Causes and Associations of Amblyopia in a Population-Based Sample of 6-Year-Old Australian Children

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Objectives: To describe the prevalence of amblyopia and associated factors in a representative sample of 6-year-old Australian children.

Methods: Logarithm of minimum angle of resolution visual acuity (VA) was measured in both eyes before and after pinhole correction, correcting cylindrical refractive components greater than 0.50 diopter (D), and with spectacles (if worn) in a population-based sample of 1741 schoolchildren. Retinal pathological abnormalities were excluded based on photographs. Amblyopia was defined using various best-available corrected VA measures in the absence of significant organic pathological abnormalities.

Results: Using the criteria of corrected VA less than 20/40 and at least a 2-line difference between eyes, amblyopia was diagnosed in 13 children (0.7%). The inclusion of children with amblyopia who had been successfully treated (n=19) increased the amblyopia prevalence to 1.8%. Strabismus or strabismus surgery history was present in 37.5% of the children with amblyopia, anisometropia in 34.4%, both conditions in 18.8%, and isometropia in 6.3%. Mean corrected VA in amblyopic eyes was 37.7 logarithm of minimum angle of resolution letters (Snellen VA equivalent /20/40), ranging from 0 to 48 logarithm of minimum angle of resolution letters (Snellen VA equivalent <20/200-20/25). Most amblyopic eyes (58.7%) were significantly hyperopic (spherical equivalent ≥+3.00 D); 8.7% were myopic.

Conclusions: A relatively low prevalence of amblyopia in a sample of 6-year-old children is documented. The majority of these children had already been diagnosed and treated for this condition.

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Amblyopia is classically defined as a reduction in corrected visual acuity (VA) in the absence of visible organic abnormalities and is due to misdirected, blurred, or absent retinal images during development of the visual system.1 Amblyopia is the most frequent cause of monocular visual impairment in both children and adults.2-4 The best-described consequence of amblyopia is an increased risk of bilateral blindness, caused sometimes by traumatic eye injury in younger people5,6 and age-related macular degeneration in older people.6

Previous estimates of amblyopia’s prevalence have ranged from 0.2% in a population-based sample of Iranian residents7 to 5.3% of subjects from an ophthalmic clinic8 (Table 1). Prevalence variability is partly owing to differences in the VA criterion used and the age group sampled. Most previous studies were drawn from selected populations of clinic patients,9-11 and schoolchildren13-15,17,20,22 and were not population based.

Most previous population-based studies did not investigate the various factors associated with amblyopia. They also did not consider treatment and its effect on amblyopia’s prevalence. Sole application of a VA criterion without regard to previous treatment of the condition is likely to underestimate its full impact in childhood populations. Considering treated children as nonamblyopic further leads to differential misclassification of these children and precludes an accurate assessment of associated factors.

In their controversial article on childhood vision screening, Snowdon and Stewart-Brown33 called for greater research into the prevalence and natural history of amblyopia, its resultant disability, and the effectiveness of its treatment. This, to our knowledge, is the first population-based study to incorporate previous treatment of amblyopia in its definition, thus giving a potentially more accurate account of the prevalence and impact of this condition.
study sought to ascertain factors associated with amblyopia and to document the current level of usual care in an urban population of Australian schoolchildren.

### METHODS

#### POPULATION

The Sydney Myopia Study is a population-based survey of refraction and other eye conditions in a sample of predominantly 6-year-old children resident in the metropolitan area of Sydney, Australia. Methods used to identify and select the target sample as well as a description of this sample and study procedures were recently described. Methods used to identify and select the target sample as well as a description of this sample and study procedures were recently described. In brief, the study area was stratified by socioeconomic status using Australian Bureau of Statistics 2001 National Census data. These data were used to select 34 primary schools across Sydney, including 5 primary schools in the top socioeconomic status decile and the remaining schools randomly selected from the bottom 9 socioeconomic status deciles. A proportional mix of public schools and private or religious schools was included. Our study is based on data from 6-year-old schoolchildren examined between August 2003 and October 2004.

