THE ROLE OF ANISOMETROPIA IN THE DEVELOPMENT OF ACCOMMODATIVE ESOTROPIA*

BY *David R. Weakley Jr, MD*, AND *Eileen Birch, PHD* (*BY INVITATION*)

ABSTRACT

Purpose: To determine if anisometropia increases the risk for the development of accommodative esotropia in hypermetropia.

Methods: Records of all new patients with a refractive error of ≥+2.00 (mean spherical equivalent [SE] of both eyes) over a 42-month period were reviewed. Three hundred forty-five (345) patients were thus analyzed to determine the effect of anisometropia (≥1 diopter [D]) on the relative risk of developing esodeviation and of requiring surgical correction once esodeviation was present (uncontrolled deviation).

Results: Anisometropia (≥1 D) increased the relative risk of developing accommodative esodeviation to 1.68 ($P<.05$). Anisometropia (≥1 D) increased the relative risk for esodeviation to 7.8 ($P<.05$) in patients with a mean SE of <3 D and to 1.49 ($P<.05$) in patients with SE of ≥3 D. This difference was significant ($P=.016$).

In patients with esotropia and anisometropia (≥1 D), the relative risk for an uncontrolled deviation was 1.72 ($P<.05$) compared with nonanisometropic esotropic patients. Uncontrolled esodeviation was present in 33% of anisometropic patients versus 0% of nonanisometropic patients with a mean hypermetropic SE of <3 D ($P=.003$); however, anisometropia did not increase the relative risk of uncontrolled esotropia in patients with SE of ≥3 D.

Although amblyopia and anisometropia were closely associated, anisometropia increased the relative risk of esodeviation to 2.14 ($P<.05$) even in the absence of amblyopia.

Conclusions: Anisometropia (>1 D) is a significant risk factor for the development of accommodative esodeviation, especially in patients with lower overall hypermetropia (<3 D). Anisometropia also increases the risk that an accommodative esodeviation will not be fully eliminated with hypermetropic correction.

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INTRODUCTION

The term "refractive esodeviation," or "accommodative esodeviation," refers to an entity first described by Donders[1] in 1864, in which the esodeviation is thought to arise from convergence associated with accommodation to clear the visual images in uncorrected hypermetropic refractive error.

Raab[2] has summarized a number of well-known characteristic features of this entity, including childhood onset, initial intermittency of deviation, esodeviation of generally less than 40 prism diopters (PD), elimination or reduction of deviation with hypermetropic spectacles, frequent association of anisometropia and amblyopia, above-average hypermetropic refractive error, and a high accommodative convergence to accomodation (AC:A) ratio. Of these factors, both high refractive error and a high AC:A ratio are often considered to be causative factors either for the development of, or the deterioration of, accommodative esotropia.

Although anisometropia is frequently noted to occur with accommodative esotropia, especially in amblyopic patients,[2] its role as a causative factor for its development is not clear. Furthermore, the role of anisometropia in the unresponsiveness of refractive esotropia fully to spectacles, or its deterioration, has not been established. This manuscript seeks to study this association.

MATERIALS AND METHODS

All new patients over 1 year of age presenting to the ophthalmology service of Children's Medical Center of Dallas for the 42-month period from January 1, 1995, to June 30, 1998, were considered for inclusion in the study. Patients were eligible if they met the following criteria: (1) overall

*From the Department of Ophthalmology, The University of Texas Southwestern Medical Center at Dallas; and The Retina Foundation of the Southwest, Dallas. Supported in part by an unrestricted research grant from Research to Prevent Blindness, Inc.

refractive error of +2.00 D or greater (mean spherical equivalent [SE]/average of both eyes), (2) no history of, or documented, esodeviation prior to age 12 months, and (3) a minimum follow-up of 2 months for esotropic patients to determine response to spectacles. Exclusion of any esotropia presenting prior to age 1 year was with the understanding that the rare case of early-onset accommodative esotropia might thus be excluded; however, this was felt to outweigh the risk of inadvertently including patients with infantile esotropia.[3,4] Three hundred forty-five (345) patients were included in the study.

Each patient was evaluated for the following baseline factors at the initial examination: (1) age, (2) presence and constancy of esodeviation, (3) duration of esodeviation by history, if present, (4) overall SE of refraction, (5) overall SE of anisometropia, and (6) presence of amblyopia.

