# Anisometropic amblyopia: factors influencing the success or failure of its treatment

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#### Abstract

*Aim:* To provide an overview of the factors that might influence the success or failure of anisometropic amblyopia treatment.

*Methods:* A literature-based review was conducted using mainly Science Direct. Searches were restricted to English-based publications over the past 10 years, mainly focusing on children before they reach visual maturation.

*Results:* The most common factors considered within the literature are patient age, the degree of anisometropia, the depth of amblyopia, and the type of treatment and its compliance. However, methodological differences could account for the reported differences in treatment outcome.

*Conclusion:* There does not seem to be a general consensus on any factors that could determine why the success rate of anisometropic amblyopia treatment is not as high as expected. This could partly be due to varying definitions in the literature of anisometropia and the success of treatment; or simply the failure to separate strabismics from anisometropes, or hypermetropes from myopes. Potential factors that are not often considered include the presence of aniseikonia, astigmatism and the accommodation response in anisometropic amblyopes.

Key words: Anisometropia, Amblyopia, Treatment

#### Introduction

Anisometropia is an interocular difference in refractive error such that the plane of focus for each eye is different. The majority agree that a minimum interocular difference of 1 dioptre (D) is required to define anisometropia,<sup>1-11</sup> but the definition varies between  $0.5D^{12-14}$  and  $2D.^{15,16}$ 

The overall prevalence of anisometropia ranges from less than 1% to 1.6%.<sup>11,17</sup> It is a significant problem if left untreated as it can be associated with amblyopia in

the more ametropic eye. Approximately one-third of amblyopia is associated with anisometropia, one-third with strabismus and one-third with combined anisometropia and strabismus.<sup>12,18</sup> Differences exist between these three types of amblyopia; yet research into outcomes may not differentiate between them.<sup>19–27</sup>

This literature review provides an overview of the factors that might influence the success or failure of anisometropic amblyopia treatment. Science Direct and PubMed were searched in August 2011 for Englishbased articles published over the last 10 years, mainly using the keywords 'anisometropia', 'amblyopia', 'treatment', 'success' and 'occlusion'. References made to earlier articles were searched for individually and have been included. The main focus of the review is on children before they reach visual maturation, so articles concentrating only on adults were excluded, as were articles focusing only on strabismic amblyopia. However, if the presence of anisometropia was mentioned, whether or not strabismus was involved, the article was included.

#### Important factors to consider

Varying definitions within the literature might influence the way results are interpreted. As well as the definition of anisometropia, the definition of the success of treatment also varies. Generally this is defined as improvement in visual acuity (VA) to 6/9 or better in the amblyopic eye.<sup>2</sup> It can also be defined by a reduction of the interocular difference in VA, so that either no difference,<sup>2</sup> less than 0.1 logarithm of the Minimum Angle of Resolution (logMAR)<sup>3</sup> or less than 1 VA line difference remains between the eyes.<sup>8–10,13</sup>

The literature highlights the importance of separating anisohypermetropia from anisomyopia, as anisohypermetropes are more likely to become amblyopic. von Noorden,<sup>28</sup> quoting McMullen's work in 1939,<sup>29</sup> stated that in anisomyopia the more myopic eye can be used for near and the less myopic eye for distance viewing and therefore both eyes are exercised. In anisohypermetropia the least hypermetropic eye is thought to determine accommodation at all distances, with the more ametropic eye remaining blurred at all times.

The method used to calculate the degree of anisometropia may also vary. Most studies calculate the

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interocular difference in spherical equivalent and do not take into account the cylindrical refraction or its axis.<sup>7,30-33</sup> Rutstein and Corliss<sup>7</sup> compared several methods for calculating the degree of anisometropia, including calculating the difference in spherical power, the difference in power in the vertical and the horizontal meridians, and the root mean square difference. Although they found that calculating the interocular root mean square difference shows a better correlation with the depth of amblyopia as it takes into account the difference in the cylindrical axes, the difference is only slight. They concluded that the spherical difference is a simple and valid method. Leon *et al.*<sup>5</sup> also compared methods and found 76% of children to have the same degree of anisometropia whether this was calculated by a difference in spherical equivalent or by the maximum difference in any meridian. However, 24% had a higher degree of anisometropia when calculating the maximum difference in meridians. This proportion was representative of those with cylindrical anisometropia; consequently the difference in spherical equivalent should not be used to determine the degree of anisometropia in the presence of astigmatism.

