We are studying infant rhesus monkeys that have been reared under various conditions of deprivation to model infantile unilateral aphakia. Grating acuity was assessed in these monkeys from birth to approximately 1 year of age using the quick acuity card procedure. We found that an uncorrected aphakic eye develops little or no pattern vision. Undercorrection or near point optical correction of an aphakic eye with an extended-wear contact lens coupled with continuous occlusion of the opposite eye sometimes results in normal development of acuity in the aphakic eye but does so only at the cost of loss of vision in the occluded eye. Fifty percent partial occlusion coupled with near-point optical correction of an aphakic eye results in similar development of acuity for both eyes during the time tested. Monkeys wearing near-point correction in the aphakic eye and without any occlusion of the opposite eye show surprisingly good residual acuities in their aphakic eyes. Based on these results we conclude that aphakic eyes should be treated by providing them with an optical correction, and that occlusion of the opposite eye should be used cautiously. Invest Ophthalmol Vis Sci 30:2068–2074, 1989

Surgical removal of a congenital or infantile monocular cataract with optical correction of the aphakic eye thereafter rarely resulted in good visual function for the aphakic eye. This inability to retain good visual function has been attributed to a number of factors, including the age of the infant when surgery is performed. Recently, however, in selected cases it has been reported that if surgery is performed and the aphakic eye optically corrected in the first few days of life, good visual acuity can be maintained. For example, Enoch and Rabinowicz removed a monocular cataract from a 4-day-old infant and corrected the aphakic eye to a far point with a soft contact lens. The operated eye was patched during that time. Acuity showed continuous improvement in both the unoperated eye and the aphakic eye reaching an acuity level of 3.0 cycles per degree (cpd) by 4 months, which is normal for this age. Similarly, Jacobson, Mohindra and Held describe an infant diagnosed as having a monocular cataract, with surgery performed at 11.5 weeks of age. The infant was fitted with a hard contact lens in the aphakic eye and by 47 weeks of age the child had a grating acuity level of 9.0 cpd, which is also normal for that age. No patching regimen was described for this child.

Long-term longitudinal studies with larger groups of treated children also report improvement in acuity. In one study neonates had surgery performed before 6 weeks of age, wore extended wear lenses in the aphakic eye that corrected to a near point, and...
had the fellow eye patched daily from 4–8 hr. They showed acuities in the aphakic eye as high as 20/20 by 3 years of age. Other studies have found that with early surgery and a 50–80% patching regimen, grating and Snellen acuities lag behind those of the fellow patched eyes by approximately one octave.

Thus, even though studies suggest a reasonably good prognosis for treated aphakic children, many interesting problems still remain to be fully clarified. For example, can the aphakic eyes ever reach normal adult levels of vision? Are the 50–80% daily patching regimens that have been used most frequently as part of treatment for unilateral cataracts the best way to maintain vision in the aphakic eye? How important is compliance with optical correction and patching? What is the optimal distance for optical correction for the aphakic eyes?

Our research group is trying to assess these kinds of questions by studying infant rhesus monkeys that have been reared under various conditions of deprivation to model infantile unilateral aphakia. Acuity in macaque monkeys develops about four times faster than in humans and reaches adult levels at about 1 year of age. The time course of acuity development in macaque monkeys can be related to that of humans and therefore is a convenient system to use to model the development of the human visual system, as we are doing. We report here the results of grating acuity assessed using the quick acuity card procedure for each eye of these monkeys through approximately the first postnatal year.

Materials and Methods. Subjects: The infant rhesus monkeys used in this experiment were born in the breeding colony of the Yerkes Regional Primate Research Center. They were raised in incubators until approximately 1 month of age and then moved to single cages in a room where they could view objects and other monkeys at distances ranging from a few centimeters to several meters. Each infant was assigned to one of six experimental groups for the purposes of this study (Table 1): (1) near-point correction of aphakia with no occlusion of the opposite eye (ANP-UT); (2) near-point correction of aphakia with fulltime occlusion of the opposite eye (ANP-CO); (3) undercorrection of aphakia with fulltime occlusion of the opposite eye (AUC-CO); (4) near-point correction with daily partial (50%) occlusion of the opposite eye (ANP-50%PO); (5) uncorrected aphakia with no occlusion of the opposite eye (ANC-UT); and (6) normal unoperated monkeys (NL-NL). These last two groups are considered control groups for the purposes of this study.

