Successful Amblyopia Therapy Initiated After Age 7 Years

**Compliance Cures**

Helen A. Mintz-Hittner, MD; Kristina M. Fernandez, MA

**Objective:** To report successful therapy for anisometropic and strabismic amblyopia initiated after age 7 years.

**Methods:** A consecutive series of 36 compliant children older than 7 years (range, 7.0 to 10.3 years; mean, 8.2 years) at initiation of amblyopia therapy for anisometropic (19 patients; mean age, 8.3 years), strabismic (9 patients; mean age, 8.0 years), or anisometropic and strabismic (8 patients; mean age, 8.0 years) amblyopia was studied. Initial (worst) visual acuities were between 20/50 and 20/400 (log geometric mean, –0.83 [antilog, 20/134] for all patients; –0.88 [antilog, 20/151] for anisometropic patients; –0.70 [antilog, 20/100] for strabismic patients; and –0.88 [antilog, 20/151] for anisometropic and strabismic patients). Initial (worst) binocularity was absent or reduced in all cases. Therapy consisted of (1) full-time standard occlusion (21 patients; mean age, 8.0 years), (2) total penalization (7 patients; mean age, 7.8 years), or (3) full-time occlusive contact lenses (8 patients; mean age, 8.8 years).

**Results:** Final (best) visual acuities were between 20/20 and 20/30 for all 36 patients. Final (best) binocularity was maintained or improved for 22 (61%) of 36 patients, including 16 anisometropic patients (84%), 2 strabismic patients (22%), and 4 anisometropic and strabismic patients (50%).

**Conclusion:** Given compliance, therapy for anisometropic and strabismic amblyopia can be successful even if initiated after age 7 years.

Arch Ophthalmol. 2000;118:1535-1541

The response to amblyopia therapy is thought to be related to (1) type of amblyogenic stimulus (anisometropia, strabismus, or deprivation),1-4 (2) initial depth of amblyopia,3,5 (3) age at initiation of therapy (years),1,4,6-10 (4) duration of amblyopia therapy (initial and maintenance for months to years),6-8 (5) method of amblyopia therapy (penalization [complete or partial, i.e., with or without a refractive lens creating a blur]17-19 or occlusion [full-time or part-time, with an occlusive contact lens20 or with a standard patch]), and (6) compliance (despite social and psychological factors).5,6,21-24

In 1998, Flynn et al10 reviewed extensively the results of amblyopia therapy by using the pooled data from 961 patients described in 23 published studies between 1965 and 1994. Univariate analyses showed that the single factor that most clearly related to a successful outcome was age at initiation of therapy (P < .001). Success (visual acuity better than 20/40) was accomplished in 73% of patients, whose mean age was 5.2 years. Failure (visual acuity worse than 20/50) was accomplished in 27% of patients, whose mean age was 7.5 years. A second factor identified by univariate analyses was depth of visual loss before treatment for anisometropic and strabismic, but not for combined anisometropic and strabismic, amblyopia (P < .001). A third factor identified by univariate analyses was type of amblyopia (successful treatment in 78% of strabismic patients [n = 402], 67% of anisometropic patients [n = 108], and 59% of combined strabismic and anisometropic patients [n = 75]). With the use of these 3 single factors, a multivariate model (Table VI and Figure 4 in the article by Flynn et al10) showed odds for failure increased in the following age groups: from 0 to 3 years (n = 387; odds for failure, 0 [i.e., reference group]), 4 to 5 years (n = 226; odds for failure, 1.7), 6 to 10 years (n = 258; odds for failure, 4.3), 11 to 20 years (n = 26; odds for failure, 7.9), and 21 years or older (n = 14; odds for failure, 12.3). According to Flynn et al, “Odds of treatment failure are less than 1:2 for a wide range of patients who began
PATIENTS AND METHODS

Thirty-six compliant children are the subjects of this report. Each was referred after having failed a routine visual acuity screening after the age of 7 years either at school or in a pediatric clinic. Only patients with initial visual acuity of 20/50 or worse were included. This consecutive patient series intentionally excluded patients with organic amblyopia, deprivation amblyopia, and noncompliant patients. None of the children had undergone an ocular examination previously; thus, none had ever worn glasses, received amblyopia therapy, or had strabismus surgery. Most of the patients had been told by the initial ophthalmic professional that nothing could be done for their amblyopia because they were too old. They were referred to this pediatric ophthalmology practice for a second opinion.

