THE DECOMPENSATED MONOFIXATION SYNDROME (AN AMERICAN OPHTHALMOLOGICAL SOCIETY THESIS)

BY R. Michael Siatkowski MD

ABSTRACT

Purpose: To describe the clinical features and response to treatment of patients with decompensated monofixation syndrome (MFS) and to propose a hypothesis for a decompensation mechanism in such patients.

Methods: Fourteen adults with MFS who had been symptomatically stable for a mean duration of 25 years developed diplopia in the absence of neurologic or orbital disease. After retrospective chart review, they underwent detailed orthoptic testing. Results from this cross-sectional analysis were compared with similar data from 16 control subjects with stable MFS.

Results: Compared to stable MFS patients, decompensated subjects had significantly poorer horizontal fusional amplitudes but greater torsional fusional amplitudes; they were also more likely to have a small vertical strabismus and to have received initial treatment later. Stable subjects, however, also had subnormal horizontal as well as torsional fusional amplitudes. There was no difference between groups with respect to refractive error, amblyopia, type or prior treatment of strabismus, stereoacuity, or angle of deviation. After treatment, all patients regained monofixational alignment, but up to one-third had continued diplopia. Symptoms recurred in two patients whose treatment was initially successful.

Conclusions: Patients with MFS lose fusional amplitudes over time. In some cases this results in development of sensory torsion with secondary decompensation and diplopia. The rate of decompensation averages 7% per year from ages 20 to 70. Treatment for decompensation offers excellent motor results, but sensory symptoms may persist and recurrent symptoms may develop. Monitoring and maintenance of fusional vergence amplitudes should be part of the routine care for patients with MFS.

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INTRODUCTION

That some type of sensory adaptation is required in response to strabismus was first recognized almost three centuries ago by de la Hire[1,2] and further considered in the following century by Müller.[3,4] Although erroneous in their assumption that ocular misalignment was due to anatomic displacement of the foveas, and although their musings occurred prior to Wheatstone's initial explanation of normal stereopsis,[5] they laid the foundation for our current understandings of the objective and subjective changes that are present in individuals with abnormal binocular function.

Today we recognize the spectrum of binocular interaction as ranging from constant bifoveation at one end to complete monocularity at the other. Of particular interest is the subset of persons with either straight or almost-straight eyes but subnormal fusion and/or stereopsis. Although Pugh[6] first called attention to these small-angle deviations in 1936, work on this condition began in earnest in 1951, when Jampolsky[7] commented on patients with small-angle esotropia and "retinal slip." Gittoes-Davies[8] and Levinge[9] referred to such patients in terms of "fixation disparity," and Bryer[10] called the small shift seen on alternate cover testing "flick," hence the term "flicker cases." In 1955 Lyle and Foley[11] noted that subjects with very small degrees of strabismus could possess excellent peripheral fusion.

In 1956 Jampolsky[12] called attention to additional clinical characteristics of these patients. He noted that they often had phorias much larger than their manifest deviations and first postulated that their degree of ocular misalignment was sufficiently small as to permit the development of normal retinal correspondence (NRC). He also noted that despite intensive orthoptic therapy, these patients were incapable of achieving completely normal binocular function and high-grade stereopsis. Six years later, Jampolsky[13] used the phrase "fusion with disparity in fixation" (later shortened to "fusion disparity" but also sometimes "fixation disparity") to refer to patients with 6 to 10 minutes of arc deviation but in whom both maculas were capable of simultaneously functioning. He also used the phrase "heterophoria without bifoveation" to describe the phenomenon of patients with very small-angle ocular misalignment and peripheral fusion but inability to use both foveas simultaneously.

It is worth noting that while the term *fixation disparity* is found throughout a wide range of literature in association with patients with small-angle strabismus and deficient stereoacuity, it was originally used in 1949 by Ogle[14] in the context of normal binocular function. The term originally applied to the small levels of imprecision in the intersection of the visual axes while viewing any object of interest. Thus a term originally intended to describe normal visual physiology has been incorrectly used to refer to subjects with small degrees of strabismus and remains, unfortunately, indelibly corrupted.

The *fixation disparity* issue notwithstanding, further work in the 1960s, important and novel as it was, intensified the semantic dilemmas encountered in the literature on this topic. In 1961 Parks[15] coined the phrase *monofixational phoria* to describe patients with a small manifest deviation and a much larger heterophoria uncovered by prolonged alternate cover testing. This term was used by others for several years[16,17] but criticized by Lang[18] due to the presence of a manifest tropia as well as the fact that some of these patients clearly demonstrated anomalous retinal correspondence (ARC). He offered the term *microtropia unilateralis anomalo-fusionalis*, also known as *microtropia* or *microstrabismus*. "Microtropia" was also the title of Helveston and von Noorden's 1967 article,[19] which they subtitled "A Newly Defined Entity" to connote the subset of patients with strabismus so small as to be undetectable by cover testing; they noted that anisometropia was present in a large majority of such cases. In 1973 Epstein and

From the Department of Ophthalmology, Dean McGee Eye Institute, University of Oklahoma College of Medicine, Oklahoma City.

Tredici[20] evaluated a similar condition in aviation personnel, interspersing the terms *monofixation syndrome* and *microtropia* in their title and suggesting that stereoacuity of 40 arc seconds was possible in either.

The1969 American Ophthalmological Society (AOS) thesis of Marshall Parks, "The Monofixation Syndrome,"[21] represents the culmination of work performed and concepts refined over the preceding two decades, and his organized description remains the most widely cited today. Unfortunately, imprecision in verbiage persists. Even the American Academy of Ophthalmology's Basic and Clinical Science Course text intersperses both "monofixation syndrome" with "microtropia," prompting some to suggest that additional terms—such as *minitropia*, *macro-microtropia*, and *true microtropia*—could bring clarity (!) to the situation.[22]

As this author considers the thesis of Parks to be the seminal work in the description and classification of this condition, it is his definition of monofixation syndrome (MFS) that will be used in this manuscript. Parks recognized four possible etiologies of MFS: previously treated strabismus (the most common cause), anisometropia without strabismus, a unilateral macular lesion, and primary or idiopathic (no history of prior strabismus or strabismus treatment, anisometropia, or maculopathy). His 1969 criteria for the diagnosis of MFS include the following constant attributes: a horizontal strabismus of no more than 8 prism diopters (PD), orthophoria being possible and esodeviations much more common than exodeviations; facultative suppression of the nonfixating eye under binocular viewing conditions; good fusional vergence amplitudes; and inability to convert to bifoveation despite any form of treatment. The following additional clinical attributes occur variably: amblyopia and manifest strabismus (each in approximately three-quarters of cases), large phorias on alternate cover testing, and the presence of measurable stereopsis, but not better than 60 arc seconds.

The clinical profile of MFS as described by Parks has been strongly affirmed by the elegant neurophysiological work of Tyschen.[23] Using the macaque monkey, Tyschen demonstrated that a neuron in area V1 of the visual cortex could join receptive fields up to a maximum of 2.5 degrees (4.4 PD); thus two adjacent neurons could join fields up to 5 degrees, or 8.7 PD, apart, corresponding very closely to the Parks rule of a horizontal deviation of not more than 8 PD. Excellent fusional vergence amplitudes can develop, since beyond the region of foveolar suppression the excitatory binocular horizontal neuronal connections in V1 are intact. Thus patients whose horizontal ocular alignment is within 8 PD have the capacity to develop cortical fusion mediated by ocular dominance columns (and receptive fields) separated by up to two axonal lengths; this then is the neural substrate of the clinical state that Parks termed MFS several decades earlier.

In the 40 years that have passed since Parks published his thesis,[21] relatively few new clinically based insights into MFS have surfaced. Choi and Isenberg[24] established that up to 6 PD of vertical deviation is compatible with the original description of Parks, and Scott and colleagues[25] postulated primary MFS as a forme fruste or incomplete phenotypic expression of infantile esotropia, since it was found in 6% of parents of children with infantile esotropia. Additionally, in 1996 Harwerth and colleagues[26] reported a possible animal model for MFS in macaque monkeys, by surgically inducing esotropia during the critical period of visual development, and subsequently realigning the eyes.

One facet of MFS about which Parks was adamant is its long-term prognosis, namely, the stability of the condition. Parks was quite firm in his conviction that monofixation, once established, did not change. His AOS thesis contains the following statements (italics added): "The monofixators are *symptomless*, cosmetically straight, and *tend to remain unchanged with increasing age.*" "The most impressive prognostic feature of patients with the monofixation syndrome is their *static alignment state. Over the years their eyes continue to remain aligned* as well as if they were bifixating. . . .These data reveal the *tendency for the alignment of the monofixator to persist unchanged over the years*, a fact noted by many other contributors to his subject. Peripheral fusion alone seems to be just as effective as the combination of peripheral and central fusion in maintaining straight eyes." Six years later, Parks again stated, "Once the monofixation syndrome has evolved, almost invariably it remains unchanged. The patient is comfortable and all concerned are happy with the straightness of the eyes."[27]

This author became interested in the stability of MFS upon encountering an unusual case early in practice. The patient was a 58-year-old commercial airline pilot with the chief complaint of intermittent binocular diplopia for 1 year. He had a history of refractive accommodative esotropia, treated with glasses in the first decade of life through his teen years. He remained with cosmetically straight eyes and with no visual symptoms apart from presbyopia in his early 40s until age 57, at which time he began to experience diplopia. His prior evaluation had consisted of examinations by two optometrists, two ophthalmologists, a neurologist, and an internist; five different pairs of prism glasses had been prescribed. In addition, computed tomography, magnetic resonance imaging, and magnetic resonance angiography of the head were performed, as were lumbar puncture and electroencephalogram, all of which were normal.

On examination, visual acuity was 20/15 in the right eye and 20/20 in the left eye. Ocular motility was full. Via simultaneous prism-cover testing he had a left esotropia of 8 to 10 PD at distance and near, increasing to 18 PD on alternate cover testing. He could see singly with a 10 PD base-out prism, and contour stereopsis with prism correction was 200 arc seconds. Pupils, visual fields, anterior segment, and dilated fundus examination were normal bilaterally. Cycloplegic refraction was +0.50 sphere in each eye.

