STRABISMUS, ANISOMETROPIA, AND AMBLYOPIA*

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EVIDENCE will be presented in this communication to support the hypothesis that anisometropia *per se* does not produce strabismus, but that, for hypermetropes, the refraction of the better eye is an important factor. Further, the clinical entity of anisometropic amblyopia and its treatment will be discussed. Finally, some comments will be made on optical correction in anisometropia. The case records used for the statistical analysis were all obtained from Moorfields Eye Hospital (High Holborn Branch); others came from a variety of sources, including Bristol Eye Hospital.

I. ANISOMETROPIA AND STRABISMUS

The association between anisometropia and strabismus is well known. The existence of many cases of anisometropia without strabismus suggests that some factor in addition to anisometropia must play a part in producing a squint, for example a refractive error in the less ametropic eye (as Lyle, 1950, suggests) or, alternatively, the amount of spherical and cylindrical anisometropia present. In order that these factors could be investigated, comparisons were made between groups of (a) squinting and (b) non-squinting anisometropes.

Material and Methods

From the records of the Orthoptic Department, Moorfields Eye Hospital (High Holborn Branch), cases of anisometropia attending at any time between 1953 and 1958 were selected. The criterion of anisometropia was a difference between the two eyes of one dioptré or more, either of sphere or of cylinder. A squint was considered to be present only if it was manifest with and without glasses for all distances when the cover test was used. Cases of anisometropia with a history or clinical evidence of previous inflammation, injury, incomitance, etc., were excluded.

The selection of the control sample presented many difficulties which could not all be resolved completely beyond criticism. Ideally, the investigation should have made use of a cohort analysis—in this case the examination of a large number of

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children aged, say, 2 years, and the annual follow-up of those who were anisometropic to discover which would develop strabismus. This was impractical for the writer. In order that sufficient controls might be found, the records of the general Out-patient Department, in addition to those of the Orthoptic Department, at Moorfields Eye Hospital (High Holborn Branch) were searched for non-squinting anisometropes who had a one or more dioptre difference in sphere or cylinder between the two eyes. This group had many defects as a control sample but corrections were used for the main ones. The greatest difficulty was the fact that these patients were usually much older when first seen at hospital, no squint having been present to draw attention to their abnormality at an earlier age. A second difficulty was that many, unlike the squinting anisometropes, had not been refracted after cycloplegia. A third objection could be raised, *viz.* that the search for squint was less stringent in patients who merely attended for correction of their refractive errors than in those who attended the Orthoptic Department; also, the refractionists may have omitted to record a squint which was present: however, both these factors would bias the figures below against the hypothesis being tested. Cases of bilateral anisohypermetropia, bilateral anisomyopia, and antimetropia were classified separately.

For each case, a calculation was made to estimate what the refraction would have been after cycloplegia by atropine at the age of 7 years. For the non-squinting anisometropes, the older group, the result was much less certain than for the others: when no cycloplegia had been used the amount of total hypermetropia was estimated from a Table compiled by Duke-Elder (1949a); the allowance made for age was based on a Table showing the average annual change in refraction (Brown, 1938). So that confusion from the under-correction of hypermetropic errors could be avoided, the actual retinoscopic figures were used minus 1.25 (unless an unusual distance had been chosen for retinoscopy; if this was not recorded then a serious defect is present in these statistics). There was no reason to suppose that the refractionists of the squinting group were different from those of the non-squinting group. No data are available on the behaviour of astigmatic errors with increasing age so that the amount of cylinder had to be regarded as unchanged at whatever age it was found. The sex ratio in the two groups did not differ significantly ($\chi^2 = 1.75$; $0.50 > P > 0.10$).

Results

At the stage when the sample sizes were 26 and 21 for the anisometropes with and without strabismus respectively, the recently devised X-test of Waerden and Nievergelt (1956) was applied. This non-parametric test for small samples was particularly appropriate because the distribution of the observations did not seem to be so Gaussian as was expected. The test value calculated after the observations had been "ranked" was ± 4.345 , but this did not reach the level (6.25) required for 95 per cent. significance. Accordingly the samples were increased in size.

The mean spherical error, derived as described above, of the less ametropic eyes in the group of forty non-squinting hypermetropic anisometropes was +3.08; for the group of 53 squinting hypermetropic anisometropes the corresponding figure was +4.66. The difference between these two means

was highly significant ($t=3.52$; $n=91$; $P<0.001$) with good (99 per cent.) confidence limits.

