Published in final edited form as:
Ophthalmology. 2011 June ; 118(6): 1170–1174. doi:10.1016/j.ophtha.2010.10.032.

Long-term Follow-up of Acquired Nonaccommodative Esotropia in a Population-based Cohort

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Abstract

Purpose—To describe the clinical characteristics and long-term outcomes of children diagnosed over a 30-year period with acquired nonaccommodative esotropia (ANAET).

Design—Retrospective chart review of a population-based cohort.

Participants—All pediatric (< 19 years of age) residents of Olmsted County, Minnesota, diagnosed with ANAET from January 1, 1965, through December 31, 1994.

Methods—The medical records of all potential patients identified by the resources of the Rochester Epidemiology Project were reviewed.

Main Outcome Measures—Incidence, clinical characteristics, and long-term motor and sensory outcomes of children with ANAET.

Results—A total of 174 children were diagnosed during the 30-year period, yielding an incidence of 1 in 287 live births. The median age at diagnosis for the 174 patients was 4.0 years (range, 11 months to 18.2 years), and 61% (107) were male (p=0.009). Although 11% (8 of 75) of those queried were diplopic, none of the 174 were subsequently diagnosed with an intracranial lesion. During a mean follow-up of 10.9 years (range, 0 days to 37 years), 127 (73%) patients underwent strabismus surgery (mean, 1 surgery; range, 0 to 3 surgeries). Among the 127 who underwent surgery, the median final stereoacuity was 3000 seconds of arc, including 8 (6.3%) patients with 50 seconds of arc or better. Patients who were older (> 44 months) at ANAET diagnosis (p=0.005) and without amblyopia at their initial exam (p, 0.001) were more likely to achieve excellent final stereopsis.

Conclusion—In this population-based cohort, ANAET occurred in 1 in 287 children and was more prevalent among males. Although diplopia was relatively common, none of the children

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Study conducted at Mayo Clinic, Rochester, Minnesota

Presented in part at the 36th Annual Meeting of the American Association for Pediatric Ophthalmology and Strabismus, Orlando, FL, April 15, 2010

None of the authors have financial interests in the subject matter

were found to have an intracranial malignancy. Most patients achieved good motor and sensory outcomes, with the best results among those with a later onset of their deviation and no amblyopia.

Acquired nonaccommodative esotropia (ANAET) is a disorder of ocular alignment characterized by a nonaccommodative esodeviation that develops after 6 months of age in an otherwise healthy child. Conventionally, ANAET is considered to occur infrequently,[1, 2] but often raises concern for the potential of an underlying neurologic malignancy.[3–6] However, recent reports have demonstrated that this form of childhood esotropia is relatively common[7] and that an associated intracranial tumor or other central nervous system lesion is rarely present.[8] Moreover, these children can attain excellent sensory and motor outcomes, especially if the onset of the esodeviation occurs after 30 months of age.[9] The purpose of this study is to report the presenting features, management, and long-term outcomes of a large cohort of children diagnosed with ANAET over a 30-year period using a population-based medical record retrieval system.

Subjects and Methods

The medical records of all pediatric patients (< 19 years of age) residing in Olmsted County, Minnesota, who were diagnosed with ANAET from January 1, 1965, through December 31, 1994, were retrospectively reviewed. Institutional review board approval at both Mayo Clinic and Olmsted Medical Group was obtained for this study. Potential cases of ANAET were identified by using the resources of the Rochester Epidemiology Project (REP), a medical records linkage system designed to capture data on any patient–physician encounter in Olmsted County, Minnesota.[10, 11] The racial distribution of Olmsted County residents during the years of this study was greater than 95% white and less than 3% each for Asian-, African-, and Native American. The population of this county (92,006 in 1980) is relatively isolated from other urban areas, and virtually all medical care is provided to residents by Mayo Clinic or Olmsted Medical Group and their affiliated hospitals. Unaffiliated area optometrists were rarely the sole provider of eye care to children with strabismus during the years of this investigation.

The medical records of all patients < 19 years of age diagnosed with any form of esotropia from the years 1965 through 1994 were reviewed by a pediatric ophthalmologist (BGM). A diagnosis of ANAET was confirmed by the same reviewer and defined as a nonaccommodative esotropia that developed after 6 months of age. Esotropic children with developmental delay or a paralytic or sensory cause of their deviation were excluded. The majority of patients with ≥ 2.50 diopters of hyperopia were initially managed with a 4-week period of wearing their full cycloplegic refraction. However, none of these patients had a decrease of their deviation by 10 or more prism diopters and the use of spectacles was discontinued. Trained residency checkers verified each patient's residency status in Olmsted County at the time of birth and at diagnosis. Children not residing in Olmsted County at the time of their diagnosis were excluded.