Huang *et al.*<sup>34</sup> used vector dioptric distance (VDD), a method drawn from Thibos *et al.*,<sup>35</sup> which takes into account the magnitude and the axis of astigmatism in addition to the spherical component. The single figure is calculated from M, the spherical equivalent; J0, the power in the vertical or horizontal meridians; and J45, the power in the oblique meridians. This allows for simpler statistical analysis and for refractive errors to be visualised graphically.<sup>35</sup> Huang *et al.* concluded that VDD is better for calculating the degree of anisometropia than other methods because it allows for greater discrimination of amblyopia. This is the only study that appears to calculate the degree of anisometropia using VDD.

# Onset of anisometropia versus onset of amblyopia

There is a close link between anisometropia and amblyopia, with 53–60% of anisometropes having amblyopia,<sup>15,36</sup> but whether anisometropia causes amblyopia or is caused by amblyopia is still controversial.<sup>17,36–38</sup> Most literature suggests that anisometropia leads to amblyopia,<sup>16,30,32,37–39</sup> but some provide evidence that amblyopia may be the primary cause.<sup>36</sup> Either way, the onset of anisometropia and the onset of amblyopia are likely to occur at different ages.

Abrahamsson *et al.*<sup>40</sup> suggested that anisometropia can develop during emmetropisation and may disappear with age, as only 30% of those who had anisometropia of between 1D and 3D at 1 year of age still had anisometropia present at 4 years. Abrahamsson and Sjöstrand<sup>36</sup> subsequently studied anisometropia greater than 3D, and found 90% of anisometropes at 1 year of age still had anisometropia at the age of 5; of those with anisometropia between 2 and 5D, some will emmetropise whilst others will continue to be anisometropic and may develop amblyopia. Above 5 dioptres sphere (DS) children are unlikely to grow out of the anisometropia and there is an increased risk of amblyopia development. Birch and Holmes<sup>41</sup> tested 3-year-old amblyopes (younger than in most studies) and found only 5% had pure anisometropic amblyopia. This was not due to under-referral (anisometropia being difficult to detect), as a greater number of anisometropes without amblyopia were also referred. They suggest that anisometropia that persists or develops after the age of 3 years might become an aetiological factor for amblyopia.

Weakley<sup>30</sup> suggested that lower levels of anisometropia than suggested by Abrahamsson et al.40 should alert clinicians to the risk of amblyopia development. Anisohypermetropia more than 1DS, anisomyopia more than -2DS and cylindrical anisometropia (hypermetropic or myopic) more than 1.5 dioptres cylinder (DC) could cause amblyopia. The incidence of amblyopia was 100% with anisomyopia between -2DS and -3DS, and the greater the degree of anisometropia, the greater the depth of amblyopia. With anisohypermetropia both the incidence and the severity of amblyopia increases with more than 1DS anisometropia, reaching 100% incidence with more than 3DS anisometropia. Thus, although differences exist between anisohypermetropia and anisomyopia, beyond 2DS the two conditions are similar. Perhaps with anisomyopia of more than -2DS it becomes increasingly difficult to use the more myopic eye for near viewing as McMullen<sup>29</sup> suggested, resulting in amblyopia.

# **Detection and diagnosis**

Anisometropia is more difficult to detect than strabismus in unscreened populations, as there are few objective signs. It is possible that delay in detection could affect the success of treatment. Referrals before 4–5 years of age are usually because of a family history of eye problems and hence parental concerns. After this age anisometropia is most frequently diagnosed through screening, which is neither universal nor consistent with varying referral routes. Also, some studies refer to all anisometropes whilst others consider only amblyopic anisometropes.

Different aspects of patient age could determine the success of anisometropic amblyopia treatment.<sup>6,14,15</sup> The prognosis of treatment could depend on the age at diagnosis.<sup>30</sup> As in most studies the time between diagnosed and the start of treatment is unclear. Those diagnosed and treated earlier might be expected to have a better chance of achieving a normal VA, but Cobb *et al.*<sup>16</sup> and Chen *et al.*<sup>3</sup> found no difference in anisometropic amblyopia treatment response that was related to the age at which treatment was started. Hussein *et al.*<sup>32</sup> found an increased risk of failure of anisometropic amblyopia treatment only if it was started after the age of 6 years.