Based on prior history and examination, a diagnosis of nonstatic MFS (previously stable MFS in which a change in motor alignment and sensory status occurred), or " decompensated MFS," was made. A prism adaptation trial commenced, with which his angle built to 25 PD at distance and 30 PD at near. He underwent strabismus surgery with final alignment of 2 PD of esotropia at distance and near. One year postoperatively, his angle was stable, he was diplopia free, and contour stereopsis measured 80 arc seconds.

Following this encounter in the early 1990s, I began to formulate a more precise definition of "decompensated MFS" for patients who had a history of either primary MFS or MFS secondary to anisometropia or previously treated strabismus and had been symptomatically stable for many years into adulthood. This group of patients, however, at some point began to experience binocular diplopia bothersome enough to seek treatment. In some cases, a change in refractive correction or the addition of bifocals for

presbyopia solved the problem; in others, however, the etiology and treatment of the new symptoms were more elusive. Some of these patients experienced constant or intermittent diplopia along with a change in their ocular alignment. In others, alignment was stable or not visibly changed from their perspective. A retrospective review of stable vs decompensated cases of MFS was presented at the 1997 North American Neuro-Ophthalmology Society (NANOS) meeting (Ganser GL, et al, NANOS, 1997, Abstract, page 2). This study found that amblyopia was significantly more common in stable cases (48% vs 8%, *P*=.023, Fisher exact test) and that decompensated subjects tended to be exotropic rather than esotropic, although this trend was not statistically significant. This led to a hypothesis that higher levels of stereoacuity may be protective in preventing against decompensation in patients with MFS. However, a subsequent and larger study (Siatkowski RM, et al, Association for Research in Vision and Ophthalmology, 1997, Abstract B426) found no difference between stable and decompensated MFS patients with respect to angle of strabismus, underlying etiology, or level of stereoacuity. This study measured stereopsis prospectively with both contour and random dot tests; for subjects with less than 3000 arc seconds of stereoacuity, a computer-generated haploscopic display was created that could measure levels of stereopsis up to 10,000 arc seconds. Even with this device, no significant difference in stereoacuity was found between the groups.

Several other investigators have commented on long-term instability in patients with small-angle strabismus. Undoubtedly, some of these patients would meet criteria for decompensated MFS, but as these reports are incomplete in their clinical data, exact comparison is rarely possible. In 1974 Lang[28] noted 66 children (part of a larger series) with increasing angles of esotropia. However, 92% of these patients had increasing levels of hyperopia, a high accommodative convergence to accommodation ratio, or both; the remaining 8% had amblyopia. Thus these cases seem to be more parallel to the phenomenon described by Wisnicki,[29] in which primary micro-esotropes or esotropes with an accommodative component develop increasing uncorrected hyperopia causing an increase in their manifest angle. Clarke and Noel[30] also noted an increase in angle of strabismus in patients with small-angle esotropia after extensive patching for amblyopia, presumably due to conversion of a large phoria to a tropia with prolonged disruption of binocularity. These previously described patients have very different characteristics than the adults in this study.

In 1989 Arthur and colleagues[31] reported on the long-term stability of ocular alignment in patients with MFS. They found that over a mean period of 17.5 years, 26% of monofixators developed an increase in their horizontal misalignment to greater than 8 PD. Although this study relied on mean survival curves to extrapolate long-term data and included no sensory information, it definitively refutes the concept of long-term stability in these cases. Arthur and colleagues also compared unstable MFS cases to unstable cases of non-MFS strabismic patients (in whom the angle of ocular misalignment was larger than 8 PD). There was no difference between these groups with respect to initial alignment or age at diagnosis, but the MFS patients were surgically aligned earlier than the non-MFS subjects. They also noted a large difference in the mean time to instability (decompensation) between monofixating and non-monofixating strabismic patients, 32.2 years vs 9.8 years. Thus they did support the notion by Parks that the development of MFS is relatively (but not absolutely) protective against instability in motor angle. Interestingly, in a 1986 presentation at the American Academy of Ophthalmology, Parks noted, "Never can the ophthalmologist conclude, regardless of the patients' age, that once the treatment has successfully aligned the strabismic eyes they will remain straight."[32] Several years later, Shauly and colleagues[33] reported that between one-fifth and one-fourth of patients with microtropia or small-angle esotropia following surgery for infantile esotropia developed a larger angle over time. However, Rowe[34] noted that in 40 patients who were initially treated for infantile esotropia before 2 years of age, none developed a deviation beyond 10 PD over a mean follow-up period of 7 years (range, 4-10 years).

In her excellent 2001 Scobee Memorial Lecture, Arnoldi[35] also reported on long-term motor instability over time in patients with MFS, occurring in approximately one-quarter of small-angle esotropes and almost one-half of small-angle exotropes or hypertropes. She found that motor stability was associated with higher levels of both motor and sensory fusion as well as stereopsis. Instability was correlated with the presence of oblique dysfunction, pattern strabismus, amblyopia, and change in refractive error. However, the incidence of adults with diplopia in her study is not clear, since a change in alignment was the a priori definition of instability.

In 2005 Hunt and Keech[36] reported on the "deteriorated monofixation syndrome" using the Parks diagnostic criteria for the original diagnosis and subsequent development of an angle of strabismus greater than 8 PD as their definition for deterioration. They identified 29 patients from the University of Iowa database, all but one of whom had a history of esotropia. Nine patients (31%) complained of diplopia, and 20 (69%) had a history of amblyopia. All but one patient underwent surgical correction of their deteriorated angle, with 48% regaining MFS status postoperatively. However, 4 of the 9 patients with diplopia continued to experience diplopia after treatment. In the Hunt and Keech series, there was also a trend for patients with diplopia to do more poorly after surgery, that is, not to regain monofixational status. Thus these investigators also clearly demonstrate the capacity for patients with MFS to change with time; however, their work does not include any detailed sensory or psychophysical data that might help to elucidate the etiology of the deterioration.

Thus it is clear that the body of literature on this topic, including both my previous work as well as that of others, provides no compelling evidence for a definitive etiology of decompensation in patients with MFS. Given the lack of any reproducible association between decompensation and the gamut of clinical factors routinely evaluated (eg, level of stereopsis, presence of oblique dysfunction or dissociated strabismus, density of amblyopia), consideration of a different causative defect is necessary. Since central (foveal) fusion is by definition impaired in MFS, a reasonable and testable hypothesis is that, despite the statements of Parks to the contrary, *peripheral fusion is abnormal* in these subjects and is associated with decompensation, diplopia, and a change in strabismus pattern. The purpose of this study was to compare clinical characteristics of adults with stable vs decompensated MFS to attempt to identify fusional defects that may predispose to decompensation and to evaluate the prognosis after treatment for decompensated cases.

METHODS

This study protocol was submitted in 2006 and subsequently approved by the Institutional Review Board of the University of Oklahoma Health Sciences Center. The initial step was a diagnosis-sorted review of medical records of patients seen by this author from 1999 forward to identify potential subjects, followed by subject contact and assessment of potential interest in participation. Additional subjects were prospectively recruited as they were evaluated clinically. Eligible subjects were 18 years of age or older with a history of MFS and on chart review ocular misalignment of less than 8 PD, stereoacuity of no better than 60 arc seconds, Worth 4-dot fusion at near, and suppression of one eye at distance. The diagnosis of MFS and the patients' prior ophthalmologic history were confirmed via review of prior optometric, ophthalmologic, and/or surgical records, patient and parental history, and examination of old photographs when available or pertinent. Subjects were considered decompensated if they had a chief complaint of acquired, bothersome binocular diplopia, with or without a change in their angle of strabismus. Stable subjects were those patients with MFS with no diplopia or other visual complaints, and no recent change in ocular alignment. Patients were excluded if they had ocular disease that produced a nonrefractive change in visual acuity by more than 1 Snellen line (eg, cataract, epiretinal membrane) or a neurologic condition that could affect ocular motility or fusional capacity (eg, brainstem stroke, multiple sclerosis).

After discussion of the risks and benefits, and after obtaining informed consent, all subjects underwent a detailed record review, ophthalmologic examination, and orthoptic evaluation. Historical data obtained included the age at which decompensated patients became visually symptomatic; number of prior strabismus surgeries; history of glasses wear, patching, or other amblyopia therapy; treatment with orthoptic exercises; the age at which their original motility diagnosis occurred and was treated; and the original condition (infantile esotropia, esotropia with accommodative component, constant or intermittent exotropia, vertical strabismus, primary MFS, unknown). Patients' spherical equivalent refraction and astigmatism status in each eye were recorded, as was the presence of anisometropia of more than 1 diopter (D) in either the spherical or cylindrical correction.

Examination consisted of measurement of linear Snellen visual acuity in each eye, measurement of muscle balance at distance and near in the primary position by simultaneous and alternate prism cover tests, assessment of the presence of dissociated strabismus complex—which in our cases was always dissociated vertical deviation (DVD)—pattern strabismus, and ductions and versions. Sensory evaluation consisted of measurement of contour (Titmus test; Titmus Optical Company, Petersburg, Virginia) and random dot (Randot test; Titmus Optical Company, Petersburg, Virginia) stereoacuity; strength of Bangerter foil at which fixation preference switched; Worth 4-dot responses (constant or intermittent fusion, suppression of one eye or alternate suppression, diplopia, indeterminate); assessment of response to the 4-D base-out prism test (normal, suppression of one eye, alternate suppression); and response to the Bagolini glass test (NRC or ARC, with or without suppression). The following tests were performed on a synoptophore: measurement of torsional fusional amplitudes, subjective fusional responses using both simultaneous perception and fusion (partially similar image) slides, and assessment of retinal correspondence (NRC, harmonious vs unharmonious ARC, or complete suppression of one eye). Horizontal and vertical fusional amplitudes were also measured at both distance and near in free space.