All parents gave informed consent regarding the diagnosis and standard treatment of amblyopia (anisometropic, strabismic, and combined anisometropic and strabismic). Additional information was given regarding penalization (pharmacological and optical) and occlusive contact lenses when these treatment modalities were to be used.

Visual acuity was measured by means of linear Snellen optotypes. At the time that many of these patients were seen initially, devices were not available to constantly generate random letters by a computer-driven apparatus; therefore, familiarity of letters or memorization factors cannot be eliminated. A binocularity index was determined with the use of the Worth 4-dot test at near and the Titmus stereo test with a scale ranging from 0 to 4: 0 indicated complete suppression; 1, a moderate central suppression scotoma with peripheral fusion at near only indicated by fusion on the Worth 4-dot test at near; 2, a small suppression scotoma and peripheral fusion indicated by fusion of the Titmus stereo fly; 3, moderate stereoaucuity (100-400 arc seconds) on the stereo test animals (1 to 3 animals) and/or on the stereo test circles (1 to 5 circles); and 4, good stereoaucuity (≤80 arc seconds) on the stereo test circles (6 to 9 circles).

Initial therapy consisted of full optical correction (spectacle or contact lens) for the amblyopic eye and total penalization or full-time occlusion (standard occlusion with a patch or with an occlusive contact lens) for the nonamblyopic eye. Total penalization for both distance and near consisted of 1% atropine sulfate ophthalmic drops from 2 to 4 days each week (depending on iris color) with a refractive lens creating 4 to 6 diopters of blur, ie, an incorrect lens, for the nonamblyopic eye. Because the rate of recovery of visual acuity seemed to be nonlinear, follow-up visits were initially frequent (1 to 4 weeks) to give encouragement and document compliance. There was a uniformly rapid rate of improvement to the 20/200 level of visual acuity. Later, follow-up visits were less frequent (4 to 6 months) to prevent discouragement, since patients want to document improvement after each visit, and there was a slower rate of improvement to the 20/30 or 20/20 level of visual acuity. This therapy was continued until there was no further improvement in the visual acuity of the amblyopic eye. After this, partial penalization for near or part-time occlusion (with a patch or with an occlusive contact lens) was used for maintenance of the final (best) visual acuity for a minimum of 1 year to diminish recidivism. Partial penalization for near consisted of 1% atropine ophthalmic drops 1 to 2 days each week with the correct lens for the nonamblyopic eye. After maintenance therapy was discontinued, visual acuity was restested in 3 to 4 months, and if there was any decrement in visual acuity, maintenance therapy was used for a minimum of 1 additional year.

The occlusive contact lenses were obtained by ordering clear, soft contact lenses (SaturEyes [55% hioxifilcon A; base curves, 8.4 or 8.7 mm; diameter, 14.2 mm; power, +3.00 diopters; dK value [oxygen permeability factor], 20 for daily wear]; Metro Optics, Austin, Tex). These contact lenses were sent to Adventure in Colors Technology (Golden, Colo), where they were dyed with reactive black dye No. 11.

With regard to children with strabismic amblyopia, response to treatment is not better. In 1993, Epstein et al12 found that the efficiency of treatment for strabismic amblyopia decreased as a function of age and was null by the time the patient was 12 years of age (their Figure 2). Only children with anisometropic amblyopia are reported to respond to therapy at later ages. In 1977, Hedgpeth and Sullivan14 found that anisometropic amblyopia could be successfully treated at least until the age of 12 years (their Tables 1 and 2). In 1992, Wick et al15 described 19 patients older than 6 years and found that anisometropic amblyopia was amenable to treatment at any age (at least to age 49 years) (their Table 1).

