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The Final thesis

Surgical Treatment of Pediatric Congenital Esotropia

(title)

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1. SUMMARY:

Infantile esotropia is a type of ocular motility disorder characterized by an inward turning of one or both eyes, also known as "crossed eyes." Infantile esotropia is esotropia that occurs in a neurologically normal child during the first 6 months of life. Although the term "congenital esotropia" has been used interchangeably, the condition is rarely present at birth. Therefore, from here on the term “infantile esotropia” will be used. The deviation angle is constant and large (>30 PD). There are several surgical techniques available to treat infantile esotropia. Although bilateral medial rectus recessions greater than 5 mm have been an acceptable treatment, many surgeons still prefer other techniques such as three or four-muscle surgeries, botulinum toxin augmentation, etc. The main purpose of this literature analysis is to review and analyze the different surgical techniques that are used to treat this condition in addition to evaluating possible augmentations and factors affecting the postoperative surgical outcome during follow-ups. The overall conclusions are that operative treatment before the age of one bears the best long-term outcome and that procedures augmented by non-invasive methods result in better stereopsis. Currently, the choice of treatment is merited to the ophthalmic surgeon and his preference and further depends on each individual case. Additional multicenter prospective studies need to be done to properly identify a gold standard method of therapy.

1. KEYWORDS:

Strabism, esotropia, comitant, incomitant, botulinum toxin, recession, resection, rectus, stereopsis, binocularity, gaze, convergent, amblyopia, hyperopia, optokinetic, dissociated vertical deviation, cross-fixation, plication, visual acuity.

2. METHODS:

A systematic literature review was conducted on the various treatment modalities for infantile esotropia using the PubMed scientific database, Google Scholar search engines, and academic books. The search was restricted to articles available in English and German. Most of the articles were from the years 2000 to 2020. For this study, the author reviewed 47 publications in total.

3. INTRODUCTION:

Clear vision is produced when features of interest in the visual environment are pointed steadily at the specialized region of the retina with the highest photoreceptor density, called the macula. Logically, excessive motion of images on the retina degrades visual acuity. Eye movements

serve two primary functions to keep the image steady: gaze-holding and gaze-shifting. The term "gaze" refers to the direction of the line of sight or visual axis. In healthy individuals, the visual axes of both eyes are aligned. Focusing on an object in motion requires gaze-shifting, whereas focusing on a still object requires gaze-holding. (1) The movement of each eye within its orbit is controlled by six extraocular muscles (four rectus muscles and two oblique muscles). "A tug-of-war exists between the rectus and oblique muscles." (2). The four rectus muscles originate at the annulus of Zinn (common tendinous ring) at the posterior apex of the orbit, insert anterior to the equator and pull the eye posteriorly. They are named after where they insert into the sclera on the eye's medial, lateral, inferior, and superior surfaces. As a result, the primary action of the respective muscles is to adduct, abduct, depress, and elevate the globe. The two oblique muscles insert posterior to the equator and provide anterior counterforces by primarily controlling torsional movement and, to some extent, upward and downward movements of the globe. (2,3) "The extraocular muscles are innervated by lower motor neurons that form three cranial nerves: the abducens, the trochlear, and the oculomotor." (4) The primary, secondary and tertiary functions of each extraocular muscle are detailed in the picture 3 and table 2.

Figure 1: Anatomy of the extraocular muscles of the orbit, lateral and anterior view (5)

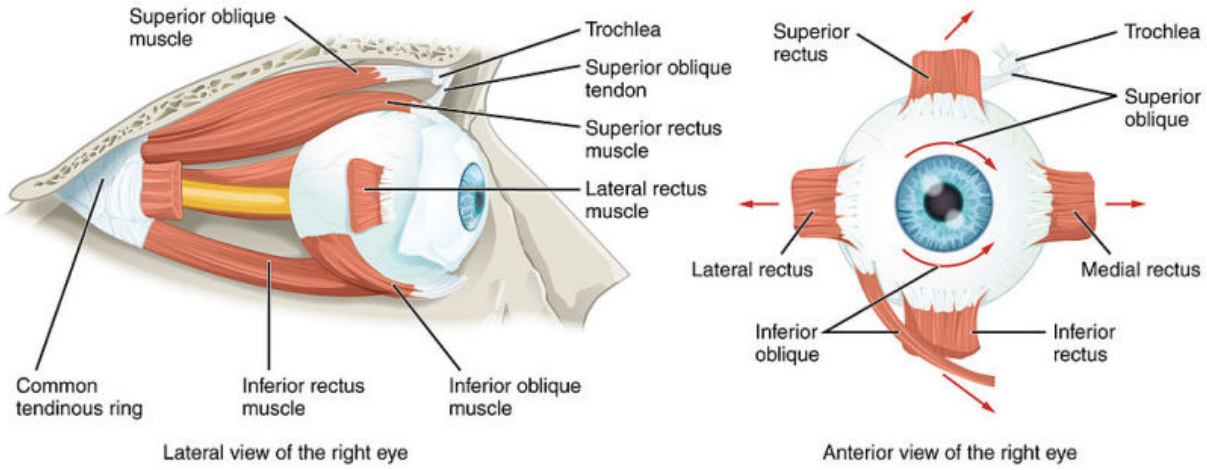
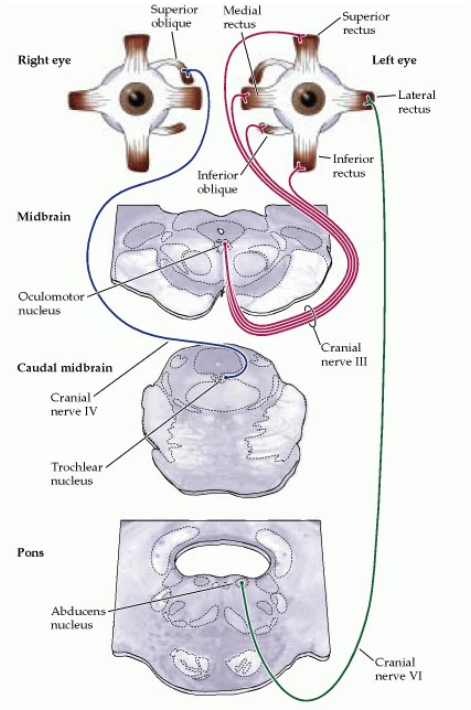


Figure 2, Table 1: cranial nerves (and nuclei) that innervate the extraocular muscles (4)

