A longitudinal study of children with a family history of strabismus: factors determining the incidence of strabismus

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Abstract
A longitudinal study of ocular refraction, position, and fixation was performed in children with a family history of strabismus. The children were examined at regular intervals between 3 months and 4 years of age, and the results are discussed in terms of changes in refraction between different ages and correlations between refraction and development of strabismus and amblyopia. Six of 34 children (17-6%) developed constant or intermittent esotropia. The strabismus was first noted between 18 and 30 months of age except in one case. All esotropic children were 4 dioptries hypermetropic or more at 6 months, and their hypermetropia remained almost unchanged through the years. Seven additional children were 4 dioptres or more hypermetropic at 6 months but did not develop a squint. In contrast to the squinting children the hypermetropia in these children changed towards emmetropia. This emmetropisation was most pronounced during the first 2 years of age. The implications of these results for an early diagnosis of strabismic amblyopia are discussed.

One main reason for examining the eyes of preschool children is to detect errors which might cause amblyopia. The simplest method is monocular testing of vision but this is difficult in small children. We doubt whether it could be performed before the age of 4 as a population screening method, since it requires trained staff and even so would probably not be reliable for all children. In Sweden all 4-year-old children have their vision screened at the Children's Health Care Centre, and those who present subnormal results are referred to an ophthalmologist for further evaluation. Köhler and Stigmar have reported a study of 2447 4-year-old randomly selected children. Of these 358 children were referred to an ophthalmologist, and 12-3% in this group were considered amblyopic.

It is generally believed that amblyopia and disorders in binocular function should be detected and treated as early as possible, but there is no easy and reliable method of detecting these disorders in young children. Nor is it known how many people are actually suffering from visual problems which could have been prevented had they been detected earlier. If the assumption is made that amblyopia therapy should be started earlier than at present, then the question arises how to find the children at risk. Ingram suggested that refraction should be the basis for screening young children. He argued that there was a close association between hypermetropia and the development of squint and/or amblyopia. He also found that amblyopia was highly likely if a child had a meridional hypermetropia of more than 3 dioptres at the age of 1 year. In many of these children the amblyopia could not be corrected.

Before even contemplating a nationwide refraction screening of small children we must be even more confident than we are today about what an individual refraction at a certain age means for the child's vision in the future. By relating his own observations to the reports of others Fabian suggested that the refractions of small children develop towards emmetropia (emmetropisation). This theory is supported by Ingram and Barr, but only if the refractions of individual meridians are considered. They found no decrease in hypermetropia between the ages of 1 and 3-5 years. Astigmatism decreased significantly, however, and anisometropia was unstable. Even if the number of anisometric children was roughly the same at 1 as at 3-5 years, they were mostly different individuals. Similar reductions in astigmatism and instability in anisometropia between 1 and 4 years have been found by Abrahamsson et al. Unstable refraction does not necessarily imply emmetropisation but instability as such creates difficulties in determining when glasses should be given. Medina has proposed a mathematical model for the emmetropisation process. The model implies a feedback mechanism operating towards reducing the refractive error, and Medina concludes that corrective lenses influence this process.

Our knowledge of the normal development of oculard refraction is still fragmentary because longitudinal studies are few. It seems that we cannot, except in special cases, predict with certainty which children are going to develop amblyopia judging from the results of one single refraction at one particular age. More longitudinal studies of the development of refraction during infancy and in early childhood are needed before we can be absolutely certain when a prescription of glasses is due in a small child, especially when the testing of visual acuity is difficult. The practical problems with glasses and amblyopia therapy are seldom mentioned in the literature. Parents are concerned about their child's vision, and they usually try very hard to follow the instructions. We must be reasonably sure that their efforts are worthwhile.

We know, however, that some groups of children run a greater risk than others of developing strabismus and amblyopia. Heredity is one factor of importance in determining the risk, though we do not know what factor is inherited nor what the mode of inheritance is.
This study we therefore chose heredity as the single determining factor in order to select newborn children for a longitudinal study of ocular refraction, position, and fixation.

Material and methods

The incidence of strabismus and the development of refraction were studied in a group of children with one common denominator: heredity for strabismus. The children were recruited from an average Swedish town and country population during a given time. All mothers who were delivered of a living child between 15 February and 30 June 1981 at the county hospital in Möln达尔, Sweden, were asked if the newborn child’s parents or siblings had or used to have a squint. The questions were asked by the paediatrician who examined the child immediately before mother and child left the ward. All mothers who had given Yes for an answer were contacted within one month by one of the authors. Additional questions were asked on the history of strabismus. Convergent strabismus was thus confirmed in parents and/or siblings of 39 children.