For patients with esodeviation at the initial examination, outcome measures at the most recent follow-up included (1) response to spectacle correction, (2) presence and degree of a high AC:A ratio, (3) response to amblyopia therapy, and (4) overall length of follow-up. Subsequent data after the initial visit from hypermetropic patients who did not have an esodeviation at the initial visit were not required for inclusion.

Alignment was measured by using the prism cover test at 20 feet and at 33 cm. Refraction was measured objectively in all patients with use of 1% or 2% cyclopentolate and phenylephrine hydrochloride 2.5% (Neo-Synephrine). Any patient with esodeviation (intermittent or constant) was prescribed the full cyloplegic refraction. Amblyopia, defined as 1 line or greater of difference in the Snellen acuity, was determined after initial spectacle correction and at the most recent follow-up by use of linear optotypes (letters, HOTV match, or Allen pictures). The AC:A ratio was determined clinically in esotropic patients by comparing the distance to the near esodeviation measured with full distance correction, as described by Parks and others.[2,5] With this method, a high AC:A ratio is defined as more than 10 prism diopters difference between the 2 measurements. Esotropia was defined as uncontrolled if a constant deviation (>8 PD at distance with full cycloplegic correction or at near with full cycloplegic correction and a +3.00 bifocal) developed and persisted at any time during the follow-up period after a minimum of 2 months in spectacles. The duration of esotropia was determined by the history of the parent(s) or primary caregiver.

Statistical analysis was performed to determine the effect of anisometropia on 2 outcome measures: (1) the presence of esodeviation and (2) whether or not the deviation was fully controlled with spectacles. Significant anisometropia was defined as 1 D or more. This level of anisometropia was chosen as "significant" on the basis of previous work of 1 of us (D.R.W.) that has suggested that this level of hypermetropic anisometropia significantly increases the incidence of amblyopia and reduces binocularity in nonstrabismic patients.[6] The effects of moderate (≥1 to <2 D) and large (≥2 D) anisometropia were also compared to each other and to nonanisometropic patients. The relative risk (derived from the odds ratio) of developing esotropia, both controlled and uncontrolled, was determined.[7]

RESULTS

Three hundred forty-five (345) patients were included in the study. The mean length of follow-up was 15.4 months (range, 0 to 53) for all patients and 20.2 months (range, 2 to 53) for esotropic patients. Anisometropia (≥1 D) was present in 28% of patients (97/345) and esotropia (including both controlled with spectacles and uncontrolled, requiring surgery) was present in 61% of patients (210/345). Further breakdown of patients is shown in Table I.

The presence of esotropia at the initial examination was strongly associated with 3 baseline factors: younger age, increasing hypermetropic refractive error, and the presence of amblyopia (P= <.001 all variables). Esotropia was also associated with the presence of a high AC:A ratio (P=< .001); however, since this was determined clinically (near deviation exceeding distance deviation by >10 PD), by definition no patient without esotropia could have a high AC:A ratio. Thus, a high AC:A ratio was not considered a baseline risk factor for esotropia as a whole but was considered in comparing risk factors for uncontrolled esotropia. Furthermore, the proportion of anisometropic patients with a high AC:A ratio (20/84) was not significantly different than the proportion of nonanisometropic patients with a high AC:A ratio (23/126) (P= .378).

The likelihood of esotropia being unresponsive to spectacles and requiring surgery (uncontrolled esotropia) was also associated with certain baseline factors, including younger age at presentation, the presence of amblyopia, and constancy of the esodeviation at presentation.

TABLE I. SUMMARY OF PATIENTS

FACTOR	ALL PATIENTS	NO (<1D) ANISOMETROPIA	ANISOMETROPIA (≥1D)
No. of patients	345/345(100%)	248/345(72%)	97/345(28%)
Esotropia absent	135/345(39%)	122/248(49%)	13/97(13%)
Esotropia present	210/345(61%)	126 /248(51%)	84/97(87%)
Controlled	145/210(69%)	90 /126(71%)	42/84(50%)
Uncontrolled	65/210(31%)	36/126(29%)	42/84(50%)

Contrary to its effect on initial development of esotropia, the mean hypermetropic SE did not increase the likelihood that an esotropia would be uncontrolled with spectacles. The presumed duration of esotropia prior to treatment, length of follow-up, and presence of a high AC:A ratio likewise did not significantly affect the likelihood of an esotropia being uncontrolled (Table II).