The purpose of this consecutive compliant patient series, studied retrospectively, is to suggest that anisometropic and strabismic amblyopia can be improved provided that the initial depth of amblyopia is not worse than counting fingers and that the method and duration of amblyopia therapy are tailored to obtain compliance, accounting for social and psychological factors. Thus, age at initiation of therapy need not be a deterrent to therapy even if greater than 7 years.
There were 36 patients: 21 boys and 15 girls. Nine were Hispanic, 3 were black, and 24 were white. Each was born between November 1, 1979, and July 31, 1991, and was initially examined ophthalmologically between October 1, 1987, and July 31, 1999. Thus, an average of only 4 patients per year met the clinical criteria for inclusion in this consecutive series of compliant patients diagnosed initially after the age of 7 years. It is not known how many patients who were given instruction for amblyopia therapy were not compliant or did not feel that therapy was working and, thus, did not return. These patients, as well as those who may have been required to have follow-up care by other physicians because of insurance carriers, were excluded from this study for lack of data, and this exclusion prevents calculation of a success rate.

The clinical variables for each of the 36 compliant patients are given in Table 1 and include sex, race, refraction of each eye, amount of anisometropia, and presence of strabismus. Table 2 details the initial (worst) amblyopia characteristics and includes age at start of therapy, method of initial therapy, initial (worst) visual acuity of the amblyopic eye and its log value, and initial binocularity index. Means are given for each subgroup of patients as well as for all of the 36 patients. Table 3 provides the final (best) amblyopia characteristics and includes age at end of therapy, years of therapy required, final (best) visual acuity of the amblyopic eye and its log value, and final binocularity index. Means are given for each subgroup of patients as well as for all of the 36 patients.
The average age at initiation of amblyopia therapy for the 36 patients was 8.2 years (range, 7.0-10.3 years). Anisometropic amblyopia was present in 19 patients (mean initial age, 8.3 years; range, 7.1-10.3 years), strabismus in 9 patients (mean initial age, 8.0 years; range, 7.0-9.0 years), and both anisometropia and strabismus in 8 patients (mean initial age, 8.0 years; range, 7.0-9.2 years). None of the patients had an angle of strabismus greater than 10 prism diopters, which undoubtedly contributed to the late age at the time of diagnosis.

The initial (worst) visual acuity ranged from 20/50 to 20/400 with best optical correction. The log geometric mean was –0.83 (antilog, 20/134) and median was 20/100 for all patients; –0.88 (antilog, 20/151) and 20/100 for anisometropic patients; –0.70 (antilog, 20/100) and 20/80 for strabismic patients; and –0.88 (antilog, 20/151) and 20/200 for combined anisometropic and strabismic patients. Binocular function was present initially for 28% (10/36 patients) of all patients, for 37% (7/19 patients) with anisometropic amblyopia, for 11% (1/9 patients) with strabismic amblyopia, and for 25% (2/8 patients) with combined amblyopia.

The final (best) visual acuity ranged from 20/20 to 20/30 with best optical correction (log geometric mean, –0.09; antilog, 20/24; and median, 20/25) for all patients. Duration of therapy was a mean of 0.6 year for anisometropic amblyopia, 1.0 years for strabismic amblyopia, and 0.8 year for combined amblyopia. Binocular function at the end of therapy was maintained or improved for 61% (22/36 patients), including 84% (16/19 patients) with anisometropic amblyopia, 22% (2/9 patients) with strabismic amblyopia, and 50% (4/8 patients) with combined amblyopia.

