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# Amblyopia Preferred Practice Pattern®

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# PEDIATRIC OPHTHALMOLOGY/STRABISMUS PREFERRED PRACTICE PATTERN DEVELOPMENT PROCESS AND PARTICIPANTS

The **Pediatric Ophthalmology/Strabismus Preferred Practice Pattern Panel** members wrote the Amblyopia Preferred Practice Pattern guidelines (PPP). The PPP Panel members discussed and reviewed successive drafts of the document, meeting in person twice and conducting other review by e-mail discussion, to develop a consensus over the final version of the document.

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The **Preferred Practice Patterns Committee** members reviewed and discussed the document during a meeting in June 2022. The document was edited in response to the discussion and comments.

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The Amblyopia PPP was then sent for review to additional internal and external groups and individuals in July 2022. All those returning comments were required to provide disclosure of relevant relationships with industry to have their comments considered (indicated with an asterisk below). Members of the Pediatric Ophthalmology/Strabismus Preferred Practice Pattern Panel reviewed and discussed these comments and determined revisions to the document.

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The disclosures of relevant relationships to industry of other reviewers of the document from January to October 2022 are available online at [www.aao.org/ppp](http://www.aao.org/ppp).

# TABLE OF CONTENTS

|   |      |
|---|------|
| <b>OBJECTIVES OF PREFERRED PRACTICE PATTERN GUIDELINES</b> .....  | P142 |
| <b>METHODS AND KEY TO RATINGS</b> .....   | P143 |
| <b>HIGHLIGHTED FINDINGS &amp; RECOMMENDATIONS FOR CARE</b> .....  | P144 |
| <b>INTRODUCTION</b> .....   | P145 |
| Disease Definition .....  | P145 |
| Refractive Amblyopia .....  | P145 |
| Strabismic Amblyopia .....  | P145 |
| Visual Deprivation Amblyopia .....  | P145 |
| Occlusion (Reverse Amblyopia) .....   | P146 |
| Patient Population .....  | P146 |
| Clinical Objectives .....   | P146 |
| <b>BACKGROUND</b> .....   | P146 |
| Prevalence and Risk Factors .....   | P146 |
| Natural History .....   | P147 |
| Rationale for Treatment .....   | P147 |
| <b>CARE PROCESS</b> .....   | P148 |
| Patient Outcome Criterion .....   | P148 |
| Diagnosis .....   | P148 |
| History .....   | P148 |
| Examination .....   | P148 |
| Criteria for Diagnosis .....  | P152 |
| Management .....  | P152 |
| Prevention .....  | P152 |
| Choice of Therapy .....   | P153 |
| Alternative Therapies .....   | P156 |
| Follow-up Evaluation .....  | P156 |
| Provider and Setting .....  | P159 |
| Counseling and Referral .....   | P159 |
| Socioeconomic Considerations .....  | P159 |
| <b>APPENDIX 1. QUALITY OF OPHTHALMIC CARE CORE CRITERIA</b> .....   | P161 |
| <b>APPENDIX 2. INTERNATIONAL STATISTICAL CLASSIFICATION OF DISEASES AND<br/>RELATED HEALTH PROBLEMS (ICD) CODES</b> ..... | P163 |
| <b>APPENDIX 3. PEDIATRIC EYE DISEASE INVESTIGATOR GROUP AMBLYOPIA CLINICAL<br/>TRIALS, 2002–2021</b> .....                | P164 |
| <b>LITERATURE SEARCHES FOR THIS PPP</b> .....   | P168 |
| <b>SUGGESTED READING</b> .....  | P168 |
| <b>RELATED ACADEMY MATERIALS</b> .....  | P168 |
| <b>REFERENCES</b> .....   | P170 |

# OBJECTIVES OF PREFERRED PRACTICE PATTERN GUIDELINES

As a service to its members and the public, the American Academy of Ophthalmology has developed a series of Preferred Practice Pattern guidelines that **identify characteristics and components of quality eye care**. Appendix 1 describes the core criteria of quality eye care.

The Preferred Practice Pattern guidelines are based on the best available scientific data as interpreted by panels of knowledgeable health professionals. In some instances, such as when results of carefully conducted clinical trials are available, the data are particularly persuasive and provide clear guidance. In other instances, the panels have to rely on their collective judgment and evaluation of available evidence.

**These documents provide guidance for the pattern of practice, not for the care of a particular individual.** While they should generally meet the needs of most patients, they cannot possibly best meet the needs of all patients. Adherence to these PPPs will not ensure a successful outcome in every situation. These practice patterns should not be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the best results. It may be necessary to approach different patients' needs in different ways. The physician must make the ultimate judgment about the propriety of the care of a particular patient in light of all of the circumstances presented by that patient. The American Academy of Ophthalmology is available to assist members in resolving ethical dilemmas that arise in the course of ophthalmic practice.

**Preferred Practice Pattern guidelines are not medical standards to be adhered to in all individual situations.** The Academy specifically disclaims any and all liability for injury or other damages of any kind, from negligence or otherwise, for any and all claims that may arise out of the use of any recommendations or other information contained herein.

References to certain drugs, instruments, and other products are made for illustrative purposes only and are not intended to constitute an endorsement of such. Such material may include information on applications that are not considered community standard, that reflect indications not included in approved U.S. Food and Drug Administration (FDA) labeling, or that are approved for use only in restricted research settings. The FDA has stated that it is the responsibility of the physician to determine the FDA status of each drug or device he or she wishes to use, and to use them with appropriate patient consent in compliance with applicable law.

Innovation in medicine is essential to ensure the future health of the American public, and the Academy encourages the development of new diagnostic and therapeutic methods that will improve eye care. It is essential to recognize that true medical excellence is achieved only when the patients' needs are the foremost consideration.

All Preferred Practice Pattern guidelines are reviewed by their parent panel annually or earlier if developments warrant and updated accordingly. To ensure that all PPPs are current, each is valid for 5 years from the approved by date unless superseded by a revision. Preferred Practice Pattern guidelines are funded by the Academy without commercial support. Authors and reviewers of PPPs are volunteers and do not receive any financial compensation for their contributions to the documents. The PPPs are externally reviewed by experts and stakeholders, including consumer representatives, before publication. The PPPs are developed in compliance with the Council of Medical Specialty Societies' Code for Interactions with Companies. The Academy has Relationship with Industry Procedures (available at [www.aaopt.org/about-preferred-practice-patterns](http://www.aaopt.org/about-preferred-practice-patterns)) to comply with the Code.

Appendix 2 contains the International Statistical Classification of Diseases and Related Health Problems (ICD) codes for the disease entities that this PPP covers. Appendix 3 summarizes the published results of the pediatric eye disease investigator group clinical trials from 2002 to 2021. The intended users of the Amblyopia PPP are ophthalmologists.

## METHODS AND KEY TO RATINGS

Preferred Practice Pattern guidelines should be clinically relevant and specific enough to provide useful information to practitioners. Where evidence exists to support a recommendation for care, the recommendation should be given an explicit rating that shows the strength of evidence. To accomplish these aims, methods from the Scottish Intercollegiate Guideline Network<sup>1</sup> (SIGN) and the Grading of Recommendations Assessment, Development and Evaluation<sup>2</sup> (GRADE) group are used. GRADE is a systematic approach to grading the strength of the total body of evidence that is available to support recommendations on a specific clinical management issue. Organizations that have adopted GRADE include SIGN, the World Health Organization, the Agency for Healthcare Research and Quality, and the American College of Physicians.<sup>3</sup>

- ◆ All studies used to form a recommendation for care are graded for strength of evidence individually, and that grade is listed with the study citation.
- ◆ To rate individual studies, a scale based on SIGN<sup>1</sup> is used. The definitions and levels of evidence to rate individual studies are as follows:

|      |   |
|------|---|
| I++  | High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias   |
| I+   | Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias   |
| I-   | Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias   |
| II++ | High-quality systematic reviews of case-control or cohort studies<br>High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal |
| II+  | Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal   |
| II-  | Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal   |
| III  | Nonanalytic studies (e.g., case reports, case series)   |

- ◆ Recommendations for care are formed based on the body of the evidence. The body of evidence quality ratings are defined by GRADE<sup>2</sup> as follows:

|                      |  |
|----------------------|--|
| Good quality         | Further research is very unlikely to change our confidence in the estimate of effect   |
| Moderate quality     | Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate   |
| Insufficient quality | Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate<br>Any estimate of effect is very uncertain |

- ◆ Key recommendations for care are defined by GRADE<sup>2</sup> as follows:

|                              |   |
|------------------------------|---|
| Strong recommendation        | Used when the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not   |
| Discretionary recommendation | Used when the trade-offs are less certain—either because of low-quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced |

- ◆ The Highlighted Findings and Recommendations for Care section lists points determined by the PPP Panel to be of particular importance to vision and quality of life outcomes.
- ◆ All recommendations for care in this PPP were rated using the system described above. Ratings are embedded throughout the PPP main text in italics.
- ◆ Literature searches to update the PPP were undertaken in March 2021 and May 2022 in the PubMed database. Complete details of the literature searches are available in Appendix 4.



## HIGHLIGHTED FINDINGS AND RECOMMENDATIONS FOR CARE

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Treatment of refractive error alone can improve visual acuity (VA) in children who have anisometropic, strabismic, or combined amblyopia. Visual acuity of children who have bilateral refractive amblyopia also can substantially improve with refractive correction alone.

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Most children who have moderate amblyopia (20/40 to 20/80) respond to initial treatment consisting of 2 hours of daily patching or weekend atropine.

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Following treatment of amblyopia caused by strabismus, anisometropia, or both, continued monitoring is necessary and additional treatment, if needed, is associated with long-term durability of the VA improvement.

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Suitable treatment options for amblyopia include optical correction, patching, pharmacological treatment, optical treatment, Bangerter (translucent) filters, and digital therapeutics, in addition to managing the underlying cause of amblyopia.

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Amblyopia treatment may be effective in older children and adolescents, particularly if they have not previously been treated.

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# INTRODUCTION

## DISEASE DEFINITION

Amblyopia is a unilateral or, less often, bilateral reduction of best-corrected visual acuity (BCVA) that usually occurs in the setting of an otherwise normal eye. It is a developmental disorder of the central nervous system that results from the abnormal processing of visual images, leading to reduced visual acuity (VA). Less commonly, amblyopia occurs in association with a structural abnormality involving the eye or visual pathway. Patients with amblyopia experience a reduction in VA that cannot be attributed solely to a structural abnormality; such eyes may also have a deficit in contrast sensitivity and accommodation. Often the fellow eye is not normal but has subtle functional deficits.<sup>4,5</sup>

Amblyopia is classified by cause:<sup>6</sup>

- ◆ Refractive
  - ◆ Anisometropic
  - ◆ High bilateral refractive (isoametropic)
- ◆ Strabismic
- ◆ Visual deprivation
  - ◆ Media opacities
  - ◆ Ptosis
- ◆ Occlusion (reverse)

### Refractive Amblyopia

Amblyopia may develop because of untreated unilateral or bilateral refractive errors.<sup>7-11</sup> Anisometropic amblyopia, a form of unilateral amblyopia, develops when unequal refractive error causes the image on one retina to be more poorly focused than in the fellow eye. This form of amblyopia may occur with or without strabismus. Anisometropic amblyopia is thought to result partly from the direct effect of image blur on the development of VA in the involved eye and partly from interocular competition or inhibition similar to (but not necessarily identical to) that responsible for strabismic amblyopia. Greater degrees of anisometropia or astigmatism result in increased risk and severity of amblyopia (See Pediatric Eye Evaluation PPP, Table 2).<sup>11-13</sup>

Bilateral refractive amblyopia (isoametropic) is a less common form of refractive amblyopia with bilateral reduction in VA. It is thought to result from the effect of bilateral blurred retinal images alone.