Donahue<sup>6</sup> found both the prevalence and severity of amblyopia to increase with age. Only 14% of anisometropes under the age of 2 years had amblyopia. Over the age of 3 years this percentage increased to approximately two-thirds, but after this age the further increase was only small. However, VA testing in young children is difficult and less accurate than in older children, in whom logMAR VA can be assessed, which may have influenced the results. Despite the number of anisometropes having amblyopia stabilising, Donahue found, along with Leon *et al.*,<sup>5</sup> that the depth of amblyopia continues to increase with age.

Stewart *et al.*<sup>42</sup> studied both anisometropic and strabismic amblyopia and found that depending on the outcomes measured age may or may not be a factor. Children over the age of 6 years had milder amblyopia at the start of treatment in comparison with the younger age groups, thus the change in VA in terms of lines of improvement is limited, but age is a factor. However, if the outcomes measured are residual amblyopia or the proportion of amblyopia corrected then this bias is removed and age is no longer significant.

It is debatable whether the degree of anisometropia determines the success of treatment. A higher degree of anisometropia would be expected to result in deeper amblyopia and thus be more difficult to treat with a higher risk of failure. Ying *et al.*<sup>43</sup> tested a cohort of 3728 children and found that the percentage of children with amblyopia increased with the degree of anisometropia: 2% in those with just 0.5DS anisometropia, 10% in anisometropia between 0.5DS and 0.75DS, and 50% in anisometropia over 1.75DS.

Chen *et al.*<sup>3</sup> found 4D of anisometropia to be associated with a poor outcome, perhaps due to a worse initial VA or to aniseikonia. These results are similar to those of Leon *et al.*,<sup>5</sup> who found 80% of anisometropes with less than 2D of anisometropia had no or mild amblyopia. When the anisometropia was greater than 4D, 60% of children had moderate to severe amblyopia. Chen *et al.* stated that children with a higher degree of anisometropia are at greater risk of developing severe amblyopia and hence treatment should be started at a younger age. However, both these studies failed to separate anisohypermetropes from anisomyopes (who may have had less severe amblyopia). While only 2.5% of Leon *et al.*'s<sup>5</sup> participants were myopic it might still have slightly skewed the results.

In a study separating myopes and hypermetropes, Tanlamai and  $Goss^{44}$  found the degree of anisometropia to be proportional to the incidence of amblyopia. Amblyopia was present in 100% of patients with anisohypermetropia greater than 3DS and anisomyopia greater than -6.5DS. Weakley<sup>45</sup> found an increasing incidence and severity of amblyopia in anisomyopia greater than -2DS and anisohypermetropia greater than +1DS. This lower degree of anisometropia than that reported by Tanlamai and  $Goss^{44}$  could be because their participant group consisted of adults as well as children. Also, the amblyopic children had presented to an ophthalmology clinic, so those with mild amblyopia may not have been included.<sup>5</sup>

Rutstein and Corliss<sup>7</sup> agreed that amblyopia is more likely to develop in those with higher degrees of anisometropia and studied the difference between anisohypermetropes and anisomyopes (children and adults). They found a relationship between the degree of anisometropia and the depth of amblyopia in anisohypermetropes, but not in anisomyopes. However, Townshend *et al.*<sup>46</sup> found the degree of anisometropia correlated better with anisomyopia than with anisohypermetropia. Rutstein and Corliss<sup>7</sup> suggested that this could be because they did not use cyclorefraction, which is required for a reliable measurement, particularly of hypermetropia.

Although some authors have found the degree of anisometropia to be strongly correlated with the final VA<sup>2,3,16</sup> and the depth of amblyopia,  $^{6,30,45,46}$  others have found no relationship.<sup>14,15,32,47</sup> There could be numerous reasons for this difference. For example, Malik *et al.*<sup>14</sup> did not separate hypermetropes and myopes, and Hussein *et al.*<sup>32</sup> calculated the degree of anisometropia by the difference in spherical equivalent ignoring the cylindrical component.