For the cross-sectional comparison of these two groups, and based on the type of data obtained for each variable, appropriate statistical analysis was performed comparing subjects with stable vs decompensated MFS. Fisher's exact test was used to compare proportions, and two-sample *t*-tests were used to compare means of interval level variables. Measurements made with the Titmus and Randot tests did not meet the distributional assumptions of the *t*-test and so for these variables the groups were compared with the Mann-Whitney nonparametric test. All *P* values were two-sided (two-tailed). Cumulative proportions of incident decompensated MFS cases were calculated with the Kaplan-Meier product-limit estimate method. Despite numerous tests of statistical significance evaluated in this study, no multiple comparison adjustment was applied. This was to prevent an increase in type II (beta) error, although there is the possibility of alpha inflation as a result.

RESULTS

From August 1, 1999, to July 31, 2009, this author evaluated a total of 12,079 individual patients (not patient visits) at the Dean McGee Eye Institute/Department of Ophthalmology, University of Oklahoma College of Medicine. Of these, 221 (1.84%) met criteria for diagnosis of MFS. Of these 221, 26 (11.8%) met criteria for the definition of decompensated MFS. (An additional 6 patients with prior MFS and an increase in their angle of strabismus were found but excluded from this study since they had no diplopia; including these, 14.5% of patients with MFS had a change in their motor or sensory status). Of the 26 patients with diplopia, 6 were excluded because they were under 18 years of age, 3 were excluded due to neurologic disease (2 cases of stroke and 1 case of myasthenia gravis), and 1 was excluded due to an overlying functional or nonphysiologic component to her responses. A total of 16 eligible adult subjects with decompensated MFS remained. Of these, 14 (87.5%) consented to be part of this study. Of these 14, 10 were evaluated and treated prospectively in their decompensated condition; 4 had been treated for decompensated MFS by this author prior to the start of the study. For these 4, retrospective data from chart review prior to treatment for decompensation was extracted. An additional 16 patients with stable MFS were randomly selected as controls, matched by age and sex as closely as possible. None of the subjects in the control group had undergone surgery for decompensated MFS; additionally, none of the subjects in either cohort in this study were related to one another.

Because the patients who had been treated for decompensated MFS prior to the start of the study did not have complete data sets at the time they were in the decompensated state, statistical analysis was performed both with and without these 4 decompensated patients.

The groups were strikingly similar with respect to baseline demographic and clinical characteristics (Table 1). There was no difference between stable and decompensated MFS patients with respect to age at study examination, glasses wear, history of patching or orthoptic exercises, or number of prior strabismus surgeries. There was no significant difference between the groups in interocular visual acuity difference, or in the presence or absence of amblyopia (with definitional cutoffs of 1, 2, or 3 or more lines difference between groups). The two groups were also similar with respect to the mean difference in refractive error between eyes, the prevalence of more than 1 D of spherical and cylindrical anisometropia, and the amount of astigmatism. (Additional analysis, not listed in Table 1, also showed no difference in proportion of eyes with cylinder axis >15 degrees from either 90 or 180 degrees).

TABLE 1. HISTORICAL AND CLINICAL FEATURES OF PATIENTS WITH STABLE AND DECOMPENSATED MONOFIXATION SYNDROME

CHARACTERISTICS	DECOMPENSATED*	STABLE	*P* VALUE*
Mean age (SD)	47.8 (15.9) / 45.3 (16.7)	37.4 (20.1)	.180/.259
Mean age in years at original diagnosis (SD)	21.5 (26.5) / 16.6 (23.5)	4.7 (4.0)	.076/.084
Glasses wear	9 (90%) / 13 (93%)	16 (100%)	.39/.47
Prior patching therapy	2 (20%) / 3 (21%)	5 (31%)	.44/.69
Prior orthoptic treatment	1 (10%) / 2 (14%)	4 (25%)	.34/.66
Number of prior strabismus surgeries			.12/.13
0	5 (50%) / 8 (57%)	7 (44%)	
1	1 (10%) / 1 (7%)	3 (19%)	
2	1 (10%) / 2 (14%)	3 (19%)	
3	3 (30%) / 3 (21%)	0	
4	0/0	3 (19%)	
Mean interocular logMAR acuity difference (SD)	0.09 (0.13) / 0.07 (0.11)	0.07 (0.14)	.77/.83
Presence of amblyopia			.38/.38
1-line IOD	1 (10%) / 1 (7%)	3 (19%)	
2-line IOD	1 (10%) / 1 (7%)	2 (13%)	
≥3-line IOD	2 (20%) / 2 (14%)	1 (6%)	
Original diagnosis			.63/.79
Infantile ET	5 (50%) / 5 (39%)	5 (31%)	
Accommodative ET	1 (10%) / 3 (23%)	5 (31%)	
XT or X(T)	1 (10%) / 2(15%)	1 (6%)	
Vertical	0/0	0	
Primary	3 (30%) / 3 (23%)	4 (25%)	
Unknown	0/0	1 (6%)	
Mean SEQ interocular			
Refractive error difference (SD)	1.14(0.93) / 0.99(0.83)	0.61 (1.22)	.25/.33
Anisometropia >1 D	6 (60%) / 6 (43%)	2 (25%)	.11/.44
Mean (SD) of average cylinder (D)	0.86 (0.60) / 0.75 (0.57)	0.94 (1.06)	.84/0.56
Anisoastigmatism >1 D	2 (20%) / 2 (14%)	1 (6%)	.54/0.59
Age at onset decompensation symptoms (range)	37.5 / 38 (16-65)	NA	
Mean years of stability prior to decompensation	23.1 / 26.5	NA	
Mean years of symptoms prior to diagnosis (range)	4.6 / 4.6 (0.5-15)	NA	

D, diopters; ET, esotropia; IOD, interocular difference; NA, not applicable; SD, standard deviation; SEQ, spherical equivalent refractive error equivalent; XT, exotropia; X(T), intermittent exotropia.
*Calculated without/with cases treated entirely prior to inception of study.

Similarly, there was no difference between groups in the distribution of original diagnosis preceding the development of MFS; however, there was a trend for the decompensated MFS group to have received their original diagnosis and treatment much later than the stable group (21.5 vs 4.7 years [*P*=.076, two-sample *t*-test] for patients studied prospectively; 16.6 vs 4.7 years [*P*=.084, two-sample *t*-test] including all decompensated patients). The mean age at onset of symptoms in the decompensated patients was 38 years (range, 16 to 65 years). Decompensated patients had been stable without symptoms for 23 to 26 years on average. Symptoms persisted for a mean of 4.6 years (range, 6 months to 15 years) prior to diagnosis of decompensated MFS. A few significant differences in motor findings between the groups were evident. Decompensated MFS patients were more likely than stable MFS patients to have a vertical deviation (50% vs 6%, *P*=.018/.012, Fisher's exact test), and the mean deviation of vertical strabismus tended to be larger in decompensated patients (1.1 PD vs 0.1 PD, *P*=.055/.025, two-sample *t*-test). There was a trend toward a larger distance angle of strabismus (irrespective of direction of deviation) among decompensated patients (*P*=.053/.004, two-sample *t*-test) and a larger angle of esotropia by alternate prism and cover testing in the decompensated group (10.9 PD for prospective cases and 17.7 PD for all

decompensated cases vs 6.89 PD for stable cases, *P*=.021/.008, two-sample *t*-test). There was a trend toward a larger esophoria at both near (*P*=.071/.069, two-sample *t*-test) and distance (*P*=.070./057, two-sample *t*-test) in decompensated patients, but the clinical significance was minimal, with mean differences only approximately 3 PD. Otherwise, stable and decompensated MFS patients did not differ with respect to the presence of DVD, ductional or versional abnormalities, pattern strabismus, and other aspects of horizontal strabismus (Table 2).

TABLE 2. CLINICAL MOTOR FEATURES OF PATIENTS WITH DECOMPENSATED VERSUS STABLE MONOFIXATION SYNDROME

CHARACTERISTICS	DECOMPENSATED*	STABLE	*P* VALUE*
Presence of vertical deviation	5 (50%) / 7 (50%)	1 (6%)	.018/.012
Presence of DVD	1 (10%) / 2 (14%)	3 (19%)	.50/.99
Full versions	7 (70%) / 10 (71%)	9 (56%)	.39/.47
Presence of pattern strabismus	0/0	0	
Mean angle of strabismus (SD)			
Distance SPCT	5.9 (3.4) / 6.25 (4.1)	4.3 (3.3)	.25/.18
Distance APCT	8.5 (5.0) / 11.1 (6.6)	5.1 (3.6)	.053/.004
Near SPCT	6.4 (4.9) / 7.6 (7.2)	5.6 (4.5)	.34/.18
Near APCT	8.6 (5.6)11.4(9.6)	5.2 (4.6)	.10/.039
Vertical	1.1 (1.4) / 1.1 (1.5)	0.1 (.05)	.055/.025
Mean angle distance strabismus (SD)			
Esotropia			
SPCT	7.1(3.2) / 6.5(3.5)	6.44(2.4)	.63/.039
APCT	10.9(3.8) / 17.7(5.4)	6.89 (2.3)	.021/.008
Exotropia			
SPCT	2.5(2.1) / 6.3(6.8)	2.8 (2.2)	.90/.36
APCT	2.5(2.1) / 8.3(10.2)	4.8 (4.1)	.52/.54
Mean angle near strabismus (SD)			
Esotropia			
SPCT	6.5(5.1) / 5.9(5.8)	6.1 (3.5)	.71/.91
APCT	10.2(6.5) / 13.1(8.9)	6.0 (3.7)	.14/.043
Exotropia			
SPCT	7.3(3.1) / 11.8(9.2)	5.8 (6.2)	.71/.32
APCT	7.3(3.1)13.0(11.6)	7.3 (5.6)	.98/.41
Mean deviation, signed tropias†			
Distance SPCT	−5.0 (6.8) / −3.0 (7.3)	−3.0 (4.6)	.33/.99
Distance APCT	−7.9 (6.8) / −7.8 (11.2)	−2.8 (5.7)	.055/.12
Near SCPT	−1.9 (8.6) / 0.5 (11.1)	−1.6 (6.3)	.93/.52
Near APCT	−3.6 (10.0) / −4.1 (15.3)	−1.5 (6.9)	.53/.55
Phorias (APCT-SPCT)			
Distance			
ET	3.7 (4.8) / 4.5 (5.0)	0.44 (1.3)	.070/.057
XT	0.0 (0.0) / 2.0 (3.5)	2.0 (4.0)	.54/.99
All	2.9 (4.5) / 3.8 (4.6)	1.0 (2.5)	.23/.091
Near			
ET	3.7 (4.3) / 4.3 (4.9)	0.5 (1.4)	.071/.069
XT	0 (0)/1.3 (2.5)	1.5 (3.0)	.44/.90
All	2.4 (3.8) / 3.5 (4.5)	0.8 (2.0)	.23/.072

APCT, alternate prism and cover test; DVD, dissociated vertical deviation; ET, esotropia; SD, standard deviation; SPCT, simultaneous prism and cover test; XT, exotropia.*Calculated without/with cases treated entirely prior to inception of study.†Negative values indicate an esodeviation; positive values, an exodeviation.