We did not attempt to find any records of their strabismus for two reasons. First, we had no intention of studying heredity as such; secondly, we wanted to see if an amblyopia risk group could be defined in a simple and clinically applicable way. We judged it impossible to find strabismus records for all parents after, in many cases, more than 20 years. All parents of the 39 children were willing to take part in the study with their child. During the time of the study (four years) five children were lost from it. Three moved to other parts of Sweden and could not be reached, one parent refused to let us give cyclopentolate, and one child did not turn up in spite of repeated calls. Thirty four children completed the whole study.

During the first visit the parents were informed about the purpose of the study. They were told to look for signs of strabismus and were instructed about what to look for. They were encouraged to call and report if they made any observations of interest. The children were

**Figure 1.** Refractions at four different ages for the whole material (34 children). On the x axis seven groups of columns with four columns in each group are shown. The groups except the one to the far right each represent a certain refraction span, indicated below the group. The single group to the right represents those who could not be examined at those particular ages. The four columns in each group represent from left to right 3 months, 6 months, 2 years, and 4 years of age. The y axis indicates the number of children in the different columns. The stripes and dots together represent the hypermetropic group, the stripes the eso group and the dots the non-eso group (see text for explanations). By definition the column representing +4 D or more at 6 months (the second column in the sixth group) consists of only stripes and dots, since the hypermetropic group is defined by being +4 D or more at 6 months. At 4 years only the eso group is still +4 D or more.

**Figure 2.** Mean and standard deviation for the refractions of the most ametropic meridian of the most (left) and the least (right) ametropic eye for the hypermetropic group. The eso group is represented by filled circles and the non-eso group by open circles.
examined at 3, 6, 12, 18, and 24 months, and at 4 years. On all these occasions fixation, position, motility, and the ocular fundus were examined.

At 3, 6, 12, and 24 months, and at 4 years a retinoscopy after repeated instillations of 1% cyclopentolate solution was performed. At four years the visual acuity was measured by means of linear Es. Those who developed strabismus were treated conventionally with glasses and if necessary with occlusion. All examinations were performed by the authors except in some rare cases when the child at 4 had moved to a distant part of Sweden. In those cases the child was examined by the local ophthalmologist. Some of the children have been followed up beyond the age of 4.

Results

DEVELOPMENT OF REFRACTION

In Figure 1 the refractions of the most ametropic meridian of the most ametropic eye are shown for the whole group. We have chosen to compare the results of the retinoscopy at 3 months, 6 months, 2 years, and 4 years of age. There were some children who either did not come or could not be examined properly on all these occasions. Especially at 1 year there were some children in whom we failed to achieve a reliable retinoscopy. We have therefore refrained from including the figures for refraction at 1 year old when making comparisons for the whole group. The largest ametropia was found at 6 months. In the majority of cases the hypermetropia was less at 3 months than at 6 (Fig 1, Fig 2, Table 1).

Thirteen of the 34 children, more than 3/5 of the whole group were 4 dioptres hypermetropic or more at 6 months. These 13 children have been followed up beyond the age of 4 years, and this article will mainly deal with their development. In this text they will be referred to as the hypermetropic group.

During the length of the study the refraction changed towards emmetropia in the majority of the children. A detailed analysis of this change has been done only for the hypermetropic group. Seven children in this group showed a decrease of hypermetropia from 6 months to 4 years; they started to become emmetropic. Since those 7 children did not show any strabismus they are called the non eso group. The remaining 6 children in the hypermetropic group had no decrease of hypermetropia; they failed to become emmetropic. Since they all developed an esotropia they are called the eso group.

The greatest changes towards emmetropia occurred during the first two years. At 2 years only one child had 4 dioptres hypermetropic or more and at 4 years only five. These five children together with a sixth child to be described below (no. 6 on Table 1) constitute the eso group, since they all eventually had an esotropia. Child no. 6 belongs by definition to the hypermetropic group, since her refraction at 6 months was +4 (Table 1). At both 2 and 4 years her retinoscopic refraction was +3.5. The girl was very uncooperative, however, but because her mother had repeatedly and increasingly observed, from about 4 years, that the child’s left eye squinted she got another appointment at about 4½ years of age. On that occasion the examination was easy; her refraction was +4, and a cover test showed an esophoria with slow restitution. Because she was thought to be on the verge of manifest esotropia she was given glasses. Because of her failure to become emmetropic, and, because of the observations made by her mother and us, we decided that she should belong to the eso group, though with some hesitation, since we had not observed a spontaneous strabismus.