Procedure: All procedures were performed in compliance with the ARVO Resolution on the Use of Animals in Research. At 7 to 14 days of age, the natural lens was surgically removed (Ocutome™, Cooper Vision, Palo Alto, CA) from one eye of all animals except the normal control monkeys to simulate the removal of a unilateral cataract in a human infant. The lensectomy was conducted under deep anesthesia and sterile conditions. Monkeys in groups wearing occluder lenses were fitted with the occluder lens on the same day the surgery was performed on the aphakic eye. Occluder lenses are extended-wear contact lenses dyed black on both sides so they are opaque. They are used in this experiment to block light input to an eye, much as an ophthalmologist would do when treating a human infant with a patching regimen. The aphakic eyes of all monkeys except for uncorrected aphakics were fitted with a high-plus extended-wear contact lens approximately 1 week after surgery. These lenses yielded a refractive error of −2 to −5 D (near-point) or +5 to +8 D (undercorrection). Compliance in wearing lenses was monitored 24 hr a day at 2 hr intervals and lenses replaced as necessary. A more detailed description of our contact lens protocols and rearing methods is provided by Fernandes et al.

Acuity was evaluated using the quick acuity card procedure. The acuity cards (VisTech Consultants, Inc., Dayton, OH) are designed with a homogeneous grey field displayed on one side of the card and square wave gratings presented on the other side. The gratings range in spatial frequency from 0.23 to 28.5 cpd, and are of 82 to 84% contrast with the mean luminance matched to the surrounding grey card within 1%. The monkey's face was held 38 cm in front of a cardboard screen constructed of grey cardboard to match the acuity cards. Each acuity evaluation began by showing the monkey a very low spatial frequency grating followed by a blank card to observe looking patterns for that monkey in each case. The cards were then shown in order of increasing spatial frequency. The experimenter was masked as to the actual spatial frequency of the card as well as the side of the card the grating was on. The looking patterns of the monkey were observed through a peephole in the center of the card and a judgement made as to whether the monkey looked towards the side of the card where the stripes were present. Each card was presented at least twice. The side of the card on which the stripes appeared was rotated between trials. If both trials were correct, the next card was presented. If one or both trials were incorrect, three to four more trials were collected. Attention was checked by presenting a very coarse grating periodically and observing looking behavior. Cards were shown until a threshold card was reached—defined as the highest spatial frequency grating that the experimenter judged the monkey could see.
Table 1. Experimental groups and treatment conditions

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment cond.</th>
<th>Animal designations</th>
<th>Symbol</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ANP-UT</td>
<td>Rnn1 Rnl1</td>
<td>[n = 5]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rqol Rap20</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rrnl</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>ANP-CO</td>
<td>Rkl1 Rap15</td>
<td>[n = 5]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rskl Rkl1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rpl1</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>AUC-CO</td>
<td>Rap22 Rap24</td>
<td>[n = 4]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rap23 Ral1</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>ANP-50%PO</td>
<td>Rqol Rnl1</td>
<td>[n = 3]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rlrl</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Normal control</td>
<td>Rpo1 Ryrl</td>
<td>[n = 12]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rbo1 Rko1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rml1 Rpl1</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Aphakic control</td>
<td>ANC-UT Rbn1 Rnl1</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rvl1 Rml1</td>
<td>[n = 5]</td>
</tr>
</tbody>
</table>

Abbreviations for treatment conditions: ANP—Aphakic eye wearing Near Point optical correction; AUC—Aphakic eye wearing optical Under Correction; ANC—Aphakic eye with No optical Correction; NL—untreated eye in a Normal control; UT—Untreated eye in an aphakic control; CO—Continuously Occluded eye; 50% PO—Partially Occluded eye—occluder lens worn 6 hours a day.

Monkeys were tested monocularly. The eye not being tested was occluded with either a patch or an occluder lens. Unless stated otherwise, each aphakic eye was tested wearing an appropriate optical correction. Both monocular tests for a single monkey were done within the same testing session. Test time per monkey was approximately 20 min.