Sensory responses to various tests differed between groups (Table 3). Decompensated patients had significantly poorer convergence and divergence fusional amplitudes. Convergence amplitudes averaged 16.9 PD vs 6.4 PD (*P*=.001, two-sample *t*-test) at distance and 20.6 vs 8.1 PD (*P*=.004, two-sample *t*-test) at near. Mean divergence amplitudes were 9.9 PD vs 4.0 PD at distance (*P*=.049, two-sample *t*-test) and 11.3 PD vs 4.5 PD at near (*P*=.010, two-sample *t*-test). Vertical fusional amplitudes were similar between groups, but the decompensated patients had significantly larger cyclovertical amplitudes than the stable groups.

TABLE 3. CLINICAL SENSORY FEATURES OF PATIENTS WITH DECOMPENSATED VERSUS STABLE MONOFIXATION SYNDROME

CHARACTERISTICS	DECOMPENSATED* (SD)	STABLE (SD)	*P* VALUE*
Fusion amplitudes			
Distance (PD)			
BO	6.4 (5.2)	16.9 (8.7)	.001
BI	4.0 (3.4)	9.9 (7.5)	.049
BD	3.4 (3.9)	5.0 (3.6)	.40
BU	3.6 (4.1)	4.7 (3.2)	.54
Near (PD)			
BO	8.1 (8.0)	20.6 (10.4)	.004
BI	4.5 (3.3)	11.3 (10.8)	.10
BD	4.8 (3.6)	7.4 (6.5)	.41
BU	3.4 (3.0)	6.3 (5.90)	.30
Excyclovergence (degrees)	9.1 (2.7)	3.3 (1.5)	<.001
Incyclovergence (degrees)	7.1 (4.3)	3.1 (1.9)	.041
Mean Bangerter strength	0.24 (0.40)	0.16 (0.22)	.58
Mean stereoacuity (arcsec)			
Titmus (range)	1700 (80-blind)/400 (80-blind)	400 (50-blind)	.59/.61
Measurable	7 (70%)/10 (71%)	13 (81%)	.64/.68
Randot (range)	Blind (0-blind)	600 (100-blind)	.76
Measurable	4 (44%)	9 (56%)	.69
Worth 4-dot, near			.56/.37
Fusion			
Constant	7 (70%)/10 (71%)	11 (69%)	
Intermittent	0/0	2 (13%)	
Suppression			
One eye	1 (10%)/1 (10%)	1 (7%)	
Alternate	1 (10%)/1 (10%)	2 (13%)	
Diplopia	1 (10%)/2 (14%)	0	
Worth 4-dot, distance			.046/.027
Fusion			
Constant	3 (30%)/3 (21%)	5 (31%)	
Intermittent	0/0	2 (13%)	
Suppression			
One eye	1 (10%)/2 (14%)	8 (50%)	
Alternate	3 (30%)/4 (29%)	3 (19%)	
Diplopia	3 (30%)/5 (36%)	0	
Bagolini responses			.23
No suppression	6 (75%)	7 (47%)	
Suppression	2 (25%)	8 (53%)	
Synoptophore fusion slides			.49
Fusion	7 (70%)	12 (75%)	
No fusion	1 (10%)	3 (19%)	
Indeterminate	2 (20%)	1 (6%)	
Simultaneous perception slides			.44
NRC	4 (40%)	9 (56%)	
Harmonious ARC	1 (10%)	3 (19%)	
Unharmonious ARC	4 (40%)	2 (13%)	
Total suppression	1 (10%)	2 (13%)	

ARC, anomalous retinal correspondence; BD, base down; BI, base in; BO, base out; BU, base up; NRC, normal retinal correspondence; PD, prism diopters; SD, standard deviation. *Calculated without/with cases treated entirely prior to inception of study.

Mean excyclovergence amplitudes were 9.1 degrees in the decompensated group vs 3.3 degrees in the stable group ($P<.001$, two-sample *t*-test); incyclovergence amplitudes were 7.1 degrees vs 3.1 degrees ($P=.041$, two-sample *t*-test). There were no significant differences in the density of Bangerter foil strength required to switch fixation or responses to Bagolini lens testing or amblyoscope testing with either fusion or simultaneous perception slides. Worth 4-dot responses at near were similar between decompensated and

stable patients, whereas at distance there was a greater tendency for stable patients to constantly suppress the same eye and for decompensated patients to report diplopia (*P*=.046/.027, Mann-Whitney test).

Levels of both contour and random dot stereoacuity were similar between groups. Since the lowest level of stereoacuity testable on both the Titmus and Randot tests is 3000 arc seconds, data were analyzed in two ways. In the first analysis, patients who had no measurable stereoacuity on either test were assigned an arbitrary score of 5000 arc seconds, and data were analyzed with the Mann-Whitney rank sum test rather than the *t*-test. In the second analysis, the proportion of patients in each group who had no measurable stereoacuity on either test was evaluated. There was no significant difference between groups with either analysis, both including and excluding the cases with data prior to treatment.

Table 4 shows the workup each decompensated patient underwent prior to the diagnosis. Among 14 patients, 5 neuroimaging studies and 1 orbital echogram were performed. Patients had a mean of 2.71 prior examinations and had received a mean of 2.57 prior pairs of glasses, including 5 patients with 4 or more examinations and 3 patients with 5 or more pairs of glasses. Only 1 patient among all 14 decompensated cases received the diagnosis of decompensated MFS on the first visit to a medical care provider.

TABLE 4. PRIOR WORKUP AND MANAGEMENT OF PATIENTS WITH DECOMPENSATED MONOFIXATION SYNDROME

PATIENT	EVALUATIONS AND TESTS	COST IN 2009 DOLLARS (CHARGE/MEDICARE ALLOWABLE)*
1	MRI, CT, orbital echography, 1 eye exam, 1 neuro exam	$3155 / $1130.18
2	3 eye exams, 6 pairs glasses	$1506 / $1074.06
3	MRI, 2 pairs glasses, 1 eye exam, 1 neuro exam	$1607 / $988.85
4	1 eye exam, 1 pair glasses	$376 / $232.02
5	MRI, edrophonium test, 4 eye, 1 neuro exam	$2005 / $1092.54
6	1 eye exam, 2 pairs glasses	$452 / $358.02
7	4 eye exams, 10 pairs glasses	$2260 / $1684.08
8	No prior workup	0
9	MRI, 3 neuro exams, 1 eye exam	$1565 / $908.36
10	2 eye exams, 2 pairs glasses	$752 / $464.04
11	4 eye exams, 2 pairs glasses	$1252 / $676.08
12	3 eye exams, 2 pairs glasses	$1002 / $570.06
13	3 eye exams, 5 pairs glasses	$1380 / $948.06
14	5 eye exams, 4 pairs glasses	$1754 / $1034.10
Mean		$1168 / $797

CT, computed tomography; MRI, magnetic resonance imaging.*2009 Dean McGee Eye Institute charges and Oklahoma Medicare reimbursements of: Level III evaluation, $105/$56.85; Level IV evaluation, $155/$85.76; sensorimotor exam, $95/$49.17; MRI brain with/without gadolinium, $1000/$545.06; CT head with/without contrast, $450/$243.34; intravenous edrophonium chloride test, $90/$37.35; prism glasses, $126/$126.

Table 5 provides selected individual clinical details on the 14 decompensated patients. Most patients had a prior diagnosis of esotropia (5 infantile and 3 with an accommodative component). Three had primary MFS and 2 had intermittent exotropia, presumably monofixational in nature. The mean age (and range) at onset of decompensation was 39.6 years (range, 16-53 years) for patients who had infantile esotropia, 43.3 years (range, 30-63 years) for those with an accommodative component to their esotropia, 45 years (range, 23-65 years) for the primary monofixators, and 18 and 53 years for the 2 exotropes. One patient's original diagnosis could not be definitively determined from old record review, although it was clear that he had some type of esotropia.

All but 1 decompensated patient underwent treatment. Six had strabismus surgery, 4 were treated with orthoptic exercises, 3 were treated with prisms, and 2 were prescribed a change in glasses without prisms. One patient was treated with Bangerter foil occlusion. Among the patients who were treated surgically, a monofixational angle of strabismus was achieved in all cases postoperatively, with a follow-up of at least 15 months in each case. However, contour stereopsis improved (defined as at least a 2-octave increase on the Titmus test) in only 1 of these patients postoperatively; an improvement in stereopsis was noted in 1 additional patient who was treated with orthoptic fusional vergence exercises. Prior to treatment, as part of our diagnostic criteria, all patients suffered diplopia. After treatment, 77% of patients had an improvement in their symptoms, with 9 patients being diplopia-free and 1 patient who had had prior constant diplopia experiencing only intermittent diplopia. Two patients who before treatment had constant diplopia and 1 who had intermittent symptoms remained unchanged.

Table 6 provides additional clinical information on the decompensated patients, including the number of years each patient had been stable prior to onset of symptoms and individual horizontal and torsional fusional amplitudes, where data is available. Convergence and divergence amplitudes at distance and near were measured in free space, whereas cyclofusional amplitudes were assessed on the synoptophore using a target that subtended a visual angle of 9 degrees horizontally and vertically. Further details regarding these data will be addressed in the next section.