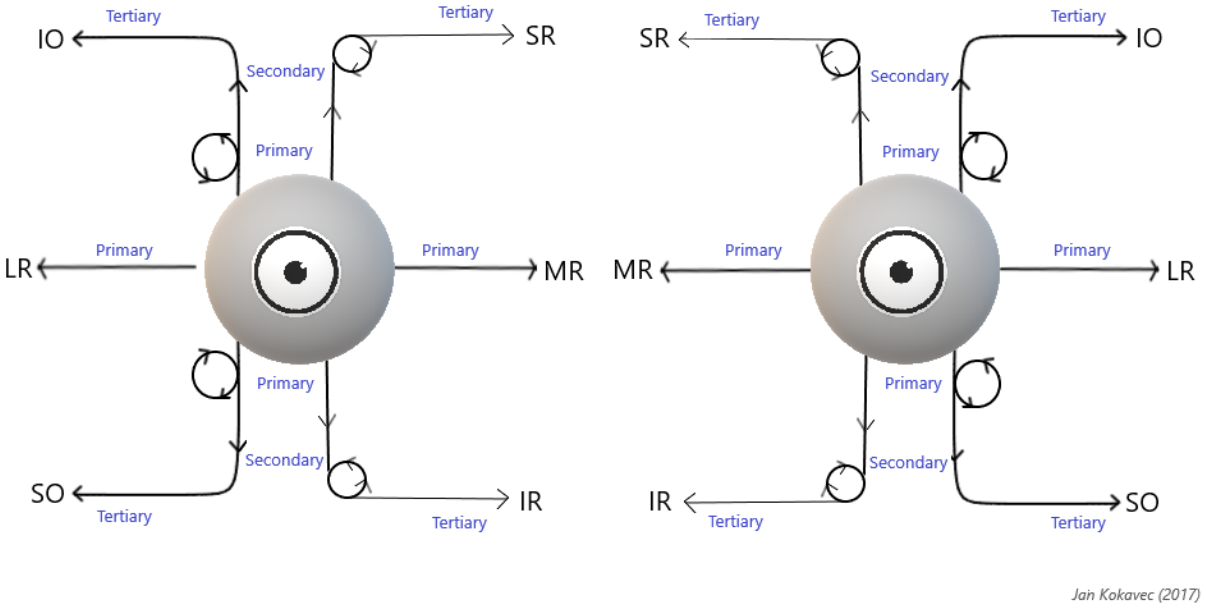
Muscle	**Innervation**
Lateral rectus (LR)	Abducens nerve (VI)
Medial rectus (MR)	The oculomotor nerve (III)
Superior rectus (SR)	Oculomotor nerve (III)



Inferior rectus (IR)	Oculomotor nerve (III)
Superior oblique (SO)	Trochlear nerve (IV)
Inferior oblique (IO)	Oculomotor nerve (III)

Figure 3, Table 2: The actions of the extraocular muscles (6)

Muscle	**Primary**	**Secondary**	**Tertiary**
Lateral rectus (LR)	Abduction	None	None
Medial rectus (MR)	Adduction	None	None
Superior rectus (SR)	Elevation	Intorsion	Adduction
Inferior rectus (IR)	Depression	Extorsion	Adduction
Superior oblique (SO)	Intorsion	Depression	Abduction
Inferior oblique (IO)	Extorsion	Elevation	Abduction



4. STRABISMUS:

To achieve proper binocular vision, the eyes need to see clearly, be aligned (looking in the same direction), and focused on the same object. To maintain eye alignment, the eyes must also move together. (7) Misalignment of the eyes causes deviation of one eye (the deviated eye) from the usual visual axis of the healthy eye that is fixed on what the person intends to look at (fixing eye). (7,8) This phenomenon is referred to as strabismus. Strabismus can be classified according to several criteria. For a qualitative assessment for diagnostic purposes five criteria stand out: the size of deviation, direction of deviation, accommodation, state of fusion, and comitancy. Horizontal deviations are convergent (eso-) or divergent (exo-) misalignment. Vertical deviations are upward (hyper-) or downward (hypo-) deviations. Finally, cyclo- refers to torsional strabismus, which occurs when the eyes rotate around the anterior-posterior axis. The accommodative system can affect/cause the misalignment, so we differentiate between accommodative and non-accommodative types. The state of fusion is a factor that differentiates constant strabismus of one eye (manifest) from strabismus that only occurs contralaterally while the ipsilateral eye is covered (latent). (8,9) Comitancy describes the presence or absence of variation in the degree of misalignment in different visual axes. "A comitant deviation has the same degree of misalignment in all gaze directions. An incomitant deviation varies in degree of misalignment depending on gaze direction." (8)

Table 3: Overview of strabismus classification

Comitancy	Comitant			Incomitant		
State of fusion	Manifest: Tropia	Intermittent	Latent: Phoria	**Mechanism**	Paralytic	Paretic
Direction	Eso Exo Hyper Hypo Cyclo			**Etiology**	Neurogenic, myogenic, mechanical	

5. ESOTROPIA:

A convergent strabismus is termed an esotropia. Most patients with esotropia present before school age, generally between the ages of 2 and 3 years. Esotropia is often constant. In most cases, intermittent esotropia occurs initially associated with accommodative esotropia or decompensated esophoria (a tendency of one eye to deviate inward). The intermittency of accommodative esotropia is attributed to the fluctuating accommodative status of the patient at the onset of the deviation. Without treatment, intermittent esotropia is likely to become constant. (10) Fusional vergence is the eye's movement that enables the fusion of monocular

images producing binocular vision. It helps to correct an esodeviation, however, our innate divergence amplitudes are typically weak and therefore contribute to the poor control of esodeviation. Because of esodeviations' early onset and constant character, they tend to disrupt binocular visual development and can be associated with amblyopia. (11) The scope of this paper focuses on comitant esotropia. Therefore, incomitant esotropia, such as the paralytic and paretic forms are not discussed in-depth. It is best to classify comitant esotropia according to clinically relevant criteria. First, we must differentiate between infantile, acquired, secondary and micro-esotropia. Esotropia manifested in the first six months of life is called “infantile”. “True congenital esotropia, which is present at birth, is considered extremely rare”. Acquired esotropia occurs after the first six months of age, usually in children with normal binocular vision prior to the condition's onset. Acquired esotropia can be further classified into accommodative, nonaccommodative, acute, mechanical, and consecutive. Accommodative esotropia is associated with the activation of accommodation. It is attributed to either uncorrected hyperopic refractive error and/or a high accommodative convergence/accommodation (AC/A) ratio and treated by correcting the hyperopic refractive error surgically and/or with glasses. Nonaccommodative esotropia is not associated with accommodation. “Correcting any coexisting hyperopia has minimal or no effect on the size of the esotropia.” Acute esotropia develops suddenly without any apparent etiology in a school-aged or older patient with previously normal binocular vision. Associated sudden diplopia may result from an underlying and potentially life-threatening cause. Its onset can often be traced precisely. Mechanical esotropia is caused by a mechanical restriction or tightness or a physical obstruction of the extraocular muscles. Consecutive esotropia occurs after surgical overcorrection of an exotropia. Finally, in micro-esotropia the angle of deviation is less than 10 PD, beginning in a child under 3years of age, and, in some cases, may escape diagnosis by conventional methods. (10)

Table 4: Types of esotropia

Infantile	**Secondary**	**Acquired**	**Micro-esotropia**
	Sensory Consecutive	Accommodative Non-accommodative Acute Mechanical	

Pediatric infantile esotropia is the “constant convergent deviation of one eye of a child present from birth”. One can deduce important specificities of this condition simply from its name.

