Cyclopegic and Noncycloplegic Refractions of Chinese Neonatal Infants

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Purpose. To examine Chinese neonatal infants with both cycloplegic and noncycloplegic retinoscopy and to compare the distribution of refractive errors for the two techniques.

Methods. Cycloplegic retinoscopy was performed by two experienced pediatric ophthalmologists on 81 neonatal infants randomly selected from a group of 185 neonates who had undergone noncycloplegic retinoscopy. All infants were between 1 day and 6 days of age and were born without incident at full term.

Results. The mean cycloplegic spherical equivalent (CSE) was highly hyperopic (+3.55 diopters [D] ± 2.39 D). The mean noncycloplegic spherical equivalent (nCSE) was +0.58 D ± 2.32 D. The high reliability of the refractive measurements was demonstrated by high correlations between examiners (CSE: OD, $r = 0.96$; OS, $r = 0.97$; nCSE: OD, $r = 0.94$; OS, $r = 0.93$ OS) and between eyes (CSE: examiner 1, $r = 0.94$; examiner 2, $r = 0.95$; nCSE: examiner 1, $r = 0.95$; examiner 2, $r = 0.97$). The correlation between CSE and nCSE was much lower (examiner 1: OD, $r = 0.76$; OS, $r = 0.73$; examiner 2: OD, $r = 0.72$; OS, $r = 0.70$). Prevalence of astigmatism was very low (1.6% ≥ 1.0 D).

Conclusions. The level of hyperopia was very high in these infants, and the offsetting tonic accommodation demonstrated by the difference between CSE and nCSE was much higher than in any previous report. Low amounts of infantile hyperopia and high astigmatism are associated with future myopia in the West. The Chinese neonates in this study had high amounts of hyperopia and little astigmatism, yet they are at high risk to become myopic. (*Invest Ophthalmol Vis Sci.* 2011;52: 2456–2461) DOI:10.1167/iovs.10-5441

Refractive error is a major eye care problem throughout the world primarily because of the rapid increase of myopia in modern Asian cities. To understand the development of refractive error during childhood, it is important to understand its starting point, refractive error at birth. We can then consider how much the purely maturational process of prenatal eye growth contributes to the development of postnatal refractive errors. In the West, infants tend to be hyperopic with wide variability in their spherical equivalent refractive errors. There are limited modern data on the refractive errors of newborn infants and virtually none for East Asian neonates. Thus, we felt it was important to carefully document the refractive errors of a group of newborn infants in China.

A number of large-scale studies of refractive error in neonates were performed in Europe during the nineteenth and early twentieth centuries. Under atropine cycloplegia, Wibaut[1] found that 70% to 99% of 2398 neonates were hyperopic, with refractive means ranging between 2.0 diopters (D) and 3.0 D. In 1952, Cook and Glasscock[2] found that 70% of their 1000 infants were hyperopic during the first month of life, with a mean refractive error of approximately 2.5 D. Duke-Elder[3] declared at this time that "At birth all eyes are hypermetropic to the extent of 2.50 D to 3.00 D."

Studies continue to show that cycloplegic refractive errors of infants shortly after birth have 2.4 D to 3.0 D of hyperopia with atropine in large samples (98–275 full-term neonates)[4–6] and lesser amounts (0.75 D–2.0 D) with a combination of cyclopentolate and phenylephrine in smaller samples (30 and 54 infants).[7,8] Only Saunders et al.,[9] using two drops of 0.5% cyclopentolate per eye, deviate from this pattern and report a mean spherical equivalent of +3.47 D for 38 full-term neonatal infants.

Most recent studies of infant refraction start to examine infants at 1 to 3 months of age and use a milder cycloplegic (cyclopentolate) or noncycloplegic techniques. Wood et al.,[10] using cyclopentolate, showed a mean spherical equivalent error of +1.44 D for 58 infants at 2 weeks of age, which increased to +2.84 D at 12 weeks of age. Mayer et al.[11] also used cyclopentolate (on 118 infants) but showed a mean refractive error of about +2.2 D from the first to the fourth month of age that then declined. Similarly, Mutti et al.,[12] using cyclopentolate, showed a mean refractive error of +2.2 D in 221 infants 3 months of age.

