APPENDIX A

TITLE PAGE

MANIFEST, DELAYED, AND CYCLOPLEGIC REFRACTIONS IN HYPEROPIA

by

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APPENDIX B

APPROVAL PAGE

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APPENDIX C

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MANIFEST, DELAYED, AND CYCLOPLEGIC REFRACTIONS IN HYPEROPIA

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APPENDIX D

ABSTRACT

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Background: This literature review discusses the diagnosis and treatment of latent hyperopia, and the effectiveness of delayed and cycloplegic refractive techniques. Cycloplegic refraction and delayed subjective refraction are two common techniques that optometrists use to find additional hyperopic refractive error or less myopic refractive error in a patient after a standard subjective refraction has been performed. Cycloplegic refraction is performed after the patient's accommodation has been neutralized by pharmacologically induced cycloplegia using an agent such as cyclopentolate or tropicamide. Delayed refraction is performed without the use of a pharmacological agent. Numerous studies have shown that cycloplegic refraction typically finds a more hyperopic refractive error correction than a standard subjective refraction. *Methods:* A literature search was performed using the PubMed database. *Results:* In cases of latent hyperopia, cycloplegic refraction will find the maximum amount of hyperopia. Delayed refraction will typically show more hyperopia than a standard manifest refraction. *Conclusions*: Delayed refraction findings can be helpful to find the maximum amount of plus power that can be accepted by the patient. Performing a delayed refraction before cyclopleging, along with ocular posture findings and subjective symptoms will give the practitioner more information with which to make a final decision in regards to spectacle prescription.

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Hyperopia is refers to the state of refractive error where the refractive power of the eye is insufficient, or the eye is too short, for the unaccomodating eye to focus the image of a distant object directly on the retina. Unlike myopic refractive error, hyperopic refractive error can be overcome by the eye's accommodative system. The influence of the accommodative system affects the amount of hyperopia found during a refraction, so it is important to measure both the manifest hyperopia – the hyperopic refractive error found in a noncycloplegic refraction – and the latent hyperopia, the amount of additional hyperopic refractive error found in refraction after the patient has been cyclopleged and the accommodative system thus neutralized.[1] Accurate measurement of hyperopia in infants and young children is important for proper vision development. Significant hyperopia (+4.00D or higher) in infants is associated with delays in visual and motor development.[2] Children with +3.50D or more of hyperopia as measured at age 7-9 months, if left uncorrected, are 13 times more likely to develop strabismus and 6 times more likely to have decreased visual acuity by age 4. [3]

Cycloplegia can be effectively produced by several pharmaceutical agents. Cyclopentolate is most commonly used, as it produces the best cycloplegic effect within a reasonable time frame.[4,5] Atropine can be used for maximum cycloplegic effect,[6] however the duration of the cycloplegia associated with atropine makes it impractical. When prescribing a spectacle correction for a hyperopic patient, it is best to take into account a number of factors, including the manifest and latent hyperopia, as well as other data such as ocular posture, binocular function, age, and subjective symptoms on the part of the patient.

Between the two extremes of the manifest refraction, which typically underestimates hyperopia and overestimates myopia[7]; and the cycloplegic refraction, which gives a more accurate measure of the eye's true power but may not acceptable or comfortable to the patient as a spectacle prescription; there is the technique of the delayed refraction. A delayed subjective refraction is performed on a noncyclopleged patient and helps to stimulate acceptance of additional plus power when compared to a standard noncycloplegic refraction.[8]