### Strabismic Amblyopia

Constant tropias that are not alternating or are unequally alternating (typically esodeviations) can cause amblyopia. Strabismic amblyopia is thought to result from competitive or inhibitory interaction between neurons processing the nonfusible inputs from the two eyes, which leads to dominance of cortical vision centers of the fixating eye and chronically reduced responsiveness to input from the nonfixating eye.

### Visual Deprivation Amblyopia

Visual deprivation amblyopia is caused by complete or partial obstruction of the visual axis, resulting in a degraded retinal image. A common cause is a congenital or early-onset cataract. Corneal opacities, infectious or noninfectious intraocular inflammation, vitreous hemorrhage, and ptosis may also be associated with visual deprivation amblyopia. Deprivation amblyopia is the least common form of amblyopia, but it is often the most severe and difficult to treat. Amblyopic visual loss resulting from a unilateral obstruction of the visual axis tends to be greater than the loss produced by bilateral deprivation of similar degree because interocular competition adds to the direct amblyogenic impact of severe image degradation. Visual acuity is often 20/200 or worse. Newborns with a visually threatening unilateral cataract have a better

prognosis when the cataract is removed and optical correction is in place by 2 months of age.<sup>14-16</sup>

Dense central cataracts are likely to cause amblyopia in young children. Polar cataracts, around which retinoscopy can be performed readily, and lamellar cataracts, through which a reasonably good view of the fundus can be obtained despite difficult retinoscopy, typically cause mild to moderate amblyopia or may have no effect on visual development. With many partial cataracts, there is an associated refractive error that needs to be corrected.

Vision loss in the setting of a structural abnormality of the retina or vitreous (e.g., optic nerve hypoplasia, myelinated nerve fiber layer, macular dragging from retinopathy of prematurity, uveitis) may have a component of treatable amblyopia, either attributable to the structural abnormality (analogous to form deprivation) or as a result of coexisting strabismus and/or refractive error.<sup>17, 18</sup> Conversely, subtle or unrecognized abnormalities of the retina or optic nerve may contribute to vision loss in some eyes in addition to their strabismic or anisometric amblyopia.<sup>19-22</sup>

### Occlusion (Reverse Amblyopia)

Occlusion amblyopia (reverse amblyopia) is a specific form of deprivation amblyopia that is seen after therapeutic patching or pharmacologic cycloplegia of the nonamblyopic eye. In one prospective randomized trial, after 6 months of treatment, VA in the fellow eye was reduced by 2 lines or more in 1% of children patching 6 or more hours per day and in 9% of children given one drop daily of topical atropine.<sup>23</sup> However, in many of the atropine-treated cases, the VA was not measured with optimal correction, so these may not all have represented reverse amblyopia. In nearly every case, the fellow eye VA returned to baseline with no active therapy but simply with discontinuation of the therapy and continuation of the optical correction. In subsequent studies of lower doses of patching and atropine, few cases of reverse amblyopia were noted.<sup>24, 25</sup>

## PATIENT POPULATION

Infants and children through 17 years of age with amblyopia or who have risk factors for development of amblyopia.

## CLINICAL OBJECTIVES

- ◆ Identify children at risk for amblyopia
- ◆ Examine the child with amblyopia risk factors at the earliest possible age
- ◆ Inform the patient, as appropriate, the family/caregiver, and the primary care provider about the diagnosis, associated conditions like refractive error and strabismus, treatment options, care plan, and prognosis
- ◆ Treat infants and children who have amblyopia to improve visual function and to reduce the likelihood of vision-related disability<sup>26, 27</sup>
- ◆ Re-evaluate the child and adjust the treatment plan as necessary

## BACKGROUND

### PREVALENCE AND RISK FACTORS

Amblyopia is an important public health problem because it is prevalent among children, and if it is not treated the visual impairment from amblyopia is lifelong and can be profound.<sup>28</sup> Both amblyopia and its treatment can have a substantial impact on quality of life.<sup>29-31</sup> Prevalence estimates from population-based studies in children ages 30 to 71 months<sup>7-9, 32-34</sup> range from 0.7%<sup>9</sup> to 2.6%,<sup>8</sup> whereas school-based studies of older children typically report higher rates (range, 1.0% to 5.5%); prevalence estimates vary depending on the age, race, and ethnicity of the population studied; on study methodology; and on the definition of amblyopia used.<sup>7-9, 11, 32-51</sup> Amblyopia is most often unilateral. However, bilateral amblyopia does occur, with a proportion varying considerably based on VA criteria, from as low as 5% up to 41% of cases of amblyopia.<sup>9, 33, 34, 42, 44-46</sup>

Unilateral amblyopia is associated with strabismus in 19% to 50% of cases and with refractive error in 46% to 79% of cases.<sup>10, 33, 34, 44, 45</sup> A third of infants 9 to 14 months old with esotropia<sup>52</sup> and over a quarter of preschool children with esotropia have amblyopia,<sup>11</sup> as do a third of children with 2 diopters (D) of anisometropia.<sup>11</sup> Odds of amblyopia are 4.5 times greater when 1 D to 2 D of spherical equivalent anisometropia is present compared with less than 0.5 D, and 40 times greater for more than 2 D of anisometropia.<sup>11</sup> Odds of amblyopia are 2.7 to 18 times greater when strabismus is present.<sup>11, 13, 33, 44, 53</sup> Amblyopia and its risk factors are more common in children who are premature, small for their gestational age,<sup>54-62</sup> have developmental delay,<sup>62</sup> or have a first-degree relative with amblyopia.<sup>63, 64</sup> Environmental factors, including maternal smoking and drug or alcohol use during pregnancy, have been reported to be associated with an increased risk of amblyopia or strabismus in some studies.<sup>65-72</sup> However, other population-based studies have not found an association between amblyopia and maternal smoking.<sup>32, 33, 44, 73</sup>

## NATURAL HISTORY

With rare exception, amblyopia results in lifelong visual loss if it is untreated or inadequately treated in early childhood.<sup>74, 75</sup> All children should have periodic vision screenings. (See Pediatric Eye Evaluation PPP, Table 1.) The potential for successful treatment of amblyopia is greatest in young children, though recent studies show that treatment in older children can improve VA.<sup>74-80</sup>

Untreated deprivation amblyopia due to significant media opacities present in the first 3 postnatal months produces profound and permanent reductions in high contrast (e.g., grating or optotype) acuity, typically to 20/200 or worse in the affected eye(s).<sup>57, 58, 81, 82</sup> The VA reduction may be less profound for deprivation amblyopia developing after 3 months of age.<sup>57, 58, 81, 82</sup> Even brief visual deprivation in infancy can cause amblyopia. Early visual deprivation from cataracts is strongly associated with development of sensory nystagmus in bilateral cases and strabismus in both unilateral and bilateral cases.<sup>83, 84</sup> Deprivation amblyopia developing at later ages shows a slower rate of vision loss, and affected children are more likely to respond to treatment.<sup>82</sup>

Similar but less severe VA deficits are seen in children who have untreated refractive or strabismic amblyopia. In these cases, reduced acuity in one or both eyes may be evident in infancy. When an amblyopia risk factor develops later in life, the risk of amblyopia is less.<sup>81</sup>

Amblyopia is a risk factor for the development of strabismus and subnormal binocularity. In young children, amblyopia treatment may improve vision and foster the development of binocular vision.

## RATIONALE FOR TREATMENT

Timely treatment of amblyopia usually improves VA, may improve binocularity,<sup>23, 85</sup> and decreases the likelihood of a visual handicap if there is loss of vision in the fellow eye later in life. Amblyopia treatment is also cost-effective.<sup>86, 87</sup> Amblyopic children have been found to have reduced eye-hand coordination,<sup>88</sup> more fixation instability, reduced self-perception of peer acceptance and physical competence, slower reading speed, and reduced motor skills, even in the absence of strabismus.<sup>89-92</sup> However, there is insufficient evidence that these deficits contribute to diminished academic achievement.<sup>93</sup> The lifelong risk of bilateral visual impairment is approximately doubled for patients with amblyopia.<sup>94</sup> A retrospective study found that vision loss in the fellow eye was more likely to occur in children with amblyopia compared with those without amblyopia.<sup>95</sup> Accidental trauma with injury of the fellow eye was associated with more than one-half of the cases of total vision loss.<sup>95</sup> In older patients, loss of VA in the fellow eye is usually related to retinal abnormalities such as retinal vein occlusion, age-related macular degeneration, and other macular disorders.<sup>27</sup>

Untreated or insufficiently treated amblyopia may impact a person's career choice. There are specific VA and binocularity requirements, including stereopsis, for a variety of career fields, such as the military, law enforcement, aviation, and surgery.<sup>96, 97</sup> However, there is insufficient evidence that unilateral amblyopia is an impediment to education or career performance.<sup>74, 98-102</sup>

Maintenance of good vision in each eye with appropriate amblyopia treatment is an important part of successful management of strabismus.<sup>103, 104</sup> If the visual system is structurally sound, all children with amblyopia should be offered treatment regardless of age.<sup>105-107</sup>

# CARE PROCESS

## PATIENT OUTCOME CRITERION

- ◆ Improved visual function

## DIAGNOSIS

The initial evaluation of a child suspected of having amblyopia includes a comprehensive ophthalmic evaluation,<sup>108</sup> with attention to risk factors for amblyopia such as strabismus; anisometropia; a family history of strabismus or amblyopia; and the presence of ptosis, a media opacity, or structural defects.