Investigators have used a noncycloplegic technique in the dark, near retinoscopy, to measure refractive errors in infants.[13] Given that a retinoscopic beam does not provide adequate stimulus for accommodative focus,[14] this procedure actually measures the dark focus of the eye. In accordance with this, Mohindra[15,16] has shown a consistent mean difference of about +0.75 D between near retinoscopy and retinoscopy with cyclopentolate in schoolchildren and college students. Thus, the results of near retinoscopy are always reported with a +0.75 D correction. Saunders and Westall[17] found this correction to be slightly greater for infants in the second half year of life (+1.25 D) when they compared retinoscopy with cyclopentolate and near noncycloplegic retinoscopy.

Mohindra and Held[18] used a rapid screening method of noncycloplegic near retinoscopy and found that infants had a mean refractive error of −0.70 D during the first month and remained slightly myopic until about 4 months of age. Thorn et al. [19] noted that infants tend to accommodate at the onset of near retinoscopy but relax accommodation during the next 2 minutes, normally stabilizing at a hyperopic level. Thus, they waited patiently for about 2 minutes before taking their near

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retinoscopy readings and therefore obsrved more hyperopia than Mohindra and Held,[18] a mean refractive error of approximately +0.6 D during the first month that increased to +1.0 D by 3 months of age.[19] These differences suggest that near retinoscopy depends on the exact method used by the retinoscopist and may include varying amounts of tonic accommodation. Unfortunately, cycloplegic retinoscopy, the presumed gold standard, has also provided an uneven array of refractive findings in young infants.

The reported refractive errors in early infancy are inconsistent and do not address the population now experiencing a myopia epidemic in eastern Asia. In the present study, we present refractive data from neonatal infants in the first week of life in China. The infants are examined with cycloplegic retinoscopy to measure the physical limits of refraction with the ciliary muscle paralyzed and with noncycloplegic near retinoscopy to estimate the manifest refractive error during normal viewing.

Subjects and Methods

Subjects

Overall, 216 neonates participated in the study. All infants were born at full term in the Second Affiliated Hospital of the Wenzhou Medical College and were between 1 and 6 days of age at the time of the refractive examination. All were healthy at birth, and deliveries were normal.

Data for a group of 185 infants examined without cycloplegia were used in the study (nC group). Of these, a subgroup of 81 infants was examined with both cycloplegia and noncycloplegia (C/nC subgroup). Data from 31 infants were not used for the following reasons: 17 were examined by only one doctor; 10 were too difficult to examine because of such factors as eye movements, small pupils, narrow tarsal fissures, and crying; one was very underweight; two had unusually large measurement differences between the examiners; and one showed inconsistent differences before and after cycloplegia. Most infants who did not undergo cycloplegia did so because of the busy schedules of the examining ophthalmologists; therefore, a routine was established to randomly select the infants who received cycloplegia. A few parents did not agree to the use of cycloplegia on their infants. Characteristics of the infants whose data were analyzed are shown in Table 1.

This study was approved by the research review board of the Wenzhou Medical College before it was undertaken. Informed consent was obtained from at least one parent of each infant, and all were treated in accordance with the tenets of the Declaration of Helsinki.

Procedures

Parents were contacted through a brief written description of the program and through discussions with attending obstetricians and nurses who told them about the neonatal refraction research program. The use of cycloplegia in the examination was also explained. Most parents agreed to participate and signed the informed consent form.

The examination room was dimly illuminated, and the temperature was kept at 30°C. Each infant was held in the crook of a parent's or relative's arm while the infant was examined. Each ophthalmologist performed retinoscopy with a spherical lens bar, examined pupils and eye posture with a penlight, and entered the data into the examination form. The examination of each infant started after breastfeeding, when the infant was relaxed and quiet, whether it was asleep or awake. If an infant was agitated or crying, the examination was suspended. The examination continued when the infant became quiet and contented.