The relationships between initial (worst) and final (best) visual acuity (log) and age at start of therapy are shown in Figure 1 for all patients and for patients with anisometropic, strabismic, and combined amblyopia. The relationships between initial and final visual acuity (log) and anisometropic amblyopia are shown in Figure 2 for the same 4 patient groups. In this series, visual acuity was uniformly improved (100%).

The relationships between initial and final binocular function (0 to 4 binocularity index) and the age at start of therapy are shown in Figure 3 for the same 4 patient groups. The relationships between initial and final binocular function (0 to 4 binocularity index) and anisometropic amblyopia are shown in Figure 4 for the same 4 patient groups. In this series, binocular function was often maintained or improved (84%) if anisometropic amblyopia was the only amblyogenic stimulus (Figures 3C and 4C) but was less frequently improved (35%) if strabismus was an amblyogenic stimulus (Figure 3B and D; Figure 4B and D).

There are 3 periods for any visual function: (1) the period of development of the visual function; (2) the period for interrupting the visual function; and (3) the period for recovering the visual function. These 3 periods are different for each of the 3 types of amblyopia: anisometropic, strabismic, and deprivation. These 3 periods are also different for binocular function.

In this consecutive patient series, when compliance was obtained, visual acuity could be recovered uniformly for anisometropic and strabismic amblyopia; however, binocular function was easier to recover for anisometropic amblyopia than for strabismic amblyopia. It is understood that congenital strabismus will not spontaneously improve; however, anisometropic amblyopia has been documented to increase, remain stable, or decrease at early ages. Of course, in this series of patients, who were not seen before the age of 7 years, all early data for amblyopia are unknown. Nevertheless, this is just one example of the differences between anisometropic and strabismic amblyopia that allow one to predict that anisometropic amblyopia has a much more favorable progno-

<table>
<thead>
<tr>
<th>Table 3. Final (Best) Amblyopia Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient</strong></td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td><strong>Anisometropic Amblyopia</strong></td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>6</td>
</tr>
<tr>
<td>7</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>9</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>11</td>
</tr>
<tr>
<td>12</td>
</tr>
<tr>
<td>13</td>
</tr>
<tr>
<td>14</td>
</tr>
<tr>
<td>15</td>
</tr>
<tr>
<td>16</td>
</tr>
<tr>
<td>17</td>
</tr>
<tr>
<td>18</td>
</tr>
<tr>
<td>19</td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td><strong>Strabismic Amblyopia</strong></td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>6</td>
</tr>
<tr>
<td>7</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>9</td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td><strong>Anisometropic and Strabismic Amblyopia</strong></td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>6</td>
</tr>
<tr>
<td>7</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td><strong>All 36 Patients</strong></td>
</tr>
<tr>
<td>Mean</td>
</tr>
</tbody>
</table>

©2000 American Medical Association. All rights reserved.
sis for the development of binocular function than does strabismic amblyopia.

To obtain compliance, several methods of “coercion and bribery” were used. In addition, to assist indigent parents, patches, atropine eye drops, glasses, contact lenses, and office visits were provided at no charge as needed. These programs represent our most aggressive penalization and occlusion schedules because of the sense of urgency to obtain improvement quickly for both psychological and physiological reasons.

Figure 1. Relationship between initial (worst; squares) and final (best; triangles) visual acuity (log) vs age at the start of amblyopia therapy. Thick solid vertical lines indicate patch therapy; thin solid vertical lines, occlusive contact lens therapy; and thick dashed vertical lines, total penalization therapy.

Figure 2. Relationship between initial and final visual acuity (log) vs anisometropia. See the legend to Figure 1 for explanation of symbols.
In general, occlusive contact lenses were chosen for the older, cooperative, strabismic patients whose initial visual acuity was 20/200 or worse (more severe initial depth of amblyopia). Total penalization was chosen for the younger, uncooperative, anisometropic patients whose initial visual acuity was 20/100 or better (less severe initial depth of amblyopia).