A cycloplegic refraction is a refraction performed where the eye is in the condition of cycloplegia and the accommodative component of the eye's overall power has been removed as a variable. This is important because when the eye is able to accommodate normally, a standard noncycloplegic manifest refraction is likely to find a prescription for more minus or less plus power.[7] An "overminused" spectacle prescription can cause discomfort and eyestrain for a patient, and contribute to changes in phoric posture, accommodative esotropia and amblyopia in severe cases. By neutralizing the accommodative component, a cycloplegic refraction allows for a spectacle prescription with the maximum plus power to be prescribed avoiding these problems. Multiple studies support the use of cycloplegic refractions for pediatric patients.[2,3,7] Cycloplegic refraction should be performed after a routine dry refraction. For children two years of age and older, cyclopentolate 1.0% is recommended, and cyclopentolate 0.5% for younger children.[8] After waiting for the cyclopentolate to reach its maximum effectiveness between 20 and 45 minutes after instillation[9], retinoscopy and subjective refraction, if the patient is able respond, may be performed according to routine techniques.[8]

The most notable disadvantage of a cycloplegic refraction is that it requires cycloplegic pharmaceutical agents to be instilled into the patient's eyes. Patients may refuse dilation for a number of reasons – the time involved in waiting for the agent to take effect, the discomfort of having one's eyes dilated for an extended period of time, or simply a dislike of having anything put in one's eyes. In addition, all pharmaceutical agents have the possibility to cause adverse reactions when used. In cases where it is not possible to perform a cycloplegic refraction, a delayed refraction will find more latent hyperopia, if present, than a typical noncycloplegic refraction. A delayed subjective refraction is performed binocularly on a noncyclopleged patient after a routine dry refraction. The NRA test is performed as the last part of the complete refraction, leaving the patient at the point of first sustained blur with plus lenses at near. The near point card is removed from the phoroptor to allow the patient to view an isolated line of letters in the size of the patient's best corrected visual acuity on a distant chart. The patient should be fogged at this point and unable to read the letters. At this point, the plus power in the phoropter is slowly reduced binocularly in 0.25D steps until the patient reports that he or she can read the chart clearly.[8] If the patient is indeed a latent hyperope, a delayed refraction is likely to result in greater plus power acceptance than a routine dry refraction.

This literature review will discuss the advantages and disadvantages of, and differing results found in cycloplegic versus noncycloplegic refractions, and the relative accuracy of delayed refraction. Is a delayed refraction sufficiently accurate in cases of latent hyperopia to estimate the results of what a cycloplegic refraction would likely find, and allow one to comfortably write a prescription based off results without performing a full cycloplegic refraction?

METHODS: Journal articles referenced in this review were found in the PubMed Online Database, accessed through the Ferris State University library. The search strings "cycloplegic refraction," "delayed refraction," "cycloplegic vs. delayed refraction," and "latent hyperopia" were used to search for results. There were disappointingly few articles discussing the differing results of cycloplegic and noncycloplegic refractions, and little if any research into the question of whether or not delayed refraction is of any value. A similar search of the VisionNet Database did not yield any additional useable articles. Effort was made to choose more recent literature to evaluate, preferably within the past ten years; however, the overall dearth of content in this field made it necessary to include some older articles.

Textbooks referenced in this review, *Clinical Pearls in Refractive Care, Visual Development, Diagnosis, and Treatment of the Pediatric Patient, Clinical Ocular Pharmacology, and Clinical Procedures for Ocular Examination* are part of the required texts for the curriculum of the Michigan College of Optometry at Ferris State University.

RESULTS: Without cycloplegia, hyperopic refractive error can go undetected or underestimated not only at young ages but well into adulthood. One study found that noncycloplegic autorefraction, when compared to cycloplegic autorefraction, overestimated myopia for 4-7% of patients between ages five and 50.[7]

Hyperopia is the most common refractive error in pediatric patients.[10] It is in the pediatric population that hyperopia is most likely to go undetected due to the greater accommodative power of younger patients, but this population is also at the greatest risk of developing permanent visual problems from uncorrected hyperopia. Hyperopia of +4.50D or greater were found to have and 8.6% prevalence of isoametropic, or bilateral, amblyopia as well as an increased chance of strabismus in one study.[11] Hyperopia of +4.00D or greater in infants is associated with increased incidence of strabismus and decreased visual acuity by age four. Spectacle correction improved visual outcome[2] and decreased the incidence of strabismus[3] when compared to an uncorrected control group, and did not affect the process of emmetropization.[2]