During retinoscopy an assistant opened the infants' eyelids without pressing on the eye to avoid inducing corneal astigmatism. For each retinoscopic examination (with or without cycloplegia), the doctor performed the retinoscopy three times and calculated the mean of the results as the refractive error. Then +0.75 D was added to the mean of the noncycloplegic retinoscopy results in accordance with Mohindra's near retinoscopy adjustment.[13]

Fewer than 10 infants were examined in a single session. The order of the subjects examined on any day was randomly determined. Noncycloplegic retinoscopy was performed first on each infant by both examiners. Cycloplegia was administered after the noncycloplegic refraction was completed to just the first two to five infants in the session; the other infants were returned to the ward immediately after noncycloplegic retinoscopy. For the infants undergoing cycloplegic retinoscopy, 1 drop of an equal mixture of 0.5% cyclopentolate and 2.5% phenylephrine was administered to each eye. A second drop was instilled 10 minutes later.[20] An assistant checked the infant's pupil size with a pupil ruler 20 minutes after instillation of the second drop. The examiners performed cycloplegic retinoscopy when the pupil diameter was 6 mm or greater.

Statistical Analysis

The examiners recorded sphere, cylinder, and axis for each measurement, calculated the spherical equivalent for each measurement, and then calculated their mean. The method of calculation does not affect equivalent sphere, so this was safe and correct. If there had been a significant level of astigmatism (as we at first expected), we would have used the M_o, J_o, J_{45} system to calculate astigmatism.[21] The level of astigmatism was so low (<2% had ≥1.0 D of astigmatism) that estimates were easy and there was no need to use the M_o, J_o, J_{45} system.

Of the three subjects excluded because of their data, one showed a 2.32 D difference between the two examiners for OD noncycloplegic spherical equivalent (nCSE), whereas the other cycloplegic spherical equivalents (CSEs) were within 1.0 D of each other. Another showed a difference between examiners of 2.68 D OD nCSE and 1.87 D OS nCSE. These differences are certainly outliers compared with the data of the included infants. Both examiners found the nCSE of the other excluded subject to be highly myopic on the first measurement (nCSE about −6.0 D), but the nCSE never returned to a level of myopia approaching this after cycloplegia had worn off. Both examiners felt these were especially difficult refractions and had far less confidence in the data for these infants than for the others.

Distributions are shown in graphs, and mean, SD, skew, and kurtosis are shown for each distribution. Differences were tested with *t*-tests, and relationships between data samples were estimated with Pearson correlations.

Results

Results for CSE will be presented first, followed by those for nCSE and then astigmatism.

Table 1. Demographic Characteristics of C/nC and nC Groups

Group	Number	Mean Gestation (weeks)	Mean Birth Weight (g)	Postnatal Age (days)	Sex	
					Boys	Girls
C/nC	81	39.5 ± 1.1	3378 ± 446	2.20 ± 0.84	28	53
nC	185	39.3 ± 1.2	3346 ± 448	2.35 ± 1.01	103	82

C/nC group, subgroup who underwent cycloplegic and noncycloplegic retinoscopies; nC group, all subjects who underwent noncycloplegic retinoscopy.

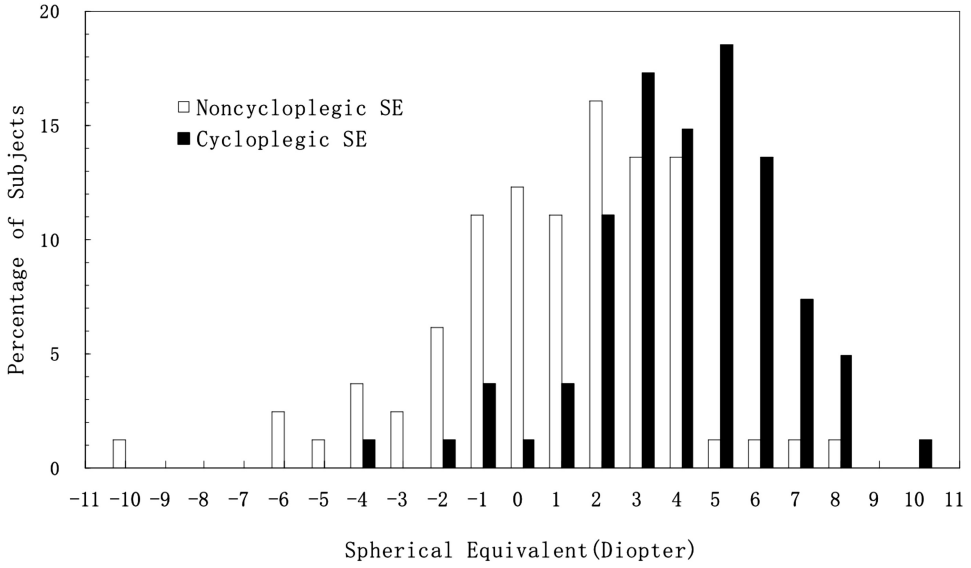

FIGURE 1. Distributions of CSE and nCSE of both eyes of the 81 infants in group C/nC (mean of the two retinoscopists).

