The Timing of Surgical Alignment for Congenital (Infantile) Esotropia

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CLINICAL STUDIES

The advantage of early (prior to age 2) surgical alignment in the management of congenital (infantile) esotropia is well established. Initially skeptical of the value of early surgical alignment, von Noorden stated in his 1987 Jackson Memorial Lecture, "A Reassessment of Infantile Esotropia," that "As the age at completion of surgical therapy increased, the probability of optimum outcome (subnormal binocular vision) decreased (p<0.02)." This concept of early surgical alignment resulting in a greater yield of binocularity in congenital esotropia had been previously demonstrated in clinical studies by Taylor, Ing and colleagues, Foster and colleagues, Ing, Zak and colleagues, and Robb. Furthermore, studies performed outside North America also supplemented and supported the concept of a better clinical result from early surgery. These latter studies were performed by Stump in Germany, Gale in Australia, and Uemura in Japan.

Much of the controversy of early versus later (after age 2) surgical alignment revolved around the difficulty in defining "cure" for congenital esotropia. Costenbader was the first to report any functional result in the treatment of congenital esotropia in 1958 when he reported a case that he had aligned, at what was then considered an early age—16 months. This patient, at age 5, demonstrated phoria responses on cover testing and the ability to fuse Worth four-dot (W4D) lights at 13 in.

Prior to Costenbader's case report, the relatively gloomy concept proposed by Worth—that no functional cure could result from alignment in infantile esotropia because these patients lacked a fusion center—prevailed. The only significant challenge to this pessimism was a concept proposed by Chavasse, who in 1939, argued that, after the barriers of satisfactory vision were removed and the deviation was surgically eliminated, a functional result could be expected to develop. Chavasse, how-

EDUCATIONAL OBJECTIVES

1. To review clinical evidence for the desirability of achieving early surgical alignment in the management of congenital (infantile) esotropia.

2. To review previous and more recent laboratory studies that elucidate the clinical findings associated with achieving early alignment and binocularity.

3. To review recent clinical studies concerning very early (prior to 6 months) alignment versus early (prior to age 2) alignment.

Quiz on page 85.
ever, offered no written report of cases to back his claim, and the literature remained devoid of written clinical evidence until Costenbader’s report.

Ing, in his 1981 American Ophthalmological Society thesis, called attention to the fact that many of the clinical congenital esotropia studies based their conclusions on the age at initial surgery rather than age of initial alignment, and that the latter did not always match the former. As pointed out by von Noorden, the timetable for the development of sensory binocularity is initiated by adequate surgical alignment rather than the timing of the initial surgery. Indeed, it was the inability of the ophthalmologists to accurately predict adequate surgical alignment that had prevented a prospective study in this area of previous controversy.

Ing concluded that a masked, independent, retrospective study of adequately aligned patients would be the most reliable source of data concerning the timing of surgical alignment. The patients were selected by five US participating ophthalmologists, along with one Canadian and one Swiss physician. Examination bias was minimized by having all tests standardized and using the same instruments and the same method of examination. All the tests were performed by the author prior to any knowledge of the clinical history.

For the purposes of comparison, the patients were divided in four subgroups according to the age of initial adequate alignment. All the subgroups were similar in 10 areas:
- length of follow-up time from the initial adequate alignment;
- length of follow-up time from the last surgical procedure;
- initial refractive error;
- initial deviation;
- number of horizontal muscle procedures;
- number of vertical muscle procedures;
- incidence of amblyopia;
- postoperative nurturing of the results by spectacles or miotics;
- incidence of dissociated vertical deviation (DWD); and
- motor alignment at the time of the study.

The Ing study clearly showed that the one major parameter with a statistically significant difference was the evidence for binocularity on sensory testing. Binocularity results in patients who were aligned after age 24 months were substantially less than those aligned before that age (p<0.001) (Fig 1).