More concretely, it is defined as an esotropia that begins before the age of six months, is associated with a constant, large angle of strabismus (> 30 PD), has no or mild amblyopia, small-to-moderate hyperopia, latent nystagmus, dissociated vertical deviation, and limited abduction (due to cross fixation), as well as absent or reduced binocular vision without other neurological disease.." (12). “The terms "infantile esotropia," "essential infantile esotropia," and "congenital esotropia" are often used interchangeably. (10) It is known that newborns usually do not have straight eyes. A large population study documented that merely 30% of healthy neonates have straight eyes, 70% have a transient exotropia or a variable angle strabismus, and less than 1% have esotropia. In that study, only 2 of 2271 healthy neonates had an esotropia at birth and, in both cases, the esotropia resolved by 2 months of age. This important study indicates that esotropia infrequently occurs at birth, whereas exodeviations are common. (13) Usually, neonatal misalignments are fleeting, large-angle ocular deviations, occurring commonly in the first two months of life. The neonatal misalignments disappear by 4 months of age except in children who develop infantile esotropia. According to a study by the same researchers, the usual time of onset of infantile esotropia was between 2 and 4 months, therefore suggesting that it is not a strictly congenital disorder. (14) “Infantile esotropia accounts for approximately 8.1 percent of cases of esotropia, affecting 1 in every 100−500 people. “ (10)

Epidemiology:

Infantile esotropia has been called the most common form of strabismus for decades. Prior studies suggest that it occurs in 1% to 2% of all new-born children, and even recent publications mention it as one of the most common forms of pediatric strabismus. A 2009 study, however, found that only 1 in 403 newborns were diagnosed with infantile esotropia. Other recent reports have reported similar results, with infantile esotropia making up only 8.1% of all forms of esotropia, when previously thought to account for 28-54% of all esotropias. The previously reported higher incidence of infantile esotropia included children with CNS disorders or distinct forms of early-onset acquired nonaccommodative esotropia that has been shown to occur more frequently than infantile esotropia, also as a result of the higher accuracy of the diagnostic differentiation of different types of esotropia. (15)

Table 5: Risk factors associated with infantile esotropia (16)

Birth factors
Prematurity
Decreased birth weight (<2,500 g)

Use of supplemental oxygen
Cesarean section
Perinatal complications
Family and pregnancy history
Strabismus or amblyopia in family
Gestational hypertension
No prenatal care
Chronic conditions
Secondary ocular disease (+4D)
Cardiovascular disease
Gastrointestinal disease
Respiratory disease
Any systemic disease

Etiology:

Worth first put forward the first theory about the etiology of infantile esotropia. In his theory, the "faculty of fusion" develops typically in the first few months of life. He acknowledged that the motor coordination of the eyes is only partially developed at birth and unstable, allowing the eyes to converge or diverge frequently to a small extent. However, according to him, before the age of 6 months, only a defect in the fusion faculty causes squint. After the development of the fusion faculty, by 6 months of age, only a muscular paralysis due to n. abducens palsy can cause squint.

Chavasse disavowed his mentor's concept about defective fusion faculty. He believed that infantile esotropia was caused by pathology either in the motor nerves innervating the extraocular muscles or by anatomical abnormalities within the muscles. He considered fusion to be a conditioned reflex with a limited developmental period. Hence, early straightening of the eyes could result in fusion developing in a patient with infantile esotropia. "He illustrates three patients with bilateral congenital or infantile abducens paresis or palsy, straightened by surgery at a young age. One was operated during infancy. All have normal abduction postoperatively. The child operated during infancy developed stereopsis, disproving his mentor's idea that these patients were unable to achieve binocular vision."

Costenbader speculated that the normal vision, produced by cortical inhibition of exuberant convergence in childhood, was impaired. Therefore, infantile esotropia was thought to result from deficient cortical function which seemed somewhat creditable due to the frequency of

esotropia in brain-damaged children. “In 1953, he established that Chavasse's claim was correct; his first case found that proved fusion was produced in a infantile esotrope whose eyes were straightened at 16 months.”

For more than 2 decades, a defect in the motor fusion mechanism has been thought to be the factor responsible for infantile esotropia. If both eyes are not appropriately used together at an age when the binocular visual system retains its plasticity, the normal disparity detection mechanism, motor fusion, deteriorates. During convergence, the eyes deviate from a baseline due to sensory input. When sensory input is withdrawn, the eyes return to baseline because of tonus. Brodsky and Freyi identified monocular esotonus as a cause of infantile esotropia. Further, they relate infantile esotropia to dissociated deviation. “These theoretical considerations are promising for our understanding of the etiology of infantile esotropia.” (17) What makes this condition astonishing is that one or both eyes are held in an adducted position even though the child is able to fully abduct each eye. Under paralyzing general anesthesia, the eyes assume a normal position, signifying that infantile esotropia must result from increased baseline innervation (tonus) to the medial rectus and inferior oblique muscles in the awake state. In neurology, it is considered axiomatic that movements are innervated by the cortex, whereas subcortical centers innervate individual muscles. Thus, hyper-innervation of individual extraocular muscles in infantile esotropia and its association with binocular torsion (absent in isolated lesions of the visual cortex) provides evidence for this condition to originate at the subcortical prenuclear ocular motor pathways. (18)

Evidence for a subcortical pathophysiology:

In humans, within the first few months of life, this subcortical optokinetic system produces a phenomenon known as monocular nasotemporal asymmetry (MNTA) secondary to horizontal optokinetic stimuli. At this stage, the optical axes of the eyes can be physiologically deviated. In the 2nd to 3rd month of life, binocular cells form in the visual cortex, which are bidirectionally sensitive to horizontal optokinetic motion. These cells begin connecting to the nucleus of the optic tract (NOT) and the dorsal terminal nucleus of the accessory optic system (DTN-AOS) in the midbrain. (18) Optokinetic stimuli are now essentially modulated by the binocular cells of the visual cortex through binocular foveal pursuit, and no longer by the subcortical monocular optokinetic system. As a result, MNTA is corrected, and binocular vision is produced. Approximately 6 months after birth, monocular horizontal responses to optokinetic stimuli are symmetrical. When sensory input is received on the fovea, the NOT and DTN-AOS generate eye movements by sending visual motion signals via the vestibulocerebellum to the vestibular nucleus, which causes the eyes to move by moving them at the appropriate speed and

direction in order to minimize the **retinal slip**. (18,19) "According to the Hoffmann hypothesis, in infantile esotropia, no binocular corticotectal connections are established because there are no binocular cells in the primary visual cortex. And because "neurons that fire together wire together" (Hebb, 1949), only the crossed nasal fibers from the contralateral eye can stream through the ipsilateral visual motion cortex (MT/MST) to hook up to the ipsilateral NOT-DTN, because these are the pathways that have the same directional sensitivity." (19)

Figure 4: Human visual pathway (20)

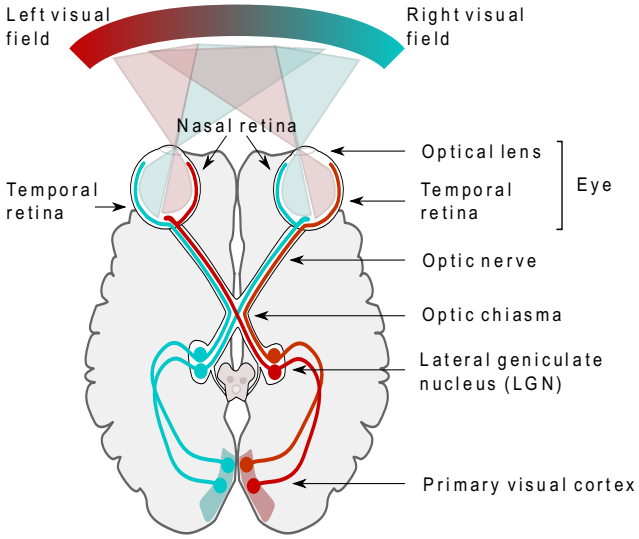
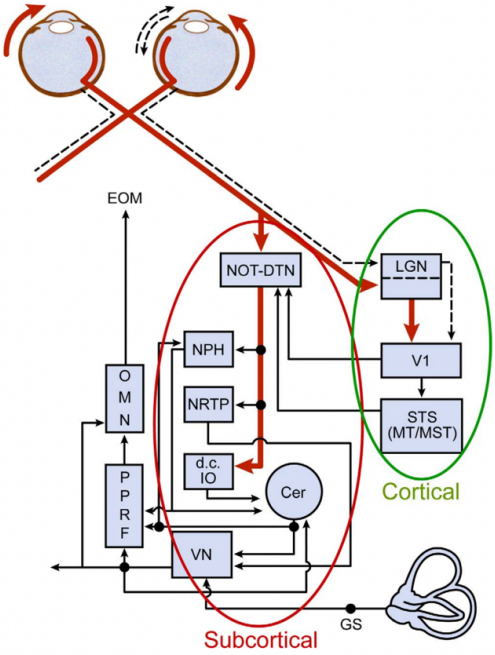