TABLE 5. TREATMENT AND OUTCOME OF PATIENTS WITH DECOMPENSATED MONOFIXATION SYNDROME

PATIENT	ORIGINAL DIAGNOSIS/AGE AT DECOMPENSATION	TREATMENT	ANGLE OF STRABISMUS*		STEREOPSIS (ARCSEC)		DIPLOPIA	
			Pre	Post	Pre	Post	Pre	Post
1	Infantile ET/16	declined rx	ET 12	NA	NMS	NA	int	NA
2	Primary/47	prism, orth	ET 8	LH 2	200	200	const	const
3	Infantile ET/53	prism, orth	XT 10	ortho	NMS	NMS	int	none
4	Primary/65	prism	RHT 4	RHT 4	100	100	const	none
5	Infantile ET/38	EMS	ET 14	ET4	200	200	const	int
6	Accommodative ET/37	EMS	ET 10	ortho	400	200	int	none
7	Infantile ET/46	EMS	ET 14	ET 4	NMS	NMS	int	none
8	Infantile ET/45	Bang	XT 4	XT 4	NMS	NMS	int	int
9	Primary/23	orth	ET 14	ET 4	80	80	const	const
10	X(T)/53 orth	orth	XT 8	X 1	3000	100	const	none
11	Accommodative ET/30	glasses	ET 14	ET 4	3000	3000	int	none
12	X(T)/18	EMS, glasses	XT 30	X 2	400	100	int	none
13	Accommodative ET	EMS	ET 14	ET 1	100	100	const	none
14	ET/46	EMS	ET 30	ET 8	NMS	NMS	int	none
Summary			100% with MFS angle of strabismus		2 of 13 with 2 octave difference		9 of 13, none2 of 13, int2 of 13, const77% improved	

Bang, Bangeter filter; const, constant; EMS, eye muscle surgery; ET, esotropia; int, intermittent; LH, left hyperphoria; NA, not applicable; NMS, no measurable stereopsis; orth, orthoptic exercises; ortho, orthotropic; RHT, right hypertropia; X, exophoria; X(T), intermittent exotropia. *Measurements represent results of alternate prism and cover testing.

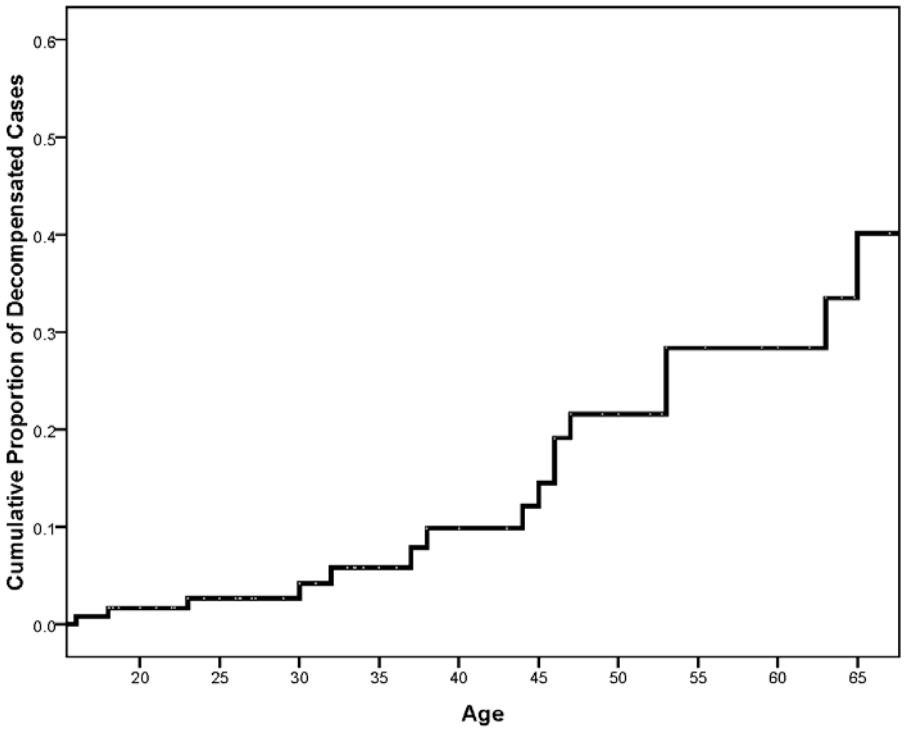
TABLE 6. FUSIONAL AMPLITUDES OF INDIVIDUAL PATIENTS WITH DECOMPENSATED MONOFIXATION SYNDROME

PATIENT	FUSIONAL AMPLITUDES			
	CONVERGENCE DISTANCE/NEAR(PD)	DIVERGENCE DISTANCE/NEAR(PD)	EXCYCLOVERGENCE (DEGREES)	INCYCLOVERGENCE (DEGREES)
1	1/1	1/1	10	4
2	25/4	no data	10	4
3	1/10	6/1	12	10
4	2/4	6/1	12	7
5	8/6	8/6	8	5
6	12/12	8/6	No data	No data
7	18/12	8/10	7	7
8	1/1	2/4	4	3
9	14/14	No data	No data	No data
10	2/2	2/2	15	12
11	No data	No data	No data	No data
12	No data	No data	No data	No data
13	No data	No data	No data	No data
14	No data	No data	No data	No data

PD, prism diopters.

DISCUSSION

Although occurring in a minority of cases, loss of stability of motor and/or sensory status in patients with previously static and asymptomatic MFS constitutes an important clinical entity. In this series, a change in either the angle of strabismus and/or the onset of diplopia occurred in 32 of 221 (14.5%) of all MFS patients (adults and children) seen by a single physician over a decade. Sixteen adult patients (7.2%) with MFS experienced new-onset binocular diplopia during this period. These patients represent 0.13% to 0.27% of all patients seen in an academic practice of pediatric ophthalmology, strabismus, and neuro-ophthalmology. Although the denominator and time period are unclear, these data are not markedly disparate from the report by Hunt and Keech[36] of 29 deteriorated MFS patients, presumably seen over several decades at the University of Iowa, and the calculation of Arthur and colleagues[31] that 26% of MFS patients developed a decompensation over a mean 17.5-year period. In the current study, all cases of stable MFS patients were diagnosed prior to age 18; therefore, it makes good sense to calculate risk of decompensation in adults with MFS (aged 18 years or older) relative to age. Analyzing all of the adults with MFS (age range, 20-95 years) evaluated over the 10-year period of this study, one can derive a Kaplan-Meier analysis of the rate of cumulative decompensation over time (Figure). (The 109 MFS patients seen only as children cannot contribute meaningfully to the risk estimate because they have not had a chance to decompensate yet and are not included in the Kaplan-Meier curve.) Additional data regarding the decompensation rates is available in Table 7. This curve suggests that the risk of decompensation is modest (<5%) for individuals under 30 years of age but increases linearly through the sixth decade of life to involve 20% to 30% of MFS cases. For older ages, the study's sample size is relatively small, but the data suggest that for every decade of life beyond age 40, an additional 10% of previously stable patients with MFS decompensate.



FIGURE

Kaplan-Meier curve of rate of decompensation for 112 adults with monofixation syndrome seen over a 10-year period.

Lang[37] estimated the prevalence of microtropia to be approximately 1% in the general population, similar to the estimated prevalence of MFS.[25] As noted in the "Introduction" section, heredity may play a role in the etiology of MFS, with 9% of first-degree relatives of patients with infantile esotropia demonstrating MFS.[25] Cantolino and von Noorden[38] also found microtropia in 25% of first-degree relatives in a series of 20 patients with the same condition, and Lang[39] noted a higher incidence of microtropia in monozygotic twins with ocular motility disorders. Cibis[40] reported microtropia in almost half of all treated esotropes and one-quarter of treated exotropes in a series of over 500 consecutive patients in his practice. Excluding twin cases and disregarding the clinical overlap in some cases of microtropia vs MFS, up to 3.2 million persons in the United States may have MFS. According to the analysis of Arthur and colleagues,[31] 26% of patients with MFS experience a worsening of alignment over a 17.5-year period. Of our patients with worsening alignment, 62% experienced diplopia, and in the series by Hunt and Keech,[36] 29% had double vision. Averaging these rates of diplopia and assuming a linear rate of decompensation per annum, slightly over 20,000 patients annually in this country would present with diplopia following decompensation of a previously stable monofixational state.

TABLE 7. CUMULATIVE PROPORTION OF PATIENTS WITH DECOMPENSATION OF MONOFIXATION SYNDROME WITH AGE IN DECADES

AGE	PROPORTION DECOMPENSATED (SE)	NUMBER OF PATIENTS REMAINING STABLE
20	1.7% (1.2%)	112
30	4.2% (2.1%)	64
40	9.1% (3.8%)	41
50	21.6% (5.9%)	28
60	28.4% (7.1%)	17
70	40.0% (9.7%)	6

SE, standard error.

There are approximately 1,000 practicing pediatric ophthalmologists and approximately 400 practicing neuro-ophthalmologists in the United States. Assuming that 75% of decompensated diplopic patients would eventually be evaluated by a pediatric ophthalmologist, strabismologist, or neuro-ophthalmologist, then each such provider would see on average about 11 new such patients annually. Using the numbers provided in this study (7% of adults with MFS decompensating with diplopia over a decade, and 10% per decade new compensations after age 40), along with the assumptions discussed above, would result in a figure of about 12 new decompensated MFS patients annually per pediatric ophthalmologist, strabismologist, or neuro-ophthalmologist in the United States. The results of these two calculations are remarkably similar; although these figures may seem higher than what occurs in practice, they are certainly plausible, especially since the prevalence data are likely inflated given the selection bias of patients seen in a tertiary care, university setting. Adults with diplopia are commonly evaluated in clinical practice, and many cases in which there is no neurologic or orbital explanation for symptoms are diagnosed as "decompensated phorias" or "long-standing strabismus"; it is likely that a more detailed analysis of some proportion of these patients would support a diagnosis of decompensated MFS. Additionally, there remains the possibility that a relatively large number of patients aged 40 or older with decompensated MFS are either being seen by primary care vision providers (comprehensive ophthalmologists and optometrists) or simply not seeking care at all.