The three cycloplegic pharmaceutical agents most often referred to in literature are cyclopentolate, tropicamide and atropine. Cyclopentolate in 0.5% or 1.0% concentration, depending on the age of the patient, was the most commonly recommended.[1,5,8] Tropicamide 0.5% or 1.0% is sometimes suggested due to its comparable time to maximum effect and shorter overall duration.[9] Studies have shown that 1% tropicamide is less effective as a cycloplegic than 1% cyclopentolate, leaving 0.47D more residual accommodation as measured with an autorefractor,[5] and measuring 0.14 +/-0.30D more hyperopia.[4] Atropine is noted for providing the maximum amount of cycloplegia[6] but the long duration of the cycloplegic effect renders it impractical in most situations, although it may be warranted in cases of accommodative esotropia.[9]

Table 1 –Maximum Effect and Duration of Cycloplegics

	Time to maximum cycloplegic action (minutes)	Duration of cycloplegic effect (hours)
Cyclopentolate 0.5%	20-45	6-24
Tropicamide 1.0%	20-45	6
Atropine 1.0%	60-180	168-288

The high prevalence and magnitude of childhood hyperopia and the increased risks of strabismus, amblyopia, and delayed visual and motor development, all suggest that cycloplegic refraction is most important in pediatric patients. Cycloplegic refraction should not necessarily be limited to pediatric patients, but can be a valuable tool for adults up to age 50 who may overcorrected for myopia by a noncycloplegic refraction,[7] especially if they are experiencing symptoms of asthenopia, headaches, or blurred vision that are not explained by a noncycloplegic refraction.

The delayed refraction technique is a useful tool for patients who refuse cycloplegia or for whom cycloplegia is contraindicated, such as patients with narrow angles at risk for angle closure glaucoma, or patients with previous hypersensitivity or other adverse reactions to cycloplegic agents.

When deciding which cycloplegic agent is the best to use, there are several factors to take into consideration. Cyclopentolate is the most recommended for drawing out the maximum amount of latent hyperopia. For myopic patients, or patients with low to moderate amounts of hyperopia, tropicamide may be sufficient and has the advantage of a shorter overall duration.[4] Cyclopentolate is known to cause central nervous system disturbances such as drowsiness, hallucinations, and rarely seizures.[9] It is recommended that one use no more than 0.5% cyclopentolate for children under the age of two[8], and patients with brain damage or other central nervous system dysfunctions.[9] In such cases it might be preferable to use tropicamide, especially if a large amount of latent hyperopia is not suspected. Atropine is known for being the most potent cycloplegic available and is the standard of comparison by which other cycloplegics are judged, but again, the long duration of the cycloplegic and mydriatic effect render atropine unsuitable for use in most situations,[9] and some studies suggest there is no statistically significant difference between refractive measurements of eyes cyclopleged with cyclopentolate vs atropine.[12] However, other studies disagree and state that atropine does uncover a larger hyperopic refractive error than cyclopentolate and tropicamide combined.[13] For most cases, cyclopentolate should be sufficient.

Latent hyperopia should be considered in the patient who presents with an esophoric or esotropic binocular posture, subjective symptoms such as headaches, asthenopia, and frequent blinking or rubbing of the eyes, poor school performance, or avoidance of near activities.[14]

When latent hyperopia is found, there is a question of whether to prescribe a correction, and if so, how much of the correction to prescribe. Young children whose refractive error puts them at increased risk of strabismus or amblyopia should certainly be corrected.[15] An esophoric posture that is improved with refractive correction is another indication. A spectacle correction in the full amount of refractive error found by cycloplegic refraction may not be accepted by the patient, and he or she may find it uncomfortable or complain that his or her vision is blurry with this correction and seems clearer without any glasses. It is important, here, to take into account the amount of latent hyperopia as compared to the amount of manifest hyperopia. As well, the delayed refractive findings are useful as they will give a better estimate of how much plus the patient can be pushed to accept. Patients with subjective symptoms will benefit from a hyperopic correction, but may find a distance correction uncomfortable and benefit more from a near-only correction. Many patients with low to moderate amounts of hyperopia are most comfortable wearing spectacle correction only part time.[1]