Figure 5: optokinetic system in the right half of the brain (19)



In Figure 5, the left eye receives nasalward optokinetic input, which crosses through the chiasm to the NOT and DTN of the AOS in the right half of the brain. Conversely, these structures respond to rightward optokinetic input (nasalward for the left eye), for example during leftward rotation of the visual world.

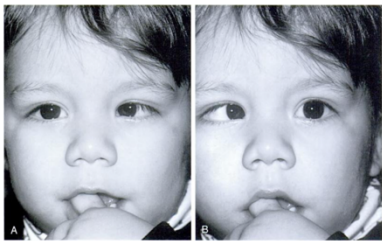
Potential role of prolonged subcortical neuroplasticity:

"Since subcortical motion pathways normally shut down as cortical motion pathways develop, one could question whether the persistence of subcortical reflexes could be a secondary consequence of a primary dysgenesis within the visual cortex." It is plausible that corticotectal connections with NOT-DTN provide a contributory signal to inactivate retinotectal pathways. However, the evidence suggests that subcortical pathways have a predefined period, of several months of infant life, at the end of which they shut down, regardless of corticotectal connections with the NOT-DTN. In children with infantile esotropia, subcortical motion pathways within the human accessory optic system remain operational. A mutation or metabolic perturbation

within the subcortical pathways could enhance their neuroplasticity and preserve their function, increasing baseline esotonus and causing a secondary remodeling of the visual cortex. (19)

6. DIAGNOSTIC WORK-UP:

Children with new-onset esotropia require a thorough anamnesis and comprehensive examination. In addition to general ocular examination, the examination must include vision assessment, ocular motility, strabismus measurements at distance and near and cycloplegic refraction. Most children with infantile esotropia are developmentally normal otherwise. however, in the setting of neurologic or developmental disorders, esotropia can be observed. This emphasizes the significance of a thorough history and examination. The ability to test vision, motility, and ocular alignment efficiently and accurately is critical to a successful ocular examination. The CSM method is one method of testing visual acuity in preverbal or nonverbal children. C refers to the centrality of the corneal light reflex. S stands for the fixation stability. M refers to the ability to maintain alignment assessed on a target and then assessing monocular fixation maintenance under binocular conditions. Amblyopia is characterized by the inability to maintain fixation. Obtaining ocular alignment measurements in young children can be more difficult. The Hirschberg and Krimsky methods can be used to estimate the deviation. When a patient prefers to fixate with either eye in adduction, this is referred to as cross-fixation. A cross-fixation pattern does not imply spontaneous or equal alternation or the absence of amblyopia. Pay attention to the point at which the alternation occurs.(21)



Presentation:

A paradigmatic infant with infantile esotropia usually presents to the ophthalmologist at approximately two months. Parents typically note that their child began crossing their eyes shortly after birth and feel that it worsens. They also note that the crossing is worse when the child is tired and alternates between the right eye and the left eye. Sometimes when they may notice an upward drift of one eye when the other eye is looking at a target. Amblyopia, characterized by a fixation preference for one eye, is more often seen in patients who present after the age of six months. The patient may present with any risk factors presented in Table 6. Associated conditions such as dissociated vertical deviation (DVD) and inferior oblique overaction (IOOA) tend to develop most frequently after the age of two years.

Table 6: Possible ocular motor signs associated with infantile esotropia

Amblyopia
Cross-fixation
Inferior oblique overaction
Hyperopia
Pursuit asymmetry
Motion visual-evoked asymmetry
Face turn
Dissociated vertical deviation
Latent fixation nystagmus

Figure 6: Cross-fixation phenomenon (22)

Figure 7: Same magnitude of angle of deviation in all directions of gaze (22)

Diagnosis:

An infant's complete evaluation for the presence of essential infantile esotropia can be completed in a short period of time with little discomfort to the infant. Before beginning the examination, it is critical to obtain a family history and record it in the chart. This infant's birth weight and family history of strabismus should be always documented. The timing of the deviation's onset is critical. Most infants with essential infantile esotropia have crossed eyes since birth or shortly after. Parents tend to focus on the times when their child's eyes are crossed rather than the brief periods when they are straight. Essential infantile esotropia can be diagnosed at the age of four months. An esotropia confirmed by a reliable observer by 6 months of age is considered to have been present sufficiently early to qualify for the diagnosis of infantile esotropia, according to convention. After 6 months, an esodeviation may be acquired esotropia. In an affected infant, gross motor evaluation usually reveals general developmental delay or cerebral palsy. However, in a very young child, this may be overlooked during the initial examination. It can be difficult to determine whether an infant prefers fixation with one or both eyes. The majority of infants object to having one of their eyes occluded. As a result, the cover test in an infant should be performed in a nonthreatening manner. Motor evaluation is typically done binocularly with evaluating versions. This can be accomplished by rotating the baby to elicit the oculocephalic, or doll's head, reflex. Unfortunately, evaluating ductions in infants is nearly impossible because they usually object strongly to having one eye covered. Infant sensory function testing is limited due to a lack of reliable subjective responses. However, sensory anomalies are frequently inferred from other examination findings. All infants with esotropia undergo retinoscopy. A hypermetropia of +3.00 diopters indicates that a refractive accommodative component must be ruled out. An examination of the fundus and media in an infant with esotropia is required to rule out

pathologic conditions such as cataract, coloboma, optic nerve hypoplasia, atrophy, and retinal tumors. (23)

7. TREATMENT:

At the initial clinic visit, it is crucial to assess the angle of deviation, refraction and coexisting oculomotor conditions. (24) The ultimate objectives of treatment are correcting the ocular misalignment and facilitating the development of binocular vision. To achieve these objectives, we must aim to eliminate any amblyopia, ensure the long-term stability of eye position. (25,26) Different modalities exist in the treatment of infantile esotropia and can be summarized into surgical, non-surgical and combined treatment. The mainstay of treatment currently is surgical with non-surgical augmentation. There are several non-surgical treatment modalities of infantile esotropia. Non-surgical treatments range from changing the refractive correction to using pharmacological chemo-denervation with botulinum toxin to supplement surgical approaches.