The age at onset, when recorded in the primary care or ophthalmic records, was based on the parental history. The angle of deviation was measured by the Hirschberg estimate or Krimsky test in infants, and by the prism and alternate cover test at both distance and near for children old enough to cooperate with testing. Stereoacuity was assessed with the Titmus test. A cycloplegic refraction, using either atropine or cyclopentolate, was performed in all patients. The entire medical record of those diagnosed with ANAET was carefully reviewed through the date of their final examination.

Continuous data were tabulated as a mean or as a median with a range. Categorical data were calculated as counts and percentages. Comparisons between two groups for continuous

variables were completed using Wilcoxon rank-sum tests. While comparisons between two groups for categorical variables were completed using Fisher's Exact test. All statistical tests were two-sided, and the threshold of significance was set at $\alpha=0.05$. The cumulative probability of surgery was estimated using the Kaplan-Meier method.[12]

The annual incidence rates for each sex and 10-year age groups were calculated by dividing the number of cases diagnosed in that group by decennial Olmsted County census data for the 1965–1994 time period. Estimates from the State of Minnesota Demographer's Office were used to aid with linear interpolation between census years. The 95% confidence intervals for the rates were calculated assuming Poisson error distribution. The relation of incidence rates to age were assessed by fitting generalized linear models assuming a Poisson error structure.

Results

One hundred seventy-four new cases of acquired nonaccommodative esotropia were diagnosed among residents of Olmsted County during the 30-year study period, yielding an incidence of 17.7 per 100,000 individuals < 19 years (95% confidence interval [CI]: 15.05 – 20.3), or a birth prevalence of 1 in 287 live births. There was no significant difference in the incidence rate throughout the 30-year study. Pertinent historical and initial clinical exam characteristics of the 174 study subjects are shown in Table 1. After adjusting for decade of diagnosis and age at diagnosis, there was a significant difference between genders, with males comprising 61% of the patient population (p=0.009). A family history of strabismus was positive in 54 (34%) of the 157 patients for whom this data was documented, and the median age at diagnosis for the 174 subjects was 4.0 years of age (range, 10 months to 18.2 years).

Amblyopia was diagnosed in 72 (41%) of the study patients at the initial examination. The median horizontal angle of deviation at diagnosis was 25 prism diopters (PD) at near (range, 0 to 60), and 20 PD at distance (range, 0 to 90). Six patients (3%) had a vertical deviation (mean 0, range 0 to 20 PD), 39 (22%) had inferior oblique dysfunction, while none of the patients had dissociated strabismus. The mean initial cycloplegic refractive error (spherical equivalent) was +1.42 diopters of hyperopia (range, −12.23 to +3.75).

One hundred twenty-seven (73.3%) of the study children underwent surgery and their clinical characteristics are shown in Table 2. The mean duration of time from diagnosis to the first surgical procedure was 10.6 months (range, 1 day to 18 years). Most of those who underwent surgery had one procedure (range, 1 to 3) during a median follow-up of 10.9 years (range, 0 to 37 years) after their diagnosis. In addition to horizontal muscle surgery, which most commonly consisted of a unilateral recess-resect procedure, fifteen (12%) also underwent inferior oblique muscle surgery, and one (1%) required the recession of a single superior rectus muscle. Of the 127 surgical patients, 29 (22.8%) underwent a second surgery, and 5 (3.9%) underwent a third. The Kaplan-Meier rate of undergoing a second strabismus surgery in this population was 25% (95% CI: 15–33%) at 5 years, 28% (95% CI: 18–37%) at 10 years, and 35% (95% CI: 20–47%) at 20 years.

Of the 174 study patients, a final exam was recorded for 171 (98%), with data available for 169 (97%) at a mean age of 11.9 years (range, 3.7 to 42 years). None of the 174 patients were subsequently diagnosed with an intracranial lesion or malignancy during the follow-up period (95% CI: 0.00–2.1%). Patients who underwent surgery were significantly more likely (73%) than nonsurgical patients (47%) to have a final horizontal alignment of ≤ 10 prism diopters (p=0.004). The final median stereoacuity for those who underwent surgery was 3000 seconds of arc (range, 40 seconds to no stereoacuity), including 8 (6.3%) patients with

50 seconds of arc or better. Table 3 shows those factors which were significantly associated with excellent final stereoacuity values (≥ 60 seconds of arc) compared to those with moderate (80–3000 seconds) or poor (no stereopsis) outcomes. Excellent final stereoacuity was correlated with a later age at strabismus onset (4.6 years, p=0.004) and diagnosis (5.9 years, p=0.005). None of the children diagnosed before 44 months of age were found to have excellent stereopsis on the final follow-up visit. The presence of amblyopia at initial exam was also strongly correlated with poor final stereoacuity (p=<0.001), with 71% (34 of 48 for whom data was available) of amblyopic children having no stereopsis at final exam.