Another hypothesis which could explain, in part at least, why squint affected one group and not the other is that the anisometropic difference between pairs of eyes, and hence the dissociative tendency, might have been greater in the squinting group. The reverse, though not very significantly ($0.05>P>0.02$; $n=91$; $t=2.21$), was found to be the case, for the mean anisometropic difference in the squinting group (2.17) was *less* than that in the non-squinting group (3.06). The presence of astigmatism made the calculation of the amount of anisometropia difficult. If the effect on visual acuity of cylinders, as opposed to spheres, is accepted as a criterion (Eggers, 1945), the dissociative tendency produced by a one dioptre cylinder, depending on its axis, would be less than that of a one dioptre sphere. Accordingly, although spherical anisometropia was given its full dioptric value, cylindrical anisometropia was scaled down to an admittedly arbitrary 75 per cent. of its actual value, irrespective of axis, for purposes of the calculation.

This finding was rather surprising. It had the effect of reducing the significance of the difference between the means of the spheres of the more ametropic eyes in the two groups very slightly below the 98 per cent. level of significance (P just >0.02 ; $t=2.33$; $n=91$). To disentangle statistically the effect of the spherical from astigmatic anisometropia was very difficult, especially because of the variable angles of the cylinders. One aspect of that problem could, however, be investigated: if the proportion of patients in each group with astigmatism of two or more dioptres in the more ametropic eye is compared, there is no significant difference (approximately 50 per cent. in each group).

It was impossible, with the information available, to separate cases of axial anisometropia from refractive or mixed ones, except in so far as astigmatism existed (above). Hence, the effect of aniseikonic (in uncorrected axial) anisometropia could not be differentiated from iseikonic (in uncorrected refractive) anisometropia.

The above observations concern only anisometropes who were bilaterally hypermetropic. Of eighteen cases of bilaterally *myopic* anisometropia, only one had a squint—divergent—and none was amblyopic. This finding is consistent with the results reported by Jampolsky, Flom, Weymouth, and Moses (1955) who explain the absence of amblyopia in such cases by the fact that the more myopic eye receives a clear image at some object distance so that “disuse” is not constant. That explanation is unlikely to apply to cases in which one eye is very markedly myopic. A more general explanation may be that the age of onset of anisomyopia is later than that at which amblyopia is likely to occur.

Antimetropes were also few (20). Thirteen of them had no squint; five of the seven squinting antimetropes showed divergence and two convergence. A convergent squint was present if the hypermetropic eye had over +4

dioptries of error. Manifest divergence occurred even when the better eye was approximately emmetropic; in these, however, the myopic fellow had a very marked error (more than -7 D sph. or, in one case, -4 D cyl. with -3 D sph.).

II. ANISOMETROPIC AMBLYOPIA (WITHOUT STRABISMUS)

The term anisometropic amblyopia does not seem to be in current use to describe the poor visual acuity often present in the more ametropic of a pair of anisometropic eyes which are normal in every other respect. This term is suggested for use when the degree of the refractive error cannot alone account for the poor acuity in the more defective eye, because it describes the condition without implying the exact mechanism. The cause may be "disuse", *i.e.* the blurred condition of the retinal image from an early age in the affected eye prevents the macula from "learning" the form sense; or more active "suppression" because of difficulty in fusing dissimilar images, especially if they be unequal in size. Aniseikonia may well be important if the anisometropia is mainly axial; correction with spectacles in such cases, as well as clarifying the blurred images, would also reduce, but not abolish, the aniseikonia (if spectacles are worn behind the anterior focal point of the eye, as is usual).

It is curious that the condition as such receives little attention in standard text-books. McMullen (1939) discussed the condition and stated his belief that disuse is the cause. Sugar (1944) used the term "suppression amblyopia". Lebensohn (1957) preferred "accommodative amblyopia". Copps (1944) also drew attention to the condition. Kramer (1949) suggested that disuse initiates the poor acuity which is then followed by suppression.

Treatment by total occlusion of the eye with the better acuity has produced good results in many cases in this series.

A girl aged 13 years, whose visual acuity was 6/6 in the right eye with $+1.25$ D sph., $+0.5$ D cyl., axis 90° , and 6/24 in the left with $+3.5$ D sph., $+0.5$ D cyl., axis 90° , improved to 6/12 in the left eye after 3 months of occlusion of the right lens (her parents refused to allow occlusion to be put on the face or to continue occlusion longer).

On the other hand, a boy aged 6 years who had been found to have poor visual acuity in the left eye at a routine school examination, had visual acuity 6/9 in the right eye with $+3$ D sph. and 6/36 in the left with $+8$ D sph. After 2 months' occlusion of the right eye, the visual acuity in the left had improved only to 6/18, but treatment is being continued.

