to the visual environment of the primate nursery for 8 weeks (4180) and 9 weeks (31580), respectively.

In order to test that no light could enter the occluded eye, visually evoked cortical potentials (VECPs) were recorded through the closed lids of each eye of both monkeys 3 days after the initial surgery. The eye not being tested was covered with black electrical tape. Platinum-iridium electrodes were inserted underneath the scalp near the inion and referenced to an electrode placed under the tongue. A Grass photoflash tube located at 25 cm distance from the monkey's face served as a stimulator. Thirty-two responses were averaged from each eye for various intensities.

The results of the experiments are shown in Fig. 2 and are compared with previously published striate single-unit eye dominance histograms from infant monkeys (403, A-85, N-8) who were visually deprived by unilateral lid suture of the right eye at similar ages for periods ranging from 6 to 8 days followed by periods of normal visual stimulation ranging from 10 to 17 weeks. For either treatment, there is marked shift of cortical dominance in favor of the nonoccluded eye and a com-
**Fig. 1a.** Cortical light-evoked potentials of monkey 4180 stimulated by flashes of different intensity delivered through either the normal closed eyelid (A) or the eyelid containing the opaque implant (B). Note in B that the highest intensity flash failed to produce any response and was not different from those control trials where no flash was delivered. From these measurements, it is concluded that the occlusion did prevent light from stimulating the retina.

**Fig. 1b.** Monkey 31580. For legend see Fig. 1a.

plete absence of binocularly driven cortical neurons. The data from total light deprivation are indistinguishable from the cortical histograms obtained after unilateral lid suture.

The results of cell size comparison between corresponding deprived and nondeprived LGN layers are listed in Fig. 3. This comparison shows significantly smaller cells in all deprived binocular layers. No such difference exists between the deprived and nondeprived monocular segments.

**Discussion.** The results of this study show that total exclusion of light from one eye in visually immature monkeys causes severe electrophysiological changes in the striate cortex as well as histologic anomalies in the binocularly innervated portions of the LGNs. These changes were not reversed by subsequent normal visual stimulation and are comparable in severity to those reported after short- and long-term unilateral lid suture in monkeys of similar ages.\(^3\)\(^,\)\(^5\)\(^,\)\(^6\)

Lid suture in monkeys reduces by approximately 90% the amount of light that reaches the retina.\(^7\) It is
reasonable therefore to assume that the residual diffused light entering the eye through the sutured eyelids creates sufficient incongruity of the visual input to the cortex to cause abnormal binocular interaction, thereby contributing to the visual deprivation syndrome. However, even if no light reaches the retina, ganglion cells continue a spontaneous discharge through the LGN into the cortex and this discharge may still constitute a competition for cortical synaptic space with input received from the open eye. Thus a fair test of the total occlusion hypothesis may be virtually impossible and the hypothesis itself irrelevant. Nevertheless, the data presented in this study may be explained in part on the basis of abolished visual stimulation of the occluded eye (amblyopia ex anopsia). That such monocular disuse may indeed be a factor in addition to competitive binocular interaction in causing the visual deprivation syndrome in monkeys has been previously proposed by us and after having shown that the histological anomalies in the monkey LGNs after long-term lid suture and experimental anisometropia are not limited only to the binocularly innervated portions but occur also in the monocular LGN segment where binocular interaction cannot take place. The finding that the monocular LGN segments were uninvolved in the present experiments does not mitigate against this concept as the monocular segment shows no changes after brief periods of lid suture (GK von Noorden and MLJ Crawford, unpublished observations) and longer periods of deprivation are required to affect its cell sizes.

Noorden and MLJ Crawford, unpublished observations) and longer periods of deprivation are required to affect its cell sizes. 4, 9, 14

Our data do not support the belief that the visual system will react differently during visual immaturity, qualitatively or quantitatively, to comparable periods of complete unilateral occlusion or light diffusion by lid suture. In view of the severity of the changes in the primate visual system following total unilateral occlusion, we also reject the recommendation that complete unilateral occlusion be considered as a delaying option until surgery can be performed in an eye with a unilateral congenital cataract. On the basis of the data presented in this study we would expect such treatment to have a deleterious effect on the afferent human visual system.

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Key words: monkeys, evoked cortical potentials, lateral geniculate nucleus, occlusion, lid suture, binocular interaction, disuse, monocular segment

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