

Natural history of infantile anisometropia

Maths Abrahamsson, Johan Sjöstrand

Abstract

Aims/background—In a previous study longitudinal changes of anisometropia were investigated. It was shown that anisometropia arises and vanishes during the emmetropisation process and that the associated risk for amblyopia is low. The aim of this study was to follow acuity and refraction longitudinally in children with marked anisometropia at 1 year of age.

Methods—Refractive errors and visual acuity were estimated every sixth month for a selected group of 20 children with marked anisometropia ≥ 3.0 D (spherical equivalent) at 1 year of age from approximately 3 to 10 years of age.

Results—The children could be classified into three groups. In six subjects the anisometropia increased (mean 1.4 D) and they all developed amblyopia. The remaining children could be classified into two groups of equal size. One group developed no amblyopia and the anisometropia decreased with a mean of 3.0 D. The seven remaining children developed amblyopia and/or strabismus; the mean anisometropia decrease was 1.2 D.

Conclusion—Anisometropia at 1 year of age that is larger or equal to 3.0 D will in 90% of the cases still be there at 10 years of age. There is a substantial risk of this group developing amblyopia (60%).

(*Br J Ophthalmol* 1996;80:860-863)

Anisometropia has been assumed to be one of the leading causes of amblyopia. The mechanisms of anisometropic amblyopia are poorly understood; von Noorden¹ suggests that there may be active inhibition of the fovea of the defocused eye to eliminate sensory interference caused by superimposition of a focused and a defocused image. There is no doubt that anisometropia is closely related to amblyopia²⁻⁴ and strabismus.⁵⁻⁶ The use of anisometropic amblyopia as a generic term⁷⁻⁸ implies a strong causative effect of anisometropia in the development of amblyopia. There are findings, however, that can be interpreted in such a way that anisometropia is a secondary phenomenon⁹⁻¹¹ and that the causative relation between anisometropia and amblyopia must be reconsidered. In cases with convergent squint there is a common tendency to develop anisometropia after the onset of strabismus.^{6,9,10}

The non-fixing eye ceases to emmetropise and subsequently the child develops anisometropia.

Another important aspect of anisometropia as a cause for amblyopia is its transitory behaviour during childhood.¹⁰⁻¹³ Abrahamsson *et al*¹⁰ longitudinally followed cases with anisometropia and showed that a substantial anisometropia (5 D) could vanish during growth and that children developed anisometropia as a part of the emmetropisation process. This anisometropia then vanished with time. In approximately 30% of the cases with anisometropia at 1 year of age the anisometropia was still present at 4 years of age. The studies were mostly concerned with cases with anisometropia less than 3 D. These data coincide with findings presented by Birch *et al*¹⁴ who found that 25% of the children with anisometropia at 1.5 years were still anisometropic at 4 years. Almeder and coworkers¹¹ showed that all their cases had a reduction in anisometropia during subsequent visits and ended with a refractive error within normal limits.

It can be stated that there is a relation between anisometropia and amblyopia although it is difficult to analyse the mechanism involved. It seems as if limited anisometropia can be common among young children without affecting their visual development. The aim of this study was to evaluate the natural history of marked anisometropia (≥ 3.0 D). In an earlier study we examined the variability of anisometropia, where the anisometropia in most cases was between 1 and 3 D.¹⁰ In this study we concentrate on those cases with an anisometropia of 3 D or more at 1 year of age.

Methods

In the city of Västerås, Sweden, all children were offered a voluntary ophthalmological control at the age of approximately 1 year through the children's health care centres. The examination consists of assessment of motility and alignment as well as of cycloplegic retinoscopy. The children were refracted by retinoscopy 30 minutes after instillation of cyclopentolate (1%). Retrospectively we studied the refraction data for children born between 1980 and 1983. Twenty consecutive children with anisometropia (spherical equivalent) greater than or equal to 3.0 at 1 year of age were selected among these children for this study.

Institute of Clinical Neuroscience,
Department of Ophthalmology,
Göteborg University,
Göteborg, Sweden
M Abrahamsson
J Sjöstrand

Correspondence to:
Maths Abrahamsson,
Institute of Clinical Neuroscience, Department of Ophthalmology, Göteborg University, 413 45 Göteborg, Sweden.

Accepted for publication
28 June 1996

Table 1 Study population

	Esotropia	Exotropia	Orthotropia
Group A	3*	0	3*
Group B	1	1*	5*
Group C	0	0	7

Group A = six children with increasing anisometropia; group B = seven children with decreasing anisometropia; group C = seven children with decreasing anisometropia and no amblyopia or strabismus.

*Cases with amblyopia.

Among these cases no one had an anisometropia greater than 5.5 D.