**LABORATORY STUDIES**

Laboratory studies, somewhat belatedly, supported the accumulation of clinical evidence of the value of early surgical alignment. In 1962, Hubel and Weisel began a series of reports that are felt to be a laboratory rational for the concept of early surgical alignment. These Harvard researchers first showed in 1962 that 80% of the cortical visual neurons in the cat were binocularly driven, 10% were driven by the ipsilateral eye, and 10% by the contralateral eye. According to these authors, the receptive fields of binocularity-driven neurons lay on corresponding points, and their simultaneous stimulation would result in the summation of response.

These investigators artificially disrupted the development of vision in cats during the first 3 months by various means, such as suturing the lids or applying an occluder lens over one eye. In 1965, the researchers found there was a loss in the cortical cells that could be binocularly driven and a substantial decline in the number of cells that could be influenced by the deprived eye. More importantly, they also described that these consequences occurred when normal binocularity was disrupted.
by artificially creating strabismus in the cats by section of one or more of the recti eye muscles.

Hubel and Wiesel also discovered that the results of closing one eye depended somewhat on whether the other eye was closed and the resulting damage might not simply be disuse, but perhaps, dependent on the interaction of the two pathways.

In 1970, Guillery and Stelzner also contributed to the knowledge of deprivation effects when they found that unilateral closure affected the binocular segment of the lateral geniculate nucleus in the cat. In 1972, Guillery also showed that geniculate cells compete for development for available synaptic surfaces on cortical cells, and that success in this completion depended on the nature of the visual input. In 1978, Guillery stated, “The visual loss, the response properties of cortical cells, and the growth of geniculate cells are all affected much more severely in the binocular segment in the nucleus than in the monocular segment, and the difference between the effects seen in the two segments provides a good measure of the extent to which each of the changes is produced by competitive interaction.”

Sherman also pointed out that the abnormalities in the cat depended on visual deprivation in the first few postnatal months. Blakemore and Van Sluyters examined the extent to which physiological effects of monocular deprivation could be reversed in kittens within the sensitive period. These investigators concluded that there was a definite postnatal time window in which the reverse suture was effective and, also, that the binocular neurons required a binocular visual development.

Later, other investigators, such as Baker and colleagues and von Noorden and Middlelitch showed that artificially created strabismus primarily affected binocularly driven cortical cells and that histiologic changes occurred in the dorsal parvocellular layers of the deprived lateral geniculate body.

Van Sluyters demonstrated in 1978 that cortical binocular neurons were the substrate for binocular function in stereopsis. This author demonstrated that stereopsis would be deficient in cats lacking these binocular cortical cells. The author reported that animal studies on recovery from monocular deprivation suggest the following guidelines for treatment of human amblyopia:

- treatment should be instituted in life as early as possible; although procedures which use imbalanced visual stimulation can improve performance through the amblyopic eye, they may do so at the expense of binocular vision; and

- when binocular stimulation techniques are employed, proper eye alignment must be maintained at all times.

In his opinion, this investigator felt that the likelihood of cortical connections serving binocularity being more fragile and irreparable was a distinct possibility, but he acknowledged that the final answer could only come from carefully controlled clinical studies.

Bridging the gap between the animal experiments in the laboratory and the clinical studies by ophthalmologists was a group of psychophysical investigations of the interocular transfer of the tilt aftereffect in humans. This investigation showed that by exposing one eye of persons with normal binocularity to a high-contrast grating tilted slightly away from the vertical, then presenting the other eye to a vertical test, for a short time, the grating appeared to be rotated in the direction opposite the first. If the adapting grating is viewed by one eye and the test grating with the other, interocular transfer is defined as the quantity of the transfer of the aftereffect from the adapted eye to the unadapted eye.

In 1972, Movshon tested three groups of people. One group had normal binocularity; the second group had no history of strabismus, but no demonstrated stereopsis; and the third group had strabismus and lacked stereopsis. The persons with normal binocularity were found to have a mean transfer of 70%; the nonstrabismic persons without stereopsis had a moderate transfer of 40%; those with strabismus and no stereopsis showed a grossly reduced mean transfer of only 12%.

Studies by Mitchell and Ware in 1974 with their interocular transfer of the tilt aftereffect confirmed the previous investigators. These authors felt that both stereoview and the extent of intraocular transfer depended on the proportion of cortical cells that were binocular as opposed to monocular.