### History

Although a history generally includes the following items, it varies with the child's problems and needs:

- ◆ Demographic data, including sex, date of birth, and identity of parent/caregiver
- ◆ The identity of the historian and relationship to the patient, and any language barriers that may exist
- ◆ The identity of health care providers involved in the child's care
- ◆ The chief complaint and reason for the eye evaluation
- ◆ Current eye problems
- ◆ Ocular history, including prior eye problems, diseases, diagnoses, and treatments
- ◆ Systemic history, birth weight, gestational age, prenatal and perinatal history that may be pertinent (e.g., alcohol, tobacco, and drug use during pregnancy), past hospitalizations and operations, and general health and development, including the presence of developmental delay
- ◆ Current medications and allergies
- ◆ Family history of ocular conditions and relevant systemic conditions
- ◆ Review of systems

### Examination

The eye examination consists of an assessment of the physiological function and the anatomic status of the eye and visual system. Documentation of the child's level of cooperation with the examination can be useful in interpreting the results and comparing results over time. In general, the examination includes the following key elements:

- ◆ Binocular red reflex (Brückner) test
- ◆ Binocularity/stereoacuity testing
- ◆ Assessment of VA and/or fixation pattern
- ◆ Binocular alignment and ocular motility
- ◆ Pupillary examination
- ◆ External examination
- ◆ Anterior segment examination
- ◆ Cycloplegic retinoscopy/refraction with subjective refinement when indicated
- ◆ Funduscopic examination

The examination may also include color-vision testing, external examination, anterior segment examination, and visual field testing. (Refer to the Pediatric Eye Evaluations PPP, Section II. Comprehensive Ophthalmic Examination.<sup>108</sup>)

#### Binocular Red Reflex (Brückner) Test

In a darkened room, the examiner sets the ophthalmoscope lens power at "0" and directs the ophthalmoscope light toward both eyes of the child simultaneously from approximately 18 to 30 inches (45 to 75 centimeters). The Brückner test should be performed prior to pupillary dilation, because subtle differences in the red reflex are difficult to detect once

the pupils are dilated.<sup>109</sup> A symmetric red reflex observed from both eyes is normal. Opacities within the red reflex, a markedly diminished reflex, the presence of a white or yellow reflex, or asymmetry of the red reflexes are all considered abnormal. The appearance of the red reflex varies based on the amount of retinal pigmentation; therefore, it varies by race and ethnicity. Significant hyperopia will present as an inferiorly placed brighter crescent in the red reflex. Significant myopia presents as a superiorly placed brighter crescent.

### **Binocularity/Stereoacuity Testing**

Binocularity, or binocular vision, has several components, including sensory fusion, stereopsis, fusional vergence (motor fusion), and other coordinated binocular eye movements. Sensorimotor fusion is sensitive to disruption by amblyopia, strabismus, refractive error, and/or deprivation. Binocular vision may be affected to different degrees depending on the underlying diagnosis, and tests to evaluate each of these components of binocular vision vary accordingly. The Worth 4-Dot Test is used to evaluate sensory fusion, the Randot Stereo Test is used to evaluate stereopsis, and a prism bar or rotary prism is used to assess fusional motor vergence.<sup>6, 110, 111</sup> Assessment of stereoacuity is an important component of binocular alignment testing because high-grade stereoacuity is associated with normal alignment. Testing of sensory function should be performed before using any dissociating examination techniques (e.g., occluding an eye to check monocular VA or cover testing to assess alignment).

### **Assessment of Visual Acuity and/or Fixation Pattern**

#### *Fixation*

Visual acuity measurement of the infant and toddler involves a qualitative assessment of fixation and tracking (following) eye movements. Fixation and following are assessed by drawing the child's attention to the examiner's or caregiver's face or to a hand-held light, toy, or other fixation target and then slowly moving the target. Fixation behavior can be recorded for each eye as "fixes and follows" or "central, steady, and maintained," along with any qualifying findings, such as eccentric, not central, not steady, or not maintained.

Fixation preference can be assessed by observing the vigor with which the child objects to occlusion of one eye relative to the other. Children with poor vision in one eye usually resist having their fellow eye covered.<sup>112-114</sup> Grading schemes can be used to describe fixation preference. For strabismic patients, fixation pattern is assessed binocularly by determining the length of time that the nonpreferred eye holds fixation. Fixation pattern can be graded by whether the nonpreferred eye will not hold fixation, holds momentarily, or holds for a few seconds (or to or through a blink), or by observation of spontaneous alternation of fixation. For children with small-angle strabismus or no strabismus, the induced tropia test is typically done by holding a base-down prism of 10 to 20 prism D or base-in prism over one eye and then over the other eye and noting fixation behavior.<sup>114-116</sup> Studies have shown that these tests cannot stand alone as highly accurate screening tests for differentiating amblyopia from normal VA.<sup>113, 117-119</sup> However, when used in a clinical setting and interpreted in the context of other key findings, tests of fixation preference are useful diagnostic tools to help determine whether there is amblyopia of sufficient severity to warrant treatment.

Qualitative assessment of VA should be replaced with a recognition VA test based on optotypes (letters, numbers, or symbols) as soon as the child can perform this task reliably.

#### *Visual Acuity*

Recognition VA testing, which involves identifying optotypes and the names for letters, numbers, or symbols, is preferred for assessment of VA to detect amblyopia. The optotypes may be presented on a wall chart, computer screen, or hand-held card. Visual acuity is routinely tested at distance (10 to 20 feet or 3 to 6 meters) and at near (14 to 16 inches or 35 to 40 centimeters). Visual acuity testing conditions should be standardized so that

results obtained over a series of visits can be readily compared. High-contrast black optotypes on a white background should be used for standard VA testing.<sup>120, 121</sup>

A child's performance on a VA test will be dependent on the choice of test and the examiner's skills, rapport with the child, and the child's level of cooperation. To reduce errors, the environment should be quiet and free of distraction. Younger children may benefit from a pretest on optotypes presented at near, either at the start of testing or in a separate session. Before monocular testing, the examiner should ensure that the child is able to perform the test reliably. Allowing children to match optotypes to those found on a hand-held card will enhance performance, especially in young, shy, or cognitively impaired children. Visual acuity testing of children with special needs can provide quantitative information about visual impairment and reduce concerns of parents/caregivers about the child's vision.<sup>121</sup> A shorter testing distance can also facilitate testing in younger children.<sup>122</sup>

Visual acuity testing should be performed monocularly and with best refractive correction in place. Ideally, the fellow eye should be covered with an adhesive patch or tape. If such occlusion is not available or not tolerated by the child, care must be taken to prevent the child from peeking and using the "covered" eye. Sometimes the child will not allow monocular occlusion, in which case binocular VA should be measured. Monocular VA testing for patients with nystagmus or latent nystagmus requires special techniques such as blurring of the fellow eye with a plus lens or using a translucent occluder rather than an opaque one. Binocular VA testing can also be performed on these patients to gain additional information about typical visual performance.

An age-appropriate and consistent testing strategy on every examination is essential. The choice and arrangement of optotypes can significantly affect the VA score obtained.<sup>123-125</sup> Optotypes should be high-contrast, standardized, and not reflect a cultural bias.<sup>120</sup> LEA SYMBOLS® (Good-Lite Co., Elgin, IL), a set of four symbol optotypes developed to test young children, are useful because each optotype blurs similarly as the child is presented with smaller symbols, increasing the test's reliability.<sup>123, 126</sup> Another method for testing young children involves using a design containing only the letters H, O, T, and V.<sup>123, 127</sup> Because the LEA SYMBOLS and the HOTV optotypes include only four possible responses, these acuity tests are easier for younger children. Children who cannot name the LEA SYMBOLS or HOTV letters may be able to match them using a hand-held card. For older children, Sloan letters are preferred.

Several other symbol tests have serious limitations in testing VA of young children. These include Allen pictures,<sup>128</sup> Lighthouse symbols, and the Kindergarten (Sailboat) Eye Chart are less useful.<sup>129,130</sup> The optotypes in these tests may not be standardized, are often presented as single symbols, and some of the symbols are culturally biased.<sup>131</sup> The Tumbling E Chart is conceptually difficult for young children and leads to high untestability rates.<sup>129</sup>

The desirable optotypes for older children and teenagers are Sloan letters used with consistent logMAR-size progression and proportional spacing of letters and lines, as in Early Treatment Diabetic Retinopathy Study (ETDRS) tests.<sup>132</sup> Snellen charts are less desirable because the chart design is typically not standardized, the individual letters are not of equal legibility, and the spacing of the letters does not always meet World Health Organization standards.<sup>120, 133-136</sup>

The arrangement of optotypes on a VA test is important.<sup>131</sup> Optotypes should be presented in a full line of five whenever possible.<sup>111</sup> If a child needs assistance knowing which optotype to identify, the screener may point to the optotype and immediately remove the pointer. The majority of optotypes must be correctly identified to "pass" a line. The same number of optotypes with equal spacing on each line being tested is preferred.<sup>137</sup> In the setting of amblyopia, VA testing with single optotypes is likely to overestimate VA<sup>138-140</sup> because of the lack of adjacent contours that are known to reduce the legibility of individual letters (i.e., crowding phenomenon). Therefore, a more accurate assessment of monocular VA is obtained in amblyopia with the presentation of a line of optotypes. In order to preserve the crowding effect of adjacent optotypes, they should not be covered or masked as the examiner points to each successive optotype. If a single optotype must be used to facilitate VA testing for some children, the single optotype should be surrounded (crowded)

by bars placed above, below, and on either side of it to account for the crowding phenomenon and to avoid overestimating VA.<sup>141-143</sup>

Forced preferential looking using Teller Acuity Cards (Precision Vision, Woodstock, IL) can provide an assessment of grating acuity in infants, and the patient's measurement can be compared with normative data; however, this method of testing overestimates the VA obtained by recognition VA methods in children with amblyopia.<sup>144, 145</sup>

For details of charts used for VA testing, see Appendix 3 in the Pediatric Eye Evaluations PPP.<sup>108</sup>

### Binocular Alignment and Ocular Motility

The corneal light reflection, binocular red reflex (Brückner) test, and cover tests are commonly used to assess binocular alignment. Cover/uncover tests for tropias and alternate cover tests for the total deviation (latent component included) in primary gaze at distance and near should be measured using accommodative targets. The cover test is performed by covering one eye and observing for a refixation movement of the fellow eye; if refixation of the fellow eye occurs, then a tropia is present. Cover tests require sufficient VA and cooperation to fixate on the desired target. Ocular versions and ductions, including into the oblique fields of gaze, should be tested in all infants and children. Eye movements may be tested using oculocephalic rotation (doll's head maneuver) or assessed by observing spontaneous eye movements in the inattentive or uncooperative child. Binocular alignment testing should be done before cycloplegia, because alignment may change after cycloplegia.

### Cycloplegic Retinoscopy/Refraction

Determination of refractive errors is important in the diagnosis and treatment of amblyopia or strabismus. Patients should undergo cycloplegic refraction with retinoscopy, followed by subjective refinement when possible.<sup>6</sup> Retinoscopy, done prior to cycloplegia, provides a rapid assessment of accommodation and may be helpful in evaluating a child with asthenopia who has high hyperopia or a child with accommodative insufficiency.<sup>146,147</sup> Accurate accommodation when viewing a small target near the retinoscope light is seen as a neutral retinoscopic reflex or minor "with" movement. In dynamic retinoscopy, the examiner evaluates the change in the retinoscopic reflex from a "with" motion toward neutrality as the patient shifts fixation from a distant to a near target.