The children were prescribed glasses that fully corrected the anisometropia at 2 to 3 years of age. The use of the spectacles was only checked by reports from the parents. The reported spectacle use did not differ significantly among the three groups of patients described below. The refractive errors were then measured at a regular interval of about 6 months and visual acuity was measured at the same time. Refractive errors and visual acuity were followed until the child reached 10 years of age. Amblyopia was treated according to clinical practice.

In this study we describe refraction and refraction changes in infants and young children. The reliability of the data depends on the accuracy of the refraction data. All refraction data in the study on young children up to 6 years of age were obtained by one experienced ophthalmologist, while some refraction data in older children were measured by several other ophthalmologists at different eye clinics. We tried to minimise the effects of having different people measuring refraction.

Results

Refraction and visual acuity were tested in 20 children with anisometropia of 3.0 D or more spherical equivalent at 1 year of age. Although the degree of anisometropia changed during growth, 90% of the children were still anisometric at 5 years of age and 70% (14/20) at 10 years of age using 1 D spherical equivalent or more as a definition for anisometropia. Presence or absence of emmetropisation, especially of the more hyperopic eye, divided the population into three groups. In six patients the emmetropisation failed completely (Tables 1 and 2). The ametropia as well as the anisometropia increased during the 10 year test period. All cases developed amblyopia which was treated with reasonable success. The acuity in the amblyopic eye at end of treatment was 0.65 or better in all cases. In three of the cases convergent squint was added to the amblyopia (Table 1). The mean increase of anisometropia during the period was 1.4 D, ranging from 0.5 to 2.0 D. There was also an increase in overall ametropia.

Table 2 Change in mean anisometropia during the test period from 1 to 10 years of age

	Group A	Group B	Group C
Anisometropia decrease	-1.4 D*	1.2 D	3.0 D

* The anisometropia increased during the test period.

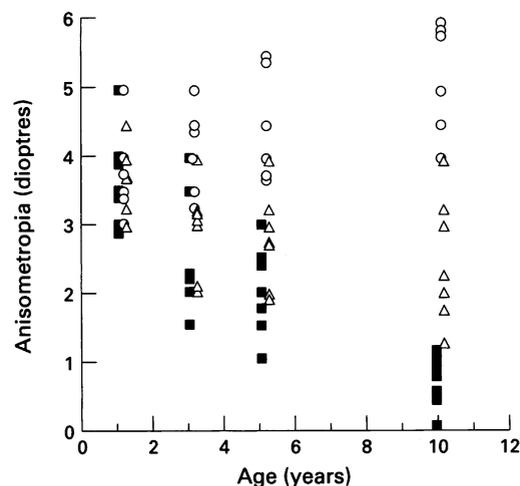


Figure 1 The three groups of patients with anisometropia are marked with open circles (six children with increasing anisometropia), open triangles (seven children with decreasing anisometropia), and filled squares (seven children with decreasing anisometropia and no amblyopia or strabismus). Anisometropia at 1, 3, 5, and 10 years are presented. In order to increase visibility in the diagram two of the groups are displaced with 0.1 units of time each.

In the remaining 14 cases the anisometropia as well as the ametropia decreased with growth. These cases could be classified into two groups of equal size by visual outcome. In one group consisting of seven children the emmetropisation was marked and no visual disorder such as amblyopia or strabismus could be seen (Tables 1 and 2). The mean anisometropia decrease was 3.0 D with a range from 2.5 to 4 D for the whole 10 year period.

The remaining seven cases consisted of six children developing amblyopia and one child with convergent squint, but no acuity difference between the eyes. One of the patients with amblyopia resisted treatment and visual acuity remained below 0.3 in spite of intensive occlusion therapy. It is impossible to conclude if this is a result of resistance to treatment or a consequence of poor compliance. The mean anisometropia decrease in this group was 1.2 D, ranging from 0 to 1.75 D during the 10 years studied. For all three groups the most pronounced change in anisometropia and ametropia took part during the first 4 years of life. The changes in anisometropia from 1 to 10 years of age are given in Figure 1.

The anisometropia was hypermetropic in 19 cases and in one case a crossing over with one myopic and one hyperopic eye. Thus, 39 hyperopic eyes and one myopic eye were followed in the study. The ametropia in all cases except two was a compound of hypermetropia/myopia and astigmatism. Two cases had no astigmatism in either eye during the follow up period. Among the rest the astigmatism component varied from 0.5 to 3 D. There was no systematic difference in the spherical refractive error/astigmatism ratio between the groups at the beginning of the test period. Among those with decreasing anisometropia the astigmatism also decreased. In the other two groups the astigmatism could increase, decrease, or stay unchanged. No obvious relation between amount of astigmatism and amblyopia could be identified.