Optical correction

Refractive errors have a significant impact on esotropia and its management. Optimal visual acuity may result in better management of the misalignment. In contrast, esotropia may be recognized only after refractive error correction, due to the switch of fixation to the non-dominant eye. Furthermore, "following surgical alignment, spectacle correction may be of considerable value in improving a small residual deviation." (27)

Occlusion therapy

Occlusion therapy uses an eye patch to cover the non-amblyopic eye for a couple of hours each day to train the amblyopic eye. It is one of the principal methods to reduce amblyopia. Performing corrective surgery on patients with infantile esotropia leads to poorer surgical outcome if moderate amblyopia is present at the time of surgery. Mild amblyopia, however, does not adversely affect surgical outcome in patients with infantile esotropia, hence improving surgical outcome. (27,28)

Vision therapy:

"The goal of vision therapy is to activate the undeveloped sensory processes". Examples include inhibition of cross-fixation using binasal occlusion, practicing abduction calisthenics to encourage abduction and increasing peripheral awareness through activities. More research is necessary to reveal the validity and usefulness of this treatment option. (29)

Botulinum toxin (BNT):

The toxin is injected intramuscularly and remains at the nerve terminal for several days to weeks where it inhibits the release of acetylcholine, resulting in muscle weakness or paralysis within 3 to 5 days after the injection. “Although an irreversible binding occurs, extra-junctional acetylcholine receptors may develop. The nerve reinnervates the muscle with a reversal of the paralysis and eventual recovery. Extraocular muscle paralysis usually lasts from 2 to 8 weeks.” (27) In a prospective randomized control study conducted by Mayet et all in 2021, surgery was proven superior to Botulinum toxin in children with large-angle esotropia. Nevertheless, BNT has a definite role as a primary treatment option in selected children. The success of BNT treatment was associated with small to moderate angles of esotropia. At the same time, BNT in younger children had a significantly higher success rate than older children “The explanation is probably based on increasing contracture of the medial rectus muscles over time.” (30) Single bilateral medial rectus injection of botulinum toxin at 5–10 mm posterior to the muscular insertion without electromyography is an effective alternative to surgery in early treatment. However, complications associated with early treatment, such as vertical deviation and ptosis, increase the risk of amblyopia in young children. “The addition of sodium hyaluronate may decrease drug diffusion to other muscles, and thus decrease the potential for ptosis and vertical deviations.” (31) Botulinum toxin is a less invasive method of treatment in children with early esotropia which, when effective, significantly reduces the number of secondary surgeries. In addition, some studies have shown that even if a surgery is decided for, the surgical procedure is associated with better outcomes in patients that have previously received botulinum toxin injection therapy. (32)

Surgery:

It is widely accepted that that some form of surgical intervention is necessary to treat IE. “Surgery is indicated for the treatment of infantile esotropia when the size of the deviation is stable, amblyopia has been treated, and an accommodative component of the esodeviation has been eliminated.” Esotropia with an angle of less than 40 PD and with onset in very early infancy frequently resolves whereas “esotropia with a deviation greater than or equal to 40 PD presenting after 10 weeks of age has a low likelihood of resolution." It is, therefore, that although surgery can be performed safely in 3 to 4 months old patients, many surgeons prefer to wait until the patient is 6 months of age to permit stability of the ocular deviation in order to minimize the risk of later occurring secondary ocular misalignment, associated secondary amblyopia and secondary strabismus surgery. Patients with infantile esotropia who underwent surgical alignment before the age of 24 months showed improved binocular function compared with those who achieved alignment after the age of two. Surgical correction of IE during the

first year of life is associated with better stereoacuity in children who achieve stereopsis after surgery, because the period of misalignment of the visual axes is shorter. (33) The aim of surgery is therefore to align the eyes as closely to the orthotropic position as possible by adjusting the horizontally acting extraocular muscles.

Surgical correction of IE can be divided into three types: 1. unilateral medial rectus recession and lateral rectus resection; 2. bilateral medial rectus recession or lateral rectus resections; 3. bilateral combination of recessions and resections. (34) Standard surgery of choice is bilateral recession of the medial rectus muscles. In patients with a large angle esodeviation of 70 PD or more, a bilateral symmetric medial rectus recession can be performed in combination with a unilateral or bilateral lateral rectus resection. For patients with monocular amblyopia and patients with prior contralateral eye surgery, a unilateral recession-resection procedure is recommended as well as a medial rectus recession of the preferred eye combined with a lateral rectus resection on the non-preferred eye. Associated inferior oblique overaction is treated with a simultaneous inferior oblique muscle recession surgery. (33)

Ideally, the result of the operation should be a full correction of the deviation and parallel alignment of visual axes at distance and near. Measurements are made with the Krimsky test for infants. However, in reality, surgery is considered successful when the postoperative deviation is within 10 prism diopters of orthotropic. Successful alignment early in life does not ensure long-term stability." Frequent follow-up visits are recommended at least through the first 5 years of life are recommended. Three distinct outcome categories can be identified; those who retained stable ocular alignment after the first operation, those who had good alignment that remained stable for a period and then decompensated, and those who had unstable alignment throughout the study period. The prevalence of these categories is approximately equal. Secondary and tertiary operations may be required with ocular alignment decompensation or instability and the possible consequences. Stereopsis "rarely develops in patients who have infantile esotropia, regardless of age at surgical alignment. Clinical evidence suggests that alignment before 2 years of age is associated with development of some degree of binocular vision." (34)

Conjunctival incisions for rectus muscle surgery:

Any strabismus surgery requires an incision through the conjunctiva and Tenon's fascia for access to the episcleral space in which the surgical manipulation occurs. The limbal and the fornix approaches represent the two most utilized surgical approaches for strabismus surgery.

The fornix approach is the method of choice in pediatric strabismus surgery. Hence, in accordance with the topic of this paper, only this approach will be elaborated upon.

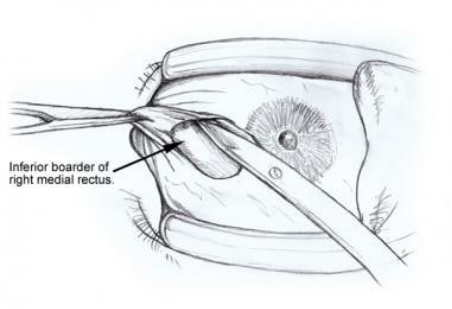
Fornix (cul-de-sac) approach

A fornix conjunctival incision is made preferably in an inferior oblique quadrant parallel to the lid margins between adjacent rectus muscles, approximately, 8–10 mm posterior to the limbus. "The globe is rotated to expose the incision site. The conjunctiva is grasped, placed under mild anterior traction, and a 6–8 mm incision is made." (35) The Tenon's fascia is then incised to gain access to the episcleral space. (35)

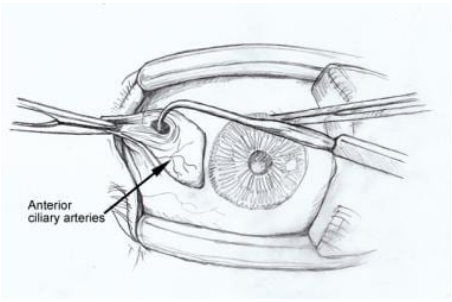
Muscle Weakening Procedure: Recession of the Medial Rectus Muscle

Dissection and muscle hooking

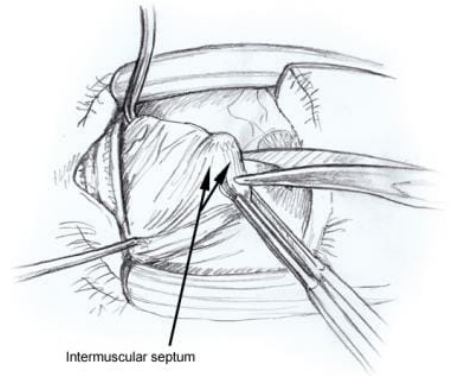
Figures 8-15: Visual representation of the surgical step described. (36)



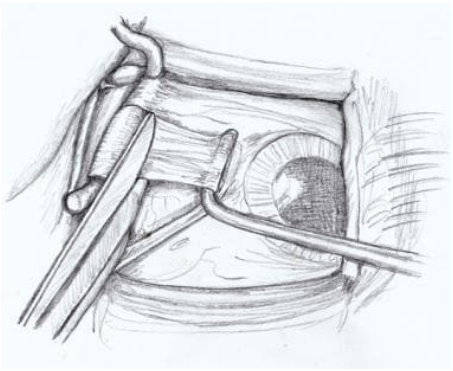
Following the incision into the conjunctiva in the area of the inferior nasal fornix, the conjunctiva and Tenon's capsule are grasped and pulled up to expose the inferonasal quadrant in which a buttonhole is made under the intermuscular septum.