Adequate cycloplegia is necessary for accurate retinoscopic refraction in children because of their increased accommodation compared with adults. At present, there is no ideal cycloplegic agent that is safe, has rapid onset and recovery, provides sufficient cycloplegia, and has no local or systemic side effects.<sup>148</sup> Cyclopentolate hydrochloride 1% is useful because it produces rapid cycloplegia that approximates the effect of topical ophthalmic atropine 1% solution but with a shorter duration of action.<sup>149</sup> Cyclopentolate 1% solution is typically used in term infants over 12 months old. The dose of cyclopentolate should be determined based on the child's weight, iris color, and dilation history. In eyes with heavily pigmented irides, repeating the cycloplegic eyedrops or using adjunctive agents, such as phenylephrine hydrochloride 2.5% (which has no cycloplegic effect) or tropicamide 1.0%, may be helpful to achieve adequate cycloplegia and dilation to facilitate retinoscopy and ophthalmoscopy.<sup>148</sup> Tropicamide (0.5%) and phenylephrine hydrochloride (2.5%) may also be used in combination to produce adequate dilation and cycloplegia. For children younger than 6 months, an eyedrop combination of cyclopentolate 0.2% and phenylephrine 1% is often used.<sup>150</sup> In some children, higher concentrations or a repeat application may be necessary. In rare cases, topical ophthalmic atropine sulphate 1% solution may be necessary to achieve maximal cycloplegia.<sup>149</sup>

The use of topical anesthetic prior to the cycloplegic agent reduces the stinging and promotes penetration of subsequent eyedrops.<sup>151</sup> Uncommon short-term side effects of cycloplegic medications include hypersensitivity reactions, fever, dry mouth, rapid pulse, nausea, vomiting, flushing, somnolence, and, rarely, behavioral changes (i.e., delirium). Punctal occlusion may be useful to reduce these side effects. If the reaction is severe, the child should be referred to an emergency care setting and physostigmine may be given.



## Fundusoscopic Examination

The optic disc, macula, retina, vessels, and the choroid should be examined, preferably using an indirect ophthalmoscope and condensing lens after adequate pupillary dilation is achieved. It may be impossible to examine the peripheral retina of the awake young child. Examination of the peripheral retina with an eyelid speculum and scleral depression may require swaddling, sedation, or general anesthesia.

## CRITERIA FOR DIAGNOSIS

A diagnosis of amblyopia requires detection of a VA deficit (see Table 1) and identification of the likely cause. Amblyopia in the absence of strabismus, unequal refractive error, media opacity, or structural abnormality is rare.<sup>152</sup> A careful search for an alternative diagnosis with associated visual loss should be carried out if an obvious cause is not present.

TABLE 1 DIAGNOSTIC CRITERIA FOR AMBLYOPIA

| Assessment                      | Finding   |
|---------------------------------|---|
| <b>Unilateral Amblyopia</b>     |   |
| Response to monocular occlusion | Asymmetric objection  |
| Fixation preference             | Failure to initiate or maintain fixation, or strong preference for one eye                            |
| Preferential looking            | Interocular difference of two or more octaves*  |
| BCVA                            | Interocular difference of two or more lines, with the better eye within the normal range <sup>†</sup> |
| <b>Bilateral Amblyopia</b>      |   |
|                                 | Age 3 to <4 years: VA worse than 20/50 in both eyes <sup>153, 154</sup>                               |
|                                 | Age 4 to <5 years: VA worse than 20/40 in both eyes   |
| BCVA in each eye <sup>†</sup>   | Age ≥5: VA worse than 20/30 in both eyes  |

Note: A unilateral or bilateral amblyogenic factor needs to be present, along with the corresponding VA deficit.

BCVA = best-corrected visual acuity; VA = visual acuity.

\*A 2-octave difference is a 4-card difference in the full set of Teller Acuity Cards.

<sup>†</sup>In cases of bilateral amblyopia, the visual acuity may not be symmetrical

## MANAGEMENT

### Prevention

Vision screening is important to identify significant refractive error or strabismus that predisposes to amblyopia.<sup>78, 155, 156</sup> The earlier these are detected and treated, the greater the likelihood of preventing and/or successfully treating amblyopia.<sup>157</sup> (See Table 3 in the Pediatric Eye Evaluations PPP for guidelines on refractive correction in infants and young children.<sup>108</sup>) When amblyopia is present, the potential for successful treatment is greatest in young children, although improvement in VA can reasonably be expected in older children and teenagers.<sup>158-160</sup> A study of treatment of moderate strabismic and/or anisometropic amblyopia demonstrated that the VA of the amblyopic eye improved to 20/30 or better 6 months after initiating treatment in approximately three-quarters of children under 7 years of age.<sup>23</sup>

Children with risk factors for amblyopia should have at least one comprehensive ophthalmic examination, generally when the risk factor is identified. Amblyopia risk factors include uveitis; ptosis; gestational age of less than 30 weeks; a birth weight less than 1500 grams; delayed visual or neurologic maturation of unclear etiology;<sup>108</sup> cerebral palsy; syndromes with ocular involvement, such as Down syndrome; and a family history of amblyopia, strabismus, childhood cataract, or childhood glaucoma.

## Choice of Therapy

Success rates of amblyopia treatment decline with increasing age.<sup>78, 161, 162</sup> Treatment may be offered to children regardless of age, including older children and teenagers, especially if they have not been treated previously.<sup>78</sup> The prognosis for attaining normal vision in an amblyopic eye depends on many factors, including the age of onset; the cause, severity, and duration of amblyopia; the history of and response to previous treatment;<sup>78</sup> adherence to treatment recommendations;<sup>23</sup> and concomitant conditions.<sup>10</sup>

Several strategies are used to improve VA in amblyopia. The first is to correct any cause of visual deprivation. The second is to correct refractive errors that are likely to cause blur. The third is to promote use of the amblyopic eye by occluding, fogging, or reducing the contrast of the image seen by the fellow eye. Although not always achievable, the goal of treatment is equal VA between the two eyes. The recommended treatment should be based on the child's age, VA, and adherence and response to previous treatment as well as the child's physical, social, and psychological status.

Treatment for amblyopia in children includes the following elements:

- ◆ Optical correction of significant refractive errors<sup>78, 163-165</sup>
- ◆ Patching<sup>23, 24, 85, 166-168</sup>
- ◆ Pharmacological treatment (atropine)<sup>23, 25, 78, 85, 166, 169-173</sup>
- ◆ Optical treatment (e.g., overplussed lenses)\*, <sup>174</sup>
- ◆ Bangerter (translucent) filters (Ryser Optik AG, St. Gallen, Switzerland)<sup>175</sup>
- ◆ Binocular (dichoptic) digital therapy<sup>176</sup>
- ◆ Surgical correction of visual axis occlusion causing deprivation amblyopia (cataract, ptosis, etc.)
- ◆ Refractive surgery<sup>177-179</sup>

Appendix 3 shows results of randomized controlled trials of amblyopia therapy completed by the Pediatric Eye Disease Investigator Group.

### Optical Correction

Treatment of refractive error alone is the initial step in care of children 0 through 17 years of age with amblyopia.<sup>70, 142, 155, 156</sup> Often there is immediate improvement in VA from improved image clarity. (That is, BCVA is better than uncorrected VA though still subnormal. Note that immediate normalization of VA with refractive correction would indicate simple refractive error, not amblyopia.) Continued wear of refractive correction for 18 weeks can improve VA in the amblyopic eye by two or more lines in at least two-thirds of children 3 to 7 years old who have untreated anisometropic amblyopia.<sup>164</sup> A study in children 7 to 17 years old found that amblyopia improved two or more lines with optical correction alone in about one-fourth of the children.<sup>78</sup> In another study, even children who had residual strabismus when wearing eyeglasses experienced substantial improvement in the amblyopic eye with optical correction alone.<sup>180</sup> A study of children with bilateral refractive amblyopia found their VA substantially improved with refractive correction alone.<sup>181</sup>

In general, eyeglasses are tolerated well by children, especially when there is improvement in visual function. Obtaining an accurate fit and maintaining proper adjustment facilitate acceptance. Flexible single-piece frames with head straps are useful in babies and young children; straps, cable temples, and spring hinges are helpful in keeping eyeglasses on active young children. Impact-resistant lenses provide greater safety and are preferable for children, especially those with amblyopia.

### Patching

Patching is an appropriate choice for amblyopia treatment for children who do not improve with refractive correction alone or who have incomplete resolution of their VA deficit.<sup>18, 159</sup>

The improvement in VA with patching is likely related to the associated decrease in neural signals from the fellow, or nonamblyopic, eye, as demonstrated by recordings from the visual cortex in experimental animals.<sup>182, 183</sup> Patching is best administered by applying an

\*Wynanski-Jaffe T, Kushner BJ, Moshkovitz A, et al. An eye-tracking-based dichoptic home treatment for amblyopia: A multicenter randomized clinical trial. *Ophthalmology*. 2023;130:274-285.

opaque adhesive patch directly to the skin surrounding the fellow eye. Prescribed eyeglasses are worn over the patch. A cloth patch mounted on the eyeglass frame can be effective, but it is a less preferred alternative because children can look around the cloth patch.<sup>184</sup>

A randomized clinical trial found that 6 hours of prescribed daily patching produces an improvement in VA that is similar in magnitude to patching prescribed for all but 1 waking hour when treating severe amblyopia (20/100 to 20/400) in children under 7 years of age (see Appendix 3).<sup>185</sup> In children who have moderate amblyopia (20/40 to 20/80), initial therapy of 2 hours of prescribed daily patching produces an improvement in VA that is similar in magnitude to the improvement produced by 6 hours of prescribed daily patching.<sup>24</sup> The treatment benefit achieved by the patching appears stable through at least 15 years of age.<sup>186</sup>

A small percentage of children treated with patching develop occlusion amblyopia.<sup>104, 185, 187</sup> Strabismus may develop or worsen during patching in some children, but conversely a similar proportion of children may show improvement of their pre-existing strabismus.<sup>104, 187</sup> Mild skin irritation from the adhesive is common with patching (41% of a treatment cohort); the irritation is moderate or severe in an additional 6%,<sup>23</sup> but it can be minimized by switching to a different patch or applying skin lotions to irritated areas when the child is not wearing the patch. The parent/caregiver needs to be advised that a child wearing a patch should be monitored carefully to avoid accidents. In addition, even if the parents and child are committed to treatment, they may experience some distress associated with patching.<sup>31, 188</sup> Educating the parents and children about the importance of treatment does improve compliance with patching.<sup>189</sup> (*I+, Good, Strong*)

Visual deprivation amblyopia, most commonly from unilateral cataract, is difficult to treat successfully. Patching is typically the first line of therapy.<sup>167</sup> (*I-, Moderate, Discretionary*) Some patients have good visual outcomes after occlusion; however, most have persistent, significant visual impairment.<sup>190, 191</sup>

Patching should be considered for older children and teenagers, particularly if they have not previously been treated.<sup>78</sup>

Patching as initial therapy after refractive correction has been implemented should be considered for children with moderate amblyopia (20/40 to 20/80) with a prescribed dose of 2 hours of daily patching.<sup>23,24</sup> For amblyopia worse than 20/80, 6 or more hours of patching is often prescribed,<sup>185, 192</sup> even though 2 hours of patching have been successful in some cases.<sup>193</sup> (*I+, Good, Discretionary*)

## Pharmacological Treatment

Pharmacological treatment that produces cycloplegia of the nonamblyopic eye, most often with atropine 1% solution, is a reasonable choice for treatment of children who do not improve with refractive correction alone.<sup>168, 25</sup> This technique may also be considered in the presence of latent nystagmus or occlusion failure, or for maintenance treatment.<sup>23, 194</sup>

Pharmacological treatment works best when the nonamblyopic eye is hyperopic. The cycloplegia optically defocuses the nonamblyopic eye. In a child wearing full refractive correction, the nonamblyopic eye is defocused at near; in a child with uncorrected hyperopia, the nonamblyopic eye is more defocused at near and is also defocused at distance.