Twelve developed amblyopia and five convergent or divergent squint among the 20 children examined, while seven cases had a 'normal' visual development. Among the latter cases the visual acuity was 1.0 or better in both eyes.

Discussion

Anisometropia, an interocular difference in refractive state, has been historically considered to be a significantly amblyogenic factor. The concept of anisometropic amblyopia which implies a causative relation between anisometropia and amblyopia is easy to conceive. The differences in refractive state cause differences in the retinal image, size, and sharpness of the image between the two eyes. Several studies of animal models have shown that monocular image degradation results in amblyopia and anisometropia. Raviola and Wiesel¹³ have demonstrated this most convincingly in studies of monkeys. Degradation of the retinal image will cause amblyopia and elongation of the eyeball. However, studies of infantile anisometropia have shown that it is transitory and represents little risk for the development of amblyopia^{10,11} especially in young children 1 to 3 years of age. Abrahamsson *et al.*¹⁰ showed that prevalence of anisometropia at any given age level, between 1 and 4 years of age was constant, although the individuals were different. Considerable magnitude of anisometropia (up to 5 D) could vanish or at least decline to 1 dioptre or less during this period. It also seemed as if a low level of anisometropia (≤ 2.5 D) arises and vanishes as a part of the emmetropisation process. The reduction of hyperopia had a degree of independence in the two eyes and possibly in the different axis of each eye. Most important was that these children usually did not develop any amblyopia. Their visual acuity increased in both eye in a perfectly normal way and the transitory anisometropia had little consequence for the visual development.

In order to further examine the variability of anisometropia during childhood we studied 20 patients with anisometropia ≥ 3.0 D at 1 year of age and without signs of any ocular disease or malformation. Data from this group differed from the results presented in an earlier study.¹⁰ The anisometropia examined in that group was mostly ≤ 2.5 D and approximately 30% of those children with anisometropia at 1 year of age were still anisometropic at 4 years of age. In the present study 90% of the children were anisometropic at 5 years and 75% at 10 years of age. These data coincide with results presented by Birch *et al.*¹⁴ In that study 28% remained anisometropic at 4 years among those with anisometropia ≤ 2.5 D and 82% in the group with marked anisometropia.

The association between anisometropia and amblyopia has been pointed out in numerous studies. The studies of deVries⁴ and Phelps and Muir¹⁵ indicate that anisometropia was accompanied by strabismus in approximately 40% of cases. They also demonstrated that amblyopia was present in 60% of all cases with orthotropic anisometropia. In our study amblyopia

was present in eight out of 15 (53%) of the cases with marked orthotropic anisometropia. In an earlier study¹⁰ we found that 30% of children with persistent anisometropia from 1 to 4 years of age developed amblyopia.

It is notable that among the seven cases with normal visual development two cases are anisometropic (≥ 1 D) at 5 years of age and only one (≥ 1 D) at 10 years of age, although their anisometropia ranged from 3 to 5 D at 1 year of age. In these cases it seems as if the anisometropia is taken care of by the emmetropisation process.

The results in this study indicate that anisometropia of approximately 5 D is at the limit of what the visual system can handle during early childhood. When the anisometropia becomes larger the regulatory mechanisms of the visual system become inefficient; the anisometropia increases and the child develops amblyopia. In the interval between 2 and 5 D some children grow out of their anisometropia and they may have a normal visual development. Their visual development is not affected by the difference in retinal image quality and size between the two eyes. This is to be compared with the children within the same anisometropia interval which show increasing anisometropia—that is, a failure to emmetropise and consequently develop amblyopia. This stresses essential questions: is the marked anisometropia at 1 year of age already present at birth and the result of a growth delay in the more hyperopic eye? Is transitory anisometropia during childhood a part of natural development? Does it cause amblyopia? Does amblyopia cause the emmetropisation to stop and thereby make the anisometropia persistent? Does amblyopia create anisometropia? Answers to these questions can only be speculations. One possible way of explanation is to consider amblyopia as the main problem and persistent anisometropia as a consequence of a fault in the growth regulation of the eye and that one of the features of amblyopia is to induce such a fault.

An interesting parallel to animal studies of amblyopia and anisometropia can be pointed out. Hung *et al.*¹⁶ use monkeys, *Macaca mulatta*, and induced an anisometropia of plus or minus 3 and 6 D. The monkeys with an anisometropia of 3 D could adapt to the induced refractive error and developed a permanent anisometropia opposite to the optically induced one. When 6 D lenses were used the monkeys were unable to adapt. Induced anisometropia of 6 D or more is the amount commonly used in animal models of amblyopic anisometropia. The fact that the induced anisometropia in animal models is more marked than that normally present in human children can explain why the relation between amblyopia and anisometropia is much stronger in the monkey studies.¹⁶

When it comes to older children it is much less clear how the anisometropia changes with time. Studies indicate^{4, 17} that anisometropia becomes more stable in older children. Several studies have indicated a prevalence of anisometropia between 2.5 and 5%^{4, 15, 18, 19} among

schoolchildren. Still, our earlier studies have taught us to be cautious with interpreting cross sectional prevalence data. In order to gain knowledge on stability we must perform longitudinal studies of refractive changes in individuals.