Weakley<sup>30</sup> found the depth of amblyopia to be the most predictive factor for treatment outcome, and factors such as age and the degree of anisometropia to be less reliable. Stewart *et al.*<sup>42</sup> found a greater depth of amblyopia to result in greater residual amblyopia, yet other studies have been unable to replicate this finding.<sup>8,15</sup>

#### Microtropia

A microtropia is a small-angled strabismus with some binocular vision. In 'microtropia without identity' there is small movement on the cover test and hence its presence can easily be detected.<sup>48</sup> In 'microtropia with identity' there is no movement on the cover test but there is eccentric fixation which can be identified using a visuscope or fixation ophthalmoscope.<sup>48</sup> Microtropia is frequently associated with anisometropia<sup>49</sup> and both are associated with amblyopia.<sup>50</sup> Most studies do not consider microtropes,<sup>2–7,9,10,12,13</sup> especially those 'with identity' where no manifest strabismus is detectable. Stewart *et al.*<sup>1</sup> placed both types of microtropia into their strabismic cohort but found that the presence of eccentric fixation is related to a poorer outcome. Failure of anisometropic amblyopia treatment in some studies could be due to a proportion of undetected microtropia.

One article that did study microtropia in anisometropic amblyopia<sup>14</sup> found a relationship between the depth of amblyopia and the degree of eccentric fixation, but no relationship between the degree of anisometropia and the degree of eccentric fixation. This could also imply that there is little association between the degree of anisometropia and the depth of amblyopia. However, this study failed to separate anisohypermetropes and anisomyopes.

#### Treatment of anisometropic amblyopia

The treatment method undertaken, such as the duration of refractive adaptation, the type of occlusion, the duration of occlusion and its compliance, are all factors that could influence outcome. Research studying these factors may not differentiate the response to treatment individually in strabismic and anisometropic amblyopes.

It has been argued that strabismic and combined amblyopia are more severe conditions<sup>12</sup> due to differences in cortical inhibition and suppression, with higher risk of treatment failure. However, it is unclear why some anisometropic amblyopes fail treatment. Even if two patients have similar risk factors such as age or the type and degree of refractive error, their response to treatment can still differ. Anisometropic amblyopia is caused by a difference in refractive error, so that the retinas receive a different image only in terms of size and sharpness, not disparity. During the critical period VA may fail to develop due to a lack of visual stimuli or be inhibited by suppression. Correction of this refractive error will restore a clear image to the amblyopic eye, which ought to improve neuronal sensitivity<sup>1</sup> and thus resolve the amblyopia, but as the success rates show, this is not always the case and therefore other factors are clearly involved.

### **Response to treatment**

The overall success rate of amblyopia treatment falls between 30% and 95%.<sup>15,32,51</sup> Generally, the success rate is higher for anisometropic amblyopes, followed by strabismic amblyopes and then combined amblyopes.<sup>16,20,31,52</sup> However, others report that the success rate is equal for all three types.<sup>1,2,42,53</sup> When articles specify pure anisometropic amblyopia, the success rate is approximately 65–75%.<sup>31–33</sup> Some studies have found success rates as high as 94%.<sup>2,10</sup>

Cobb *et al.*<sup>16</sup> reported a high success rate of 81%. Their definition of success was a final Snellen VA of 6/12 or better and from their graphs we can calculate that with a more common definition of 6/9, the success rate falls to approximately 40%.

Holmes and Clarke<sup>54</sup> questioned why some amblyopes have an initial improvement in VA but then plateau before reaching normal. Lithander and Sjöstrand,<sup>8</sup> who considered compliance with treatment in 44 children with any of the three types of amblyopia, suggested that no further improvement in VA is due to an early onset of amblyopia in the first years of life.

#### Refractive adaptation

Refractive adaptation is now recognised as an important part of amblyopia treatment. Spectacles alone can fully treat anisometropic amblyopia.<sup>1,9</sup> Agervi *et al.*<sup>10</sup> reported a resolution of amblyopia in 94% of their anisometropic amblyopes, in an average time of 3.9 months.