Even slight degrees of amblyopia are worth treatment by occlusion. A boy aged 10 years who had visual acuity 6/12 in the right eye with $+3.5$ D sph., and 6/6 in the left with $+1$ D sph., $+0.5$ D cyl., axis 90° improved to 6/6 (partly) in the right eye after 3 months of occlusion; this improvement having been achieved, the wearing of glasses was discontinued.

If anisohypermetropia is axial in origin, and marked, equal visual acuities should not be expected from occlusion, because the retinal image will be smaller in the worse eye than in the better, even when both are fully corrected (see below under "Optical Correction of Anisometropia").

No attempt was made to detect any difference between the morphoscopic and angular visual acuities, *i.e.*, between the acuities measured by letters and Landolt's rings (see Foster, 1957); unilateral macular agnosia rather than general suppression might exist in these cases.

Occlusion, however, has a danger: it may add another "dissociative" factor to the anisometropia and precipitate or aggravate a squint, especially in young children who are very hypermetropic. No such case has been found in this series which concerns, mainly, older children. A preliminary period without occlusion in which the patient wears a full spectacle correction may be advisable in order that all possible improvement in vision, binocular and unocular, be achieved without increased risk of a squint. As soon as visual acuity commensurate with the refractive error in the more ametropic eye has been reached, occlusion must, of course, cease, although supervision at intervals should be maintained.

McMullen (1939) advised occlusion for patients under the age of 10 years. Bishop (1957), in an excellent survey of the subject, advised intermittent occlusion, supplemented by a final period of total occlusion before the patient is pronounced "cured"; patients over the age of 11 years he found to give poor results though a trial of occlusion was worthwhile until the age of even 14 or 15.

III. PERIPHERAL FUSION IN ANISOMETROPIC AMBLYOPIA

The frequent absence of squint, even in very marked anisometropic amblyopia, implies that some form of binocular vision probably exists. Few eyes with poor visual acuity, including unilaterally aphakic eyes, avoid a divergent strabismus. The importance of "peripheral fusion" in general has attracted little attention. Burian (1939) seems to have been the first to show the importance of peripheral stimuli for fusion, and Lyle and Foley (1955) have investigated the problem recently. The only mention found of the possible relation of peripheral fusion to the absence of squint in anisometropic amblyopia is by Sugar (1944).

The cause of anisometropic amblyopia may be mere "disuse", or "suppression". It is reasonable to suggest that the tolerance of the peripheral retina of an image slightly more than usually blurred without the development of disuse amblyopia will be greater than that of the macula; similarly, tolerance by the two peripheral retinæ of aniseikonia is also likely to be greater. Thus the peripheral retinæ can be expected to retain their binocularity in optical circumstances in which the maculae are unable to do so—hence the absence of squint in cases of anisometropic amblyopia. Ferree

and Rand (1932) have shown that a stigmatic image is produced on the retina only within a circle of angular radius 10° . Beyond this angle even emmetropic eyes can exhibit marked irregularities, most characteristically a vertically positive astigmatism. This subject has more recently been investigated by Weale (1956). Cone density decreases from the macula to the periphery but to a less extent than would explain the greater fall in acuity (Weale, 1956); Ten Doesschate (1946 and 1949) explains this as due to the subservience by a single nerve fibre of a number of cones greater than in the central area. These facts all tend to suggest, though they do not provide good evidence, that the peripheral retinae could tolerate a greater aniseikonia than the maculae. Real evidence exists in the finding that Panum's areas are larger in the periphery (Panum, 1858). In anisometropia, pairs of peripheral images may differ proportionately more or less than central ones: this would be an interesting subject for investigation.

The threshold level of anisometropia above which peripheral fusion would be expected to become impossible would vary with circumstances, *e.g.* the refraction of the better eye in anisohypermetropia, as has been shown by implication earlier in this communication. Inspection of the records of divergent squints with one eye emmetropic suggests that a level of more than -7 dioptres of difference is incompatible with the retention of (peripheral) binocular vision. It is the usual experience that the $+10$ dioptres of difference induced by unilateral aphakia causes complete dissociation.

Theoretically, unequal axial lengths of the globes could be combined with appropriate powers of corneae and crystalline lenses to produce images on both retinae which, though clear, would be unequal in size. Such a situation would be very likely to permit peripheral fusion but produce a pure aniseikonic isometropic amblyopia. (Duke-Elder, 1949b, used the term "relative anisometropia": it would produce isometropic aniseikonia.) A careful search was made for possible cases but only one potential candidate was found in whom no cause had been discovered clinically for unilateral poor vision; on investigation, however, the very small differences in powers between the refractive surfaces in his eyes, and therefore the difference in axial lengths of his globes, were well within the experimental error of the method of investigation.