Discussion

This study provides population-based data on a 30-year cohort of 174 children diagnosed with acquired nonaccommodative esotropia. In this population, ANAET occurred in 1 in 287 live births, was more common among males, and demonstrated no significant change in incidence over the 30-year study period. Although at least 1 in 9 patients presented with diplopia, none of the 174 were subsequently diagnosed with a central nervous system (CNS) lesion. Nearly three-quarters of those who underwent surgery were well-aligned after a mean duration of one decade, and most patients had measurable stereopsis, including 6% with a functional cure.

ANAET has been traditionally considered a rare form of strabismus, receiving only brief mention in discussions of childhood esotropia.[2,13,14] Within the last two decades, Wright's textbook on pediatric ophthalmology devoted a single paragraph to the entity and characterized it as uncommon,[2] and an American Academy review on acquired esotropia failed to mention this form at all.[13] However, ANAET was diagnosed relatively frequently in this cohort, which is consistent with recent reports in which it was the second most prevalent form of esotropia, accounting for 14.4% [15] to 16.6% [7] of all forms of childhood esotropia.

Children presenting with ANAET often provoke concern regarding an underlying intracranial malignancy,[3–6] yet none of the 174 patients in this cohort were subsequently diagnosed with a CNS lesion during a mean follow-up of one decade. While there are multiple case reports of children presenting with ANAET as the initial manifestation of a brain tumor,[16–18] the results of this series suggest that such an occurrence is sufficiently rare that brain imaging of all patients presenting with ANAET may not be justified. Clinical experience would suggest that imaging is indicated in the subset of ANAET patients with characteristics suggestive of an underlying intracranial process, such as lateral incomitance, a greater deviation at distance compared to near, and the presence of focal neurological deficits.[3, 4] Further research is warranted to identify which children with an acquired nonaccommodative esotropia are at the greatest risk for harboring a CNS lesion.

The majority of the children with ANAET in this study achieved good motor and sensory outcomes after a single surgery. One hundred twenty-seven (73.3%) of the patients underwent a mean of 1 surgery during a median follow up time of 10.9 years from diagnosis. Approximately three-fourths of children who underwent surgery had a final horizontal alignment within 10 PD and some degree of stereopsis. These findings are consistent with the short-term outcomes previously reported by Kitzmann and coauthors.[9] Moreover, these results suggest that, unlike other forms of strabismus such as congenital esotropia[19] or intermittent exotropia,[20] patients with ANAET are more likely to have a successful long-term outcome.

Prior research has demonstrated that an older age at onset (> 30 months of age) is associated with a significantly better postoperative stereoacuity.[9] In this study, patients whose deviation

began after a median of 37 months were more likely to have at least a moderate level of stereopsis at their final exam, with the best outcomes (≥ 60 seconds of arc) occurring among children with an onset after 4 years of age. Additionally, amblyopia appears to be negatively associated with sensory outcomes, with only one-third of amblyopic children achieving any level of stereopsis. However, the duration of time from the onset of strabismus to surgical intervention did not appear to influence the stereoacuity outcome for this form of childhood esotropia.

There are several limitations to the findings of this study. Its retrospective design is limited by non-standardized and incomplete data collection. Additionally, only a small portion of the patients in this study underwent brain imaging to confirm the absence of a CNS lesion. However, the complete medical record of each patient was thoroughly searched for any indication of the development or treatment of such lesions through September 31, 2009. Third, it is possible that, despite the strict study criteria and uniform retrospective identification of subjects, some of the cohort children with a low hyperopic refractive error may have had an accommodative rather than nonaccommodative esotropia, as a trial of full refractive correction was only consistently attempted in those with a refractive error > 2.50 diopters of hyperopia. Furthermore, despite Olmsted County's relative isolation, some residents with ANAET may have sought care outside the region, thereby potentially underestimating the incidence of ANAET in this population. Finally, the relatively homogeneous ethnic composition of Olmsted County may limit the ability to generalize the study findings to other populations.

