Objective: To evaluate the clinical performance of the Pediatric Vision Screener (PVS) in children in a pediatric ophthalmology office setting.

Methods: Seventy-seven subjects between 2 and 18 years of age received gold-standard orthoptic examinations and were classified as at risk for amblyopia if strabismus or anisometropia (>1.50 diopters) was present. Strabismus was subclassified as variable or constant. The subjects were then tested with the PVS, which produced a pass or refer recommendation based on a binocularity score. The PVS also produced a yield score to indicate the subject’s interest in the target. Sensitivity and specificity for amblyopia risk detection were calculated.

Results: Binocularity as determined by the PVS was greater than 65% for all controls and less than 20% for all subjects with constant strabismus. Binocularity ranged from 0% to 52% in subjects with variable strabismus. All subjects with anisometropia and no strabismus had binocularity scores less than 10%.

Conclusions: The PVS identified strabismus, when present, in all subjects and identified 3 subjects with anisometropia as well. The PVS shows potential to address a lack of screening instrumentation appropriate for use with preschool-aged children.

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AMBLYOPIA IS DEFINED AS poor vision in a structurally sound eye, and with a prevalence of 3% to 5%, it is the leading cause of vision loss in childhood. Amblyopia results from the inability of the brain to correctly interpret visual input because of deprivation or suppression. Anatomical risk factors for this condition include strabismus, anisometropia, cataract, certain forms of astigmatism, and hyperopia. Early detection and treatment are essential to prevent irreversible vision loss, but the risk factors can be difficult to detect. Although comprehensive eye examinations have been mandated in some areas, in most cases this solution is not economically feasible and tends to be instituted later than is optimal for amblyopia detection. Ideally, all children would be screened for amblyopic risk factors before the age of 4 or 5 years.3,4

Unfortunately, no commercially available screener has sufficiently high testability, sensitivity, and specificity to reliably identify children at risk for amblyopia. Visual acuity tests have been the most widely used approach to vision screening. However, visual acuity testing may be no better than other screening tests for detecting amblyopia. No currently implemented vision-screening protocol can accurately identify binocular misalignment, one of the major risk factors for amblyopia.

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Guyton et al have developed a method of using retinal reflections of polarized light to determine foveal fixation. Prototype instruments designed to detect binocular alignment were designed and built at Johns Hopkins Hospital (Baltimore, Md) using this technique. The second prototype, the Pediatric Vision Screener (PVS), was designed to detect both ocular focus and alignment. The PVS was described in detail in the first article of this series. The object of the PVS is to provide a first-stage screening device that will differentiate between children in need of referral to an ophthalmologist and those not at risk, without attempting diagnosis. The output of the device is binary (either “refer” or “pass”) to facilitate use by nonophthalmologists. In a pilot study, presented as the second article of this series, the PVS demonstrated high sensitivity and specificity for detection of amblyopia risk factors in 40 adults aged 22
METHODS

STUDY DESIGN AND POPULATION

Pediatric patients and controls were prospectively recruited from patients and accompanying siblings at the Department of Ophthalmology at Children’s Hospital Boston. Subjects were excluded for glaucoma, cataract, nystagmus, retinal disease, prior strabismus surgery, or developmental delay. An orthoptist or pediatric ophthalmologist performed a gold-standard examination, measuring best-corrected visual acuity (using an Early Treatment Diabetic Retinopathy Study [ETDRS] acuity chart or LEA symbols), cycloplegic refraction (after administration of 1% cyclopentolate hydrochloride), binocular vision (using the Titmus test), and ocular motility (by prism and cover testing). The appropriate institutional review boards approved the study, informed consent was obtained from the parents or legal guardians of all subjects, and assent was obtained from all subjects, in accordance with the Declaration of Helsinki.

On the basis of the orthoptic evaluation results, subjects were categorized into the following groups: control, constant strabismus, variable strabismus, or anisometropia. Subjects were considered controls if they had no history of major ocular problems and if both eyes had less than 3.25 diopters (D) of myopia, less than 3.25 D of hyperopia, 1.50 D or less of anisometropia, and no strabismus. No separate criterion was set for astigmatism, a limitation that will be addressed in subsequent studies. Subjects were considered as having constant strabismus if they had clinically documented ocular misalignment of more than 0 prism diopters (PD) that was always present. Subjects were classified as having variable strabismus if they had ocular misalignment but were able to compensate for this either through intermittent fusional eye movements or by using a compensatory head position to achieve some degree of binocularity. Subjects were classified as having anisometropia if they had a refractive error difference of more than 1.50 D and no strabismus. Refractive error of control subjects ranged from −3.00 to +3.00 D in spherical equivalents. Subjects with constant strabismus had refractive errors from −1.25 to +8.00 D, and those with variable strabismus had errors from −16.50 to +7.75 D.