DISCUSSION: The article "Infant hyperopia: detection, distribution, changes and correlates-outcomes from the cambridge infant screening programs" discusses the use and effectiveness of photorefractive screening programs in an infant population. Photorefraction was performed both with and without cycloplegia. By comparing the two procedures, it was determined that a high accommodative lag in noncycloplegic photorefraction was an indicator for significant hyperopia. While this does not directly relate to the comparison of delayed and cycloplegic refractions, it does show that hyperopia can indeed be detected in a noncyclopleged state, and allows one to infer that delayed refractions may also correlate with cycloplegic results in such a fashion. However, the noncycloplegic photorefraction in this study was only intended to be used as a screening mechanism, not as a substitute for a complete cycloplegic refraction before prescribing a spectacle correction. This demonstrates that the idea of using delayed refraction to predict results of cycloplegic refraction has potential use, but in the end it may not be accurate enough. The study used a population of 8308 infants to assure a large enough sample size to base conclusions upon.[2]

The article "Two infant vision screening programmes: prediction and prevention of strabismus and amblyopia from photo- and videorefractive screening" details an earlier study comparing a screening program using photorefraction with cycloplegia in a 7-9 month old infant population and a screening program using videorefraction without cycloplegia in a similar population, with the stated goal of ascertaining risk factors for the development of strabismus and amblyopia and the effectiveness of partial spectacle correction in preventing these conditions. In the second program, only those individuals who were found to have significant refractive error in the noncycloplegic screening were given a follow-up cycloplegic refraction. The study concluded that noncycloplegic screening is viable because most of the refractive errors noted in the noncycloplegic screening were confirmed by a cycloplegic refraction on follow-up.[3] However since those individuals who passed the screening were not cycloplegically refracted it leaves the question of how many cases may have been missed by the screening. The study's information on how partial spectacle correction reduced the risk of development of strabismus and amblyopia is useful, but there is not enough information given to usefully correlate noncycloplegic screening results to the amount of hyperopia found on later cycloplegic refractions.

The article "Comparison of cyclopentolate versus tropicamide cycloplegia in children" used a double-masked study to compare cycloplegic refractive error found with two different cycloplegic agents using several different methods of measuring refractive error. The study found that cyclopentolate was more effective at inhibiting accommodation and that autorefraction measurements showed more hyperopia with cyclopentolate than tropicamide, but no difference between the two cycloplegic agents with distance retinoscopy or subjective refraction. The authors concluded that tropicamide, while less effective at inhibiting accommodation, was still useful for determining distance refractive error for low to moderate amounts of hyperopia. While this study was well-organized, only 20 subjects between the ages of 6 and 12 participated. Increasing the sample size to 30 or more participants would have increased the reliability of this study's conclusions.[4]

The article "The effect of cycloplegia on measurement of the ocular components" also compared cyclopentolate and tropicamide, using not only autorefraction but also measurement of the crystalline lens power and vitreous chamber depth. This study also found that tropicamide was less effective than cyclopentolate at inhibiting accommodation, but again had minimal effect on the distance refractive error. One problem with this study is that it did not even test subjective refractive error, which is what an optometrist performing a refraction would consider to be the main factor in determining the final spectacle prescription. The objective measurements are useful, but not necessarily applicable to a typical exam situation. This study also used only 20 participants, and again, a larger sample size would have been more reliable.[5] Between this study and the previous, one can conclude that tropicamide is an acceptable cycloplegic agent in most cases, but in cases of high amounts of hyperopia or situations where it is important to reduce the accommodative response as much as possible, cyclopentolate is really the best cycloplegic agent.