Atropine 1% ophthalmic solution administered to the nonamblyopic, or fellow, eye is an effective method of treatment for mild to moderate amblyopia in children 3 to 15 years of age, and there has been some success with amblyopia worse than 20/80.<sup>23-25, 85, 166, 169</sup> The benefit achieved by pharmacologic treatment of amblyopia due to strabismus, anisometropia, or both appears stable through 15 years of age.<sup>186</sup> Atropine appears to be as effective as occlusion.<sup>23, 166, 168, 195</sup> (*I+, Good, Strong*)

Pharmacological treatment has been prescribed using a variety of dosage schemes to the fellow eye. Traditionally, daily dosing was used and has been shown to be as effective as patching for initial treatment.<sup>23</sup> Atropine 1% given on two consecutive days per week for 4

months was as effective as once daily atropine 1% for moderate amblyopia, treated for 4 months.<sup>25</sup> Modest improvement of 4.5 lines (95% confidence interval [CI], 3.2–5.8 lines) from twice weekly dosing has been reported for children from 3 to 12 years of age with severe amblyopia.<sup>196</sup> There may be a small benefit to augmenting atropine therapy by undercorrecting the hyperopic fellow eye with a plano lens for children who have stopped improving with atropine 1%.<sup>197</sup> (See Appendix 3.) Atropine as initial therapy after refractive correction should be considered for children with moderate amblyopia (20/40 to 20/80) using a prescribed dose of twice weekly.<sup>23, 185</sup>

Pharmacological treatment of amblyopia may have ocular and systemic side effects. It has been associated with transient reduction of VA in the nonamblyopic eye, especially when used in combination with reduced hyperopic correction.<sup>198</sup> Transient reduction of VA in the fellow eye is reported more often with atropine therapy compared with patching for amblyopia management.<sup>23</sup> Less commonly, reverse amblyopia may develop. Monitoring the VA of each eye of a child being treated is essential. Fellow eye acuity can be assessed more accurately when atropine is discontinued at least 1 week before testing. In a few cases, atropine 1% has been associated with the development of esotropia, but an equal proportion of children have improvement of pre-existing strabismus.<sup>104, 166</sup> Atropine 1% solution has been reported to cause photosensitivity in 18% of children and conjunctival irritation in 4%.<sup>23</sup> Light sensitivity may limit the use of atropine in areas that have high sun exposure. Adverse systemic effects include dryness of the mouth and skin, fever, delirium, and tachycardia. Use of atropine 1% for amblyopia in children younger than 3 years has not been studied in clinical trials, and this age group may be more susceptible to systemic side effects.

Applying direct digital pressure over the lacrimal sac and puncta may reduce systemic absorption and toxicity when using atropine or other cycloplegic agents.

### Optical Treatment

Altering the refractive correction of the fellow eye, typically by adding 1 to 3 D of plus sphere to the cycloplegic refraction to blur vision at distance, has been used to treat amblyopia.<sup>199, 200</sup> However, the effectiveness of this technique has been variable and has not been evaluated in randomized clinical trials.<sup>174</sup>

### Bangerter (Translucent) Filters

Filters are an appropriate choice for treatment for children with mild amblyopia who do not improve with refractive corrections alone.<sup>151</sup>

Bangerter filters (Ryser Optik AG), translucent membranes that adhere to the eyeglass lens of the fellow eye, are an option for mild to moderate amblyopia. This filter has been used mostly as maintenance treatment after initial treatment with either patching or atropine. A randomized controlled trial assessed the effectiveness of the filters as primary treatment for amblyopia compared with 2 hours per day of patching.<sup>175</sup> On average, the patching and filter groups had similar improvement in VA for moderate amblyopia.<sup>201-206 207, 208</sup> (*I+*, *Good, Discretionary*)

### Binocular (Dichoptic) Digital Therapy

Binocular therapy has been used to treat amblyopia in children with no strabismus or small-angle strabismus with some binocularity. Images are presented dichoptically; typically, high-contrast images are presented to the amblyopic eye and low-contrast images are presented to the fellow eye. Binocular treatment has been adapted to tablet devices and early versions used a “falling blocks” game, with red-green anaglyphic eyeglasses to allow dichoptic presentation. Although data from early nonrandomized studies were promising,<sup>201-204</sup> results from three randomized trials of early software applications failed to demonstrate that game play prescribed 1 hour per day was as good as patching prescribed 2 hours per day or better than placebo game play.<sup>205, 206, 209</sup>

A randomized trial of second generation programming comparing binocular therapy with continued glasses alone in 7- to 12-year-olds found no benefit.<sup>210</sup> However, a parallel trial in

children 4 to 6 years of age found clinically important improvement at 4 weeks, although the benefit was not sustained at 8 weeks.<sup>211</sup>

Software and hardware development has continued and has been associated with improved outcomes. A randomized clinical trial of a digital dichoptic treatment using virtual reality headsets to deliver reduced contrast images to the nonamblyopic eye with masking of portions of the image visible to each eye, while viewing web-based content, found at 12 weeks that the mean amblyopic eye VA improved by 1.8 lines in the treatment group compared with 0.8 lines in the continued glasses group ( $P = 0.0011$ ).<sup>212</sup> A randomized trial of movie viewing on a hand-held device using contrast reduction and complementary areas of image masking found improvement similar to that achieved with 2 hours of patching after 2 weeks of treatment.<sup>213</sup> Research with this technology is ongoing, which will be used to delineate use of binocular therapy for treatment of amblyopia.<sup>208</sup> Another randomized prospective clinical trial studied a digital therapeutic using a desk based computer platform, red-blue anaglyph glasses and an eye tracker found at 16 weeks the therapeutic (2.8 lines of improvement to be non-inferior to patching 2 hours per day (2.3 lines of improvement).\* (*I* +, *Good, Discretionary*) (See Appendix 3.)

## Surgery

Surgery may be indicated when the cause of the amblyopia can be attributed to opacification of the ocular media (such as cataract, nonclearing vitreous opacity, corneal opacities) or other occlusion of the visual axis (such as from blepharoptosis) when it is severe enough to prevent successful amblyopia therapy without surgical correction. Although strabismus surgery for improved ocular alignment may facilitate amblyopia management in selected cases, it usually does not eliminate the need for amblyopia treatment.<sup>177</sup>

Opacification within the posterior segment from hemorrhage or inflammatory debris may produce deprivation amblyopia and necessitate vitrectomy. If subluxation of a clear lens causes significant optical defocus that is not correctable with eyeglasses or contact lenses, a lensectomy with subsequent optical rehabilitation may be necessary.<sup>178</sup>

Keratorefractive surgery for children is an off-label use of an FDA-approved device. Studies have shown that photorefractive keratectomy can be safely performed for children with anisometric amblyopia who are noncompliant with refractive correction.<sup>179</sup> Best-corrected visual acuity and stereopsis improved, even in older children.<sup>179</sup> Photorefractive keratectomy, phakic IOL and other refractive surgery may have a role in the management of amblyopia in certain children who fail conventional treatment.<sup>214</sup>

## Alternative Therapies

Active interventions including antismpression and vergence activities, accommodation, and eye-hand coordination exercises and perceptual learning have been used to treat amblyopia in the office and in home settings.<sup>215-217</sup> These interventions are often prescribed for the treatment of amblyopia as an adjunct to patching.<sup>215, 216</sup> There is no convincing evidence for treatment success with these activities for amblyopia.

Intermittent occlusion therapy using liquid crystal or polarized eyeglasses has been introduced as an alternative treatment for amblyopia that may be associated with better treatment compliance. In one method, the eyeglasses alternate between a clear and opaque lens before the fellow eye. Two publications suggested efficacy,<sup>218, 219</sup> and one pilot randomized trial found that 4 hours of wearing the specialized glasses was similar in effectiveness to 2 hours of patching.<sup>220</sup>

Another eyeglasses approach uses polarization in the lenses to show an image on a tablet to only the amblyopic eye. A randomized trial of 46 children (mean age, 4.8 years) found that these specialized lenses were superior to glasses alone, with high acceptance.<sup>221</sup>

\*Wynanski-Jaffe T, Kushner BJ, Moshkovitz A, et al. An eye-tracking-based dichoptic home treatment for amblyopia: A multicenter randomized clinical trial. *Ophthalmology*. 2023;130:274-285.

## Follow-up Evaluation

The purpose of the follow-up evaluation is to monitor the response to therapy and adjust the treatment plan as necessary. Determining the VA of the amblyopic eye is the primary goal of the follow-up evaluation, but it is also important to include interval history, especially adherence to the treatment plan; side effects of the treatment; and VA in the fellow eye. Visual acuity measurement is often difficult in children, and it helps to maintain a consistent care team, testing environment, and VA testing method over the follow-up period. Using similar charts in a setting comfortable for the child enhances the ability to obtain reliable results at follow-up visits. When a child is first able to test using letters instead of symbols, it is important to test using both at that visit, to allow comparison to previous visits, because test results are typically better with symbols. Visual acuity results in either eye can vary because of changes in refractive error, poor test reliability, reverse amblyopia, and persistent cycloplegia in an atropine-treated eye.

In general, a follow-up examination should be arranged 2 to 3 months after initiation of treatment, but timing will vary according to the intensity of the treatment and the age of the child. The VA outcome is dependent on performance during the follow-up examination as well as on adherence to treatment. These factors should be considered when the treatment regimen is adjusted as follows:<sup>222, 223</sup>

- ◆ If the VA in both eyes is unchanged and the VA data are reliable and adherence with therapy has been good, increasing treatment intensity or changing treatment modality should be considered. For example, if currently patching the fellow eye 2 hours per day, increasing patching to 6 hours per day or switching to pharmacologic treatment should be considered. When improvement ceases with patching 2 hours per day, increasing the patching dosage to 6 hours daily results in more improvement in VA after 10 weeks compared with continuing 2 hours daily (mean difference of VA adjusted for acuity at randomization = 0.6 lines; 95% CI interval, 0.3–1.0;  $P=0.002$ ).<sup>224</sup> Alternatively, some clinicians intensify treatment by adding topical atropine, although one study found no benefit to adding atropine to the patching regimen for a child who has stabilized on 6 hours per day of patching.<sup>225</sup>
- ◆ If the VA in the amblyopic eye is improved and the fellow eye is stable, the same treatment regimen should be continued.
- ◆ If the VA in the amblyopic eye is decreased and the fellow eye is stable, VA should be retested, the pupillary examination should be repeated to assess for the presence of an afferent pupillary defect (such as might accompany an occult optic neuropathy), the refractive status should be rechecked, and adherence should be confirmed.
- ◆ In cases where children fail to demonstrate any improvement in VA despite adherence to the treatment regimen, and especially if there is worsening VA, the ophthalmologist should consider an alternative diagnosis, such as optic nerve hypoplasia, subtle macular abnormalities, or other anterior visual pathway disorders.
- ◆ If the VA in the fellow eye is decreased by two or more lines, VA should be retested, the refractive status of both eyes should be rechecked, and the diagnosis of reverse amblyopia or an alternative diagnosis should be considered. If the diagnosis of reverse amblyopia is made, the active treatment should be interrupted and follow-up should take place within a few weeks. The VA should be retested to determine whether it has returned to the pretreatment level prior to resuming amblyopia therapy. If the decline in vision persists, the child should be evaluated for an optic neuropathy or maculopathy.
- ◆ If the VA stops improving and is within one line of the fellow eye over a period of 3 to 6 months, decreasing or stopping the treatment should be considered.
- ◆ If the VA in binocular ametropic amblyopia fails to improve despite adherence to refractive correction, and especially if VA worsens over time, the child should be evaluated for an optic neuropathy or maculopathy.