In 1975, Banks and colleagues conducted a series of tests demonstrating that a sensitive period for the development of binocularity begins several months after birth and peaks between 1 and 3 years of age. In cases of congenital esotropia, early corrective surgery appears to be indicated for the
development of cortical binocularity.

In 1993, Birch concluded that infants show the abrupt onset of stereopsis at age 3 to 5 months in normal development. Factors that may influence the attainment of stereopsis in these normal infants may include:

- maturation of the macula sufficient to support minimal level of monocular resolution;
- the attainment of accurate vergence control; and
- sufficient cortical maturation to preserve eye of origin information and to support disparity coding. According to Birch, after the abrupt onset of stereopsis at age 3 to 5 months, the normal infant attains a stereocuity of 60 seconds or better by 6 months of age.

**FUSION**

Fusion, a different facet of binocular function, appears to emerge nearly simultaneously with stereopsis in normal development. However, as pointed out by Birch, the ideal age for the evaluation of the innate capacity for stereopsis in congenital esotropes would be 3 to 5 months but only a small proportion of these patients are diagnosed and referred at this early age. Furthermore, misalignment of the visual axes present in these patients precludes stereopsis because images are not presented within Panum's fusional area and cannot be fused, even if the sensory capacity for fusion is intact. Birch concluded, “The seemingly normal onset of stereopsis in infantile esotropia raises the possibility that under ideal conditions, infants with esotropia may be capable of achieving normal binocular single vision.”

A more recent laboratory study by Norcia and colleagues in 1995 demonstrated that patients who had been aligned before the age of 2 showed lower levels of response asymmetry in testing with monocular motion visual-evoked potentials (MVEPs) than those aligned after age 2. These authors concluded that these laboratory data imply that binocular motion processing systems in patients with congenital esotropia are capable, to a degree, of some recovery, but that this plasticity is restricted to a critical period of visual development. The demonstration that patients with congenital esotropia show a decline in the degree of postsurgical asymmetry MVEP argues against a fundamen-

tal incapability of the motion pathway development in most patients.

They reasoned that one could argue that the substrate for MVEP is present in patients with congenital esotropia at birth, but maturation of the motion response is delayed and is independent of the state of alignment of a binocular interaction. These authors point out, however, that if this were true, one would not expect the age at surgery to make a difference in the degree of motion asymmetry; and yet, retrospective data show that the magnitude of motion asymmetry was significantly greater in the later-treated group independent of the ultimate quality of the postoperative eye alignment. These results appear to indicate that patients with congenital esotropia do not spontaneously lose their motion abnormalities over time.

Recently, Jampolsky and colleagues have suggested that both interruption and abnormal binocular interaction secondary to congenital esotropia may play a role in delaying the development of cortical motion mechanisms. These investigators found that the magnitude of MVEP asymmetry prior to surgery was lower in patients who had been alternately occluded compared with infants of a similar age who had not been occluded.

Both groups had interrupted binocular vision—one group resulting from a large angle of constant strabismus, the other because of constant occlusion—but the competitive interaction constantly present in the nonoccluded group was reduced or absent in the alternately occluded group. This recent laboratory finding has led to the initiation of a prospective clinical study, coordinated by Smith-Kettlewell Eye Research Institute, San Francisco, in which patients with congenital esotropia will be randomly assigned to alternating occlusion or nonalternating occlusion prior to their surgical alignment. The results of this study, both motor and sensory, should shed light on whether occluding prior to surgical alignment in congenital esotropia is beneficial for the development of a greater yield, or perhaps, a greater quality of binocular vision.