We calculated the relative risk for patients with anisometropia to develop any esotropia, compared with nonanisometropic patients. Anisometropia (≥1 D) increased the relative risk for the presence of esotropia to 1.68 when adjusting for age, overall SE, and amblyopia.

TABLE II. ASSOCIATION BETWEEN BASELINE FACTORS AND ESOTROPIA

BASELINE FACTORS	ANY ESOTROPIA	UNCONTROLLED ESOTROPIA
Age	$P = <.001$	$P = <.001$
Mean SE	$P = <.001$	$P = .99$
Amblyopia present	$P = <.001$	$P = <.001$
High AC:A ratio	NA	$P = .58$
Constant esotropia at presentation	NA	$P = <.001$
Duration untreated esotropia	NA	$P = .35$
Length of follow-up	NA	$P = .09$

AC:A. accomadative convergence to accommodation; NA, not applicable; SE, spherical equivalent.

This increased relative risk was the same for patients with 1 to <2 D of anisometropia as for those with ≥2 D (Table III.).

We calculated the relative risk for patients with esotropia to have an uncontrolled deviation while adjusting for age and the constancy of deviation at presentation. The relative risk of an esotropia being uncontrolled once present was increased by the presence of anisometropia (≥1 D) to 1.72. The relative risk for an uncontrolled esodeviation increased to 1.64 for ≥1 to <2 D of anisometropia and to 1.95 with ≥2 D of anisometropia. The increased relative risk for both controlled and uncontrolled esotropia persisted in all age-groups, with greatest effect in older patients (≥60 months old) (Table III.).

Anisometropia of ≥1 D also increased the relative risk of a deviation being constant at presentation to 2.23. Patients with ≥1 to <2 D of anisometropia had an increased relative risk of 1.59, and patients with anisometropia of ≥ 2D an increased relative risk of 2.57 (Table III). A constant deviation at presentation, in turn, increased the likelihood that an esotropia would not be controlled with spectacles ($P<.001$) (Table I).

When patients were stratified by mean SE, anisometropia (≥1 D) was found to significantly increase the risk of developing esotropia at lower levels of hypermetropia. In patients with a mean SE of <3 D and anisometropia, relative risk of any esotropia was increased by a factor of 7.8, compared with nonanisometropic patients with the same overall SE. This was significantly higher than the effect of anisometropia on the relative risk for esotropia (1.49) in more hypermetropic (≥3 D SE) individuals ($P = .0172$). In both anisometropic groups, the relative risk for esotropia was significantly higher than in nonanisometropic patients. When patients are further stratified into 1 D groups, the largest effect on relative risk for esotropia is again most notable in patients with lower hypermetropic refractive error (Table IV). As noted in Table I, overall SE did not affect the likelihood of an existing esodeviation being uncontrolled.

As noted in Table I, there was a significant association between the presence of amblyopia and both the development of esotropia and the likelihood of an esotropia being uncontrolled. For the purpose of analysis, amblyopia was not considered a baseline factor but rather was assumed to be secondary to esotropia, anisometropia, or both. Thus, because of the significant association between amblyopia and anisometropia (82% of anisometropic patients were amblyopic) and the strong correlation between both of these variables and esotropia (82% of

TABLE III: ANISOMETROPIA AND RELATIVE RISK FOR ESOTROPIA*

LEVEL OF ANISOMETROPIA	(RR) OF ANY ESOTROPIA (95% CI)	RR OF UNCONTROLLED ESOTROPIA (95% CI)	RR OF CONSTANT DEVIATION AT PRESENTATION (95% CI)
None (<1D)	1.0	1.0	1.0
All pts (≥ 1D)	1.68 (1.47-1.80)	1.72 (1.17-2.28)	2.23 (1.27-3.94)
≥1D to <2D	1.68 (1.42-1.82)	1.64 (1.05-2.26)	1.59 (.95-2.47)
≥2D	1.68 (1.31-1.85)	1.95 (1.08-2.73)	2.57 (1.41-3.90)

RR, relative risk.
*Adjusted for significant baseline factors.