Consensus suggestions for adjusting patching or atropine treatment dosage during treatment are detailed in Table 2.

TABLE 2 RECOMMENDATIONS FOR ADJUSTING TREATMENT IN AMBLYOPIA

| Treatment Response   | Change in Treatment  |
|--|--|
| Visual acuity is not improved after 3 months.  | Maintain or increase patching or atropine, or consider alternative therapy.  |
| Severe skin irritation develops with patching.   | Select alternative therapy.  |
| Visual acuity is not improved with occlusion.  | Consider alternative treatment, taper or terminate treatment if prior treatment has been sufficient.                             |
| Treatment unsuccessful due to underlying pathology (e.g., optic nerve hypoplasia).                                 | Taper or terminate treatment.  |
| Strabismus and/or diplopia develop.  | Temporarily stop treatment and monitor eye alignment and vision.   |
| Visual acuity decreases in the fellow eye by two or more lines.  | Temporarily stop treatment, review diagnosis, and monitor. If reverse amblyopia, consider patching the previously amblyopic eye. |
| Visual acuity is stabilized at normal or near normal over a period of 4 or months confirmed on two or more visits. | Taper or terminate therapy.  |

NOTE: These recommendations are generated by consensus based on professional experience and clinical impressions.

When the ophthalmologist, optometrist, orthoptist, or other qualified health care provider is convinced that maximal VA for the child has been obtained, treatment intensity can be tapered to maintenance therapy.<sup>226</sup> Maintenance methods include lower-dose occlusion, full- or part-time optical treatment, use of Bangerter (translucent) filters, or part-time cycloplegic treatment. If VA in the amblyopic eye is maintained as therapy is tapered, the treatment may be stopped but with follow-up planned, because approximately one-fourth of children successfully treated for amblyopia experience a recurrence within the first year off treatment.<sup>166, 172</sup> For children under age 8 treated with 6 or more hours of daily patching, data suggest that the risk of recurrence is greater when patching is stopped abruptly than when it is reduced to 2 hours per day prior to cessation.<sup>223</sup> To minimize the possibility of recurrent amblyopia, ametropia should continue to be corrected with either eyeglasses or contact lenses until visual maturity is reached, typically by the early teens. In cases of recurrent amblyopia, patching or pharmacologic treatment will usually restore the VA to its previous best-corrected level.<sup>78</sup>

The outcome of therapy depends in part on patient adherence to the treatment plan as well as the cause of amblyopia. In one clinical trial of anisometropic or strabismic amblyopia with long-term follow-up, 78% of the children achieved 20/32 or better vision.<sup>186</sup> Adherence to treatment recommendations may be compromised if the child does not tolerate the patch, eyeglasses, or eyedrops. In one study of 419 children 3 to 7 years old, a slightly higher degree of acceptability was reported for those treated with atropine compared with 6 or more hours of daily patching, based on a parent questionnaire.<sup>23</sup> Parents/caregivers of pediatric patients who understand the diagnosis and rationale for treatment are more likely to adhere to treatment recommendations.<sup>189, 227-229</sup> A study that used an educational cartoon story for 4-year-old children beginning occlusion therapy for amblyopia demonstrated improvement in adherence to the treatment plan.<sup>229</sup> It is also important to obtain the commitment of older children to the proposed treatment program. Because improved communication produces better results, written instructions are helpful for the parent/caregiver to understand, remember, and reinforce the plan.<sup>227</sup>

For children with unilateral vision impairment due to amblyopia, the risk of vision loss in the better eye due to disease or injury has been estimated to be approximately 1:1000.<sup>95</sup> Because of this, amblyopic children who have vision of 20/50 or worse need to wear proper protective eyewear full time, even if they do not benefit from optical correction. A frame approved by the American National Standards Institute Standard No. Z87.1 with impact-resistant lenses (ASTM F803) should be worn daily and for low-eye-risk sports. For most ball and contact sports, impact-resistant goggles should be worn, and integrated head and face protection should be added for higher risk activities.<sup>110, 230</sup> Functionally monocular patients should use approved protective eyewear when participating in contact sports or other potentially harmful activities,

such as those that involve balls, pellet guns, paintballs, and personal use of fireworks.<sup>231-237</sup> Special goggles, industrial safety glasses, side shields, and full-face shields should be used in these cases. Functionally monocular patients should be aware of the need to have regular eye examinations throughout their lives.

## PROVIDER AND SETTING

Although the performance of certain diagnostic procedures (e.g., VA measurement, motility testing) may be delegated to appropriately trained auxiliary personnel (e.g., certified orthoptist) supervised by the ophthalmologist, interpretation of these procedures requires the clinical training, judgment, and experience of the ophthalmologist with pediatric training and experience. Certified orthoptists may manage amblyopia in conjunction with the ophthalmologist. Consultation with or referral to an ophthalmologist who has expertise in the diagnosis and treatment of amblyopia may be desirable for cases in which the diagnosis or management is in question or when the amblyopia appears unresponsive to treatment.

When surgery is part of the treatment plan, the operating ophthalmologist should ideally perform the preoperative evaluation, because this will allow the surgeon to formulate the surgical plan and establish a relationship with the patient prior to surgery. The surgical facility should comply with local, state, and federal regulations and standards governing the setting of care. Inpatient surgery may be necessary if there is a need for complex anesthetic or surgical care, multiple procedures, or postoperative care requiring an acute-care setting.

## COUNSELING AND REFERRAL

Amblyopia is a long-term problem that requires commitment from the child, parent/caregiver, and ophthalmologist to achieve the best possible outcome. The ophthalmologist should discuss the findings of the evaluation with the parent/caregiver and, when appropriate, with the child. The ophthalmologist should explain the disorder and the proposed therapy, including duration, as well as recruit the family in a collaborative approach to therapy. Provision of instructions on paper, reading materials, website links, and video information about the condition may promote better understanding.<sup>189</sup> Parents, caregivers, and children who understand the diagnosis and rationale for treatment are more likely to adhere to treatment recommendations.<sup>227, 228, 238</sup>

## SOCIOECONOMIC CONSIDERATIONS

Amblyopia is a medical condition that requires medical treatment.<sup>239</sup> Health care insurance plans should cover management of all types of amblyopia, including timely screening, treatment, and monitoring for recurrence, because treatment is associated with long-term vision improvement. Detection includes maintaining a schedule of vision screening during childhood and adolescence consistent with the Bright Futures initiative of the U.S. Health and Human Services (<http://brightfutures.aap.org>) and the U.S. Preventive Services Task Force recommendations.<sup>160</sup> Children identified with amblyopia or risk factors need to have access to a comprehensive eye examination and optical correction, such as eyeglasses and contact lenses. Optical correction is, in most cases, the first step in the medical management of amblyopia. Barriers to care, bias, and other socioeconomic factors may contribute to disparities in outcomes of amblyopia treatment. A study from the Intelligent Research in Sight (IRIS) Registry found among children 3 to 7 years old in ophthalmology practices, the success of amblyopia therapy was significantly reduced among African-American and Latinx children compared with white children.<sup>10</sup>

Data about the long-term socioeconomic impact on an individual with amblyopia are limited. Rahi et al reported that 429 of 8861 individuals (4.8%) in a birth cohort in the United Kingdom had residual unilateral amblyopia.<sup>98</sup> They found no association between reduced visual function at 16 years of age and having a paying job at 33 years of age for either men or women. Furthermore, although there were VA requirements for various jobs, only one amblyopic person did not meet the visual requirements for his or her current occupation. When compared with a control group, there was no difference in the self-reported assessment of poor health, depression, sports involvement, or work injury.

However, there is at least a doubled life-time risk of bilateral visual impairment in patients with unilateral amblyopia, often because of trauma to the fellow eye.<sup>74, 94</sup> In older subjects, loss of VA in



the fellow eye is usually related to retinal abnormalities such as retinal vein occlusion, age-related macular degeneration, and other macular disorders.<sup>27</sup> Disorders of binocular vision including amblyopia are associated with a 27% higher risk of musculoskeletal injury, fracture, or fall in patients 65 and older.<sup>240</sup> Amblyopia treatment in childhood improves VA (as well as binocularity)<sup>23, 85</sup> and, therefore, decreases the likelihood of severe visual handicap if there is loss of vision in the fellow eye later in life.

# APPENDIX 1. QUALITY OF OPHTHALMIC CARE

## CORE CRITERIA

*Providing quality care  
is the physician's foremost ethical obligation, and is  
the basis of public trust in physicians.*

*AMA Board of Trustees, 1986*

Quality ophthalmic care is provided in a manner and with the skill that is consistent with the best interests of the patient. The discussion that follows characterizes the core elements of such care.

The ophthalmologist is first and foremost a physician. As such, the ophthalmologist demonstrates compassion and concern for the individual, and utilizes the science and art of medicine to help alleviate patient fear and suffering. The ophthalmologist strives to develop and maintain clinical skills at the highest feasible level, consistent with the needs of patients, through training and continuing education. The ophthalmologist evaluates those skills and medical knowledge in relation to the needs of the patient and responds accordingly. The ophthalmologist also ensures that needy patients receive necessary care directly or through referral to appropriate persons and facilities that will provide such care, and he or she supports activities that promote health and prevent disease and disability.

The ophthalmologist recognizes that disease places patients in a disadvantaged, dependent state. The ophthalmologist respects the dignity and integrity of his or her patients and does not exploit their vulnerability.

Quality ophthalmic care has the following optimal attributes, among others.

- ◆ The essence of quality care is a meaningful partnership relationship between patient and physician. The ophthalmologist strives to communicate effectively with his or her patients, listening carefully to their needs and concerns. In turn, the ophthalmologist educates his or her patients about the nature and prognosis of their condition and about proper and appropriate therapeutic modalities. This is to ensure their meaningful participation (appropriate to their unique physical, intellectual and emotional state) in decisions affecting their management and care, to improve their motivation and compliance with the agreed plan of treatment, and to help alleviate their fears and concerns.
- ◆ The ophthalmologist uses his or her best judgment in choosing and timing appropriate diagnostic and therapeutic modalities as well as the frequency of evaluation and follow-up, with due regard to the urgency and nature of the patient's condition and unique needs and desires.
- ◆ The ophthalmologist carries out only those procedures for which he or she is adequately trained, experienced and competent, or, when necessary, is assisted by someone who is, depending on the urgency of the problem and availability and accessibility of alternative providers.
- ◆ Patients are assured access to, and continuity of, needed and appropriate ophthalmic care, which can be described as follows.
  - ◆ The ophthalmologist treats patients with due regard to timeliness, appropriateness, and his or her own ability to provide such care.
  - ◆ The operating ophthalmologist makes adequate provision for appropriate pre- and postoperative patient care.
  - ◆ When the ophthalmologist is unavailable for his or her patient, he or she provides appropriate alternative ophthalmic care, with adequate mechanisms for informing patients of the existence of such care and procedures for obtaining it.
  - ◆ The ophthalmologist refers patients to other ophthalmologists and eye care providers based on the timeliness and appropriateness of such referral, the patient's needs, the competence and qualifications of the person to whom the referral is made, and access and availability.
  - ◆ The ophthalmologist seeks appropriate consultation with due regard to the nature of the ocular or other medical or surgical problem. Consultants are suggested for their skill, competence, and accessibility. They receive as complete and accurate an accounting of the problem as necessary to provide efficient and effective advice or intervention, and in turn respond in an adequate and timely manner.
  - ◆ The ophthalmologist maintains complete and accurate medical records.