Perhaps, however, as suggested by Helveston in his 1993 Costenbader lecture, “The onset and clinical picture of congenital esotropia is satisfactorily explained by a theory first suggested by Worth that the strabismus is caused by an inborn defect in the motor function mechanism and aggravated by esotropial factors as suggested by Chavasse.”
THE DEFINITION OF OPTIMUM RESULT

The relative dearth of refined stereoacuity (40 seconds of arc or better by Titmus or 20 to 40 seconds of arc by random dot stereotesting) when analyzing aligned congenital esotropes has been demonstrated in studies by Taylor, Inglis, and Parks. In fact, at least two major investigators in this area feel that subnormal binocularity is probably, with rare exception, the optimum result that one can expect from early surgical alignment of a patient with congenital esotropia. According to Parks, patients with negligible or small (up to 8 prism diopter [Δ]) motor deviation, who also demonstrate fusion (with fusional amplitudes) and only gross stereoacuity, should be included under the monofixation syndrome.

Park’s definition of the monofixation syndrome would include subnormal binocularity results and those of microtropia (which von Noorden defines with fusional amplitudes). Obviously, it is a matter of semantics whether subnormal binocular function and the monofixation syndrome are the same clinical entity.

Both von Noorden and Parks appear to be in agreement that there can be a clinical status in which patients with a small or negligible motor defect, nevertheless demonstrate fusion ability with reduced or absent stereoacuity, and this reduced binocularity is the generally accepted optimum result in the surgical treatment of congenital esotropia.

INSTABILITY OF THE BINOCULAR RESULT

Several investigators have documented motor instability in the congenital esotropes despite early initial alignment. In 1980, Hiles and colleagues reported a series of 54 patients who were followed at least 5 years in which 69% showed nystagmus (often rotary), 78% had overaction of the inferior obliques, and 76% manifested DVD. Although fusional responses could be elicited with W4D lights at 13 in 63% of their patients, during at least some of the follow-up period, this binocular function fluctuated as did the stereoacuity. Furthermore, a very high percentage, 52 out of 54, required the use of miotics or glasses to stabilize the alignment during the follow-up period.

Inglis reported that, despite achieving fusion and stereopsis in a high percentage of patients well aligned before the age of 2, when analyzed at an average of 8½ years follow up, 55% required secondary horizontal muscle surgery. In 1989, Arthur, Smith, and Scott also drew attention to the instability of the initial result. In addition, in 1998, Julio and Ignacio Prieto-Diaz have shown that early binocular alignment in their series followed an average of 14.7 years did not guarantee a stable outcome.

All of the above authors, therefore, have shown instability of the binocular result, undoubtedly as a result of the threat of amblyopia and other factors, such as reoccurrence of a horizontal deviation, nystagmus, or vertical deviation, and necessity for treatment of refractive errors, particularly acquired accommodative esotropia. In addition, in 1996, Kushner demonstrated that at least part of this instability may be related to the accuracy of the alignment. In Kushner’s series, orthotropia was superior to a small angle (8 diopters [D] or less) esotropia, which in turn, was superior to small-angle exotropia in maintaining a binocular result.

VERY EARLY VERSUS EARLY SURGICAL ALIGNMENT

Although the superiority of the timing of alignment to be achieved before age 2 seems well established, controversy concerning whether alignment before age 1 is superior to alignment between ages 1 and 2 remains. Theoretically, the earlier alignment should have an advantage over the later alignment within the time window. However, Inglis found no significant difference in the percentage of patients with binocularity aligned at 6 months versus 12 months versus 24 months.

In 1994, Shaul and colleagues reported that patients with a smaller angle of preoperative deviation or surgery completed by age 1 demonstrated an increased incidence of optimum results including the establishment of subnormal binocularity. Unfortunately, Shaul’s series did not compare outcomes of those aligned at 1 year versus 2 years.

The comparison of binocular results of alignment at 5 to 8 months, 9 to 12 months, and 13 to 16 months showed no difference in the percentage of patients with random dot stereopsis when analyzed by Birch and colleagues in 1995. However, these authors did report a higher incidence of a more refined stereoacuity (60 seconds of arc to 200
seconds of arc) as a result for patients aligned before 12 months versus 13 to 16 months.

Helveston and colleagues in 1990 and Wright and colleagues in 1994 pushed the envelope of congenital esotropia surgery to a “very early” age by performing alignment procedures before the age of 6 months. Indeed, Wright has reported high-grade stereoaucuity in three of his series of seven patients. This latter author has become an advocate of very early surgery theorizing that alignment at age 6 months or later has already missed the time window of opportunity to achieve any binocularity other than the heretofore described optimum result of a monofixation syndrome.