Cycloplegic Refractions

Mean CSEs were highly hyperopic (OD, +3.47 ± 2.43 D; OS, +3.64 ± 2.43 D). The distribution was Gaussian with a trivial amount of skew (0.59) and leptokurtosis (0.76). The refractive distribution is shown in Figure 1.

CSE means and standard deviations are described for each examiner (CJ, HL) in Table 2. CSE distributions were very similar for the two examiners, with examiner CJ finding mean CSEs to be less hyperopic than HL by an insignificant 0.10 D for OD and 0.12 D for OS (Table 3). CSEs were highly correlated between the two examiners (OD, $r = 0.93$; OS, $r = 0.97$) and between the two eyes (examiner CJ, $r = 0.94$; examiner HL, $r = 0.95$), indicating that the measurements were very reliable.

Noncycloplegic Refractions

The mean nCSE of the full sample of 185 subjects was almost emmetropic (+0.58 ± 2.42 D). The distribution was Gaussian, with a slight skew (−0.94) toward myopia. There was a significant level of leptokurtosis (2.99) because of several highly myopic and hyperopic subjects (outliers) rather than a peaked distribution. The refractive distribution is shown in Figure 2.

The nCSE data for all subjects are described for each examiner in Table 2. nCSEs were highly correlated between the two examiners (OD, $r = 0.90$; OS, $r = 0.89$). There was a small systematic difference of approximately 0.14 D between the two examiners, with examiner CJ showing slightly more hyperopia than HL. This difference approached but did not reach statistical significance (Table 3). In addition, nCSEs were highly correlated between the two eyes (examiner 1, $r = 0.93$; examiner 2, $r = 0.97$).

The nCSE for the C/nC subgroup was slightly less hyperopic and had slightly broader distributions than for the noncycloplegic larger group (OD, +0.39 ± 3.05 D; OS, +0.36 ± 2.98 D). The nCSE distribution for the C/nC group had a trivial skew (−0.78) and leptokurtosis (1.41).

The nCSEs for this group are described in Table 2 for both examiners. The mean difference between examiners for nCSE was about the same as in the large group. Correlations between the two eyes were also highly correlated (examiner 1, $r = 0.95$; examiner 2, $r = 0.97$).

Correlations between examiners and eyes described were very high ($0.89 < r < 0.97$). However, the correlation between CSE and nCSE was much lower (examiner 1: OD, $r = 0.76$; OS, $r = 0.73$; examiner 2: OD, $r = 0.72$; OS, $r = 0.70$). The major axis slope of the C versus nC function was 0.80, which does not differ significantly from a slope of 1.0, and a Bland-Altman analysis showed that the difference between CSE and nCSE was independent of the mean spherical equivalent for both examiners.

The mean differences between CSE and nCSE in the C/nC subgroup were 3.08 D OD and 3.28 D OS, indicating that the infants had a very high level of tonic accommodation. However, the amount of tonic accommodation was not correlated with CSE (examiner 1: OD, $r = 0.017$; OS, $r = 0.072$; examiner 2: OD, $r = 0.123$; OS, $r = 0.183$).

TABLE 2. Mean Spherical Equivalent Refractive Errors and Standard Deviations by the Two Examiners

		Mean CSE	Mean nCSE	
Examiner	**Eye**	**C/nC Group**	**C/nC Group**	**nC Group**
CJ	OD	3.42 ± 2.42	0.44 ± 3.13	0.64 ± 2.47
HL	OD	3.51 ± 2.45	0.34 ± 3.06	0.49 ± 2.40
Mean	OD	3.47 ± 2.41	0.39 ± 3.05	0.57 ± 2.37
CJ	OS	3.58 ± 2.43	0.40 ± 3.10	0.67 ± 2.47
HL	OS	3.70 ± 2.46	0.33 ± 2.96	0.53 ± 2.31
Mean	OS	3.64 ± 2.43	0.36 ± 2.98	0.60 ± 2.32

CSE and nCSE refractive errors in the C/nC subgroup ($n = 81$) and nCSE for the overall noncycloplegic group nC ($n = 185$).