TABLE IV: ANISOMETROPIA (≥1D), MEAN SPHERICAL EQUIVALENT, AND RELATIVE RISK OF ANY ESOTROPIA

MEAN SPHERICAL EQUIVALENT (D)	PREVALENCE OF ESOTROPIA WHEN ANISOMETROPIA PRESENT (N=97)	PREVALENCE OF ESOTROPIA WHEN ANISOMETROPIA ABSENT (N=248)	RELATIVE RISK OF ANY ESOTROPIA WITH ANISOMETROPIA (95% CI)
All patients	87% (84/97)	51% (126/248)	1.68 (1.31-1.85)
Two subgroups			
< 3 D	92% (11/12)	12% (4/34)	7.79 (4.46-8.43)
≥ 3 D	86% (73/85)	57% (122/214)	1.49 (1.32-1.60)
One-D subgroups			
2 to <3 D	92% (11/12)	12% (4/34)	7.79 (4.46-8.43)
≥3 to <4 D	81% (13/16)	38% (22/58)	2.14 (1.38-2.14)
≥4 to <5 D	89% (17/19)	73% (36/49)	1.22 (.86-1.33)
≥5 to <6 D	88% (23/26)	57% (24/42)	1.55 (1.16-1.69)
≥6 D	83% (20/24)	63% (39/65)	1.32 (.96-1.49)

anisometropic patients and 93% of amblyopic patients were esotropic), there was little opportunity to examine the effect of anisometropia free of amblyopia. However, in nonamblyopic patients, anisometropia increased the relative risk for esotropia to 2.14 (Table V).

DISCUSSION

Refractive, or accommodative, esodeviation is a well-described entity in which esodeviation is presumed to result from the convergence associated with accommodative effort to clear retinal images in uncorrected hypermetropia. However, it is unclear why some patients with significant hypermetropia never develop an esodeviation and why others with low hypermetropia do. Furthermore, while some accommodative esodeviations respond readily to spectacle correction, others either fail to ever respond fully or deteriorate after initial successful alignment.

In this study, we have examined the role of anisometropia in both of these issues. First, we have examined the effect of anisometropia in the initial development of accommodative esodeviation in hypermetropic patients. Additionally, in the subset of patients with accommodative esodeviation, we have examined the effect of anisometropia on the unresponsiveness to spectacle correction or later deterioration.

INITIAL DEVELOPMENT OF ESODEVIATION

The degree of overall hypermetropia and a high AC:A ratio are the most commonly cited contributing factors in accommodative esotropia.[2,5] Atkinson[8] has shown that early correction of significant hyperopia reduces accommodative esotropia by at least 50%, also lending credence to the theory that hypermetropia is a major cause of accommodative esotropia. Fulton and associates[9] noted a significant increase in esotropia and amblyopia in patients under 3 years of age with ≥ +2.76 D of hypermetropia, compared with those with ≤ 2.75 D of hypermetropia.

TABLE V: ASSOCIATION BETWEEN AMBLYOPIA, ANISOMETROPIA, AND ESOTROPIA

ANISOMETROPIA	PATIENTS WITH ESOTROPIA WHEN AMBLYOPIA PRESENT (N=166)	PATIENTS WITH ESOTROPIA WHEN AMBLYOPIA ABSENT (N=179)
None (<1D)	93% (81/87)	29% (47/161)
≥1D	92% (72/79)	61% (11/18)
RR for esotropia (95% CI)	.99 (.85-1.05)	2.14 (1.27-2.84)

RR, relative risk

Notably, these investigators did not find a significant difference in the distribution of anisometropia between normal and esotropic patients. Parks[5] and Raab[2] both noted a higher-than-normal hyperopic refractive error in patients with acquired esotropia with normal AC:A ratios. In this series we also found a strong correlation between increasing SE of refractive error and accommodative esodeviation ($P<.001$) and have controlled for this in evaluating the effect of anisometropia.

An abnormally high AC:A ratio has also been suggested to contribute to the development of accommodative esotropia, especially in patients with relatively normal hyperopic refractive errors. Parks[2] noted that 57% of patients with acquired esodeviation had a high AC:A ratio as defined in this study. He further noted an average hypermetropia of only +2.25 D in these patients versus +4.75 for acquired esotropia patients with a normal AC:A ratio. Raab[2] noted similar findings, with 50% of his series of accommodative esotropia patients having a high AC:A ratio and, additionally, a lower overall hypermetropic refractive error than patients with a normal AC:A ratio; he noted, however, that a high AC:A ratio can also be important in patients with moderate and high hypermetropia.

Von Noorden and Avilla[10] have documented a low AC:A ratio and a reduced near point of accommodation in a number of significantly hypermetropic individuals without esotropia. These investigators postulated that an intrinsically low AC:A ratio can protect some individuals from developing accommodative esotropia by allowing accommodation without excess convergence, arguing against Donders,[1] who suggested that failure to make sufficient accommodative effort to fully clear the retinal image could account for absence of strabismus in patients with significant hypermetropia. Thus, while a high AC:A ratio may contribute to the development of accommodative esotropia, especially in patients with normal or near-normal refractive error, a low AC:A may protect against it.