Our results suggest that the period of visual acuity recovery for anisometropic, strabismic, and combined amblyopia should be extended from the conventional view.

Figure 3. Relationship between initial and final binocular function (binocularity index) vs age at the start of amblyopia therapy. See the legend to Figure 1 for explanation of symbols.

Figure 4. Relationship between initial and final binocular function (binocularity index) vs anisometropia. See the legend to Figure 1 for explanation of symbols.
of 7 years of age as an upper limit for treatment, but they do not imply any specific age as an upper limit for treat-
ment. Our results also extend the period of recovery of binocular function, especially if the loss of binocularity is
due to anisometropia alone. Amblyopia therapy is one of the most cost-effective methods of restoring vision, and
treatment should be undertaken aggressively. Although this report is only a small, single-center, retrospectively
analyzed, consecutive case series of compliant patients, it suggests that large, multicenter, prospective ambly-
opia studies should include older patients.

Accepted for publication April 13, 2000.

This work was supported in part by unrestricted grants
from the Hermann Eye Fund and the J. M. West Texas Corp,
Houston, Texas, and from Research to Prevent Blindness Inc,
New York, NY, and Vision Core grant EY10608 from the
National Institutes of Health, Bethesda, Md.

Reprints: Helen A. Mintz-Hittner, MD, 6410 Fannin,
Suite 920, Houston, TX 77030-5204 (e-mail: Helen.A
.Mintz-Hittner@uth.tmc.edu).

REFERENCES

1. Wick B, Wingard M, Cotter S, Scheiman M. Anisometropic amblyopia: is the pa-
147.
3. Levartovsky S, Oliver M, Gottesman N, Shimshoni M. Factors affecting long term
results of successfully treated amblyopia: initial visual acuity and type of ambly-
4. Flynn JT, Schiffman J, Feuer W, Corona A. The therapy of amblyopia: an analy-
sis of the results of amblyopia therapy utilizing the pooled data of published stud-
5. Woodruff G, Hiscox F, Thompson JR, Smith LK. Factors affecting the outcome of
and results of treatment for amblyopia in children more than 8 years old.
7. Brown MH, Edelman PM. Conventional occlusion in the older ambylope. Am Or-
thopt J. 1976;26:34-38.
8. Levartovsky S, Gottesman N, Shimshoni M, Oliver M. Factors affecting long-
term results of successfully treated amblyopia: age at beginning of treatment and
223.
9. Quah BL, Tay MTH, Chew SJ, Lee LKH. A study of amblyopia in 18-19 year old
85:428-430.
12. Epelbaum M, Milleret C, Buissere P, Dufier JL. The sensitive period for strabis-
13. Ham O, Clarament M, Diaz T. Strabismic amblyopia: final results of occlusion
15. Bremner MH. Visual acuity in the primary school child aged four to twelve years:
a review of amblyopia treatment in this age group at Princess Margaret Hospi-
1976;26:37-42.
17. Regka MX, Ray JM. The efficacy of optical and pharmacological penalization. Oph-
thalmology. 1993;100:769-775.
18. Simons K, Stein L, Seiser EC, Vitale S, Guyton DL. Full-time atropine, intermit-
tent atropine, and optical penalization and binocular outcome in treatment of
19. Simons K, Gotzfier KC, Vitale S. Penalization versus part-time occlusion and
1997;104:2156-2160.
20. Tsubota K, Yamada M. Treatment of amblyopia by extended-wear occlusion soft
22. Leach C. Compliance with occlusion therapy for strabismic and anisometric
23. Smith LK, Thompson JR, Woodruff G, Hiscox F. Factors affecting treatment com-
24. Hudak DT, Magoon EH. Poverty predicts amblyopia treatment failure. J Am As-
505.
27. Keech RV, Kutschke PJ. Upper age limit for the development of amblyopia. J Pe-
sample of astigmatic children, II: the changeability of anisometropia. Acta Oph-