#### PROCEDURES

Written consent from at least 1 parent plus the assent of each child were obtained prior to examination. Approval for the study was obtained from the Human Research Ethics Committee, University of Sydney and Department of Education and Training, New South Wales, Australia.

Distance VA was tested in each eye separately using a logarithm of minimum angle of resolution (logMAR) chart. The chart was retroilluminated with automatic calibration to 85 candela/square meter (Vectorvision CSV-1000; Vectorvision, Inc, Dayton, Ohio) and read at 8 ft (244 cm). Visual acuity was assessed with and without spectacle correction, if worn, and with a 1.2-mm pinhole aperture for reduced vision (VA < 20/25) or if there was more than a 1-line (5-letter) difference between the 2 eyes. In addition, noncycloplegic autorefration was performed on all of the children with reduced vision, and cylinders greater.

### Table 1. Selected Past Prevalence Studies of Amblyopia

<table>
<thead>
<tr>
<th>Source</th>
<th>Diagnostic Criteria</th>
<th>Subjects, No.</th>
<th>Prevalence, %</th>
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</thead>
<tbody>
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<tr>
<td>Downing (1945)</td>
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<td>Hopkisson et al (1982)</td>
<td>≥2-Line difference</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Series 1</td>
<td></td>
<td>4499</td>
<td>4.8</td>
</tr>
<tr>
<td>Series 2</td>
<td></td>
<td>4071</td>
<td>4.0</td>
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<tr>
<td>Clinic populations</td>
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<tr>
<td>Cole (1959)</td>
<td>VA &lt; 20/40</td>
<td>10000</td>
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<tr>
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<tr>
<td>Preschool and school populations</td>
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<td>≥2-Line difference</td>
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<td>Yassur et al (1972)</td>
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<td>Ross et al (1977)</td>
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<td>Vinding et al (1991)</td>
<td>≥2-Line difference and history of difference from childhood</td>
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<td>Attebo et al (1998)</td>
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<td>Murthy et al (2002)</td>
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<td>Naik et al (2003)</td>
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<td>4890</td>
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<td>He et al (2004)</td>
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<tr>
<td>Zhao et al (2000)</td>
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<td>5884</td>
<td>0.9</td>
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<tr>
<td>Maul et al (2000)</td>
<td>VA ≥0/32 and other criteria</td>
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<td>Fotouhi et al (2004)</td>
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<td>4565</td>
<td>0.2</td>
</tr>
<tr>
<td>Tabbara and Ross-Degnan (1986)</td>
<td>VA ≥20/60</td>
<td>16810</td>
<td>0.8</td>
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</table>

Abbreviation: VA, visual acuity. Ellipses indicate that the 2 different criteria sets were applied to the same sample of 3654 subjects.
DEFINITIONS

Amblyopia was initially defined as corrected VA less than 0.3 logMAR unit (ie, <40 letters, equivalent to Snellen VA < 20/40) in the affected eye not attributable to any underlying structural abnormality of the eye or visual pathway plus a difference of at least 2 logMAR lines between the 2 eyes. Such stringent VA criteria could potentially have eliminated treated or mild cases of amblyopia (eg, those with a 1-logMAR line differential). When amblyopia was suspected on grounds of minimally reduced corrected VA in the presence of an amblyogenic risk factor, corroborative evidence from the parental questionnaire was sought. Parental report of “lazy eye” or amblyopia was taken into account for each child with potential amblyopia, as were reports of previous treatment in the form of occlusion therapy, use of atropine sulfate, or previous strabismus correction surgery.