TABLE 3. Mean Spherical Equivalent Differences and Correlations between the Two Examiners

C or nC	Group	Eye	Mean SE Differential	*r*	P_r
CSE	C/nC	OD	−0.10 ± 0.71	0.93	<0.001
		OS	−0.12 ± 0.62	0.97	<0.001
nCSE	C/nC	OD	0.10 ± 1.11	0.94	<0.001
		OS	0.08 ± 1.17	0.96	<0.001
	C	OD	0.15 ± 1.11	0.90	<0.001
		OS	0.13 ± 1.31	0.89	<0.001

Astigmatism

The prevalence of astigmatism was very low. In the large group, only 4 of 370 eyes (1.1%) had astigmatism ≥1.0 D. Under cycloplegia, 3 of 162 eyes (1.8%) had astigmatism ≥1.0 D.

Comparison of SE with Other Factors

Correlations between mean nCSE and CSE for each eye and a number of other variables are shown in Table 4. An infant's refractive error was not related to its sex or weight at birth. The range of gestational ages was very narrow (C/nC group, 39.5 ± 1.1 weeks; nC group, 39.3 ± 1.2 weeks; Table 1), and the infant nCSE was not correlated with a longer gestational period (OD: $r = 0.16$, $P = 0.03$; OS: $r = 0.13$, $P = 0.08$ OS). For the C/nC group, these correlations were similar and also not significant. The range of postnatal ages was much narrower than for the gestational age (C/nC group, 2.20 ± 0.84 days; nC group, 2.35 ± 1.01 days; Table 1), yet CSE was negatively correlated with age ($r = -0.28$, $P = 0.01$; $r = -0.28$, $P = 0.01$). There was no correlation between nCSE and age in days for this group, but for the larger group the correlation did approach significance.

DISCUSSION

Cycloplegic Refractions

We have found the most hyperopic refractive distribution (mean, +3.55 D) reported for infants with the exception of Saunders et al.,[9] who found +3.47D for full-term neonates. Previous studies that used multiple instillations of atropine showed mean SEs between +2.25 and +3.0 D.[1–6] Other studies in which cyclopentolate was used reported slightly less hyperopia.[10–12]

We used a mixture of 0.5% cyclopentolate and 2.5% phenylephrine. Caputo and Lingua[22] have shown that combinations of cycloplegics and mydriatics are more efficient than either drug alone. Bolt et al.[20] showed in a clinical trial that the mixture we used is a more effective cycloplegic than cyclopentolate alone in premature infants several weeks after birth. Our infants were similar to their premature infants in gestational age, and the new combined drug might have enhanced hyperopia in our subjects. However, Rodriguez et al.[7] and Cook et al.[8] used similar combinations on neonates and found lower mean hyperopic values in the West (+1.80 D and +0.87 D, respectively). It is unlikely that the combination we used was more effective than multiple drops of atropine. Thus, we must conclude that Chinese neonates are prone to equal or perhaps even higher amounts of hyperopia than neonates in the West.

Noncycloplegic Refractions

The noncycloplegic refractions in the Chinese neonates (mean, +0.37 D) are similar to those for older infants in the West.[19] Thus the difference between CSE and nCSE in the present study is unusually high, 3.18 D. Given that nCSE includes Mohindra's +0.75 D standard correction factor,[13] the neonatal infants have a mean tonic accommodation level of almost 4.0 D so that their mean manifest focus is −0.38 D. This average level of tonic accommodation provides a relatively clear focus for the infants to see across a room. This focal distance is similar to that of a typical emmetropic adult with a distance refractive error of +0.38 and a tonic accommodation of 0.75 D.