**Results.** We present the results of our two control groups in Figure 1. These results serve as a standard for comparison to the results presented below for the rest of the experimental groups. Figure 1A shows the development of acuity in each eye of 12 normal infant monkeys. In terms of absolute values, acuity improves from 1–3 cpd during the first week after birth to about 30 cpd at 1 year of age. The differences in acuity between the two eyes for a single normal monkey at a given age are never greater than one octave, as demonstrated in Figure 1B.

Figure 1C depicts acuity development in our aphakic control group. The acuities in the untreated eyes of these monkeys develop similarly to those of our normal controls. During the first 2 weeks after birth there are no apparent differences between the untreated eyes and the aphakic eyes in these monkeys. Furthermore, the aphakic eyes have similar acuity values to the untreated eyes at these early ages when acuity is relatively poor for both eyes, whether they are tested with a near-point optical correction in place or not. At 7 to 8 weeks of age acuity is still similar in the untreated and aphakic eyes if the aphakic eye is tested with an optical correction in place, but acuity is more than an octave poorer in the uncorrected aphakic eye. These results indicate that the aphakic eye is experiencing the functional effects of optical defocus at these ages but has not yet developed an amblyopia. Thereafter, acuity development in the aphakic eye lags behind regardless of whether it is tested with or without an optical correction in place, resulting in a severe amblyopia of over 3 octaves by 1 year of age (Fig. 1D).

Figure 2A is a plot of acuity development for the group with aphakic near-point correction with no occlusion of the opposite eye (ANP-UT). The results from the untreated eyes of these monkeys are similar to the untreated eyes of our control groups. The data show that the aphakic eyes for these animals show
Fig. 1. (A) Plot of acuity for normal infant monkeys. Acuity is reported in cycles per degree (cpd) and age in weeks for this and subsequent acuity graphs. Snellen equivalents are shown on the right axis of each of these graphs. Icons of eyes in the upper left corner for each graph correspond to the experimental groups as presented in Table 1. The open circle symbols are acuity measurements for the right eye and the plusses are acuity measurements for the left eye. The shaded area includes the entire range (100%) of individual differences we encountered for normal controls and is reproduced in subsequent figures to facilitate comparisons of normal acuity data to other experimental group data. (B) Plot of the interocular differences in acuity for normal infant monkeys. Each point (Δ) on the graph is the difference in octaves between left and right eye acuities for one monkey. The shading encompasses a ±1 octave stepsize and demonstrates that the difference in acuity values between two normal eyes is never more than an octave. This shading is also reproduced on future graphs to facilitate easy comparisons. Points connected by lines on this graph and future interocular difference plots show longitudinal data collected during the study. In this and subsequent graphs upward direction of the line indicates that the acuity of the eye corresponding to the icon on the right is better than that of the icon on the left. A downward slanting line indicates that the acuity of the eye corresponding to the icon on the left is better than that of the icon on the right. (C) Plot of acuity for ANC-UT animals. The open circles represent the acuity for aphakic uncorrected eyes, the open squares represent the acuity for aphakic eyes from the same group that were corrected to a near point at the time of the test, and the plusses represent the untreated eyes of these animals. (D) Plot of the interocular differences for this same group. In this case, the open square symbols represent interocular differences for monkeys tested with the appropriate optical correction in the aphakic eye for the acuity test. The open circle symbols represent interocular differences for monkeys tested without any optical correction for the aphakic eye.

gradual improvement in acuity during the first year, but consistently lag slightly behind the untreated eyes after the first few weeks of age. By 1 year of age, the aphakic eyes have acuities that range from 3.6 to 9.8 cpd, about two octaves below untreated eye levels. Monkeys in this treatment group demonstrate that even in the absence of any occlusion of the opposite eye, continuous near-point correction reduces the magnitude of amblyopia compared to that seen in the aphakic control group (Fig. 2B).