The MFS patients in our study, by definition, met the Parks criteria for diagnosis,[21] but their sensorial adaptations are similar to others throughout the world who have reported on MFS, microtropia, and similar conditions since his AOS thesis was published.[41-45] The question remains, What causes these patients who have been stable and asymptomatic, generally for decades, to decompensate? Kushner[46] has written eloquently of the development of diplopia in adults with long-standing strabismus who had been asymptomatic for years. In his algorithm, the majority of such patients with new binocular diplopia have experienced a change in their angle of strabismus. The second most common cause was a change in refractive need or correction, that is, onset of presbyopia, latent hyperopia in an accommodative esotrope, or fixation switch diplopia due to change in acuity in the dominant eye. His series reported a success rate of 84% after changing optical correction and/or performing strabismus surgery. However, it is unclear what proportion of the patients in this study had decompensated MFS. Only 2 of our decompensated patients were treated with a change in glasses prescription (1 with accommodative esotropia and 1 with intermittent exotropia who also underwent surgery), and both were successful. Thirteen of our patients with MFS did experience an increase in their angle of strabismus (although only 6 were treated surgically); of the 12 who were treated, 10 (83%) experienced an improvement in symptoms.

Pratt-Johnson and Tillson[47] have commented on the possibility of unstable or variable suppression patterns in patients with strabismus. Their work clearly supports the contention of Parks of a stable, small central scotoma and NRC in patients with MFS. Hence it is unlikely that any type of variable hemiretinal suppression (like that which can operate in patients with larger angles of strabismus and ARC) plays a role in the decompensation of MFS patients. Arnoldi[35] found the presence of stereopsis to be protective against motor deterioration in patients with MFS, but in this series and in this author's work in this area, neither the presence nor the degree of stereopsis was associated with stability in monofixators. Hahn and colleagues[48] found higher degrees of stereopsis in patients with a later onset of strabismus who eventually developed MFS, implying a shorter period of misalignment prior to treatment. This study found an important trend in this regard, namely, that stable adult patients had been initially diagnosed and treated, on average, over a decade earlier than decompensated adults with MFS. Although not statistically significant, this difference is likely clinically important and represents a real trend, since the mean age of stable and decompensated subjects was similar; additionally, there is no concern for selection bias, since age at initial diagnosis was not part of the selection criteria. Thus, minimizing the period of initial ocular misalignment by treating patients more promptly probably confers the benefit of a higher likelihood of stability through adulthood once MFS is established.

There was no difference between stable and decompensated MFS patients in the antecedent strabismic conditions prior to the development of MFS or in the prevalence of primary monofixators between groups. Like most other series,[21,31,35] this study found esotropia, particularly infantile esotropia, to be the most common original condition in adults with MFS. The development of a stable, monofixational state has been reported in 25% to 50% of patients after surgery for infantile esotropia,[49-51] although its incidence is lower in children with myopia.[52] Esotropia with an accommodative component was our next most common diagnosis prior to development of MFS. MFS is a common outcome in such patients, with bifixation developing in only a minority after treatment.[53,54]

The next most common condition among this series of patients with decompensated disease was primary, idiopathic MFS,

occurring in 3 cases. In all such cases it was the presence of new-onset diplopia that prompted medical evaluation. Interestingly, none of these patients had a family history of strabismus in any first-degree relatives.

Two of the decompensated patients in this series had intermittent exotropia as their original diagnosis. Intermittent strabismic deviations have a greater likelihood of allowing normal binocular function than constant ones, but Molarte and Rosenbaum[55] noted bifoveation in fewer than half of patients with intermittent esotropia. Intermittent exotropia has been classically taught as a condition that develops in previously fusing individuals with normal stereopsis, and development of MFS in such patients has been considered a treatment failure. However, we now know that intermittent exotropia may in fact be monofixational from onset, based on both the higher-than-anticipated prevalence of MFS postoperatively as well as direct serial observation of such patients.[56-60] Nevertheless, there are certainly still some patients with bifoveation and intermittent exotropia who have the capacity to lose stereopsis and convert to MFS if treatment is delayed and a prolonged period of misalignment exists.[61]

The presence of anisometropia in patients with MFS has been well established. However, in this series there was no difference in the presence or degree of anisometropia (or refractive error, for that matter) between stable and decompensated patients with MFS. Although there was a trend for a higher incidence of anisometropia in decompensated cases, this was not statistically significant. Given that almost half of all mildly amblyopic (20/40 or better) anisometropes have monofixation or microtropia,[62] it is notable that none of our decompensated patients had anisometropia with orthophoria or a microstrabismus. Although the frequency of patients with this condition is not ascertainable in prior reports of decompensation or deterioration,[31,35,36] the absence of such patients among this study's decompensated group suggests that patients with anisometropia and no measurable strabismus, even if amblyopia is present, may be less likely to decompensate and develop diplopia and measureable strabismus later in life.

This study revealed no differences in the presence or degree of amblyopia between stable and decompensated MFS patients. Ganser and colleagues (NANOS, 1997, Abstract, page 2) showed a significantly lower percentage of amblyopia in decompensated compared to stable patients with MFS; in a larger study, this difference was noted only when there were 4 or more lines of difference in interocular acuity (Siatkowski RM, Oral presentation, Squint Club, 2006). This led to speculation that perhaps amblyopia was protective against diplopia and decompensation. However, given the findings of this study, as well as the presence of amblyopia in 69% of the deteriorated patients reported by Hunt and Keech,[36] it is reasonable to conclude that the presence or severity of amblyopia is not related to the possibility of future decompensation after MFS has been established. Thus, from the perspective of long-term monofixational stability, there is no rationale not to be aggressive with amblyopia management in the first two decades of life.

Although there remains no documented case in which an adult with stable, asymptomatic MFS has converted to bifoveation, the plasticity of the cortical control of the binocular visual system is not in doubt, with evidence that the function of the fusion mechanism may either improve or deteriorate over time. Matsuo and colleagues[63] and Houston and colleagues[64] have both demonstrated improved stereopsis after treatment for amblyopia or refractive error in one-quarter to one-half of children with primary microtropia. Cleary and colleagues[65] reported 9 children who had presumably originally normal binocular function but later developed anisometropia or amblyopia, with a microtropia and ARC; after treatment, equal vision in each eye was present and bifoveation was reestablished. Such improvement in binocular function has also been documented in visually mature adults. Morris and colleagues[66] reported the achievement of stereopsis of at least 200 arc seconds in 50% of subjects who had had strabismus in the first 2 years of life and underwent surgical realignment in adulthood. Kushner[67,68] has demonstrated that adults who undergo surgery for long-standing strabismus can develop postoperative fusion on the Bagolini lenses, regardless of the depth of amblyopia. Pratt-Johnson[69] even reported reestablishment of binocular vision after strabismus surgery in 2 adults with central disruption of fusion. Conversely, he has also documented central loss of fusion in adults with head trauma or long-standing cataracts.[70,71] Eustis and Parks[72] also have noted loss of bifoveation with conversion to MFS after surgical realignment in adults with acquired strabismus due to cranial mononeuropathies or thyroid eye disease.

Given such examples, it is not surprising that some patients with previously stable MFS may develop a worsening of their binocular function, including the acquired onset of binocular diplopia in the decompensated MFS. This may or may not be accompanied by a change in their ocular alignment. Such a change occurred in the majority of our patients (86%) but only was significant enough to require strabismus surgery in about half; the alignment changes in the other decompensated patients were so small as to be unnoticeable by them.

This study has identified various factors that are associated with such decompensation. First, patients who decompensated tended to be diagnosed and treated on average more than a decade later that those who remained stable; the mean age at original diagnosis for the stable monofixators was 4.7 years, as opposed to 16.6 years among all decompensated patients. Decompensated patients also had a larger angle of deviation, regardless of directionality, and tended to have larger esophorias than stable patients. Additionally, decompensated patients tended to be more likely to have a vertical strabismus (50% vs 6%, P=.012, Fisher's exact test); for those who had a vertical strabismus, it averaged only 1 PD in size, but this differed significantly in comparison with the stable patients, as only 1 stable patient had any vertical deviation.

There was a striking difference between groups with respect to horizontal fusional amplitudes, with the decompensated patients having more significantly impaired values than the stable subjects. Mean convergence amplitudes at distance were 6.4 PD for decompensated patients vs 16.9 PD in stable patients; at near they measured 8.1 PD vs 20.6 PD. Divergence amplitudes at distance were 4.0 PD in decompensated patients and 9.9 PD for stable cases; near values were 4.5 vs 11.3 PD. Stable patients also had larger vertical fusional amplitudes (2 to 3 PD larger), but this difference was not statistically significant at either distance or near.

Cyclotorsional amplitudes were also markedly different between groups. Stable patients had amplitudes of slightly over 3 degrees for both excyclovergence and incyclovergence, whereas decompensated patients had significantly larger amplitudes at 9 and 7

degrees, respectively.

These differences are quite interesting. Whereas stable patients had much better horizontal fusional amplitudes than decompensated subjects, they were still below normal values for both convergence and divergence, at both distance and at near; in fact, only one stable MFS patient had normal fusional amplitudes for all four of these values. Vergence amplitudes in individual stable patients were more abnormal at near than at distance. Stable MFS patients also tended to have greater vertical fusional amplitudes, which actually averaged in the supranormal range (4.7 to 7.4 PD), whereas the decompensated patients' vertical fusion amplitudes were normal. Stable patients had low torsional amplitudes, whereas the decompensated patients' torsional amplitudes were at the upper range of normal or supranormal. Thus the process of decompensation in MFS is accompanied by a loss of horizontal vergence amplitudes, with a corresponding increase in vertical and torsional fusional amplitudes. This concurs with a higher incidence of vertical strabismus in decompensated patients and with the fact that the binocular diplopia in all but 1 decompensated patient was horizontal and not vertical. The single patient with vertical diplopia had only a vertical deviation without horizontal misalignment.

The question then becomes, Which of these two phenomena could be an inciting mechanism for decompensation? Guyton[73] has espoused a concept of sensory torsion that is important in this regard. On the one hand, progressive loss of horizontal vergence amplitudes might allow the development of sensory torsion, with a concomitant increase in cyclovertical fusion capability (and a corresponding increase in vertical fusion amplitudes) in attempts to avoid diplopia: at some point, the cyclovertical vergence system can no longer adapt, and decompensation occurs. On the other hand, the development of sensory torsion might occur first, again with adaptative cyclofusional capability increasing until a point at which the torsional strabismus is sufficiently large that the horizontal amplitudes break down. While this study did not, unfortunately, obtain any objective measurement of fundus torsion in the study subjects, none of the decompensated patients complained of any torsional component to their diplopia.