The article "The comparison of cyclopentolate and atropine in patients with refractive accommodative esotropia by means of retinoscopy, autorefractometry and biometric lens thickness" made a similar comparison of the effectiveness of cyclopentolate and atropine. This study included 32 subjects, a reasonably large sample size, all with sufficient amounts of hyperopia to cause accommodative esotropia. The study concluded that there was no statistically significant difference between the cycloplegic effect of cyclopentolate and that of atropine.[12] Given this conclusion, there is no reason to subject a patient to days worth of cycloplegia caused by atropine when cyclopentolate is just as efficacious.

The article "Atropine versus cyclopentolate plus tropicamide in esodeviations" compared atropine with the combination of cyclopentolate and tropicamide by reviewing records of 74 patients of varying ages with esotropic deviations who had been refracted with both agents on different occasions. In contrast to the previous study, this one did find a statistically significant increase in hyperopia measured with atropine cycloplegia when compared to the combination of cyclopentolate and tropicamide across all age groups and amounts of hyperopia.[13] Because of the long duration of cycloplegia associated with atropine and the varying results of different studies, atropine should not be a first choice when choosing a cycloplegic agent, but when faced with a patient with a significant eso deviation that is not responding as well as may be expected with the amount of hyperopia found by cyclopentolate, atropine may provide additional useful information. When comparing the results of the various studies, cyclopentolate is the best overall choice for effective cycloplegia with minimal inconvenience to the patient.

The article "Validity of noncycloplegic refraction in the assessment of refractive errors: the Tehran Eye Study" compared autorefraction on 3501 patients over the age of 5, before and after cycloplegia with cyclopentolate. This study found that the noncycloplegic autorefraction underestimated hyperopia and overestimated myopia by significant amounts in all age groups up to the age of 50. Noncycloplegic autorefraction results varied too much between individuals to formulate any sort of adjustment factor that would allow cycloplegic results to be extrapolated from the noncycloplegic measurements.[7] This study used a large enough sample size to predict results over a wide range of ages. It would have been more useful if a subjective refraction – both cycloplegic and noncycloplegic – had been done in addition to the autorefraction measurements.

Based on these studies, there is a lack of research into the direct comparison of delayed and cycloplegic refraction. There is a link between the results of noncycloplegic screening tests and hyperopia found in cycloplegic refractions, but the methods studied so far are more suitable for screenings, and even as screenings appear to be more valid in an infant population and prone to inaccuracy in older children and should not be used as a substitute for a cycloplegic refraction. Noncycloplegic autorefraction is likely to underestimate the true degree of hyperopia by a highly variable amount. Delayed refraction may be more reliable, but studies need to be performed that directly measure the relationship between the amount of refractive error found by a delayed refraction and a cycloplegic refraction in a statistically large enough sample of a juvenile population, and the results appropriately analyzed in order to confirm or disprove this hypothesis.

CONCLUSION: The refractive correction of hyperopia is a complex and delicate process, taking into account multiple methods of refraction, as well as binocular testing and subjective symptoms. The delayed refraction technique can be useful both in determining how much of a hyperopic correction a patient is likely to tolerate, and if cycloplegia is impossible the delayed refraction is a useful tool in getting closer to the true amount of hyperopic refractive error. However, a cycloplegic refraction is an indispensible part of an eye exam for a hyperopic or latent hyperopic patient, allowing a more complete understanding of the patient's visual system. Based on the available literature, evidence suggests that a delayed refraction will allow a more accurate estimate of the results of cycloplegic refraction than would a standard noncycloplegic refraction, but at this point there is not enough research into this question to warrant forgoing a cycloplegic refraction in favor of a delayed refraction. A delayed refraction has the potential to be a useful tool, but a cycloplegic refraction should still always be performed when refracting pediatric patients and cases of suspected latent hyperopia.

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