While an association between anisometropia and accommodative esotropia has been described,[2] previous studies have not determined a cause-and-effect relationship, as has been suggested for overall refractive error and a high AC:A ratio. On the basis of the findings of this study, we propose that anisometropia of ≥1 D is, in fact, an additional independent risk factor in the initial development of uncorrected refractive esotropia. The data in this study demonstrate an increase in the relative risk for esotropia in hypermetropic individuals with anisometropia of ≥1 D compared with nonanisometropic patients when controlling for overall spherical error. However, this increased relative risk for esotropia did not increase with increasing degrees of anisometropia (Table III). It should be pointed out that the proportion of patients with a clinically high AC:A was not significantly different between

the groups of anisometropic and nonanisometropic patients with esotropia in this study, supporting the conclusion that anisometropia acts independently of both the AC:A ratio and overall hypermetropia.

The increased relative risk for esotropia with anisometropia was most notable in patients whose hypermetropic refractive error might be considered to be relatively normal (2 to <3 D) or only moderately above normal (3 to <4 D). We postulate that the disruption of binocularity caused by a significant amount of anisometropia allows for refractive esotropia to develop at lower levels of hypermetropia than in nonanisometropic individuals. Additionally, we would argue that while the effect of anisometropia on developing accommodative esotropia persists at higher levels of hypermetropia, its effect is masked as larger numbers of the more hypermetropic patients develop esotropia as a result of the severity of the refractive error alone (Table IV).

These data also suggest that the presence of significant anisometropia (≥1 D) increases the likelihood that an esodeviation will be constant rather than intermittent at presentation. This association was also more notable at lower levels of hypermetropia. We again postulate that the disruption of binocularity, with resultant suppression and frequent amblyopia associated with anisometropia, would be more likely to lead to a constant than an intermittent deviation. This, in turn, could be expected to increase the likelihood of unresponsiveness to spectacles (Table III).

UNCONTROLLED ESODEVIATION

In addition to examining the effect of anisometropia on the initial development of accommodative esodeviation, we have attempted to determine if significant anisometropia increases the likelihood that an esodeviation will not respond fully to spectacle correction or deteriorate after initial control. The terms "combined esotropia" and "partially accommodative esotropia" have been used to describe such patients; however, these terms may be misleading with regard to the true cause. It seems likely that hyperopic refractive error is the cause of esotropia in many of these patients, yet delay in treatment or the development of sensory abnormalities such as suppression or amblyopia, as is seen with significant anisometropia, precludes alignment with glasses alone (ie, "deterioration" may occur prior to the institution of treatment).

Little information is available regarding factors that might predispose an esodeviation to not respond significantly or fully to spectacles; however, a number of investigators have examined the issue of deterioration alone, evaluating various factors, including the AC:A ratio, constancy of deviation at presentation, delay in seeking treatment (these 2 factors are frequently associated with each other), the presence of amblyopia, and overall refractive error. Raab[2] did not note a significantly higher deterioration rate in patients with a high AC:A ratio. Dickey and Scott[11] also found that deterioration was not related to the presence of a high AC:A ratio, but did note an association between earlier onset of esotropia and an increased time between onset and treatment of the esodeviation. Contrarily, Ludwig and associates[12] did note an association between deterioration and both a high AC:A ratio and lower hypermetropia (although patients with high AC:A ratio had lower hypermetropia, and these factors may therefore not be independent). Surprisingly, delay in treatment and the presence of amblyopia were not associated with deterioration in this series.

In this study, we did not specifically examine deteriorated esodeviations; rather, we evaluated as a group all patients in whom an esodeviation was uncontrolled either through deterioration or failure to ever respond fully to spectacles. In this series, a high AC:A ratio, the overall level of hypermetropia, or delay in seeking treatment did not increase the likelihood that an accommodative esodeviation would be uncontrolled. However, constancy of deviation at presentation, the presence of amblyopia, and the presence of anisometropia were positively correlated with uncontrolled esodeviation.