This population-based study provides data on the long-term outcomes for patients with acquired nonaccommodative esotropia. ANAET occurred in approximately 1 in 287 children and was more prevalent among males. Although diplopia was relatively common, none of the children in this cohort were found to have an intracranial malignancy. The majority of patients underwent a single surgery and, after a mean follow-up of one decade, two-thirds of patients were within 10 prism diopters of orthotropia and measureable stereopsis. The best sensory outcomes occurred among those with an older age at onset and no amblyopia.

Acknowledgments

Supported in part by an unrestricted grant from Research to Prevent Blindness, Inc., New York, NY and by the Rochester Epidemiology Project (Grant #R01-AR30582 from the National Institute of Arthritis and Musculoskeletal and Skin Diseases).

References

1. von Noorden, GK. Burian-von Noorden's Binocular Vision and Ocular Motility: Theory and Management of Strabismus. 3rd ed. St Louis, MO: Mosby; 1985. p. 320-329.
2. Wright, KW., editor. Pediatric Ophthalmology and Strabismus. St Louis, MO: Mosby; 1995. chapter author. Esotropia; p. 179-194.
3. Astle WF, Miller SJ. Acute comitant esotropia: a sign of intracranial disease. Can J Ophthalmol. 1994; 29:151–154. [PubMed: 7922858]
4. Hoyt CS, Good WV. Acute onset concomitant esotropia: when is it a sign of serious neurological disease? Br J Ophthalmol. 1995; 79:498–501. [PubMed: 7612566]
5. Macpherson H, De Becker I, MacNeill JR. Beware: armed and dangerous--acquired non-accommodative esotropia. Am Orthopt J. 1996; 46:44–56.
6. Williams AS, Hoyt CS. Acute comitant esotropia in children with brain tumors. Arch Ophthalmol. 1989; 107:376–378. [PubMed: 2923560]
7. Greenberg AE, Mohney BG, Diehl NN, Burke JP. Incidence and types of childhood esotropia: a population-based study. Ophthalmology. 2007; 114:170–174. [PubMed: 17070595]

8. Mohney BG. Acquired nonaccommodative esotropia in childhood. J AAPOS. 2001; 5:85–89. [PubMed: 11304815]
9. Kitzmann AS, Mohney BG, Diehl NN. Short-term motor and sensory outcomes in acquired nonaccommodative esotropia of childhood. Strabismus. 2005; 13:109–114. [PubMed: 16251139]
10. Kurland LT, Molgaard CA. The patient record in epidemiology. Sci Am. 1981; 245:54–63. [PubMed: 7027437]
11. Melton LJ III. History of the Rochester Epidemiology Project. Mayo Clin Proc. 1996; 71:266–274. [PubMed: 8594285]
12. Kaplan EL, Meier P. Nonparametric estimation from incomplete data. J Am Stat Assoc. 1958; 53:457–481.
13. Wilson, FM., editor. Basic and Clinical Science Course, Section 6, 1991–2. Pediatric Ophthalmology and Strabismus. San Francisco, CA: American Academy of Ophthalmology; 1991. p. 263
14. Dankner SR, Mash AJ, Jampolsky A. Intentional surgical overcorrection of acquired esotropia. Arch Ophthalmol. 1978; 96:1848–1852. [PubMed: 697622]
15. Mohney BG. Update on childhood esotropia [letter]. Ophthalmology. 2002; 109:1583–1584. [PubMed: 12208692]
16. Anderson WD, Lubow M. Astrocytoma of the corpus callosum presenting with acute comitant esotropia. Am J Ophthalmol. 1970; 69:594–598. [PubMed: 5309572]
17. Harada T, Ohashi T, Ohki K, et al. Clival chordoma presenting as acute esotropia due to bilateral abducens palsy. Ophthalmologica. 1997; 211:109–111. [PubMed: 9097318]
18. Simon JW, Waldman JB, Couture KC. Cerebellar astrocytoma manifesting as isolated, comitant esotropia in childhood. Am J Ophthalmol. 1996; 121:584–586. [PubMed: 8610811]
19. Louwagie CR, Diehl NN, Greenberg AE, Mohney BG. Long-term follow-up of congenital esotropia in a population-based cohort. J AAPOS. 2009; 13:8–12. [PubMed: 18993096]
20. Ekdawi NS, Nusz KJ, Diehl NN, Mohney BG. Postoperative outcomes in children with intermittent exotropia from a population-based cohort. J AAPOS. 2009; 13:4–7. [PubMed: 18848478]

Table 1

Historical Characteristics and Initial Ophthalmologic Findings in 174 Children with Acquired Nonaccommodative Esotropia over a 30-Year Period from Olmsted County, Minnesota