A 4.0 D change in focus can produce a dramatic change in clarity in adults. The effect would be less in a young infant because infants are insensitive to high spatial frequencies. Behavioral preferential looking procedures show that the spatial vision of an infant in the first month is reduced to approximately 1.0 cyc/deg.[23,24] However, cortical visual evoked potentials show their primary visual system is responsive to higher spatial frequencies (up to 3 cyc/deg or more), which is near the contrast sensitivity function peak of adults and is sensitive to focus changes, especially of the magnitude induced

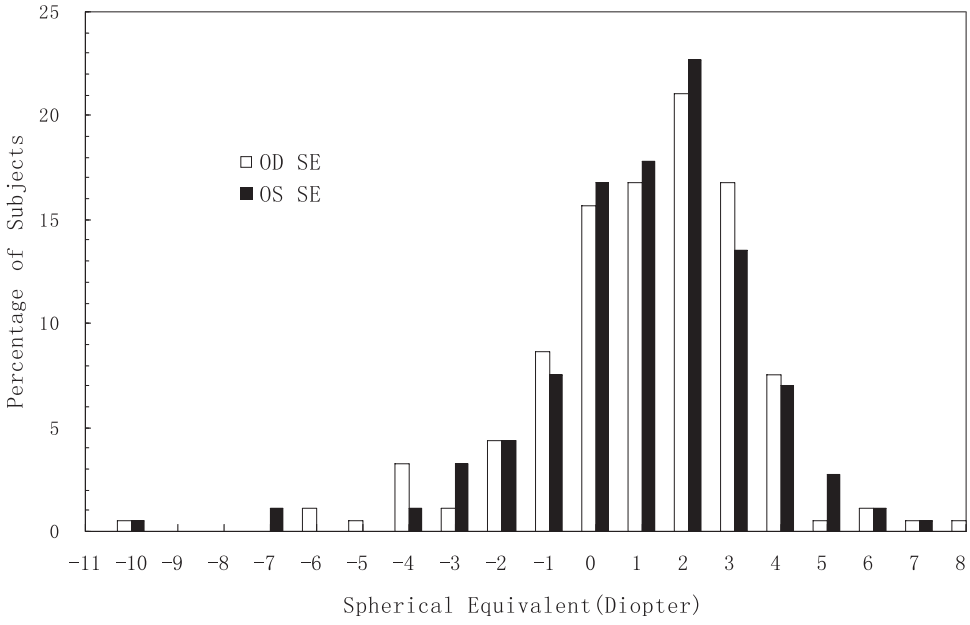

FIGURE 2. Distributions of nCSE of the right and left eyes of 185 infants (mean of the two retinoscopists).

TABLE 4. Correlations between Other Variables (Infant's Sex, Birth Weight, Gestation Period, and Age in Days) and Refractive Errors

Group C or nC	Eye	Correlation	Sex	Birth Weight	Gestation Period	Age (days)
CSE	OD	*r*	0.12	−0.05	0.15	−0.28
Gr.C/nC		*P*	0.27	0.68	0.17	0.01*
	OS	*r*	0.17	0.01	0.20	−0.28
		P	0.13	0.95	0.07	0.01*
nCSE	OD	*r*	0.04	0.04	0.13	−0.19
Gr.C/nC		*P*	0.76	0.81	0.25	0.09
	OS	*r*	0.004	0.04	0.09	−0.19
		P	0.98	0.72	0.41	0.09
nCSE	OD	*r*	0.05	0.02	0.16	−0.11
Gr.nC		*P*	0.50	0.81	0.03*	0.12
	OS	*r*	0.04	0.002	0.13	−0.08
		P	0.57	0.97	0.08	0.30

CSE and nCSE for the C/nC group ($n = 81$) and nCSE for the large nC group ($n = 185$).

by this level of tonic accommodation.[24,25] Thus, the 4.0 D change induced by tonic accommodation can greatly enhance the clarity of the infant's vision and should enhance early visual learning and the development of visually guided behavior.

Tonic accommodation enhancement of clarity must be caused by either a rapid development of tonic accommodation to compensate for the infant's cycloplegic refractive error or by an innately strong level of tonic accommodation in the newborn infant unrelated to the infant's refractive error. The fact that the mean amount of tonic accommodation almost equals the mean amount of hyperopia at first suggests a strong compensatory mechanism. However, the lack of a negative correlation between the amount of tonic accommodation and CSE indicates that the high amount of tonic accommodation is not due to a guided mechanism that compensates for the hyperopia of the individual infant. These correlations (examiner 1: OD, $r = 0.017$; OS, $r = 0.072$; examiner 2: OD, $r = 0.123$; OS, $r = 0.183$) were not significant and suggest that the CSE accounts for only 0.03%, 0.52%, 1.51%, and 3.3% of the variance for each of the four tonic accommodation distributions. Thus, the high level of tonic accommodation in the neonates is not an individually developed response to the infant's high level of hyperopia.