Figure 2C shows acuity plotted for each eye as a function of age for undercorrection and near point...
Fig. 2. (A) Plot of acuity for the ANP-UT group. The open circles depict the aphakic near point corrected eyes and the pluses are the untreated eyes. (B) Interocular difference plot for the same group. The open circles plotted are the interocular differences between the aphakic corrected eye and the untreated eye for each animal. (C) Plot of acuity for the ANP-CO and AUC-CO groups combined on one graph. Open circles depict the undercorrected aphakic eyes, open squares the near point corrected aphakic eyes; filled circles the occluded eyes for the undercorrected group and filled squares the occluded eyes for the near point corrected group. (D) Interocular difference plot for the same group. The open circle symbols represent interocular differences for the ANP-CO group and the open squares represent interocular differences for the AUC-CO group. (E) Plot of acuity for the ANP-PO50% group. The open circles represent the acuities of the aphakic near point corrected eyes and the small filled triangles represent the acuities of the 50% occlusion eyes. (F) Interocular difference plot for the same group using open circles to show the interocular differences between the aphakic corrected eye and the 50% occluded eye for each animal in this group.
correction of aphakia with continuous occlusion of the opposite eye (ANP-CO and AUC-CO) groups. The data for these two groups were combined in this figure because no obvious differences in acuity between the two are apparent at these ages with the acuity card procedure. The aphakic eye attains acuity levels that are near normal, reaching values of 19–26 cpd by 1 year of age. However, the acuity of the occluded eye deteriorates over time, dropping in some cases to levels poorer than at birth. The interocular differences in this group are as extreme as those found in the uncorrected aphakic group, though in opposite directions (Fig. 2D). Figure 2E is a plot of acuity as a function of age for each eye of the partial occlusion group (ANP-50%PO). So far in these animals, both eyes have exhibited a similar development of acuity (Fig. 2F). In terms of absolute levels, acuity development falls within the normal range for the period tested. These results for aphakic monkey eyes are similar to those found by others for human aphakic eyes.5-8

Discussion. A number of issues related to these results warrant discussion. We found no apparent differences between the ANP and AUC groups in grating acuity. This indicates that the plane of optical correction is not critical for visual acuity development in our animals. However, this factor may be more critical if the correction is not paired with continuous occlusion of the other eye, producing a condition in which only one eye is available for use. As we have not tested any AUC animals with less than continuous occlusion, we can not conclude at this time that the plane of optical correction is unimportant for visual outcome.

We have been successful in obtaining reasonably good grating acuities in some aphakic eyes. Our ANP-CO and AUC-CO groups maintained normal acuity in the aphakic eyes of some animals, but only at the expense of their occluded eyes. These results are not directly applicable to human treatment as this is not a typical patching regimen. If used clinically this procedure is monitored closely for the first signs of occlusion amblyopia, at which time occlusion therapy is decreased or discontinued, preventing the severe damage to acuity seen in this group.12 However, there are isolated cases of irreversible damage caused by occlusion amblyopia in the human literature. 13 We have demonstrated elsewhere that this occlusion amblyopia effect is long-lasting in a monkey in the aphakic near-point correction, continuous occlusion group (ANP-CO).14

Monkeys in the ANP-50%PO group exhibited similar acuity development in their two eyes during the time tested. Our ANP-UT group demonstrated surprisingly good results for their aphakic eyes given the fact that there was no occlusion of the opposite eye. We had anticipated no benefit at all of optical correction with no patching; however, these aphakic eyes definitely have better grating acuity than the uncorrected aphakic group. Carefully monitored lens wear may have placed this group at a greater advantage for developing good grating acuity. The pattern of results that we have obtained across these groups raises an important question that must be considered when deciding upon treatments for infantile aphakia. Do the potential benefits of about a two octave improvement in acuity in the aphakic eye outweigh the potential risks of damaging acuity in the occluded eye? Additional information that bears on this issue comes from reports that aphakic eyes that have good acuity may still suffer from other deficits such as asymmetric optokinetic nystagmus and field deficits.7 Binocular function is also at risk, as demonstrated by the frequent development of strabismus in humans and monkeys.15 We are currently using operant methods to explore various aspects of visual function in the eyes of these monkeys to determine exactly what deficits are created by the removal of an infantile cataract as well as the permanence of the findings presented here.14

Finally, because surgeries are performed on our animals at 7–14 days of age, our model more appropriately simulates the effects of an infantile cataract than a congenital cataract. Our animals received binocular experience for this period, which may have been enough time to account for the notably good outcomes for all of our groups, particularly the ANP-UT group. Recognizing this limitation of our current model, we are now pursuing studies with monkeys that more closely simulate congenital cataracts. We hope these studies with animals will allow new clinical treatments to be derived for human children with problems such as infantile and congenital cataracts that are safe to use and provide the optimal visual acuity in both eyes.

Key words: aphakia, grating acuity, infantile cataracts, amblyopia, macaque monkey

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