Swan[13] has reported that patients with accommodative esotropia and poor binocular function have a significantly greater likelihood of requiring surgery than those with normal binocular function. Wilson and associates[14] reported constancy of a deviation at presentation, need of esotropia surgery, and amblyopia all to be significantly more common in patients with monofixation than bifixation. Thus, poorer binocularity seems to be associated with poor control in accommodative esodeviation, although the reason for poorer binocularity is not always clear. We postulate that the disruption of fusion, with resultant suppression and often amblyopia as well, caused by significant anisometropia is 1 mechanism by which poor binocularity may result. This, in turn, can increase the risk that an esodeviation will not respond fully to spectacles. Our data demonstrate an increased risk of an uncontrolled deviation with significant anisometropia consistent with this theory.

CONCLUSIONS

Anisometropia (≥ 1 D) increases the relative risk for the development of esotropia in hypermetropic individuals, especially at lower levels of hypermetropia. Anisometropia also increases the likelihood that an accommodative esodeviation will not respond fully to spectacle correction. The effect of anisometropia should

be considered in the management of hypermetropic patients.

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DISCUSSION

DR MALCOLM L. MAZOW. The authors, Drs Weakley and Birch, have proposed that an additional characteristic should be considered in evaluating the factors that influence the development and management of accommodative esotropia. They report that an anisometropia of as little as 1 diopter increases the risk for the development of esotropia in the hypermetropic patient, and that these cases do not seem to fully respond to spectacle correction. They question whether the development of the deviation was caused by the difference in the refractive error prior to wearing the glasses and if so, was amblyopia the result of the uncorrected refractive error, therefore making fusion impossible when the prescription was given.

This was a prospective study and included all patients that presented with a refractive error of at least +2.00D without documented strabismus prior to 12 months of age with enough follow up to assess response to the wearing of correction. All cases under 12 months of age were excluded to eliminate any possible cross-over with infantile esotropia.

Certain assumptions are made by the authors. They classify as uncontrolled accommodative esotropia any deviation not responsive to optical correction. They consider one cycloplegic refraction sufficient, and the method to determine the AC/A ratio is not the universally accepted technique for attaining such measurements. Convention suggests that accommodative esotropia is classified into 2 types: 1) accommodative esotropia of the refractive type, where refractive error alone controls the deviation with the development of fusion and binocular function, and 2) the high AC/A ratio esotropia whose angle is corrected by additional plus lenses at near, resulting in binocular function.

Patients with a deviation not fully corrected by hypermetropic spectacles suggests a mixed type of esotropia. The authors here suggest that patients with anisometropia often fall into the partial or mixed esotropia category, when the deviation present is not fully corrected by glasses. In this group, the deviation is lessened but not totally corrected with the addition of lenses and binocularity is not achieved optically. Regardless of the definition of accommodative esotropia, the authors have convincing evidence that anisometropia of small amounts may lead to the development of strabismus and amblyopia, as well as true and partial accommodative esotropia. The Relative Risk (RR) for developing esotropia, regardless of the amount of anisometropia, was 1.68. The development (RR) of uncontrolled esotropia with glasses ranged from a low of 1.64 in patients with 1 to 2 diopters of anisometropia to 1.95 in those with greater than 2 diopters. Table 4 shows the development of esotropia is greater in patients who have anisometropia as compared to the prevalence of esotropia when there is no evidence of anisometropia. The differences seen here are significant in the cases with less than 4 diopters of hypermetropia and anisometropia. However, this might be explained by the troublesome image blur requiring adaptive mechanisms, such as suppression. In differences of 2 diopters to 4 diopters, as compared to no interocular refractive differences with the same hyperopic error, facultative suppression may be necessary, resulting in amblyopia and esotropia. This is also true in refractive errors >4, but with less RR.

The authors state that when patients were stratified by mean spherical equivalent (SE), anisometropia ≥ 1D was found to significantly increase the risk of developing esotropia at lower levels of hypermetropia. Patients with a mean SE of <3D and anisometropia, had a 7.8 times greater RR of any esotropia when compared to patients without anisometropia and the same overall SE. This finding was significantly greater than the effect of anisometropia on the RR for esotropia (1.49) in more hypermetropic individuals (≥3D SE, p=. 0172). In both anisometropia groups, the RR for esotropia was significantly higher than in non-anisometropic patients. When patients are further stratified into 1D groups, the greatest effect on RR for esotropia is again most notable in patients with lower hypermetropic refractive errors.