We have emphasized the correlations between examiners and between eyes for both cycloplegic and noncycloplegic refractive errors as strong indicators of the robustness of our measurements. Cycloplegic measurements and noncycloplegic measurements show considerable variability between studies with an undependable gold standard for comparisons. However, the strong internal consistency within our data provides assurance of accurate reliable measurements for this sample of infants.

Astigmatism

The prevalence of astigmatism was very low in this study; only 1.1% to1.8% of the neonates had 1 D of astigmatism. This is surprising because several highly cited studies have reported that 40% or more of infants between 3 and 7 months of age have ≥1 D of astigmatism and that >10% have ≥2 D.[11,26–28] In addition, Thorn et al.[28] demonstrated that Chinese infants in this age range have the same amount of astigmatism as Western children.[28] These papers report a rapid decline in astigmatism during the following 2 years.

For infants in the first month of life, there is a wide and inexplicable range (8%–59%) of reported astigmatism prevalence.[4–6,8,9,11] We found a much lower prevalence of astigmatism than in any of these studies, suggesting that Chinese neonates actually have less astigmatism than other neonates.

Comparison of Refractions with Other Factors

Premature infants tend to be myopic at birth primarily because the crystalline lens is near the cornea and is relatively spherical in shape. The characteristics of the lens change rapidly during the last trimester, flattening and moving away from the cornea.[29,30] Varugese et al.[6] have shown a 7 D shift from −4.86 D for neonates at 25.5 weeks to +2.40 D for full-term neonates. Thus, there is a large refractive shift from myopia to hyperopia shortly before the time of full-term birth that appears to be revealed as a small marginal correlation in the brief window of time in our study. An attempt was made to analyze this relationship in the present study even though the infants in the study were all full term and the gestational age range was narrowly restricted (SD, 1.1 or 1.3 weeks). The correlations between this narrow range of gestation periods and SE were not significant.

The correlation between CSE and postnatal age is most surprising because the range of ages was so narrow (SD, 0.86 days) and hyperopia decreases with age, which is the opposite of the trend described here. To explain this brief trend, we believe we must look at the sudden change in the eye's environment. In utero the eye has a fluid pressure on the cornea of several psi, and at birth the eye is suddenly released from this pressure. Simple modeling indicates that this release would allow the cornea to bulge slightly forward, becoming slightly more curved and powerful, similar to the change that occurs in the cornea after the removal of an orthokeratology lens. Even the time course is similar to that in orthokeratology.

Myopia

Myopia is rare in the cycloplegic refractions of neonates, but 20% of the neonates in this study show myopia when refracted without cycloplegia. A high rate of hyperopia and a low rate of astigmatism in older infants are risk factors for preventing myopia in longitudinal studies in the West.[31] Given that the prevalence of myopia in the industrialized areas of eastern China, including Wenzhou, exceeds 60%, the infants in this study must be considered at high risk for myopia. These contradictory findings suggest that the dynamics of myopia development may differ in China. The difference may simply reflect the environmental factors that come into a child's life during the school-age years.

CONCLUSIONS

Chinese neonates are highly hyperopic, have little astigmatism, and have a large amount of tonic accommodation that roughly

compensates for their hyperopia to allow for relatively clear vision across a room. The high mean amount of tonic accommodation and its great intersubject variability suggest that noncycloplegic near retinoscopy is not an appropriate procedure for determining a neonate's refractive error, but it can provide useful information in assessing the clarity of a neonate's manifest vision.

High levels of hyperopia and low prevalence of astigmatism during infancy are considered factors that protect against myopia in Western children. Yet our Chinese neonates are at high risk for myopia. Therefore, either the factors that induce myopia are different between the West and China or the relationship that links infantile refractive errors to adult myopia increases dramatically during the first year of life.

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