Stewart *et al.*,<sup>1</sup> as part of the Monitored Occlusion Treatment of Amblyopia Study (MOTAS), suggested 18 weeks of refractive adaptation before commencing occlusion therapy, as a significant proportion of children achieved normal VA in their amblyopic eye during this period. From their data we can calculate that 28% of anisometropic amblyopes achieved resolution. Although refractive adaption might be predicted to be more effective in a purely refractive problem, the strabismic amblyopia group had a similar resolution rate of 31%, although this figure did drop to 13% in the combined amblyopes.

The Pediatric Eye Disease Investigator Group (PED-IG) found a similar result, with approximately one-third of anisometropic amblyopes gaining complete resolution of amblyopia with refractive adaptation alone.<sup>13</sup> A greater chance of resolution was associated with a better initial VA, lower degrees of anisometropia and less severe amblyopia. Even if amblyopia does not resolve, refractive adaptation can improve VA to some extent and hence compliance is likely to be better with occlusion therapy.

# Compliance with treatment

Poor compliance might increase the risk of treatment failure,<sup>3,8,32</sup> although its definition varies within the literature.<sup>33</sup> Oliver *et al.*<sup>55</sup> found younger amblyopes, and Chen *et al.*<sup>3</sup> more specifically found younger anisometropic amblyopes, to be more compliant than older ones. If older children are less compliant then their treatment is less likely to be successful. In which case perhaps compliance, not age, is the significant factor, as Oliver *et al.*<sup>55</sup> suggested. Since anisometropic amblyopia is detected at a later age than strabismic amblyopia we would thus expect poorer compliance. Lithander and Sjöstrand<sup>8</sup> considered compliance to be the main factor influencing outcome, with more than 95% resolution in compliant participants (strabismics and anisometropic amblyopes) compared with 50% in their low-compliant participants.

# Less commonly considered factors affecting the response to treatment

# Aniseikonia

Aniseikonia is caused by a high degree of anisometropia<sup>4,38,39,49</sup> and has been reported to result in a poor outcome.<sup>3</sup> Paysse *et al.*<sup>39</sup> suggested that aniseikonia makes children less accepting of their spectacles. They reduced anisometropia to 3D or less through refractive surgery. A weaker prescription and thus reduced aniseikonia could improve spectacle compliance posttreatment.

# Initial VA

Some authors report a positive correlation between the initial and post-treatment VA.<sup>3,16,31,33,47</sup> Woodruff *et al.*<sup>52</sup> found this to be the main factor that determines the outcome of treatment irrespective of the type of amblyopia. Those with a poor initial VA (worse than 6/60) can improve but might have limited success, with a possible final VA no better than  $6/12.^{32}$ 

#### Astigmatism

Hussein *et al.*<sup>32</sup> found astigmatism greater than  $\pm 1.50$ DC increased the risk of treatment failure. Weakley<sup>45</sup> also found that more than  $\pm 1.5$ DC anisometropia results in a significant increase in the incidence and severity of amblyopia. Although not significant, anisometropia of  $\pm 1$ DC anisometropia was also associated with amblyopia. Ying *et al.*<sup>43</sup> found that even 0.25DC anisometropia significantly increased the risk of amblyopia from 2% to 6%. This percentage increased as the cylindrical anisometropia increased, reaching 34% with more than 1.50DC anisometropia.

Somer *et al.*<sup>56</sup> reported that the presence of againstthe-rule (ATR) anisometropic astigmatism (hypermetropic or myopic), rather than with-the-rule (WTR) astigmatism, is a factor that could contribute to the failure of treatment. In myopic and hypermetropic ATR Table 1. A summary of methodological differences that could account for the reported differences in outcome of anisometropic amblyopia treatment