Anisometropic amblyopia was assigned as the cause if there was a 1.0-D difference in spherical equivalent (SE) refraction between the 2 eyes in the absence of strabismus. Strabismic amblyopia was assigned as the cause if there was heterotropia or microsquint or if there was history of previous strabismus surgery without anisometropia or high refractive error. Mixed amblyopia was assigned as the cause if there were both anisometropia and strabismus. Isoametropic amblyopia was assigned if there was bilateral reduction in corrected VA to less than 0.3 logMAR unit in the presence of bilateral hyperopia greater than 4.0 D, bilateral myopia of 6 D or greater, or bilateral astigmatism of 2.5 D or greater. Stimulus deprivation amblyopia was assigned as the cause if congenital cataract, ptosis, corneal opacities, or other media opacities obstructed vision.

Myopia was defined as SE refraction of –0.5 D or less. Hyperopia was defined as SE refraction of +2.0 D or greater and was deemed significant if it was +3.0 D or greater. Astigmatism was defined as a cylinder of 1.0 D or greater, and anisometropia was defined as an SE refraction difference of at least 1.0 D between the 2 eyes. Absence of ametropia was defined as SE refraction greater than –0.5 D to less than +2.0 D. With-the-rule astigmatic axis was defined by the range of 90°±15°, against-the-rule astigmatism by axes in the range of 0°±15°, and oblique astigmatism by axes between 16° and 74° or between 106° and 164°. All of the definitions refer to values obtained after cycloplegic autorefraction.

The child’s ethnic origin was derived from that of both parents. Based on Australia’s ethnic mix, all of the relevant groups were represented in the questionnaire, which was translated into key languages including Chinese, Vietnamese, and Arabic. Parental education was defined as the highest level of education completed by either parent. This ranged from never having attended school to having completed a higher degree such as a master’s degree or PhD. Socioeconomic status was based on home ownership by the child’s parents as well as the parents’ employment status.

DATA HANDLING AND STATISTICAL ANALYSIS

Data were entered into a Microsoft Office Access (Microsoft Corp, Redmond, Wash) database. All of the statistical analyses were performed using SAS version 8.2 software (SAS Institute, Inc, Cary, NC). Mixed models and generalized estimating equations were used to adjust for clustering within schools. Where cluster effects were not significant, χ² tests and t tests were used. All of the sample means and mean differences are reported with their standard errors. All of the confidence intervals (CIs) are given as 95% CIs.

RESULTS

SUBJECTS

Of 2238 eligible children, 1765 (78.9%) were given parental permission to participate and questionnaire data were provided by parents. Of the 473 nonparticipants, 53.7% were boys and 46.3% were girls. Of the 1765 children with a positive response, 24 were not examined because they were absent from school during the examination period. Visual acuity measures were available for 1739 of the remaining 1741 children. The mean age of participants was 6.7 years (range, 5.5-8.4 years); 49.4% of the children were female and 50.6% were male. Most of the children (70.4%) were 6 years old, and a quarter of them (25.5%) were 7 years old.

PREVALENCE OF AMBLYOPIA

Table 2 shows the prevalence of amblyopia using various proposed criteria, including past treatment for this condition. Amblyopia was diagnosed in 32 children (1.8%); this included 23 children with a history of amblyopia at the time of examination. Amblyopia was in the right eye in 14 children (43.8%) and in the left eye in 16 children (50.0%), but this difference was not statistically significant (P = .70). Two children had bilateral amblyopia due to isometropia. Amblyopia was found in 20 girls (2.4%; 95% CI, 1.5%-3.6%) and 12 boys (1.4%; 95% CI, 0.9%-2.2%). This sex difference was not statistically significant (P = .10). Amblyopia prevalence was
The cause of amblyopia was assessed as anisometropia in 11 children (34.4%), strabismus in 12 (37.5%), mixed in 6 (18.8%), and isoametropia in 2 (6.3%). The cause of amblyopia in 1 child was undetermined. Esotropia was the most common type of strabismus, found in 11 children (61.1%) with strabismic or mixed amblyopia. Exotropia was found in 3 children (16.7%), and 4 children (22.2%) had microstrabismus. Small numbers in each category precluded meaningful sex analysis.