Guyton[73] has stated that the most common abnormality in the breakdown of the ocular alignment control system is loss of fusional vergence. Secondarily, adaptation of both vergence as well as muscle length fails. Applying this scenario to decompensated MFS, loss of horizontal fusional amplitudes may produce sensory torsion (more likely excyclotorsion than incyclotorsion). In attempts to prevent torsional diplopia, adaptation of cyclovergence is initiated, preserving or increasing torsional (and, secondarily, vertical) fusional amplitudes. However, this is overshadowed by the profoundly decreased horizontal amplitudes and horizontal diplopia results. In a series by Guyton of patients with intermittent exotropia who lost fusion postoperatively, 43% developed an A- or V-pattern strabismus,[74] implying the development of sensory torsion, followed by oblique muscle length adaptation and a pattern strabismus. None of our patients developed an A or V pattern, yet the torsional amplitudes in the decompensated patients were either at the upper range of normal or moderately increased. This difference is likely due to the fact that the intermittent exotropes whom Guyton studied initially had higher-grade fusion and stereopsis than the decompensated MFS patients; given the subnormal fusional status in the study patients prior to the development of sensory torsion, compensatory mechanisms are less robust and degrade more quickly prior to the development of oblique muscle dysfunction and pattern strabismus.

One is reminded that the horizontal and torsional fusional amplitudes of our stable monofixators were subnormal. Normal horizontal vergence amplitudes are considered to be 14 PD for convergence at distance and 38 PD at near, and 6 PD for distance divergence and 16 PD for near. Vertical amplitudes are approximately 2.5 PD at all distances.[75] Using these values as normative, as noted before, only one stable patient had normal convergence and divergence amplitudes at distance and near. Distance amplitudes among the stable patients were better than near amplitudes; 12 of 16 (75%) had normal distance convergence amplitudes and 11 of 16 (69%) had normal distance divergence amplitudes, whereas only 2 of 16 (12.5%) had normal near convergence and 3 of 16 (19%) had normal near divergence. The AOS thesis by Parks[21] specifically notes good to excellent horizontal vergence amplitudes in his patients with MFS, and this data is confirmed in monkeys after repair of surgically induced esotropia during the critical period of visual development.[76] However, the patients in the Parks thesis[21] were all 16 years of age or younger, whereas all of the stable patients in our series were adults. Given the unlikely possibility that all of our stable patients are destined to suffer a future decompensation of their MFS, this raises the possibility that horizontal fusional amplitudes in patients with MFS tend to diminish over time, and the data in this study suggest that this loss of amplitudes occurs first at near and later at distance. The near Worth 4-dot responses of some of the stable MFS patients supports this hypothesis. Of the 16 stable patients in the present study, 3 reported suppression at near during their study evaluation, yet past record review indicated near Worth 4-dot fusion on prior examinations; in addition, half of our stable patients reported some degree of suppression on the Bagolini lenses, and a fifth could not fuse partially dissimilar images on the synoptophore. The design of this study does not prove a direct cause-and-effect relationship between deficient horizontal fusional amplitudes and decompensation of MFS, that is, deficient amplitudes could theoretically be the result, rather than the cause, of decompensation; however, a cause-and-effect relationship is strongly supported by the fact that stable MFS patients had subnormal fusional amplitudes but amplitudes significantly greater than those of the decompensated patients. Since all of the decompensated patients were at one time stable, inference of continuing loss of horizontal and vertical fusional amplitudes over time is not unreasonable.

One further consideration with respect to the evolution of fusional amplitudes over time is pertinent. Although it is widely assumed and frequently taught that the natural course of human fusional amplitudes is to decline with increasing age, the prospective and population-based data in the literature do not support this tenet. Using a variable prism stereoscope and testing over 500 normal adults, Mellick[77] demonstrated an *increase* in convergence amplitudes through the seventh decade of life. With the synoptophore, he showed increases in both convergence and divergence amplitudes through the fourth or fifth decade of life, followed by either stability or a mild decrease afterward. Similarly, Kim and colleagues[78] noted no variation in vertical fusional amplitudes with increasing age in a sample of 100 normal adults. Vaegen and Pye[79] also found no variations in horizontal fusional amplitudes between children and adults

in the third decade of life. Tait[80] noted normal break points for both convergence and divergence in the majority of 500 prepresbyopic and presbyopic adults. Various investigators[81-84] have noted relative stability of both horizontal and vertical phorias with increasing age, leading to the postulate by Sethi[85] that adaptive fusional ability (vergence adapation) improves over time. Thus it is not a foregone conclusion that fusional capacity diminishes with age, and the presence of asymmetrically abnormal fusion in the stable vs decompensated MFS subjects in this study lends continued credence to the hypothesis.

The role of presbyopia is also conceivably important in the etiology of decompensation of MFS. One might postulate that decreasing accommodative tone would impair convergence ability, thus promoting decompensation. However, the Kaplan-Meier analysis shows not an abrupt spike in decompensation at the onset of presbyopia, but rather a fairly linear rate after age 30. Additionally, change in accommodative status would not be expected to have any effect on either vertical or torsional fusional amplitudes. Thus while in some individual cases loss of accommodation or inadequate treatment of presbyopia may be present contemporaneously with, or contribute to, decompensation of MFS, the data do not support the hypothesis that presbyopia is a primary cause of decompensation.

Interpretation of the data regarding retinal correspondence is limited by the fact that subjects did not undergo detailed testing in this regard prior to study entry. Only slightly over half of the stable patients had clear NRC on the simultaneous perception and fusion slides during major amblyoscope testing, with the others giving responses more consistent with ARC or complete suppression of one eye. However, 80% of subjects had NRC responses on Bagolini lens testing. Regardless of the test used, there was no significant difference in classification of retinal correspondence between groups. Interestingly, in the original description of MFS by Parks,[21] a majority of subjects actually gave responses consistent with ARC during Bagolini lens testing. He speculated that perhaps the definition of NRC was too strict or that peripheral fusion in patients with NRC is sufficiently "loose" to allow for small-angle deviations without corresponding neural adaptation. Parks based his argument on the fact that all of his MFS patients with straight eyes gave NRC responses to Bagolini testing, whereas all of those with a small angle of strabismus reported an ARC response; additionally, the other clinical findings (fusional vergences, stereopsis, suppression scotomata) were similar between patients with ARC vs NRC Bagolini responses. His final conclusion was that in everyday, binocular viewing circumstances in free space, MFS patients have functional NRC. However, Pratt-Johnson and Tillson,[86] in their determination of the size of the visual field suppressed in individuals with strabismus, noted that patients with MFS actually may have variable areas of suppression, reporting sensory responses consistent at times with NRC and at other times with ARC, despite the presence of motor stability. Since tests of retinal correspondence like the Bagolini lenses or the synoptophore are dissociating and do not simulate everyday visual experience, and since there is no prior subject data in this regard, it is not possible to determine definitively whether stable MFS patients showed a change in retinal correspondence over time. However, the results of both fusional amplitude and Worth 4-dot testing in this study do support the hypothesis that stable asymptomatic MFS patients show degrading binocular function over time, even though they remain diplopia-free and have no appreciable change in the ocular alignment. Thus the absence of symptoms may not necessarily imply biologic stability.

The torsional vergence system is both less understood and less studied than the horizontal and vertical fusional systems. Parks[87] states normal torsional fusional amplitudes as 8 to 12 degrees for excyclotorsion and 6 to 10 degrees for incyclotorsion. However, some evidence suggests that amplitudes in normal adults are lower than these levels. Physiologically, with a 30-degree head tilt, mean incyclorotation of the ipsilateral eye is 7 degrees and mean excyclorotation of the contralateral eye is approximately 8.5 degrees.[88] Additionally, Howard and Rogers[89] have demonstrated that 6 to 8 degrees would be the outer maximal level of fusional cyclovergence in normal humans. Sullivan and Kertesz[90] have shown that mean cyclofusional amplitudes are only 3.5 degrees when using alternating pattern displays subtending 50 degrees of arc in size. Torsional responses measured by scanning laser ophthalmoscopy are consistent with normal responses in primates in the 6- to 8-degree range.[91] However, Guyton[92] notes that this range of cyclofusion may apply to both sensory and motor torsional fusion, with the possibility of amplitudes of up to 15 degrees. One difficulty in measuring and comparing cyclofusional vergence amplitudes is that capability is closely dependent on stimulus size. The synoptophore slides used in this study to measure cyclovergence subtended a visual angle of 9 degrees in both horizontal and vertical meridians. Crone and Everhard-Halm,[93] using a 10-degree stimulus size, measured incyclorotational and excylotorsional fusion amplitudes in most normal subjects at 5 degrees in each direction, with the largest amount for this stimulus size recorded at 8 degrees. Finally, in the current study, all stable cases had excyclovergence amplitudes of 6 degrees or less, while all but one of the decompensated patients had amplitudes of 7 degrees or more (sensitivity 88%, specificity 100%). This lends credence to assigning an outer maximum normative value of excyclovergence with a 9-degree target at approximately 6 degrees.

Despite the lack of certainty regarding the exact capabilities of the human torsional fusion system, the data in this study clearly demonstrate a decrease in torsional fusional amplitudes in stable MFS patients. That these torsional amplitudes can increase in response to sensory torsion (as in the decompensated subjects) and that orthoptic exercises were helpful in some of our decompensated patients suggests that the fusional vergence system in patients with MFS can improve, at least for some finite period of time, once the decompensation process has begun.