Table 1 shows that the emmetropisation process for the non-eso group was most pronounced before 2 years, but in some individuals it continued and we do not yet know what happens after 4 years. We do not have complete data from one year. Nine of the 13 children in the hypermetropic group allowed a reliable retino-
scopy to be performed at 1 year, and seven of these were 4 dioptres hypermetropic or more. Five out of these seven belonged to the group who remained hypermetropic at 4 (the eso group). One child in the eso group could not be examined. Three children in the non-eso group could not be examined at 1 year. The remaining four were still hypermetropic (+3 to +4-5), but the emmetropisation process had started (Table 1).

Astigmatism was common in both the eso and the non-eso group as well as in the whole group. No obvious correlation between astigmatism and strabismus/amblyopia has been found. Anisometropia with a difference of about 1 dioptre was common. No obvious correlations can be drawn between anisometropia and strabismus/amblyopia, but it must be pointed out that we can neither confirm nor deny any importance of anisometropia in this context. All children in the eso group who required amblyopia therapy were anisometric, but so were others. The material is too small for any conclusions to be drawn in this respect.

DEVELOPMENT OF STRABISMUS
One finding is obvious from these results regarding the development of refraction: children with a hypermetropia of 4 dioptres or more at 6 months either stayed hypermetropic at about the same degree throughout the investigation or started to become emmetropic. All those who stayed hypermetropic developed a convergent squint, the eso group. None of those who became emmetropic developed a squint, the non-eso group. Five started to squint between 1-5 and 2-5 years. Three of them required amblyopia therapy, two stayed straight after they got glasses. One (the above mentioned no. 6) was observed by her mother to squint before 4 years. An esophoria was observed by us at about 4½. The reasons for including this girl in the eso group have been explained above.

VISUAL ACUITY
Visual acuity was tested with linear Es at 4 years. All children were able to attend. We have defined amblyopia as an acuity difference between the eyes of more than one line. Three children had been put on amblyopia therapy (nos. 2, 3, and 4) a short time after the strabismus had been detected. Only one, no. 3, had at 4 a deep amblyopia which had resisted all treatment. No. 4 must also be considered as amblyopic, though not to the same extent. She was still wearing occlusion intermittently as well as no. 2. On the whole the visual acuity was lower bilaterally at 4 in the eso group than in the non-eso group. All children in the non-eso group as well as the remaining 21 children had at 4 a visual acuity of 0-7 or better and no bigger difference than one line between the eyes.

Discussion
The incidence of strabismus in a Caucasian population is generally considered to be 3-4%. The risk for developing strabismus increases about four times if either of the parents have a squint. Our results correspond well to this figure, since six children of 34 (17-6%) developed a convergent strabismus, constant or intermittent. All these children were hypermetropic. Three of the esotropic children required amblyopia therapy. Ingram et al. found that uncorrectable amblyopia was likely if a child had +3-5 or more dioptres of meridional hypermetropia at the age of 1 year. At one year only 26/34 could be reliably examined. Ten of these were +3-5 dioptres or more. Since only one child in the whole group developed amblyopia at 4 years, we doubt whether uncorrectable amblyopia would be likely. Since the end result of the amblyopia therapy is not complete at 4, we must postpone a definite statement.

We started this investigation on the assumption that an inheritance for strabismus increases the risk of developing strabismus, and the high percentage of esotropes confirms this assumption. One aim was to examine what other factors are of importance. As might be expected, we found that hypermetropia is important for strabismus. The exceptional observation in this study is that all those who started to squint had roughly the same hypermetropia at 4 years as at 6 months, the so called eso group. Children with the same amount of hypermetropia at 6 months as the eso group but who later decreased in their hypermetropia did not develop a squint, the non-eso group. One conclusion from these observations is that one should probably think twice before prescribing glasses to very small children. But what is the reason for these differences?

Why did the six eso children stay hypermetropic while the seven non-eso children with the same initial hypermetropia started to become emmetropic (Fig 2)? We know little about what factors are important for the so called emmetropisation process in a normal child. The concept of emmetropisation as a mechanism, regulating the refraction of the eye towards achieving the best possible acuity, has been discussed since the 1920s. Attention was then drawn to the fact that the number of emmetropes in the population was larger than could be expected from a normal distribution. The concept of emmetropisation implies that refraction develops towards emmetropia from hypermetropia as well as from myopia and astigmatism. Evidence has accumulated during the last decades that refraction is controlled by visual input. Evans et al. recently reviewed animal experiment and human observations suggesting that defective emmetropisation is associated with deficient visual input or faulty neural transmission. Evans et al. have found that individuals with congenital achromatopsia have higher refractive errors than normal persons and also show a defective tendency to become emmetropic. They propose that retinal cones are involved in the feedback control of ocular refraction. Medina suggests a mathematical model for a feedback loop which operates by detecting a refractive error and by correcting for it. This model implies that corrective lenses may have a negative effect on the emmetropisation process. He discusses the possibility that accommodation may be involved in the emmetropisation process as a feedback.
signal but offers no definite evidence for or against.