As a first test of the instrument’s performance in a pediatric population, children of all ages were studied, with 89 children between the ages of 12 months and 18 years meeting enrollment criteria. Four eligible subjects refused to participate in the project. Eight subjects aged 12 to 24 months were judged to display insufficient interest in the fixation target for reliable results, and they were excluded from data analysis. The remaining 77 subjects ranged in age from 2 to 18 years. The study population included 5% African American, 13% Asian, 70% white, and 12% Hispanic subjects, with 38 girls and 39 boys.

Figure 1 summarizes both the study design and the demographic distribution of the subject population. Of the 37 patients with strabismus, 26 had constant strabismus (1-80 PD). Of the 11 patients with variable strabismus, 8 had intermittent strabismus (2-42 PD) controllable with fusional vergence, whereas 3 with constant strabismus in primary position (6-30 PD) were able to fully align the eyes by adopting an (anomalous) compensatory head position. Three subjects had anisometropia (3-13 D) and no strabismus. For evaluation of the influence of eye color on PVS performance, subjects were divided into 2 groups: dark eyes (brown) and light eyes (blue, green, hazel, or gray).

DEVICES OPERATION

The PVS design and operation have been described in detail elsewhere. In brief, the eyes are evaluated with binocular retinal birefringence scanning to detect alignment and with binocular focus detection to detect locus. Data were obtained as a series of 5 measurements of alignment and focus from both eyes in a total of 2.5 seconds, with the final results summarized using custom software.

For data acquisition, older children were seated in a dimly lit room using a chin rest to facilitate head positioning, with the PVS mounted on a stand for ease of testing. Children younger than 4 years (18 in total) were tested with the device in handheld mode (Figure 2). The fixation target was a near-infrared blinking point source presented in combination with a synchronized beeping tone. Figure 3 is a schematic representation of what a subject sees during testing. Data were inspected online and saved to a disk for offline analysis.
DATA ANALYSIS

Full characterization of the PVS output has been published elsewhere. In brief, to receive a pass score, both eyes must be able to focus and fixate on the target simultaneously, as shown in Figure 4A. During central fixation, the binocular retinal birefringence scanning light annulus is focused by the eye and exactly surrounds the fovea, as illustrated by the circles centered on the fovea. The device measures the number of times in a series of 5 measurements that the subject is able to binocularly fixate and produces a binocularity score as a percentage.

Binocularity was calculated as follows:

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\text{Binocularity} = \left( \frac{\text{No. of Bilateral Readings}}{\text{(No. of Unilateral Readings + No. of Bilateral Readings)}} \right) \times 100\%
\]

Thus, binocularity included only those readings in which at least 1 eye was fixating on the target. A subject who was relatively inattentive to the target therefore did not influence this parameter. If neither eye was centrally fixating, the reading was not included in the binocularity calculation; that is, a subject with 100% binocularity had bilateral alignment for every usable reading. On the basis of the results of the pilot study in adults, a binocularity score of greater than 60% was defined as passing.

A subject with strabismus is unable to fixate on the target with both eyes simultaneously. Figure 4B illustrates a condition in which the right eye is able to focus and fixate on the target, but the left eye is fixating elsewhere. The binocular retinal birefringence scanning signal for the right eye is represented as a focused circle on the retina that is not centered on the fovea. The PVS would register this individual reading as monocular fixation.

The instrument is also able to detect when the subject does not look at the target. The instrument registers this reading as inattentive because of the absence of a central fixation signal from either eye, as shown in Figure 4C. A similar signal is obtained if both eyes are closed or if the subject moves outside the range of the instrument. These inattentive readings were automatically excluded from the binocularity calculation. The percentage of readings in which the subject is fixating on the target (whether with 1 or both eyes) is designated as the yield of a sequence, with a high yield indicating a highly attentive subject.