Several investigators have examined various psychophysical and electrophysiologic findings in MFS. Struck and colleagues[94] have reported on differences in binocular visual evoked potentials (VEPs) in patients with MFS vs lesser binocular function, with the inference that recording values can change with prismatic correction of the angle of strabismus as a result of neural plasticity in adulthood. Wright and colleagues[95] have demonstrated that VEP amplitudes are indirectly proportional to the level of suppression and size of suppression scotomata in patients with anisometropic amblyopia. Fawcett and Birch[96] have demonstrated the possibility of using motion VEP recordings as a surrogate for binocular vision but noted some overlap in data between bifoveators and patients with

MFS, depending on testing circumstances. There is also data that suggests that motion perception is abnormal in patients with MFS. Price and Keck[97] showed depressed motion aftereffect in MFS patients, and Cobo-Lewis and colleagues (Association for Research in Vision and Ophthalmology, 1997, Abstract B425) documented impaired linear and nonlinear motion perception in subjects with MFS. In all of these series, there is some overlap of data between normal bifoveating subjects and those with MFS, as well as evidence of variability in results depending on testing conditions. The current study cannot assess the physiologic range of visual sensory function in stable vs decompensated MFS patients, but clearly such a range exists, as it does with response to other visual tests, such as visual fields and visual acuity. Nevertheless, the differences between groups with respect to fusional amplitudes are sufficiently large to negate the assertion that these differences are merely within the physiologic range. Moreover, the current study and those cited above support the concept that the function of the binocular visual system may vary over time, via both spontaneous worsening and improvement in response to treatment, in patients with initially subnormal function.

When first presenting for treatment of diplopia, patients with decompensated MFS may pose a challenge to the consulting physician. As noted in Table 4, these patients often have sought medical care from multiple sources and have expended significant financial resources before their condition is properly diagnosed. If only half of the patients in the United States with decompensated MFS had the average workup as did the patients in this study, a conservative estimate of $10 million annually would be wasted on unnecessary evaluations and diagnostic testing. Although the chief complaint of diplopia often raises concern for neurologic disease and suggests the need for extensive workup, awareness of the prevalence of decompensated MFS as a cause of acquired diplopia would allow clinicians to practice more efficiently and cost-effectively in this regard. If the true prevalence of decompensated MFS approaches the figures calculated previously by Arthur and colleagues[31] or the current study, then neuro-ophthalmologists and strabismologists would encounter such patients almost as frequently as those with diabetic ophthalmoplegia.[98] This underscores the need for clinicians to recognize that many patients who present with diplopia have symptoms from decompensation of long-standing nonparetic strabismus and harbor no neurologic or myopathic pathology.

One may follow the advice of Kushner[46] in attempting to determine the etiology of decompensation. Although he noted a change in refractive error or refractive need in over a third of adults with decompensated strabismus, we had only 2 patients who had a change in refractive error. One of the patients was an accommodative esotrope who required more hyperopic correction at the age of 30; the other was an intermittent exotrope who had an increase in astigmatic correction. Thus in the management of decompensated MFS patients, although assessment for a refractive change that may have affected an accommodative esodeviation or fixation preference is an important first step, alteration of refractive correction alone appears to be a successful mode of therapy in only a minority of cases. Another set of factors of which the practitioner must be aware are the vergence and alignment changes that can occur with the onset of presbyopia, and it is certainly plausible that in some patients these may play an important role. However, only 4 of our decompensated patients developed symptoms in their 40s, and there was no evidence that any of these patients developed problems related to loss of accommodative tone. Additionally, as noted earlier, the Kaplan-Meier curve demonstrates that the rate of decompensation is fairly linear from age 30 through 70 years; if the onset of presbyopia were a major heralding factor for decompensation, a spike at age 40 or 45 would be expected.

Of our patients, 6 underwent strabismus surgery as part of their treatment. Surgical correction of decompensated microtropia is well documented in the literature.[99,100] All of the patients in this study who underwent surgery had a successful motor outcome, with 100% being within 8 PD of orthophoria postoperatively; the other decompensated patients had monofixational alignment at the onset of their diplopia. However, while monofixational motor alignment is readily achievable after decompensation, sensory stability does not always ensue. Although after treatment 77% of our patients were improved with respect to their diplopia, the diplopia remained in 30%, including 2 patients each with intermittent and constant double vision. As noted before, there was little change in stereoacuity post-treatment, consistent with prior reports of lack of association between stereopsis and stability vs decompensation.

The treatment algorithm for decompensated MFS consists of first determining whether there is a change in refractive error or need with subsequent correction. If symptoms persist, any change from baseline ocular alignment is corrected with either prisms or eye muscle surgery. Although measurement of fusional vergence amplitudes would likely occur at this point, such assessment is traditionally absent from routine ophthalmologic evaluation in asymptomatic patients with MFS. This study suggests that progressive loss of amplitudes may occur over time in many patients with MFS. Measurement of these amplitudes in all patients with MFS, even those without symptoms, should become part of routine practice. When subnormal amplitudes are detected, even in asymptomatic patients, orthoptic vergence exercises should be considered; these exercises may diminish the chance of decompensation in the future.

Treatment failure, defined as no improvement in diplopia despite surgical or prismatic motor alignment, occurred in 3 patients, 2 of whom had primary MFS and 1 of whom originally had infantile esotropia. Stereoacuity ranged from 80 arc seconds to no measurable stereoacuity on the Titmus and Randot tests; fusional vergence amplitudes among these 3 showed no obvious trend when compared to the successfully treated patients. It remains unclear why symptoms persisted in these individuals.

All treated patients were followed for at least 15 months after initiation of therapy. Of the 10 successfully treated patients, 2 (patients 3 and 5) developed new symptoms. Patient 3, originally an infantile esotrope who developed a consecutive exodeviation, was re-treated with orthoptic convergence exercises. Although she had no stereopsis, she could appreciate image disparity and diplopia and experienced improvement in symptoms following a second course of orthoptic therapy, with resolution of diplopia despite stability of her motor angle. Patient 5, too, was an infantile esotrope who also had high myopia and developed an increasing esotropia with diplopia over time. In this case it was felt that she experienced progressive inferior deflection of the lateral rectus muscles with resultant abduction weakness and esotropia secondary to her elongated globes; an additional surgical intervention has been recommended for this patient.

CONCLUSIONS

Most patients with MFS remain asymptomatic throughout their lifetime. However, a minority (approximately 7% over a 10-year period or 10% per decade after age 40 according to this study) will develop a sensory perturbation that results in binocular diplopia; this may be accompanied by a worsening of their ocular alignment, requiring surgery in about 50% of cases. Physicians must be aware of the possibility of acquired diplopia due to decompensated MFS in order to avoid unnecessary and expensive consultations and diagnostic testing.

Most patients with MFS experience no visual problems; although a long-term prospective study of fusional status in both normal individuals and those with MFS would be required for proof of hypothesis, this study provides evidence that patients with MFS do not remain stable with respect to their original level of binocular function. Despite the presence of robust fusional vergence amplitudes in childhood, this study lends credence to the theory that even in stable patients, first at near and later at distance, both convergence and divergence amplitudes, as well as torsional fusional amplitudes, diminish over time. In some patients loss of the horizontal fusional amplitudes progresses sufficiently to allow the development of sensory torsion and, in some cases, an increase in the angle of horizontal strabismus that may be accompanied by a small vertical deviation. Adaptative mechanisms are initiated, including an initial increase in torsional (and vertical) vergence amplitudes, but if the binocular system is incapable of adapting fully, diplopia will result. Because of their baseline subnormal fusional status, this decompensation in patients with MFS likely occurs sooner than in patients with higher levels of binocular function (eg, intermittent exotropia or esotropia) and before complete cyclovertical muscle adaptation has occurred; thus decompensated patients typically do not demonstrate a pattern strabismus or oblique muscle dysfunction at initial presentation, although a small vertical misalignment may be present.

There is no proven therapy to prevent the future development of decompensation in persons with MFS. Since later diagnosis and treatment of any childhood strabismus is more associated with decompensation than stability, early intervention and shortening of the initial period of ocular misalignment may offer protection against decompensation in adulthood. Additionally, decompensation is less likely to occur in those monofixational patients with anisometropia and either orthophoria or no measurable strabismus. There is no evidence that the presence or severity of amblyopia differs between stable and decompensated MFS patients, and aggressive amblyopia management should be performed in all cases. Although our results show no association between decompensation and prior orthoptic therapy, they do suggest the advisability of routine monitoring of fusional vergence amplitudes in all MFS patients, with the institution of orthoptic therapy when diminishing or subnormal amplitudes arise. Maintenance of good fusional amplitudes may protect against decompensation, and orthoptic treatment is simple, inexpensive, and carries minimal risk. Indeed, Sethi[85] has noted improvement in fusional vergence adaptation when slowly advancing prism disparity is induced in normally fusing individuals. Thus institution of fusional vergence exercises in the early stages of increasing phorias and decreasing fusional amplitudes may offer protection against decompensation in MFS patients who are still asymptomatic.

When decompensation has occurred, initial management should consist of determining whether a change in refractive prescription or refractive need has occurred. Although comprising only a minority of the cases in this series, age-related loss of accommodation in patients with esotropia, early-onset presbyopia with corresponding vergence changes, and refractive changes causing fixation switch are all easily detectable and treatable. If a worsening change in ocular alignment has occurred, reestablishment of the original asymptomatic angle should be the goal, and therapy in this regard may consist of any combination of orthoptic exercises, spectacle change, prisms, and/or strabismus surgery.

The motor outcome after treatment for decompensated MFS is excellent. In this series a monofixational angle of strabismus was present or was reestablished in all cases. However, the sensory response to treatment is less satisfactory. With a minimum 15-month follow-up, only 70% of our patients had resolution of diplopia, although improvement to some extent occurred in 77%. Additionally, 2 of the 10 patients who were initially diplopia-free after treatment experienced recurrent symptoms several years later.

The goal of therapy for childhood strabismus and amblyopia is to produce optimal, comfortable, and life-long binocular function; for a large number of primary etiologies, achievement of a stable monofixational status is the highest goal possible. This study provides evidence that the most effective means to this end are to initiate treatment early to minimize the period of ocular misalignment and to engage in lifetime follow-up of these patients in order to detect progressive loss of fusional vergence amplitudes. When such declines are present, even in asymptomatic individuals, orthoptic therapy should be offered in an attempt to promote continued stability. If decompensation nevertheless ensues, current optical, orthoptic, and surgical interventions offer an excellent prognosis for motor alignment, although sensory symptoms may persist.

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