- ◆ On appropriate request, the ophthalmologist provides a full and accurate rendering of the patient's records in his or her possession.
- ◆ The ophthalmologist reviews the results of consultations and laboratory tests in a timely and effective manner and takes appropriate actions.
- ◆ The ophthalmologist and those who assist in providing care identify themselves and their profession.
- ◆ For patients whose conditions fail to respond to treatment and for whom further treatment is unavailable, the ophthalmologist provides proper professional support, counseling, rehabilitative and social services, and referral as appropriate and accessible.
- ◆ Prior to therapeutic or invasive diagnostic procedures, the ophthalmologist becomes appropriately conversant with the patient's condition by collecting pertinent historical information and performing relevant preoperative examinations. Additionally, he or she enables the patient to reach a fully informed decision by providing an accurate and truthful explanation of the diagnosis; the nature, purpose, risks, benefits, and probability of success of the proposed treatment and of alternative treatment; and the risks and benefits of no treatment.
- ◆ The ophthalmologist adopts new technology (e.g., drugs, devices, surgical techniques) in judicious fashion, appropriate to the cost and potential benefit relative to existing alternatives and to its demonstrated safety and efficacy.
- ◆ The ophthalmologist enhances the quality of care he or she provides by periodically reviewing and assessing his or her personal performance in relation to established standards, and by revising or altering his or her practices and techniques appropriately.
- ◆ The ophthalmologist improves ophthalmic care by communicating to colleagues, through appropriate professional channels, knowledge gained through clinical research and practice. This includes alerting colleagues of instances of unusual or unexpected rates of complications and problems related to new drugs, devices or procedures.
- ◆ The ophthalmologist provides care in suitably staffed and equipped facilities adequate to deal with potential ocular and systemic complications requiring immediate attention.
- ◆ The ophthalmologist also provides ophthalmic care in a manner that is cost-effective without unacceptably compromising accepted standards of quality.

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## APPENDIX 2. INTERNATIONAL STATISTICAL CLASSIFICATION OF DISEASES AND RELATED HEALTH PROBLEMS (ICD) CODES

Amblyopia, which includes entities with the following ICD-10 classifications:

|  | ICD-10 CM |
|--|-----------|
| Amblyopia, unspecified   | H53.00-   |
| Strabismic amblyopia (suppression)                                       | H53.03-   |
| Deprivation amblyopia  | H53.01-   |
| Refractive amblyopia, including anisometropic and isoametropic amblyopia | H53.02-   |
| Amblyopia, suspect   | H53.04-   |

CM = Clinical Modification used in the United States; (-) = 1, right eye; 2, left eye; 3, bilateral; 9, eye not specified.

Additional Information:

- For bilateral sites, the final character of the codes indicates laterality. An unspecified side code is also provided if the side is not identified in the medical record. If no bilateral code is provided and the condition is bilateral, assign separate codes for both the left and right side.
- When the diagnosis code specifies laterality, regardless of which digit it is found in (i.e., 4th digit, 5th digit, or 6th digit), most often you will find:
  - Right is 1
  - Left is 2
  - Bilateral is 3
  - Unspecified always follows the conventions under "unspecified" above (i.e., either a 0 or 9 depending on whether it is a 4th, 5th, 6th, or 7th digit)

# APPENDIX 3. PEDIATRIC EYE DISEASE INVESTIGATOR GROUP AMBLYOPIA CLINICAL TRIALS, 2002–2021

TABLE A3-1 PEDIATRIC EYE DISEASE INVESTIGATOR GROUP STUDIES WITH PUBLISHED RESULTS, 2002–2021

| Study   | No. of Patients<br>(age at enrollment) | Follow-up<br>Period | Result  |
|---|--|---------------------|---|
| Randomized trial comparing occlusion vs. pharmacologic therapy for moderate amblyopia <sup>23</sup><br>(ATS 1)  | 419<br>(3 to <7 years)                 | 6 months            | <ul style="list-style-type: none"> <li>• VA improved in both groups: 3.16 lines in occlusion group; 2.84 lines in atropine group</li> <li>• Mean difference = 0.34 lines (95% CI, 0.05 to 0.6)</li> <li>• VA <math>\geq</math>20/30 and/or improved by <math>\geq</math>3 lines in 79% of occlusion group and 74% of atropine group</li> </ul>  |
| Randomized trial comparing occlusion vs. pharmacologic therapy for moderate amblyopia <sup>166</sup><br>(ATS 1) | 419<br>(3 to <7 years)                 | 2 years             | <ul style="list-style-type: none"> <li>• VA improved in both groups: 3.7 lines in occlusion group; 3.6 lines in atropine group</li> <li>• Mean difference = 0.01 lines (95% CI, -0.02 to 0.04)</li> <li>• Atropine or patching for an initial 6-month period produced a similar improvement in amblyopia 2 years after treatment</li> </ul>   |
| Randomized trial comparing part-time vs. full-time patching for severe amblyopia <sup>185</sup><br>(ATS 2A)     | 175<br>(3 to <7 years)                 | 4 months            | <ul style="list-style-type: none"> <li>• VA improved in both groups: 4.8 lines in the 6 hours prescribed patching group; 4.7 lines in the full-time prescribed patching (all hours or all but 1 hour per day) group</li> <li>• Mean difference = 0.02 lines (95% CI, -0.04 to 0.07)</li> </ul>  |
| Randomized trial comparing part-time vs. minimal-time patching for moderate amblyopia <sup>24</sup><br>(ATS 2B) | 189<br>(3 to <7 years)                 | 4 months            | <ul style="list-style-type: none"> <li>• VA improvement in both groups was 2.40 lines</li> <li>• Mean difference = -0.007 lines (95% CI, -0.050 to 0.036)</li> <li>• VA <math>\geq</math>20/32 and/or <math>\geq</math>3 lines in 62% of patients in both groups</li> <li>• VA improvement similar for 2 hours of prescribed daily patching and 6 hours of prescribed daily patching</li> </ul> |

TABLE A3-1 PEDIATRIC EYE DISEASE INVESTIGATOR GROUP STUDIES WITH PUBLISHED RESULTS, 2002–2021  
(CONTINUED)

| Study  | No. of Patients<br>(age at<br>enrollment) | Follow-up<br>Period | Result   |
|--|---|---------------------|--|
| Evaluation of treatment of amblyopia <sup>78</sup><br>(ATS 3)  | 507<br>(7 to 17 years)                    | 6 months            | <ul style="list-style-type: none"> <li>For moderate amblyopia in children 7 to &lt;13 years old, 36% achieved 20/25 or better with optical correction/occlusion/atropine use compared with 14% with optical correction alone (<math>P&lt;0.001</math>)</li> <li>For severe amblyopia in children 7 to &lt;13 years old, 23% achieved 20/40 or better with optical correction/patching compared with 5% with optical correction alone (<math>P&lt;0.004</math>)</li> <li>For moderate amblyopia in teenagers 13 to 17 years old, 14% achieved 20/25 or better with optical correction/occlusion compared with 11% with optical correction alone (<math>P=0.52</math>)</li> <li>For severe amblyopia in teenagers 13 to 17 years old, 14% achieved 20/40 or better with optical correction/occlusion compared with 0% with optical correction alone (<math>P=0.13</math>)</li> </ul> |
| Randomized trial comparing daily atropine vs. weekend atropine for moderate amblyopia <sup>25</sup><br>(ATS 4)                         | 168<br>(3 to <7 years)                    | 4 months            | <ul style="list-style-type: none"> <li>VA improvement in both groups was 2.3 lines</li> <li>Mean difference = 0.00 (95% CI, -0.04 to 0.04)</li> <li>47% of daily group and 53% of the weekend group had either VA <math>\geq</math>20/25 or greater than or equal to that of the nonamblyopic eye</li> </ul>   |
| Prospective noncomparative trial to evaluate 2 hours of daily patching for amblyopia <sup>164</sup><br>(ATS 5 – eyeglasses-only phase) | 84<br>(3 to <7 years)                     | Up to 30 weeks      | <ul style="list-style-type: none"> <li>Amblyopia improved with optical correction by <math>\geq</math>2 lines in 77%</li> <li>Amblyopia resolved with optical correction in 27% (95% CI, 18% to 38%)</li> </ul>  |
| Randomized trial to evaluate 2 hours of daily patching for amblyopia <sup>241</sup><br>(ATS 5 – randomization phase)                   | 180<br>(3 to <7 years)                    | 5 weeks             | <ul style="list-style-type: none"> <li>After a period of treatment with eyeglasses until vision stopped improving, patients treated with 2 hours of daily patching combined with 1 hour of near visual tasks had an improvement in VA of 1.1 lines compared with 0.5 lines in the control group</li> <li>Mean difference (adjusted) = 0.07 lines (95% CI, 0.02 to 0.12, <math>P=0.006</math>)</li> </ul>   |
| Randomized trial comparing near vs. distance activities with occlusion <sup>193</sup><br>(ATS 6)                                       | 425<br>(3 to <7 years)                    | 17 weeks            | <ul style="list-style-type: none"> <li>At 8 weeks, improvement in amblyopic eye VA averaged 2.6 lines in the distance activities group and 2.5 lines in the near activities group (95% CI for difference, -0.3 to 0.3 lines)</li> <li>Groups appeared statistically similar at the 2-week, 5-week, and 17-week visits</li> <li>At 17 weeks, children with severe amblyopia improved a mean of 3.7 lines with 2 hours of daily patching</li> </ul>  |