**Figure 2** illustrates the SE of the refractive error for all of the amblyopic eyes compared with the right eyes of children without amblyopia. The mean SE refraction of amblyopic eyes was +3.17 D compared with a mean SE of +1.26 D OD and +1.31 D OS in children without amblyopia. Significant hyperopia (SE ≥ +3.00 D) was in 58.7% of amblyopic eyes, and myopia (SE ≤ −0.50 D) was in 8.7%.

**Figure 3** illustrates the cylindrical refraction for all of the amblyopic eyes compared with eyes of children without amblyopia. The mean cylinder was significantly greater in amblyopic eyes (0.99 D OD and 0.82 D OS) than in nonamblyopic eyes (0.29 D OD and 0.28 D OS). This difference was highly significant in both right (P = .001) and left (P < .001) eyes. The distribution of astigmatic axis was also compared in the 2 groups.

### Causes of Amblyopia

The cause of amblyopia was assessed as anisometropia in 11 children (34.4%), strabismus in 12 (37.5%), mixed in 6 (18.8%), and isoametropia in 2 (6.3%). The cause of amblyopia in 1 child was undetermined. Esotropia was the most common type of strabismus, found in 11 children (61.1%) with strabismic or mixed amblyopia. Exotropia was found in 3 children (16.7%), and 4 children (22.2%) had microstrabismus. Small numbers in each category precluded meaningful sex analysis.

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There were no significant differences between children with and without amblyopia for any of the axes.

**TREATMENT OF AMBLYOPIA**

Of the 32 children assessed as having amblyopia, 9 (28.1%) were newly diagnosed at the time of the examination and 23 (71.9%) had been previously diagnosed with and treated for amblyopia as reported by their parents. Of the 9 newly diagnosed cases, 6 had anisometropia and 3 had strabismus. The 23 previously diagnosed cases either had completed or were undergoing treatment at the time of examination. Spectacles had been prescribed for 19 children (59.4%) whereas current or previous penalization treatment with atropine was reported by the parents of 4 children (12.5%). Current or previous occlusion therapy was reported by 17 subjects (53.1%), with a reported mean treatment duration of 11.6 months. This value was heavily influenced by 2 extreme outliers, omission of which led to a mean treatment duration of 6.7 months.

**ASSOCIATIONS WITH AMBLYOPIA**

Table 3 summarizes the prevalence of amblyopia among children with and without selected ocular, gestational, and socioeconomic factors. Amblyopia was around 10-fold more likely in children with astigmatism than in those without astigmatism. Strabismus and anisometropia were also strongly associated with amblyopia (P < .01); the amblyopia prevalence was 37.0% in children with strabismus compared with 0.9% in children without strabismus. The prevalence of amblyopia in the presence of anisometropia was even higher at 56.7% compared with 0.8% in children without anisometropia.

Amblyopia was not statistically associated with any measures of socioeconomic status, including parental education, parental employment status, and home ownership. It was also not associated with maternal age at conception, history of breastfeeding, or the duration of breastfeeding. There was a borderline association with maternal smoking during pregnancy. This was more frequently reported by mothers of children with amblyopia (22.6%) than those of children without amblyopia (11.7%). Highly significant associations were found with neonatal factors, including gestational age (P < .001), birth weight (P = .03), and parent-reported admission to a neonatal intensive care unit (P < .001). Children born at less than 37 weeks gestation had a 5-fold greater risk of having amblyopia (odds ratio, 5.4; 95% CI, 2.3-12.3); 31% of children with amblyopia were born premature compared with 7.6% of children without amblyopia. Those with birth weights less than 2500 g were almost 5 times more likely to have amblyopia at the time of examination (odds ratio, 4.8; 95% CI, 1.9-11.8). Admission to a neonatal intensive care unit was more commonly reported by parents of children with amblyopia (23.3%)
than those of children without amblyopia (5.7%). The presence of this association also conferred a 5-fold increased risk of having amblyopia (odds ratio, 5.0; 95% CI, 2.1-12.0); this association remained highly significant (P<.01) in the multivariate model.