Study	Definition of aniso- metropia	Differentiate aniso- metropes and strabismics?	Aniso- metropic participants ( <i>n</i> )	Separate hyper- metropes and myopes?	Aniso- metropia calculation	Refractive adaptation	Definition of success of treatment	Include micro- tropia?	Other	Success rate
Stewart <i>et al</i> . 2004 <sup>1</sup>	≥1DS	Yes	65	No	-	Yes	_	Yes	Refractive adaptation only	28%
Scott <i>et al.</i> $2005^2$	≥lD	Yes	56	Yes	Any meridian	No	$\geq$ VA of 6/9 or equal VA		Myopes have worse	94.6%
Chen <i>et al</i> . $2007^3$	≥lD	Yes	60	No	Any meridian	Yes	≤0.1 logMAR difference	No	outcome Refractive adaptation	45%
Levi <i>et al.</i> 2011 <sup>4</sup>	≥lD	Yes	84	Yes	Include cylindrical	_	difference -	No	only –	_
Leon <i>et al</i> .	≥1D	Yes	974	No	refraction Compared	_	_	No	_	_
2008 <sup>5</sup> Donahue 2006 <sup>6</sup>	≥1D	Yes	792	No	2 methods Unclear	_	_	No	-	_
Rutstein and Corliss 1999 <sup>7</sup>	≥lD	Yes	60	Yes	Compared 4 methods	_	-	No	Include adults	-
Lithander and Sjostrand 1991 <sup>8</sup>	≥lD	Yes	17	No	Any meridian	No	≤1 line VA difference	Yes	_	>95% in compliant and 50% in non- compliant
Steele <i>et al</i> .	≥lD	Yes	28	No	Unclear	Yes	$\leq 1$ line VA	No	Only 1 myope	
2006 <sup>9</sup> Agervi <i>et al.</i> 2009 <sup>10</sup>	≥1DS ≥1.5DC	Yes	66	No	Unclear	Yes	difference ≤1VA line difference	No	Refractive adaptation	94%
PEDIG 2002 <sup>12</sup>	≥0.5DS ≥1.5DC	Yes	153	Yes	Spherical equivalent and in any	Yes	_	No	only Exclude myopes	_
PEDIG 2006 <sup>13</sup>	≥0.5DS ≥1.5DC	Yes	84	No	meridian Unclear	Yes	≤1VA line difference	No	Only 4 myopes. Refractive adaptation	27%
Malik <i>et al.</i> 1968 <sup>14</sup>	≥0.5D	Unclear	75	No	Unclear	_	-	Yes	only Unclear if results include strabismics	_
De Vries 1985 <sup>15</sup>	≥2D	Yes	37	Yes	Spherical or cylindrical power	Yes	Expressed as a ratio – an increased ratio by 0.2 is successful	Unclear		47%
Cobb <i>et al.</i> $2002^{16}$	≥2D	Yes	112	Yes	Unclear	-	$\geq$ VA 6/12	Yes	-	81%
Weakley 1999 <sup>30</sup>	Unclear	Yes	361	Yes	Compared methods	_	-	Unclear	-	_
Flynn <i>et al.</i> 1999 <sup>31</sup>	≥1.5D	Yes	54	No	Spherical	No	VA 6/12	No	≥age 10	63%
Hussein <i>et al.</i> $2004^{32}$	≥1D	Yes	104	Yes	equivalent Spherical equivalent	_	$\geq$ 3 logMAR VA lines improve- ment or $\geq$ 6/12	<u>-</u>	-	75%
Flynn <i>et al.</i> 1998 <sup>33</sup>	≥1.5D	Yes	142	No	Spherical	No		No	-	66.7%
Huang et al.	_	Yes	-	No	equivalent VDD	_	-	No	Conference	-
$2011^{34}$ Stewart <i>et al</i> .	≥1DS	Yes	20	No	Unclear	Yes	Unclear	Yes	poster –	_
2005 <sup>42</sup> Tanlamai and Goss 1979 <sup>44</sup>	$\geq$ 2D Thai, $\geq$ 1D	Yes	167 Thai, 472	Yes	Compare 2 methods	_	_	No	Include adults	_
Weakley <i>et al</i> . 2001 <sup>45</sup>	American >0DS ≥0.5DC	Yes	American 361	Yes	DS and DC aniso-metropia analysed separately.	Yes	-	Yes	-	_
Townshend <i>et</i>	≥0.75D	Yes	35	Yes	Axis ignored Compare	_	-	No	Include adults	-
<i>al.</i> 1993 <sup>46</sup> Kutschke <i>et al.</i> 1991 <sup>47</sup>	≥1D	No	124	Yes	3 methods Not stated	Yes	≥6/12	Unclear	Include fully accommo- dative esotropia in non-strabismic group	

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astigmatism the vertical meridian is clear and the horizontal meridian is blurred, whereas in WTR astigmatism the vertical meridian is blurred and the horizontal meridian is clear. Somer et al.56 suggested that this blurring of the horizontal meridian might be why treatment results are poorer with ATR astigmatism. Although they found no difference between hypermetropic and myopic astigmatism, Kutschke47 did find that anisometropic myopic astigmatism leads to a poorer outcome.