The eye is stabilized in an abducted position while the inferior nasal conjunctiva and Tenon's capsule are grasped and retracted. "Under visualization of the inferior pole of the medial rectus muscle, identified by the anterior ciliary artery, a small Steven's hook is placed perpendicular to the sclera and passed behind (under) the medial rectus muscle."

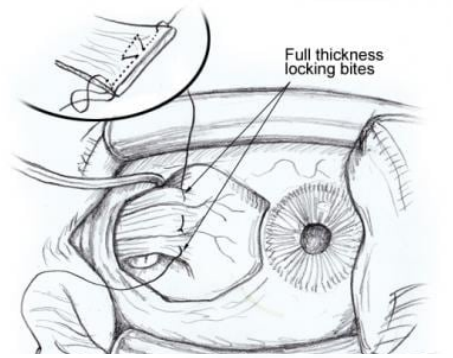


A large Jameson hook is passed parallel to the muscle insertion line and firmly pressed against the sclera until the muscle hook encompasses the entire width of the muscle. The superior nasal intermuscular septum is then folded over and incised over the tip of the Jameson hook.

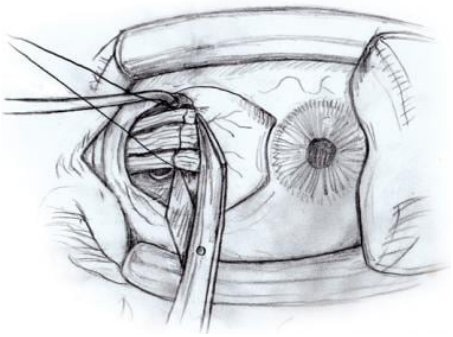


At this stage, the anterior Tenon's capsule is removed with Westcott scissors and the anterior ciliary vessels are cauterized, laying bare the medial rectus muscle. (36)

Securing the muscle and disinsertion

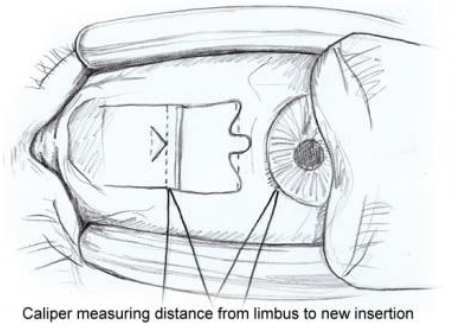


The tendon is divided into three equal segments, and a suture is passed through the muscle's anterior insertion, with a locking bite both superiorly and inferiorly. (33)



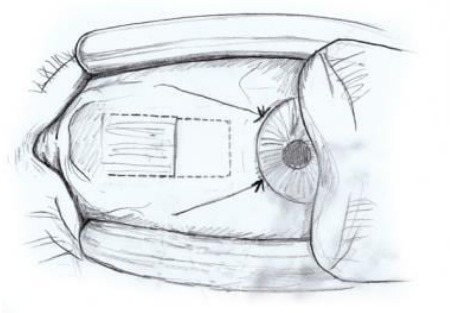
"Once the muscle is secured, the preplaced sutures are pulled up, the inferior and superior edge of the insertion is marked with a sterile marking pen, and the muscle-tendon is disinserted with Westcott scissors." (36)

<u>Recession and securing of the muscle to the sclera at its new location and closure</u>


Caliper measuring distance from limbus to new insertion

The desired amount of recession is measured from the limbus and marked with a sterile marking pen before anchoring the muscle.

Two sets of scleral passes are made through the superior and inferior end of the original insertion, each with the second scleral pass near the center of the insertion line. Subsequently, the muscle is pulled up to the level of the desired new insertion and spread uniformly against the sclera.



One suture end is cut 3 cm away from the sclera, a knot is tied, and the sutures are cut 2 mm away from the knot. The conjunctiva is finally sutured. (36)

Muscle-strengthening procedure:

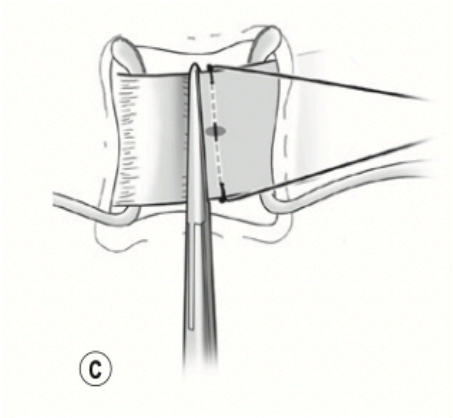
Resection of the lateral rectus muscle:

Preparation of the muscle for resection

After isolation of the rectus muscle, the intermuscular membrane and muscle capsule are dissected for suture placement posterior to the muscle insertion site. During dissection, it is imperative to avoid penetrating Tenon's capsule, "which can promote intrusion of extraconal fat into the operative site; this can produce restrictive strabismus." (35)

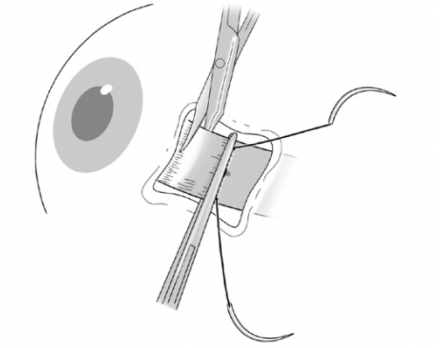
Resection of the muscle

Figures 16-20: Visual representation of the surgical step described. (35,37)



Posterior to the muscle hook, a second hook is placed between the muscle and the sclera and the position of the posterior limit of the resection is marked with a caliper.

"Transverse passes are made, followed by locking bites at the borders of the muscle. A small straight hemostat is placed anterior to the suture and the posterior muscle hook removed." (35)



The muscle is then detached from its insertion and the distal portion of the muscle is excised. The hemostat can be used to help keep the muscle at the insertion position while suturing.

Re-attaching the muscle to the sclera

The sutures are then passed through the original muscle insertion and the muscle is pulled to the site before the sutures are tied and trimmed. In the event of posterior displacement of the muscle due to the sutures, another suture is passed through each pole of the muscle, tied and cut to bring the muscle back to its proper position. (35)

Plication of the lateral rectus muscle:

Muscle plication is an alternative to resection to strengthen a rectus muscle. This procedure is especially valuable in complicated cases because during the early postoperative period it can be easily and fully reversed by merely cutting the muscle suture. Especially valuable in previously operated eyes, it preserves anterior segment circulation through the intact anterior ciliary vessels, thereby reducing the risk of anterior segment ischemia.