The PVS also quantifies the quality of the individual readings using a signal-to-noise relationship. These 2 quality measures are combined in a product quality score so that yield/signal to noise = quality score. The quality score may be used to characterize the reliability of any particular data sequence.

RESULTS

Measurements were obtained from 77 children, 40 of whom had risk factors for amblyopia. The binocularity scores for all 77 subjects analyzed are shown in Figure 5. Binocularity was greater than 65% for all control subjects and less than 20% for all subjects with constant strabismus. Subjects with variable strabismus had binocularity ranging from 0% to 52%. The separation of the different populations is characterized statistically using a box plot in Figure 6, with P<.001 by 1-way analysis of variance. As with adults, the best combination of sensitivity and specificity was obtained with a pass threshold set to 60% binocularity. The 3 patients with anisometric amblyopia and no strabismus all had binocularity scores less than 10%.

Eye color did not influence quality score (P=.17) or yield (P=.30). The PVS performed equally well in boys and girls, with no discernible difference in quality score (P=.19) or yield (P=.11).

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The PVS reliably identified children with strabismus aged 2 to 18 years. The smallest constant (measurable) angle of strabismus detected successfully in this study was an esotropia of 1 PD, and the smallest vertical angle was a hypertropia of 2 PD. The theoretical lower limit of detection of misalignment is 0.75 PD, which indicates that the device is sensitive to microstrabismus. This has been confirmed in subjects with simulated strabismus. More patients with small-angle strabismus and monofixation syndrome need to be tested to experimentally determine the lower limit of detection of this device.

Unexpectedly, the binocularity score of the PVS was able to successfully detect the presence of anisometropia; 3 patients with anisometropic amblyopia and no strabismus were tested and had binocularity scores less than 10%. Therefore, the binocular retinal birefringence scanning technique itself appears to be sensitive to anisometropia. One explanation for this observation is that good focus in both eyes is a prerequisite for accurate convergence and fusion. To achieve a passing binocularity score, a subject must be able to focus and fixate on the target simultaneously with both eyes. However, a subject with anisometropia has 1 eye out of focus. This may impair the accuracy of fixation in those eyes, leading to low binocularity scores. This concept is depicted schematically in Figure 7. An alternative hypothesis is that eyes with anisometropic amblyopia also have microstrabismus and will thus fail the highly sensitive assessment of alignment.

No patients with pure refractive error (without strabismus) were tested in this study. Symmetric myopia is not considered a risk factor for amblyopia. Symmetric hyperopia may or may not constitute a risk factor depending on whether the patient can simultaneously accommodate and converge; that is, if the patient can accommodate and converge accurately to achieve binocular fixation, a minimal risk of amblyopia exists and the patient will appropriately receive a pass score. Three of the best-performing amblyopia screening tests in the Vision in Preschoolers Study were autorefractors, which are incapable of detecting strabismus, a major cause of amblyopia. With these instruments, it is inferred that strabismus may be present if hyperopia is detected, although the threshold for increased risk varies among individuals. In contrast, the PVS detects binocular misalignment but must infer that anisometropic amblyopia is present if microstrabismus is present. Future studies...
will include subjects selected for high degrees of refractive error without strabismus to further explore the risk of amblyopia in hyperopic patients who accommodate without developing strabismus.

The ability to determine when the subject was not looking at the target proved to be a distinct advantage in young children. Eight children between the ages of 12 and 24 months were judged to have inconsistent interest in the fixation target, based on lower yield scores, and these children were not included in the data analysis. Although this is a potential limitation of the device, most screening studies (including the Vision in Preschoolers Study) do not attempt to test in this age group. The next prototype of the PVS, currently under development, will incorporate a blinking, extended white-light target with a design more appealing to young subjects, synchronized with a beeping tone. We anticipate that the new target will increase the ease of testing, particularly in preverbal children, and improve the yield scores in subjects younger than 24 months.

In summary, the PVS showed high testability in children aged 2 to 18 years. Ocular misalignment, including both variable and constant strabismus, was detected with high specificity and sensitivity. Three cases of anisometropia were also detected. The instrument shows potential as a screening device for amblyopia risk factors in preschool children for use by primary care physicians and nurses. Future studies will better characterize its performance in subjects with anisometropia, monofixation syndrome, and uncomplicated, symmetric refractive error.

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