Passing through childhood with persistent anisometropia and without corresponding amblyopia or strabismus seems to be a rare condition. Almeder *et al*¹¹ found only one case in their study of 1060 schoolchildren and calculated the incidence to be about 1%. In this study we also found only one case in a population of more than 4000 individuals at 10 years of age. Almeder *et al*¹¹ suggest that a substantial share of adult non-strabismic amblyopic subjects may, in fact, have developed their anisometropia slowly as a result of a prior microstrabismic problem. The anisometropia is caused by amblyopia and strabismus and is not its cause. The emmetropisation of the non-fixing eye is arrested and the child subsequently develops an anisometropia since the emmetropisation in the fixing eye continues.^{5 6 9}

In conclusion, marked anisometropia at 1 year of age as well as persisting anisometropia during childhood significantly increases the risk for amblyopia. In this study 60% developed amblyopia and 25% developed strabismus. Anisometropia ≥ 3.0 D at 1 year of age leads to a lasting anisometropia in the majority of cases. In our study 90% are still anisometric at 5 years of age.

This study was supported by Swedish Medical Research Council (grant 02226), Handlanden H Svensson Foundation, De

Blindas Väner Association, and Margit Thyselius Foundation. We also thank Carola Arvemark for valuable assistance.

- 1 von Noorden G. Mechanisms of amblyopia. *Doc Ophthalmol* 1977;34:93-115.
- 2 Tanlantai T, Goss DA. Prevalence of monocular amblyopia among anisometropes. *Am J Optom Physiol Opt* 1979;56:704-15.
- 3 Stevens PR. Anisometropia and amblyopia. *Br Orthopt J* 1960;17:66-73.
- 4 de Vries J. Anisometropia in children: analysis of a hospital population. *Br J Ophthalmol* 1985;69:504-7.
- 5 Abrahamsson M, Fabian G, Sjöstrand J. Refraction changes in children developing convergent or divergent squint. *Br J Ophthalmol* 1992;76:723-7.
- 6 Lepard C. Comparative changes in the error of refraction between fixing and amblyopic eyes during growth and development. *Am J Ophthalmol* 1975;80:485-90.
- 7 Kutschke P, Scott W, Keech R. Anisometropic amblyopia. *Ophthalmology* 1991;98:258-63.
- 8 Lithander J, Sjöstrand J. Anisometropic and strabismic amblyopia in the age group 2 years and above: a prospective study of the results of treatment. *Br J Ophthalmol* 1991;75:111-6.
- 9 Aurell E, Norrsell K. A longitudinal study of children with a family history of strabismus: factors determining the incidence of strabismus. *Br J Ophthalmol* 1990;74:589-94.
- 10 Abrahamsson M, Fabian G, Sjöstrand J. A longitudinal study of a population based sample of astigmatic children. II. The changeability of anisometropia. *Acta Ophthalmol (Copenh)* 1990;68:435-40.
- 11 Almeder L, Peck L, Howland H. Prevalence of anisometropia in volunteer laboratory and school screening population. *Invest Ophthalmol Vis Sci* 1990;31:2448-55.
- 12 Abrahamsson M, Sjöström A, Sjöstrand J. A longitudinal study of changes in infantile anisometropia. *Invest Ophthalmol Vis Sci (suppl)* 1989;30:141.
- 13 Raviola E, Wiesel TN. An animal model of amblyopia. *N Engl J Med* 1985;312:1609-16.
- 14 Birch E, Stager D, Everett M. Natural history of infantile anisometropia. *Invest Ophthalmol Vis Sci* 1995;(suppl 36):845.
- 15 Phelps M, Muir V. Anisometropia and strabismus. *Am Orthopt J* 1977;27:131-3.
- 16 Hung LF, Crawford MLJ, Smith EL. Spectacle lenses alter eye growth and the refractive status of young monkeys. *Nature Med* 1995;1:761-5.
- 17 Pärssinen O. Anisometropia and changes in anisometropia in school myopia. *Optom Vis Sci* 1990;67:256-9.
- 18 Ingram R. Refraction of 1-year-old children after atropine cycloplegia. *Br J Ophthalmol* 1979;63:343-7.
- 19 Laatikainen L, Erkkilä H. Refractive errors and ocular findings in school children. *Acta Ophthalmol* 1980;58:129-35.