This current controversy of very early (before 6 months) versus early (before 2 years) surgery has been addressed in editorials by Repka and Clarke, with the former commenting that it is premature to advocate the widespread use of very early surgery at this time. The latter author, with his experience of two out of three patients with medium-to-large-angle esotropia decreasing to a small-angle esotropia, and, in one case, the spontaneous development of esotropia with alternating occlusion, concluded that “there appears to be no significant advantages and, indeed, some potential pitfalls in performing very early surgery (before 6 months) in infantile esotropes.”

Supporting the message of these editorials is the sobering report by Ing who performed a masked, independent analysis of 16 patients of four other surgeons. These patients had been surgically aligned by a mean age of 4.2 months. When examined by this author at a mean age of 7 years, only one patient demonstrated refined stereoaucuity (40 seconds of arc Titmus and 20 seconds of arc Randot). This patient with refined stereoaucuity was aligned at age 3 months, and all patients aligned at 4 and 5 months demonstrated no better binocularity than that found in the previously examined group of patients aligned at 6 months.

Given the relative instability of strabismus at 3 months of age, it remains controversial to recommend surgery at that early age. Indeed, findings of Nixon and colleagues demonstrated that the majority of patients with “congenital” esotropia do not truly have that type of strabismus at birth. In addition, these latter investigators found that unsteady motor behavior, as well as absent stereoaucuity responses, were found in healthy infants before 4 months of age. Therefore, the surgeon who performs surgery in those very early months may be doing so unnecessarily, thereby jeopardizing the possibility of normal infant binocularity. In addition, both von Noorden and Parks reported cases of congenital esotropia that they examined at 3 or 4 months of age in which the strabismus had completely resolved by 6 months.

Despite the lack of convincing evidence that surgical alignment for congenital esotropia before age 1 is superior to alignment later in the 2-year time window, it is the author’s practice to not delay surgery any longer than necessary. Once accurate measurements, equal fixation preference, and a trial of spectacles for hyperopia in excess of 2.75 D is achieved, there seems no practical reason for delay. In fact, in a recent series of patients reported by the author, the majority of congenital esotropes showed a significant increase in the quantity of the deviation while being followed; therefore, any delay may actually necessitate greater amounts of surgical treatment (Fig 2).

In this same series, the mean age of initial successful alignment was 9 months, well within the first year of life. In addition, it was the author’s admonition to accurately measure the strabismus...
close to the date (within days) of initial surgery to
detect any increase in the amount of deviation that
might have occurred while the patient was under
observation.

Finally, in addition to the rare, but definite,
possibility of establishing a refined stereocuity
result by surgery at 6 months or later, van Selm47
found 40 seconds of arc stereocuity many years
after initially less refined stereocuity was estab-
lished at an earlier age. This author reported four
patients who initially achieved a stereocuity of 80
seconds of arc, which when followed for 20 years,
demonstrated 40 seconds of arc acuity on later test-
ing. As van Selm concluded, "The assessment of
stereopsis at age 4 is not necessarily final. Stereopsis
may improve with regular postoperative care or
deteriorate with neglect."

SUMMARY

At this time, the beneficial effect of accurate
alignment by age 2 in congenital esotropia has been
well established by clinical and laboratory studies.
There is, however, only scanty clinical evidence that
alignment before age 1, much less before 6 months
of age, may yield a better quality of binocularity (ie,
refined stereocuity) than alignment by age 2.

Fisfalls of very early alignment are present. In
addition, the ophthalmologist must be vigilant in
following the initially aligned patient and be ready
to treat vertical motor defects, amblyopia, and
acquired refractive errors.

The need for additional horizontal surgery after
initial alignment is also common. The optimum
result in the surgical treatment of congenital
esotropia generally shows binocularity that is with-
in the confines of a monofixation syndrome, and
refined stereocuity remains an elusive target and a
rare outcome, no matter at what age the alignment
is achieved.

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