If accommodation is involved, it should be possible to influence it. Some reports for different species, including man, support the idea that conditions favouring myopic vision may induce myopia.1-14 There have been several reports about the favourable effect of cycloplegics on stopping or at least delaying the progression of myopia,15-17 and these results naturally focus attention on accommodation as a myopia enhancing factor. However, some recent observations challenge this theory. Pärsinen et al18 have found a positive correlation between short reading distance and the development of myopia. But the progress of myopia could not be stopped by reducing accommodation. Dobson et al19 have studied the effect of glasses on the development of hypermetropia in small children, and they suggest that wearing glasses decreases the normal reduction in hypermetropia. They argue that accommodation is involved as a factor promoting emmetropisation. McBrien and Barnes20 have reviewed theories of refractive error development, and they discuss theories of the emmetropisation process and how to influence it through environmental factors. They emphasise the importance of research in this field, not least for practical reasons, in order to better understand the development of refraction and to know whether, how, and when to interfere.

Is it possible in our study to implicate differences in accommodation as the reason for the differences in emmetropisation between the two hypermetropic groups, the eso and the non-eso groups? All children in the eso group got glasses but none before the age of 2. If we compare the two groups at the age of 2, the figures indicate that the emmetropisation process has started for the non-eso group by then (Fig 2, Table 1). Thus it seems that the glasses are not responsible for the failure to become emmetropic, at least not exclusively. Our results do not indicate what possible part accommodation may play in the development of refraction. Fabian21 emphasises that the main changes towards emmetropia occur during the first two years of life. Our study confirms this. The process continues, however, in some individuals up to 4 years, and we do not yet know what happens after that age. We suggest that failure to become emmetropic is a significant factor to consider when determining the risks for strabismus, but we have no explanation to offer for this failure. Apart from the hypermetropia the eyes were completely normal, including the ocular fundi. All initially hypermetropic children whose emmetropia did not decrease started to squint. We certainly believe that the hypermetropia is essential for the strabismus. It could be that the failure to become emmetropic in itself has nothing to do with the strabismus. If the hypermetropia is large enough and, for instance, the fusional capacity is weak enough, the child may start to squint. But another explanation might be that some aberration in the refractive media is responsible for both the failure to become emmetropic and the development of strabismus. Sorsby et al21,22 postulated a mechanism by which axial length, lens power, corneal power, and anterior chamber depth correlate with each other to produce emmetropia. Failure of this correlation process would produce moderate deviations from emmetropia, so called correlation ametropia. They found that in high hypermetropia and high myopia a single component, most frequently the axial length, was abnormal, and they used the expression 'component ametropia' for this group. Our results do not warrant a subdivision of the two different hypermetropic groups along these lines, since we do not have enough data about dimensions of the refractive media. Longitudinal studies from infancy to school age, including measurements of axial lengths and other refractive parameters, would be of great theoretical and practical importance. Better knowledge of how ocular refraction develops and what factors may interfere with this development is of great significance, not least for practical clinical work. We shall possibly have to change our practice in prescribing glasses and treating strabismus.

We have postulated that strabismus in the family indicates a substantial risk of strabismus in the child,2,3 and this has been verified. Of the children in this group 17-6% developed a strabismus. We have found that those who start to squint are hypermetropic at the start of squint, have been equally hypermetropic since infancy, and will stay at the same level of hypermetropia at least until the age of 4. What practical conclusions may be drawn from these observations? We do not believe that refraction screenings of unselected groups of small children should be recommended. Screening involves many problems and great costs.23,24 Our results show that there is a substantial group of children whose refractive errors at least during the first two years are very unstable, perhaps even longer. This means that it is hard to judge which children are at risk for developing strabismus and/or amblyopia on the basis of a single refraction.

We suggest that awareness of heredity and cooperation from parents should be considered when looking for strabismus and amblyopia. Parents could be questioned on some occasion during the programme for children's health care regarding strabismus in the family. Parents in squinting families could be encouraged to be observant and opportunities created to consult an ophthalmologist if problems arise and for a routine retinoscopy at about 2-5 years. At that age it should be possible to differentiate most of the children at risk from those in the normally emmetropising group judging from the height of the hypermetropia. We do not claim to be able to find all children at risk for amblyopia, but we believe that a substantial part might be discovered.

We should like to emphasise that the parents in our study made accurate and relevant observations after having been given some superficial instruction. Rosner and Rosner25 have shown parents to be good detectors of strabismus. We suggest that they may be used actively in screening for strabismus.

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