The authors would be well advised to look at the development of accommodative esotropia and its RR in 3 different groups: refractive esotropia, high AC/A accommodative esotropia, and by their definition, partial accommodative (mixed) esotropia. By directing our attention to the development of esotropia and/or amblyopia without stratifying into the distinct groups, confusion occurs as to the relative risk of anisometropia in the purely refractive accommodative esotropia patient.

The authors show a significant increase of esotropia development when amblyopia and anisometropia are present, as they show in Table 5. Anisometropia ≥1D results in the development of esotropia in 93% of the patients studied (81/87) as compared to those patients without anisometropia and amblyopia where only 29% of the patients (47/161) developed strabismus. This difference is accentuated when comparing the two groups when anisometropia is ≥1D, (92%). This data also suggest that the presence of significant anisometropia (≥1D) increases the likelihood that an esodeviation will be constant rather than intermittent at presentation. This association was also more notable at lower levels of hypermetropia. We again postulate the disruption of binocularity with resultant suppression and frequent amblyopia associated with anisometropia, would be more likely to lead to a constant, rather than an intermittent deviation. This in turn could be expected to increase the likelihood of unresponsiveness to spectacles, as shown in Table 3.

The findings seem remarkable as suggested above. However, this may well be explained by the need to eliminate the blurred image by refractive differences between 2 and 4 diopters.

In summary, it might be said that the emphasis of this study is to incriminate anisometropia as a cause of partial or mixed esotropia. When compared to patients with similar refractive errors without anisometropia, those patients with anisometropia have a higher incidence of esotropia and amblyopia.

However, there are other issues that need to be studied and questions to be asked. Although the authors acknowledge they do not address the relationship of anisometropia and the deterioration of a once binocular accommodative esotropia, they beg an important question, which should be addressed. What is the effect of anisometropia on the breakdown of previously well-controlled accommodative esotropia? Should a patient who never develops binocularity with their refractive error be considered a true accommodative esotrope? Or is this patient really a partial accommodative esotrope, or an acquired non-accommodative esotrope?

Dr John Flynn. I would also like to congratulate Dr Weakley and to welcome him and literally a cohort of pediatric ophthalmologists who have joined our ranks recently. I look forward to a coming decade of AOS meetings where the quality of papers is definitely improved. I have a couple of questions for him. The first question is, do you have any idea from looking at this immense series, which is more important: a diopter of astigmatism or a diopter of hyperopic difference between the 2 eyes? It has been my intuitive clinical feeling that it is the difference on the hyperopic side that has a more profound effect on the failure to control accommodative esotropia. My second question is, I think it was implied but you did not state it, was your outcome variable the fact that these children needed surgery? If you had to take them to surgery, was that by definition uncontrolled? With regard to the stratification and the obvious lower incidence or lower degrees of anisometropia and hyperopia having the more profound risk of being uncontrolled, I have always in a simplistic way explained that to myself as the kids with high hyperopia are walking around with blurred images from 2 eyes, whereas the kids with lower degrees of hyperopia are walking around with one very clear image and one that is not clear. It is more likely to induce severe retinal rivalry going from a rivalist state into a suppressionist state.

Dr John O'Neal. David, I want to thank you for looking at an area that is very important to us and has not been so addressed. Without question the cases of anisometropia with accommodative deviations are all in hypermetropic or farsighted children. We certainly see a lot of myopic children also who have amblyopia and have high ACA ratios and esodeviations for near. I just wondered if you have looked at that group at all. Certainly, the group of children that you have seen that have the most problem of the hypermetropes are those with the low degrees of hypermetropia of 1 diopter or less. In the myopic group these would seem to have the least difficulty because they would use 1 eye for distance and 1 eye for near. Have you looked at the myopic group at all?

DR IRENE LUDWIG. Most of these patients come to us after strabismus or amblyopia has developed, and therefore how can we be sure that any anisometropia is not a secondary complication of strabismus in at least some patients? I have heard some anecdotal reports of children with documented normal or non-anisometropic refractions, although they had hyperopia before esotropia development and documented anisometropia after esotropia developed. I have also personally observed gradual resolution of anisometropia in a number of patients with treatment of accommodative esotropia and aggressive amblyopia treatment. Have you been able to document refractions in any of these children before strabismus development to sort out this question?