	ANAET Cases (N=174)	
Characteristic		**N used***
Male, n (%)	107 (61%)	174
Prematurity,** n (%)	17 (15%)	113
Mean birth weight in grams (range)	3126 (1320, 4852)	112
Family History of strabismus, n (%)	54 (34%)	157
Mean age in years at onset, (range)	3.0 (7 mos, 9.1yrs)	174
Mean age in years at diagnosis, (range)	4.0 (10 mos, 18.2yrs)	174
History of diplopia, n (%)	8 (11%)	75
Amblyopia, n (%)	72 (41%)	174
Nystagmus, n (%)	1 (<1%)	174
Difficulty with Pregnancy, *** n (%)	52 (44%)	118
Median PD horizontal alignment at near, (range)	25 (0, 60)	173
Median PD horizontal alignment at distance, (range)	20 (0, 90)	165
Mean refraction at initial exam, (range)	+1.42 (−12.23, +3.75)	155

* Number of patients for whom data was available within the medical record

** Less than 37 weeks gestational age

*** Included intrauterine infection, Cesarean section, forceps delivery, nuchal cords, meconium staining, low Apgar scores

ANAET=Acquired Nonaccommodative Esotropia; PD = prism diopters

Table 2

Surgical Characteristics of 174 Children Diagnosed with Acquired Nonaccommodative Esotropia over a 30-year Period

	ANAET Cases (N=174)	
Characteristic	**n (%)**	**N used***
Patients who underwent a first surgery, n (%)	127 (73%)	174
Patients who underwent a second surgery, n (%)	29 (17%)	174
Patients who underwent a third surgery, n (%)	5 (3%)	174
Mean number of surgeries per patient, (range)	1 (0, 3)	127
Mean time from diagnosis to first surgery, (range)	10.6 months (1d, 18yr)	127
Procedure(s) conducted during first surgery		127
Medial recession and Lateral resection, n (%)	70 (56%)	
Bimedial rectus recession, n (%)	55 (43%)	
Unilateral medial rectus recession, n (%)	1 (1%)	
Inferior oblique, n (%)	15 (12%)	127
Other muscles, n (%)	1 (1%)	127
Required subsequent surgery for additional correction of ET, n (%)	16 (13%)	127
Required subsequent surgery due to development of XT, n (%)	13 (10%)	127

* Number of patients for whom data was available within the medical record ANAET=Acquired Nonaccommodative Esotropia; ET=Esotropia; XT=Exotropia

Table 3

Historical and Clinical Features Among Postoperative Acquired Nonaccommodative Esotropia Patients with High Grade Final Stereopsis Compared to Those with Moderate or Poor Stereopsis

Characteristic	Final Stereoacuity of 40–60 (n=8)	Final Stereoacuity of 80 to 3000 (n=52)	No stereoacuity (n=54)	p-value
Male, n (%)	5 (63%)	31 (60%)	30 (56%)	0.92
Median Age at ANAET onset in years (range)	4.6 (3.7, 8.3)	3.1 (0.8, 9.1)	2.6 (0.0, 6.4)	0.004
Median Age at ANAET diagnosis in years (range)	5.9 (3.9, 9.5)	3.5 (0.9, 9.1)	3.6 (1.0, 6.9)	0.005
Mean time between onset and surgical correction	1.7 (1.9mo, 4.4yr)	1.3 (1.6 mo, 7.8yr)	1.8 (3.4mos, 20.0yr)	0.48
Prematurity, n (%)	0 (0%)	6 (17%)	5 (15%)	0.79
Mean birth weight in grams (range)	2856 (2090, 3760)	3110 (1520, 4220)	3053 (1675, 4180)	0.89
Family History of strabismus	1 (13%)	17 (35%)	17 (37%)	0.46
History of diplopia	0 (0%)	2 (11%)	3 (11%)	1.00
Amblyopia at initial exam	2 (25%)	12 (24%)	34 (68%)	<0.001
Median horizontal alignment at near, (range) – initial exam	20 (6, 35)	28 (0, 50)	30 (10, 60)	0.044
Median horizontal alignment at distance, (range) – initial exam	20 (2, 30)	20 (0, 40)	22.5 (10, 90)	0.14
Mean refraction at initial exam, (range)	1.1 (0.4, 2.1)	1.7 (−1.25, 3.75)	1.8 (0.6, 3.8)	0.096

- Note, final stereoacuity was available for 114/127 of the surgery patients
- Categorical variables are reported as n (%) and p-values given are based on Fisher's Exact test.
- Continuous variables are reported as median (or mean) and (minimum, maximum) and p-values given are based on Kruskal-Wallis test.

ANAET=Acquired Nonaccommodative Esotropia