### Ocular structural and cerebral abnormalities

Holmes and Clarke<sup>54</sup> suggested that poor response to treatment might be due to subtle ocular or cerebral pathology. Optic nerve hypoplasia might cause amblyopia and can be difficult to detect using indirect ophthalmoscopy. Clarke<sup>57</sup> also considered retinal or optic nerve structural abnormalities, which are not readily apparent with ocular equipment. Leffertstra<sup>58</sup> and Abrahamsson *et al.*,<sup>59</sup> despite concentrating on strabismic amblyopes, stated that a primary visual defect may result in defective emmetropisation in one eye. This theory could be transferred to anisometropia, where defective emmetropisation could result in anisometropia and failure of amblyopia treatment.

#### Accommodation in anisometropia

The link between anisometropic amblyopia and accommodation has not been considered. It is assumed that accommodation is a symmetrical process, so in anisometropic amblyopia the less hypermetropic eye determines the amount of accommodation and the more ametropic eye lags behind.48,60 Accommodation studies often exclude anisometropes, while few amblyopia studies consider accommodation at all. However, it has been reported that amblyopic eyes have poor accommodation.60-63

Rook et al.64 compared accommodative responses between amblyopic and control children using an autorefractor. Amblyopic eyes had a reduced accommodative response in comparison with the non-amblyopic eyes and the control eyes. However, the type of amblyopia and the amount of accommodative difference between the eyes is unclear.

Horwood and Riddell<sup>65</sup> presented a novel finding of a child with anisohypermetropia of 5DS with asymmetrical accommodation. This child had limited success in the amblyopic eye after correction of her refractive error and occlusion therapy. The amblyopic eye accommodated more for the distant targets than for the near targets whilst the non-amblyopic eye accommodated normally.

This might not be a unique case. Common clinical equipment only allows for uniocular measurements of accommodation whereas newer binocular techniques such as the PlusoptiXSO4 photorefractor in PowerRefII mode as used by Horwood and Riddell,65 allow binocular simultaneous recording. The reduced accommodative response usually seen from uniocular measures could be ascribed to poor VA and there is little research evidence as to what happens to accommodation of the amblyopic eye when the fixing eye is accommodating appropriately.

There is other published evidence that accommodation can be asymmetrical and that aniso-accommodation can exist. Marran and Schor<sup>66</sup> studied accommodation in a small group of adults. They induced anisometropia in these participants and trained them to aniso-accommodate. Participants that could not demonstrate anisoaccommodation were excluded. It is unclear how many participants were originally recruited, and hence it is unclear what percentage of the population could potentially be trained to aniso-accommodate, but it does provide evidence that aniso-accommodation is possible. They suggested that each eye has independent control of accommodation even in a non-developmental context. If this is true, aniso-accommodation could be beneficial as each eye having independent control of accommodation could compensate for anisometropic refractive error. It has been suggested that early convergence may initially be two separate uniocular adductions rather than binocular vergence.<sup>20</sup> Thus, perhaps symmetrical accommodation is also to some extent a learned process, so might be modifiable in visual development.

#### Conclusion

A great number of factors could determine the success or failure of treatment in anisometropic amblyopia. These include the degree of anisometropia, depth of amblyopia, method of treatment and its compliance, as well as the age of the patient. However, research refers variously to the age at onset, age at presentation, age at diagnosis or the age at the start of treatment, making it difficult to draw comparisons. Other less commonly considered factors such as aniseikonia, accommodation and astigmatism may also be influential.

Varying definitions of terms, such as anisometropia and the success of treatment, as well as the method used for calculating the degree of anisometropia, can make interpretation of the data difficult; as does the selective analysis of the relationships between factors that are studied.

Failure to separate hypermetropes from myopes is a common issue. Many studies fail to separate strabismic from anisometropic amblyopes and often do not consider the presence of a microtropia. These are important issues that should be considered in order to find a possible general consensus on factors that could affect treatment outcome.

It is likely that multiple factors determine the success of treatment and help explain why not all anisometropic amblyopia fully resolves.

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