## Amblyopia PPP

TABLE A3-1 PEDIATRIC EYE DISEASE INVESTIGATOR GROUP STUDIES WITH PUBLISHED RESULTS, 2002–2021  
(CONTINUED)

| Study   | No. of Patients<br>(age at<br>enrollment) | Follow-up<br>Period | Result   |
|---|---|---------------------|--|
| Treatment of bilateral refractive amblyopia <sup>181</sup><br>(ATS 7)   | 113<br>(3 to <10 years)                   | 1 year              | <ul style="list-style-type: none"> <li>Binocular VA improved on average 3.9 lines (95% CI, 3.5 to 4.2)</li> <li>At 1 year, 74% had binocular VA of 20/25 or better</li> </ul>  |
| Randomized trial comparing atropine vs. atropine plus a plano lens for the fellow eye in children 3 to 6 years old <sup>198</sup><br>(ATS 8)            | 180<br>(3 to <7 years)                    | 18 weeks            | <ul style="list-style-type: none"> <li>Amblyopic eye VA was 20/25 or better in 29% of the atropine-only group and in 40% of the atropine plus plano lens group (<math>P=0.03</math>)</li> <li>More patients in the atropine plus plano lens group had reduced fellow eye acuity at 18 weeks; however, there were no cases of persistent reverse amblyopia</li> </ul>   |
| Randomized trial comparing occlusion vs. atropine for amblyopia <sup>173</sup><br>(ATS 9)   | 193<br>(7 to <13 years)                   | 17 weeks            | <ul style="list-style-type: none"> <li>Similar improvement in VA in both groups</li> <li>Amblyopic eye VA of 20/25 or better in 17% of atropine group and 24% of the patching group (95% CI, -3% to 17%)</li> </ul>  |
| Randomized trial comparing Bangerter filters vs. occlusion for the treatment of moderate amblyopia in children <sup>175</sup><br>(ATS 10)               | 186<br>(3 to <10 years)                   | 24 weeks            | <ul style="list-style-type: none"> <li>Similar improvement in VA in both groups</li> <li>Amblyopic eye VA of 20/25 or better in 36% of Bangerter group and 31% of patching group (<math>P=0.86</math>)</li> <li>Patching was not superior (95% CI difference between groups, -0.06 to 0.83 lines)</li> </ul>   |
| Randomized trial to evaluate combined patching and atropine for residual amblyopia <sup>225</sup><br>(ATS 11)   | 55<br>(3 to <10 years)                    | 10 weeks            | <ul style="list-style-type: none"> <li>Before enrollment, eligible subjects had no improvement with 6 hours daily patching or daily atropine</li> <li>Intensive treatment group had 6 hours of prescribed daily patching combined with daily atropine; weaning group had 4 weeks of reduced treatment, then stopped</li> <li>Amblyopic eye VA improved similarly in both groups, an average of 0.56 lines in the intensive group (95% CI, 0.18 to 0.93) and 0.53 lines in the weaning group (95% CI, -0.04 to 1.10)</li> </ul> |
| Nonrandomized prospective trial of eyeglasses alone for strabismic and strabismic-anisometric combined amblyopia in children <sup>180</sup><br>(ATS 13) | 146<br>(3 to <7 years)                    | 28 weeks            | <ul style="list-style-type: none"> <li>Mean 2.6 lines improvement (95% CI, 2.3 to 3.0)</li> <li>75% improved <math>\geq 2</math> lines and 54% improved <math>\geq 3</math> lines</li> <li>Resolution in 32% (95% CI, 24% to 41%)</li> <li>Treatment effect was greater for strabismic amblyopia than for combined-mechanism amblyopia (3.2 vs. 2.3 lines; adjusted <math>P=0.003</math>)</li> </ul>   |

TABLE A3-1 PEDIATRIC EYE DISEASE INVESTIGATOR GROUP STUDIES WITH PUBLISHED RESULTS, 2002–2021  
(CONTINUED)

| Study | No. of Patients<br>(age at<br>enrollment) | Follow-up<br>Period | Result |
|-------|---|---------------------|--------|
|-------|---|---------------------|--------|

## Amblyopia PPP

|   |  |                 |   |
|---|--|-----------------|---|
| <p>Randomized trial comparing increased patching with the same dosage for amblyopia that has stopped improving<sup>224</sup></p> <p>(ATS 15)</p>                          | <p>169<br/>(3 to &lt;8 years)</p>                                      | <p>10 weeks</p> | <ul style="list-style-type: none"> <li>Amblyopic eye VA improved an average of 1.2 lines in the 6-hour group and 0.5 lines in the 2-hour group (difference in mean VA adjusted for acuity at randomization 0.6 lines; 95% CI, 0.3 to 1.0; <math>P=0.002</math>)</li> <li>Improvement of 2 or more lines occurred in 40% of participants patched for 6 hours vs. 18% of those who continued to patch for 2 hours (<math>P=0.003</math>)</li> </ul>   |
| <p>Randomized trial comparing adding a plano lens to the atropine vs. the same atropine dosage for amblyopia that has stopped improving<sup>197</sup></p> <p>(ATS 16)</p> | <p>73<br/>(3 to &lt;8 years)</p>                                       | <p>10 weeks</p> | <ul style="list-style-type: none"> <li>Amblyopic-eye VA improved a mean of 1.1 lines with the plano lens and 0.6 lines with atropine only (difference adjusted for baseline VA +0.5 line; 95% CI, -0.1 to +1.2)</li> </ul>  |
| <p>Randomized trial comparing levodopa plus patching vs. placebo with patching<sup>242</sup></p> <p>(ATS 17)</p>  | <p>138<br/>(8 to &lt;13 years)</p>                                     | <p>18 weeks</p> | <ul style="list-style-type: none"> <li>Amblyopic eye acuity improved by an average of 5.2 letters (1.1 lines) in the levodopa group and by 3.8 letters (0.8 line) in the placebo group (difference adjusted for baseline VA, +1.4 letters; 1-sided <math>P=0.06</math>; 2-sided 95% CI, -0.4 to 3.3 letters)</li> <li>No serious adverse effects from levodopa were reported during treatment</li> </ul>  |
| <p>Randomized trial comparing a binocular game (falling block design) vs. part-time patching<sup>206, 209</sup></p> <p>(ATS 18)</p>                                       | <p>385<br/>(5 to &lt;12 years)</p> <p>100<br/>(13 to &lt;17 years)</p> | <p>16 weeks</p> | <ul style="list-style-type: none"> <li>For younger children amblyopic eye acuity improved by an average of 1.05 lines in the binocular group and 1.35 lines in the patching group (difference adjusted for baseline VA, 0.31 lines; 1-sided 95% CI, 0.53 lines)</li> <li>For older children amblyopic eye acuity improved by an average of 3.5 letters in the binocular group and by 6.5 letters in the patching group. After adjusting for baseline VA, the difference was -2.7 letters (95% CI, -5.7 to 0.3 letters; <math>P=.082</math>) or 0.5 lines, favoring patching</li> <li>Improvement with binocular game play was not as good as with patching</li> </ul> |
| <p>Randomized trial comparing a binocular game (Dig Rush) vs. continued glasses<sup>210, 211</sup></p> <p>(ATS20)</p>   | <p>138<br/>(7 to 12 years)</p> <p>182<br/>(4 to 6 years)</p>           | <p>4 weeks</p>  | <ul style="list-style-type: none"> <li>For older children after 4 weeks, mean amblyopic-eye VA letter score improved from baseline by 1.3 (2-sided 95% CI, 0.1 to 2.6) with binocular treatment and by 1.7 (2-sided 95% CI, 0.4 to 3.0) with glasses alone</li> <li>For younger children after 4 weeks, mean amblyopic VA improved 1.1 logMAR lines with binocular treatment and 0.6 logMAR lines with continued spectacles alone (adjusted difference = 0.5 lines; 95.1% CI, 0.1 to 0.9)</li> <li>No benefit for older children</li> <li>Some benefit for younger children after 4 weeks of treatment. The benefit was not present at 8 weeks</li> </ul>             |

NOTE: In the ATS, mild to moderate amblyopia is defined as VA in the amblyopic eye of 20/80 or better; severe amblyopia is defined as VA in the amblyopic eye of 20/100 to 20/400.

Further information about the published results of the Amblyopia Treatment Study is available from the Pediatric Eye Disease Investigator Group (<http://pedig.iaeb.org/Publications.aspx>).

ATS = Amblyopia Treatment Study; CI = confidence interval; RCT = randomized clinical trial; VA = visual acuity.



## APPENDIX 4. LITERATURE SEARCHES FOR THIS PPP

Literature searches of the PubMed database were conducted in March 2021; the search strategies were as follows. Specific limited update searches were conducted after May 2022. The searches had added filters for randomized controlled trials and systematic reviews and date limiters to capture literature published since 2017. The panel analyzed 2410 studies of which 31 were included in the PPP.

Amblyopia General: amblyop\*[tiab] OR amblyopia[mh]

Prevalence: ("amblyopia/epidemiology"[MeSH Terms] OR "amblyopia/ethnology"[MeSH Terms]) OR ("amblyopia"[MeSH Terms] OR "amblyopia"[Title/Abstract]) AND ("prevalence"[MeSH Terms] OR "risk factors"[MeSH Terms])

Diagnosis: "amblyopia/diagnosis"[MeSH Terms] OR (amblyopia[tiab] AND diagnosis[tiab])

Therapy: (("amblyopia/surgery"[MeSH Terms]) OR ("amblyopia/therapy"[MeSH Terms]) OR ("amblyopia/drug therapy"[MeSH Terms]) ) OR (amblyopia[tiab] AND (therapy[tiab] OR surgery[tiab] OR surgical[tiab] OR drug\*[tiab]))

Socioeconomic:

("amblyopia"[MeSH Terms] OR amblyopia[tiab]) AND (socioeconomic factors[mh] OR "socioeconomic factors"[tiab])

## SUGGESTED READING

Taylor and Hoyt's Pediatric Ophthalmology and Strabismus, 5th ed. Edinburgh; New York: Elsevier, 2017.

von Noorden GK, Campos EC, eds. Binocular Vision and Ocular Motility: Theory and Management of Strabismus, 6th ed. St. Louis: CV Mosby, 2002. <https://cybersight.org/portfolio/textbook-von-noorden-campos-2002/>. Accessed March 6, 2022.

## RELATED ACADEMY MATERIALS

### Basic and Clinical Science Course

- Pediatric Ophthalmology and Strabismus (Section 6, 2022-2023)

**Clinical Statements** – Free download available at <http://one.aao.org/guidelines-browse?filter=clinicalstatement>.

- Amblyopia Is a Medical Condition (2017)
- Adult Strabismus Surgery (2017)

### Focal Points

- Childhood Vision Screening (2018)

**Ophthalmic Technology Assessments** – Published in Ophthalmology, which is distributed free to Academy members; links to abstracts and full text available at [www.aao.org/ota](http://www.aao.org/ota).

- Adjustable Sutures in the Treatment of Strabismus (2022)
- Binocular Treatment of Amblyopia (2019)
- Botulinum Toxin Injection for the Treatment of Strabismus (2018)
- Effectiveness of Laser Refractive Surgery to Address Anisometropic Amblyogenic Refractive Error in Children (2022)

**Patient Education Downloadable Handout**

- Amblyopia (2022)
- Amblyopia Patching (2022)
- Pseudostrabismus (2022)
- Strabismus in Children (2022)

**Patient Education Video**

- Strabismus Surgery for Children (Pediatrics Patient Education Video Collection)
- Treating Amblyopia (Pediatrics Patient Education Video Collection)

**Preferred Practice Pattern® Guidelines** - Free download available at [www.aao.org/ppp](http://www.aao.org/ppp)

- Adult Strabismus (2019)
- Comprehensive Adult Medical Eye Evaluation (2020)
- Esotropia and Exotropia (2022)
- Pediatric Eye Evaluations (2022)

To order any of the Related Academy Materials, except for the free materials, please contact the Academy's Customer Service at 866.561.8558 (U.S. only) or 415.561.8540 or [www.aao.org/store](http://www.aao.org/store).

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