DR. DAVID R. WEAKLEY, JR. Thank you Dr Mazow for that discussion, and let me see if I can try and address each of those issues as well as I can. Dr Mazow did mention the method in which the ACA ratio was determined. Probably the more appropriate method is the gradient method, versus the heterophoria or clinical method, which can be done retrospectively, that is the near/distance deviation difference. I think that method has tended to pervade in the literature. Certainly, it was used looking at earlier series of patients with accommodative esotropia, Dr Rabb's series before this society and Dr Park's series. It is easier to do, and can be done retrospectively. I do not, and I do not know how many of us do, actually measure AC/A ratios in all of our patients. A lot of the patients in this study were straight-eyed patients who were simply hypermetropic, so I will grant you that the gradient method would be considered to be a more appropriate measure; however, it is not something that could be done based on the way this study was designed. As to whether this would change the findings, I do not think so.

The other point that Dr Mazow brought up that I thought was interesting and which I touched upon in the manuscript is what is the non-accommodative component of accommodative esotropia. Why is there a non-accommodative component, and what causes a non-accommodative component? All of these patients did respond to glasses in some fashion. In other words, the esodeviation was reduced, although in many cases it was not eliminated. My argument in the paper is that this is traditionally considered to be a non-accommodative component of accommodative esotropia. I ask you, could it not be fact that it used to be accommodative and because the patients are untreated for a period of time or because they have anisometropia then develop amblyopia, suppression, etc., and fusion is lost, the eyes deviate inward you may get muscular changes, and thus it becomes non-accommodative. I feel "non-accommodative" components of these deviations can be the result of inadequate, poor, or delayed treatment in patients that initially may have a purely accommodative deviation.

I did not separate, as many authors have, deteriorated deviations from those that never responded fully. This resulted from my interest in seeing many anisometropic patients that did not ever fully respond to spectacles and went to surgery relatively soon. If you just look at deteriorated patients, that is patients who are fully corrected with spectacles initially, and then deteriorate, one obviously can argue that those patients were truly fully accommodative patients. The question was, are patients in this study who never align fully with glasses, they improve somewhat but never straighten fully, what type of patients are these? That is a difficult question, but in my mind I think many of these patients, if they had been treated early, if their anisometropia had been corrected, if they did not develop amblyopia or suppression, that the likelihood would be much higher and they would be aligned by glasses.

With regards to Dr Flynn's comments, in this study I used spherical equivalent of hypermetropia. In other words I determined the spherical equivalent of the hypermetropic error and then determined the difference that way. I did not separate spherical versus cylindrical anisometropia in this study. In the study that I referenced, my thesis, you asked about astigmatism versus spherical, in that paper, where I looked at anisometropia in non-strabismic patients, I did stratify in that study myopic, hyperopic, and astigmatic anisometropia, and this actually addresses a later question about myopia from Dr O'Neal. In that study, significant amblyopia, suppression, and poor binocularity developed at a diopter or more in spherical hypermetropia, and a diopter and a half or more of anisometropia in the purely astigmatic patients. It was consistent with the guidelines that we have all become accustomed to using for treating these patients. The other question of Dr O'Neal about myopia, I also did look at myopia in that study and I think the theory ascribed to Dr von Noorden and others that one eye is used at near and one eye is used for distance is probably true. Clearly the level of anisometropia for developing amblyopia in those patients was higher. No myopes developed any problems unless they had at least 2 diopters of anisometropia or more, and that was minimal at the 2 to 3 level, but it increased from there. Again, in this study we used a spherical equivalent so there was combined astigmatic and spherical anisometropia in some patients.

With regard to Dr. Ludwig's question, I think she has touched on the proverbial chicken egg question as to what comes first in these patients. Does esotropia result in suppression and then anisometropia develops, or does anisometropia result in suppression then result in the

development of esotropia. I think it can go both ways, that is, chickens lay eggs and eggs hatch into chickens. Certainly we have all seen patients like a unilateral aphake who are poorly corrected and gradually develop axial myopia. I do not think that there is any question that anisometropia can result in a poor seeing eye that is not being used, the biofeedback is lost and that eye changes shape. However, I am still a firm believer that anisometropia is primarily a cause rather than effect of strabismus. In my previous series the patients were not strabismic and there were plenty of patients with anisometropia who do not have any strabismus whatsoever. I do not think that there is any question in my mind that anisometropia does exist significantly in the population and does not always cause strabismus. There is a large population of patients in whom anisometropia does not result from strabismus, and in many of those patients there is no amblyopia either. I think it has to be a primary entity at least in those patients. I will grant you, however, that in some of these patients anisometropia may increase over time with poor correction of the esotropia.

Again thank you for your helpful comments, and it is a pleasure to be a new member of this society.