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Screening, Confirming, and Treating Amblyopia Based on Binocularity

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In the current issue of *JAMA Ophthalmology*, Jost and colleagues[1] present further validity testing of the Pediatric Vision Scanner, which assesses binocular retinal birefringence as a method for detecting abnormal binocularity associated with strabismus and/or amblyopia. The novel technology was developed 15 years ago by David Hunter, MD, PhD, and David Guyton, MD, and has recently become available as a portable unit that can be used for screening children in a medical office or in a school setting.[2]

Amblyopia is the most common cause of monocular vision loss in children, and treatment outcomes tend to be better with earlier detection[3] and earlier treatment,[4] notwithstanding data regarding effective treatment of some older children.[5] As we consider whether the Pediatric Vision Scanner might be a preferred method for amblyopia screening, and as we consider other methods for screening, it is worthwhile revisiting how we diagnose amblyopia. We all learn that unilateral amblyopia can be defined as a deficit in best-corrected visual acuity caused by abnormal binocular interaction, which we commonly subdivide into its causative subtypes of strabismic, anisometropic, and deprivation. Because we define amblyopia as a deficit in visual acuity, it would seem reasonable that we would diagnose amblyopia by measuring visual acuity. But therein lies a problem. As eye care providers, we often forget the inherent variability of visual acuity testing in our clinical practice. We ask “what was the patient's visual acuity?” and we read the number written, or typed, in our medical record, but that number represents a sampling of a distribution. Even with carefully designed visual acuity protocols used for clinical trials in amblyopia,[6] there is still marked test-retest variability of a single assessment of visual acuity, and the test-retest reliability of the interocular difference is no better.[6] Variability becomes particularly problematic when performance is close to any posited threshold. For example, if we were to define amblyopia as having visual acuity worse than 20/50 at 3 years of age (based on a large sample of normal data), we would be correct in assuming that a child whose visual acuity measured 20/200 would have a high likelihood of amblyopia (when associated with a risk factor), whereas a child whose visual acuity measured 20/60, very close to the threshold, might measure 20/50 or 20/40 on another day. Which side of the threshold determines how we label that child, and therefore whether we treat that child. When obtaining optotype visual acuity for younger children is not possible, most often clinicians use fixation

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preference testing, but unfortunately fixation preference testing has poor agreement with visual acuity testing for many children.

Some clinicians feel that if amblyopia is loss of visual acuity, then why not cut out all the "middle men" in screening and just test visual acuity. But, if the problem of misclassifying a child by a "gold standard" optotype visual acuity test is worrisome, it would be even more so for an abbreviated optotype presentation by lay testers. Subjective responses by children will always be associated with a great deal of noise, and that noise must inevitably lead to misclassification.

In an effort to reduce noise and provide screening modalities that can be used easily by nonexpert testers in environments such as a pediatrician's office and a school setting, "point and shoot" photorefraction technology has been developed, which assesses either refractive error alone or refractive error along with corneal reflections as an assessment of alignment. For such screening to be effective, it must rely on an association between higher levels of refractive error and amblyopia. As such, photorefraction detects risk factors for amblyopia, and consensus guidelines (for risk factors to detect) continue to evolve. Nevertheless, the weakness of this entire conceptual approach is that although, at a population level, there is an association of risk factors with amblyopia,[7] for an individual child, the relationship often breaks down, with some children having higher levels of refractive error and no amblyopia (screening false positives) and other children having lower levels of refractive error but amblyopia (screening false negatives). These problems of false positives and false negatives are further exacerbated by test-retest variability of the individual machines, which creates its own level of rarely considered misclassification. The Pediatric Vision Scanner provides a novel method of screening directly for amblyopia, rather than for its risk factors.

If we accept the weaknesses of the current "gold standard" diagnosis of amblyopia, the study by Jost and colleagues[1] has now independently confirmed the previous study by Loudon and colleagues[2] (developers of the technology) that the binocular retinal birefringence Pediatric Vision Scanner is superior to photoscreening in detecting amblyopia. Further studies in nonenriched populations are planned by these investigators, and it is likely that the Pediatric Vision Scanner will lead the next generation of screening methods. As the authors point out, screening should be performed longitudinally during the earlier years of a child's life to detect amblyopia, and the optimum screening interval deserves some consideration and study.

Returning to the problem of classifying a patient as having amblyopia or not, by use of an ideal gold standard examination, we could mitigate the effect of the variability of optotype visual acuity testing by performing multiple tests of visual acuity and by averaging, but multiple testing methods are impractical for young children who often have a limited attention span. Perhaps the Pediatric Vision Scanner should be used as more than a "screener" by pediatricians, nurses, and lay screeners and should be incorporated into routine clinical assessment by eye care providers, as a method of more definitively categorizing a child as having abnormal binocularity or not, and therefore amblyopia or not, particularly in the context of anisometropia. Further studies of the reproducibility of the Pediatric Vision Scanner are needed, but the reproducibility is likely to be very high, given

the automation and the method of averaging. Further work is also needed to understand how the Pediatric Vision Scanner assessment of binocularity changes in response to treatment, although pilot data are promising.[2]

Finally, redefining unilateral amblyopia as an essentially binocular deficit leads to considering binocular treatment of amblyopia, without patching and without other forms of penalization of the sound eye. Indeed, Hess and colleagues[8] have recently reported improvement of amblyopia eye visual acuity and stereoacuity in subjects treated using binocular paradigms, increasing the contrast to the amblyopic eye and decreasing the contrast to the sound eye, such that treatment is performed binocularly. These binocular treatments are now becoming available as binocular games on an iPod or iPad, and the Pediatric Eye Disease Investigator Group is planning a multi-center randomized clinical trial to further explore the utility of this new treatment. The Pediatric Vision Scanner not only may be an excellent screening device for amblyopia but also conceptually challenges the way we define and treat amblyopia.

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