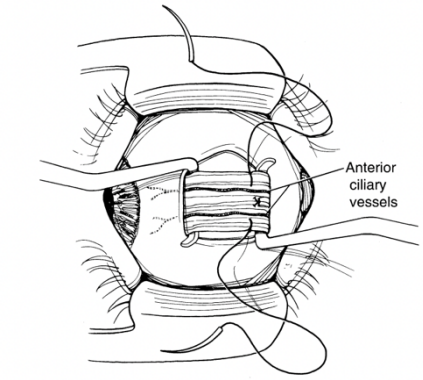
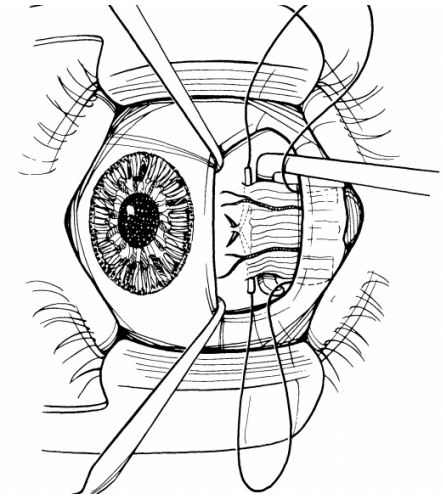


Figure 6-9

"The distal portion of the rectus muscle to be plicated is isolated, cleaned, exposed, and secured at a distance from the insertion equal to the desired plication with a double-armed suture." (37) It is essential to avoid the anterior ciliary arteries, which lie superficially on the muscle surface posterodistally to the insertion.



Next, the needles are placed through the anterior sclera in "crossed swords" fashion. The suture needle enters the sclera anterior to the pole of the insertion to obtain the tucking effect.

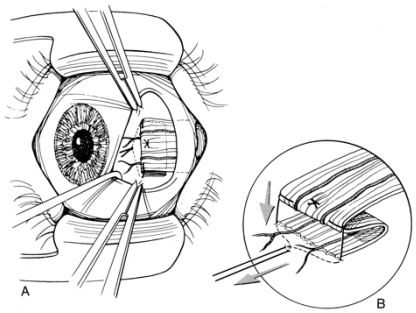


Figure 6-11

The Green muscle hook is now removed, and the sclera is grasped with a toothed forceps adjacent to each pole of the insertion (A). The posterior part of the muscle is directed beneath rather than on top of the advancing proximal muscle and tucked on the two-pole sutures (B). The muscle is then tied onto the sclera. (37)

Surgical considerations:

In infants, recessions and resections are calculated based on the Hirschberg test since prism bar cover tests are not feasible. (38) The categories for qualitative measurement of treatment success are correction of the angle of ocular misalignment and presence and quality of binocularity. Post-surgery follow-ups are recommended on days zero, seven, and six months after surgery. A successful outcome is defined as a residual angle of squint within 10° of orthotropic as measured by prism cover test, prism reflections, or synoptophore at near and distance, and any significant improvement of binocular vision measurement of stereo acuity is considered the gold standard. (39)

BMR recession:

Bilateral medial rectus recession (bimedial recession) is a retroplacement of the medial rectus muscle of both eyes from their original insertion resulting in weakening of the muscles and a corrected esodeviation as a result. (36) It is suitable for a large range of angles of esotropia and is the most commonly performed procedure in strabismus management, usually done for patients without amblyopia and with alternating convergence in previous studies, success rates between 70-90% are documented at a six month follow up. Recessions of more than 5mm were previously discouraged due to concerns about less predictability and the creation of an adduction deficit. Over time, larger BMR recessions of up to 7.5 mm proved not to cause postoperative adduction or convergence deficits. General guidelines for BMR recession to treat constant esotropia have since been updated and are well described in the literature. (38)

Table 7. Recommended amounts of recession in bilateral Symmetric Muscle Surgery (33)

Prism diopters esotropia	Medial rectus recession (mm)
30	5
35	5.5

40	6
50	6.5
60	7.0*
70	7.5*

*Adduction may be compromised

The following are complications of medial rectus muscle recession:

Slipped muscle, muscle loss, muscle split, central muscle sag under/overcorrections and severe adduction deficiency. Large bilateral medial rectus muscle recessions have been linked to late consecutive exotropia. Despite a high (92%) rate of initially successful alignments, Stager et al found that 27 percent of 88 patients who underwent 7.0-mm bilateral medial rectus muscle recessions and were followed for an average of 3.4 years developed consecutive exotropia. (39)

Unilateral rectus recession-resection:

The unilateral recession-resection, or "R&R" procedure, involves a monocular recession of the medial rectus and resection of the lateral rectus to correct the esodeviation. The result of the recession-resection of the agonist and antagonist recti is unidirectional incomitance and ocular rotation limitation. A medial rectus muscle recession reduces inward ocular rotation, and a resection of the lateral rectus muscle further restricts the medial rotation. Because in the R&R procedure some residual incomitance may persist, it is generally used to treat patients with incomitant strabismus and especially in cases of amblyopia and history of previous ocular surgery, allowing for surgery to be performed only on the amblyopic eye to minimize any risks in the better-seeing eye. (40) The lack of exact postoperative success rates with respect to the extent of correction makes a validation of the surgical dose difficult. Nevertheless, in various textbooks, tables on surgical dosage of correction for recession-resection surgery are proposed. The unilateral recession-resection procedure is associated with a 70-90% post-operative success rate, which decreases at each follow up examination. Throughout the follow-up period, persistence of good motor outcomes and a balanced rate of over-and undercorrections can be observed in most studies.

TABLE 8: Monocular Recession–Resection Surgery (33)

Prism diopters esotropia	Medial rectus recession (mm)	Lateral rectus resection (mm)
30	4.5	6
35	5	7
40	5.5	7.5

50	6	8

Three muscle surgery - bilateral medial rectus muscle recession and lateral rectus muscle resection:

This procedure involves a bilateral recession of the medial rectus coupled with monocular resection of the lateral rectus of the non-esotropic eye. It is associated with a high success rate backed up by good long-term follow-ups. Many strabismologists like to add lateral rectus muscle resections to the bimedial recessions to minimize the rate of undercorrections and the resulting stability of outcome, especially for larger angles of esodeviation. In the existing literature on overcorrection rates, after undergoing 3 horizontal muscle surgery, there is no consensus. (41)

Surgery and Botox combination:

Botulinum toxin is a relatively new approach for augmenting, rather than replacing, strabismus surgery. Given that the direct effects of botulinum toxin augmentation persist just 4 months, it is possible that botulinum toxin augments surgery by modifying the anatomy of the medial rectus muscles permanently. Furthermore, the earlier improvement in alignment in patients who had augmented surgery may boost the chance of motor fusion recovery, adding to the long-term benefit of augmented surgery over incisional surgery alone. Botulinum toxin-augmented surgery may be particularly well-suited for large-angle infantile esotropia because achieving good long-term alignment with a single procedure can be challenging with current surgical techniques. One popular approach is to perform “supra-maximal” (≥7 mm) bilateral medial rectus muscle recessions. While satisfactory success rates have been reported with supra-maximal recessions, follow-up is often short and there is a concern about long-term overcorrection. An important practical issue in the utilization of botulinum toxin-augmented surgery is the lack of dosing tables. There is significant variability among surgeons in the amount of surgery and dose of botulinum toxin used for a given angle of deviation. A dosing table comparing the surgical effect of conventional surgery to botulinum toxin-augmented surgery to help guide surgeons who wish to use this technique can be suggested using data from previous studies, but further studies are necessary to determine whether modifying the botulinum toxin dosage can influence the augmentation effect. The use of botulinum toxin either alone or combined with surgery is commonly associated with transient overcorrection and ptosis. These were both common in the augmented-surgery patients but may resolve with no long-term sequelae. Using higher concentrations of botulinum seems to reduce the incidence

and severity of post-injection ptosis. It is essential to be aware that injection of botulinum toxin will often create a short-term adduction limitation, and thus mask this complication were it to occur. (42)

8. TIMING OF SURGERY:

In terms of both high-grade stereopsis in some children and the percentage of children developing any stereopsis, recent evidence favors very early surgery (within six months of the onset of infantile esotropia) over early (up to 24 months of age) and late surgery (after 24 months of age). The specific benefits of very early surgery for infantile esotropia include decreased severity of DVD and the need for additional surgery for either DVD or inferior oblique overaction, as well as the additional benefit of minimizing sensorimotor and gross motor development delays. (43)

Table 9: Advantages and disadvantages of early and late timing of surgery (43)

Timing	**Advantages**	**Disadvantages**
Early: Before 24 months	Better stereopsis and binocular vision	Accommodative esotropia sequelae
	Reduced incidence and severity of DVD	Inaccurate estimation of angle of deviation
	Minimizes delay in sensorimotor development	
Late: After 24 months	Better accuracy of angle of deviation	Increased incidence of DVD
	Better management of amblyopia	Additional surgery requirement
	Better management of vertical misalignment	Poor stereopsis and binocular vision

The current standard age for the first surgery for IE in the United States is approximately 12-18 months, whereas surgery for IE is performed at 2 or 3 years in many European countries. Several case-series studies have found stereopsis in 35-80% of children operated on between 0 and 6 months. Recently, there has been a call for surgery within two months of the onset of esotropia. Other than the European Early vs. Late Infantile Strabismus Surgery Study, there have been no studies with prospectively assigned early- and late-surgery groups and intention-to-treat analysis. The study's primary finding was that 13.5 percent of those operated on at approximately 20 months of age recognized the Titmus Housefly, compatible with gross stereopsis, at the age of 6 years, compared to 3.9 percent of those operated on at approximately 49 months. Beyond Titmus Housefly, no benefit was found for finer stereopsis. (44) The possibility of spontaneous resolution is a frequently cited argument against early surgery. This

concern prompted the development of two studies: the Congenital Esotropia Observational Study (CEOS) and the Early Surgery for Congenital Esotropia (ESCET) collaborative clinical trial, a proposed multicenter randomized clinical trial. According to the CEOS, infantile esotropia persists in 98 percent of infants with large-magnitude (20° or 40 PD) constant esotropia that manifests after ten weeks of age and a refractive error of 3.00 diopters. As a result, the CEOS and other studies successfully defined a clinical profile of infants who would benefit from early surgery. Another issue with early surgery is the instability of deviation in young infants. A recent prospective study addressed this issue, finding that neither the instability of misalignment nor the accuracy of orthoptic measurement negatively impacted long-term eye alignment in patients who had early surgery. (45)

9. OUTCOME:

Horizontal reoperation is associated with a greater angle of preoperative deviation and a younger age at initial surgery. The risk of requiring a second surgery was higher in younger patients at the time of the first surgery and had a larger deviation angle at presentation. DVD is another significantly more common factor among patients who need reoperation. There is a link between a successful outcome and a lower prevalence of DVD. The significance of long-term regular follow-up in cases of infantile esotropia cannot be overstated. A larger angle of preoperative deviation and a younger age at the surgery are risk factors for residual esotropia. This is not surprising given that infants with large esotropias are operated on earlier than those with smaller angles. The increased rate of undercorrections in this younger group may be due to deviation instability, poor cooperation of the young patient, and difficulty obtaining accurate measurements. Longer follow-up time is associated with consecutive exotropia. It is possible that, initially, successful alignment will lead to overcorrection over time. Rajavi et al.3 discovered 30 percent gross stereopsis among successfully aligned cases with a minimum age of 5 years at final measurement in a cohort of 157 infantile esotropia patients. In a cohort of 112 patients, Na et al. reported 48.1 percent stereo acuity in infantile esotropia patients aligned within 8 PD with a single surgery. The rate of stereopsis was 36.4 percent in a cohort of 129 infantile esotropia cases aligned within 8 PD by age 24 months in a study by Birch et al.; however, it fell to 8 percent when the alignment was achieved after age one year, emphasizing the impact of age at alignment on stereopsis. The multicenter ELISSS study found a benefit for the early group (13.5 percent vs. 3.9 percent) in achieving gross stereopsis in infantile esotropia cases operated between 6–24 months (early) and 32–60 months (late). Finer stereopsis, on the other hand, provided no benefit. The authors reported that operating earlier, in the first year of life, could result in higher levels of stereopsis. (46) Even though reoperation is one of the most

common complications of IE surgery, few studies have identified factors associated with failed postoperative motor alignment. One of the most important clinical factors associated with motor and sensory outcomes is the timing of initial surgery. Surgery performed after the age of three years increases the risk of unsuccessful alignment on the first attempt; in fact, children operated on after the age of three have a significantly increased risk of reoperation. Late-operated IE patients have worse stereopsis, resulting in poorer motor alignment. Another factor to consider is the role of strabismus in the family history of IE. According to the literature, the prevalence of strabismus in the family ranges from 6% to 74%. Demographic factors such as gender and family strabismus history are linked to an increased risk of reoperation. Patients with preoperative hypertropia have a significantly lower reoperation rate. In terms of surgery timing, children who have their first operation after 36 months of age have a higher frequency of reoperation than children who have their first operation before 24 months of age. (47)

10. CONCLUSION:

In conclusion, the surgical correction of infantile esotropia is well-studied across multiple centers, but because the patients have very variable presentations with ocular and extra ocular comorbidities, the treating surgeon has the merit to choose the procedure he believes will produce the best outcome, individual to the patient. Ideally, children who have had infantile esotropia surgically treated should have no deviation of the visual axis at distance or near. However, surgery is considered successful when the postoperative deviation is less than 10 prism diopters from orthotropia. Although successful alignment early in life does not guarantee long-term stability, the prognosis for motor alignment and binocularity in the hands of trained surgeons is good. In 80 percent of cases, alignment to within 10 PD of orthotropia can be achieved. When this is accomplished before the age of two, approximately 70% of children achieve some degree of peripheral fusion and gross stereopsis (monofixation syndrome). Binocular fusion and high-grade stereo acuity are more likely with early surgery (3–4 months of age). Late surgery (after the age of two years) reduces the chances of achieving binocular fusion. Because achieving good long-term alignment with a single procedure can be difficult with current surgical techniques, botulinum toxin-augmented surgery may be particularly well-suited for large-angle infantile esotropia. Further multi-center prospective studies are needed to further explore most suitable surgical methods in accordance with the whole clinical picture of the infant.

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