**COMMENT**

The prevalence of amblyopia varies widely with the VA criteria used. The prevalence of amblyopia in an older Australian adult population residing in the Blue Mountains area west of Sydney was 3.9% when no VA criteria were applied. This prevalence was the result of an adjudication session that examined all of the potential patients and assigned the diagnosis and underlying causes of visual impairment. It took into account any history of poor vision from childhood. The current study used similar criteria to the Blue Mountains Eye Study in classifying a child as having amblyopia. We additionally used treatment of amblyopia (parental report of occlusion therapy or atropine penalization) as corroborative evidence.

The majority (71.9%) of children with amblyopia in our study had previously been diagnosed with the condition. A significant proportion (46.9%) of the total had been successfully treated, having no significant visual impairment (defined as VA <40 logMAR letters or Snellen VA equivalent <20/40) in their amblyopic eye. The corresponding prevalence of amblyopia without significant visual impairment in the amblyopic eye was 11% for Australian older adults in the Blue Mountains Eye Study, a finding that may point to improved detection and treatment of amblyopia in the intervening decades. Application of a VA criterion of 20/30 or less permits comparison of the prevalence in our study with those in a recent series of population-based studies of eye disease in similarly aged children carried out in 7 centers worldwide. Our prevalence of 1.2% using this criterion is consistent with prevalence rates ranging from 0.3% to 1.4% in these studies.

We did not have any specific data on the VA of nonparticipants, mainly because vision screening is not conducted routinely in Australian schools. We did, however, make informal note of obvious abnormalities and particularly spectacle use among the nonparticipating children within the classrooms. This did not point to any obvious participation bias.

We found no sex difference in the prevalence of amblyopia, which is in agreement with a number of previous studies. Strabismus was the most common cause of amblyopia in our population, accounting for 37.5%, and it was closely followed by anisometropia, which accounted for 34.4%. This confirms findings from previous studies that found strabismus to be the most common cause of amblyopia. Apart from strabismus, anisometropia, and high hyperopia, which are known to cause amblyopia, we found significant associations between amblyopia and many gestational factors. A low birth weight, prematurity, and admission to a neonatal intensive care unit were all found to be significantly associated with amblyopia in our study. We also found an association between amblyopia and maternal smoking during pregnancy. This is important because it represents a modifiable factor that can be targeted with education.

Strabismus, anisometropia, and refractive errors are known to be more prevalent among premature children than among full-term children. Most investigators agree that the higher incidence of ocular problems in premature children is related to the occurrence of retinopathy of prematurity. Kushner, however, reported a higher prevalence of strabismus in premature children with (34%) and without (13%) retinopathy of prematurity than in full-term children (2.5%). It appears that prematurity per se and its influence on brain development can thus affect the normal development of ocular motility. Several other factors, namely, neonatal hypoxia, kernicterus, and excessive oxygen therapy, may also play a role in the development of the central nervous system and hence increase the risk of amblyopia.

These findings are relevant to ophthalmologists, as they appear to indicate positive impacts from improvements in the detection and treatment of amblyopia, with a high proportion of children diagnosed with amblyopia already receiving treatment by age 6 years, in many cases with apparent success. The well-known causes of anisometropia, strabismus (particularly esotropia), astigmatism, and significant hyperopia were confirmed, as were important associations with gestational parameters.

In conclusion, this study reports the prevalence of both treated and untreated amblyopia in a young population. Amblyopia was found to affect boys and girls and right and left eyes equally. It was associated with many ocular factors and selected gestational factors, including maternal smoking during pregnancy, a modifiable factor. Prospective studies of the natural history of amblyopia in addition to its impact on educational achievement and performance of everyday activities would provide further valuable insights and add considerably to current knowledge in this field.

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**REFERENCES**