IV. OPTICAL CORRECTION IN ANISOMETROPIA

The usual practice in the treatment of anisometropia with spectacles is to make the difference between the two spectacle lenses as near to that between the two eyes as the patient will tolerate, though it is frequently advisable to undercorrect the more ametropic eye (Duke-Elder, 1954). In practice, it is found that myopes, children, and presbyopes who can no longer accommodate, will tolerate the full anisometropic difference in their spectacles.

A common situation occurs when a child has one emmetropic eye and a small error in the other, spherical or astigmatic. Provided that any existing anisometropic amblyopia has been eliminated and that the child is supervised at intervals to avoid its recurrence, the only benefit to be obtained from the wearing of spectacles is the slightly greater binocular efficiency than in the uncorrected state; whether the disadvantages and possible dangers of spectacles should be suffered for the improvement will depend on individual circumstances to some extent, but these patients seem usually to suffer so little disability when not wearing spectacles that their use is superfluous. And it is unlikely that stereopsis once achieved will be lost if glasses are not worn. The child often decides the question by refusing to wear prescribed glasses.

Another common problem is that of the adult with early presbyopia in whom an incidental finding is anisometropia. Prescribing of the full anisometropic correction may well result in symptoms; on the other hand, since the patient has suffered no previous trouble from his uncorrected anisometropia, the refractionist can be certain that the use of equal spectacle lenses (the less ametropic eye's reading correction determining their power) will relieve the presbyopic symptoms. This does not necessarily imply what is nevertheless quite possible, that anisometropic eyes, if both are hypermetropic, can exert unequal accommodation. Unequally myopic eyes, on the other hand, would be expected to choose to allow the accommodation of the worse eye, if it is used at all, to accompany *pari passu* the other's changes rather than maintain constant accommodation in the better eye so as to produce myopia equal to that in the worse; hence, bilateral myopes usually tolerate their full anisometropic correction well.

An example will illustrate the problem in hypermetropia.

A female stocking repairer aged 29 had begun to find blurring of vision, especially of the left eye, at work; the refraction was right +1 D sph. = 6/5, and left +2 D sph. = 6/5. When these spectacles, the lenses having been centred to avoid anisophoria, were worn, aching appeared in the left eye. The symptoms disappeared when the left lens was altered to +1 D sph.

It cannot be denied that many patients achieve clearer vision (for distance and near) with a full anisometropic correction. This would be expected at least in patients completely lacking the power of accommodation or (see above) in myopic cases. The following example is typical.

A female aged 63 achieved a visual acuity of 6/9 in each eye separately with +5.5 D sph., +1 D cyl., axis 180° in the right eye, and +5 D sph., +0.5 D cyl., axis 180° in the left, and found slight blurring if a -0.5 sphere were placed in front of the right eye or a +0.5 sphere in front of the left.

That *subjective binocular test* is useful in cases of anisometropia if there is doubt about the prescribing of a full or partial anisometropic correction.

Gillie (1956) has described an almost identical test. Turville (1946) devised a more elaborate method. The following cases illustrate its usefulness.

A female aged 28 had spectacles which she wore only occasionally, especially for close work: +1 D sph., +0.5 D cyl., axis 180° in the right eye, and +2.25 D sph. +0.5 D cyl., axis 180° in the left. Assessment of her refraction showed a similar result: visual acuity in the right eye was 6/6 with +1.25 D sph., and in the left 6/18 +1 with +2.5 D sph. With this correction in trial frames the subjective binocular test was done by asking the patient to observe any difference in clarity of, say, the 6/18 line when a -1.25 D. sph. lens was put quickly in front of the left eye; the answer was consistently that objects were clearer not only for distance but also for near work, so that the final prescription was +1.25 D sph. for each eye. There was no reduction in the acuity of the left eye tested alone with the weaker correction.

A man aged 55 years wore a correction for the right and left eyes of +5.5 D sph. (6/6) and +4.5 D sph. (6/6) respectively. The subjective binocular test for distance showed that he preferred right +5 D sph.; for near, however, the small difference seemed to be eliminated and he expressed no preference for iso- or aniso- metropic correction.

These empirical findings are difficult to interpret, especially as it is by no means invariable for anisohypermetropes who can accommodate to prefer spherical corrections differing by less than the full amount of the anisometropia. The simplest explanation would be that anisohypermetropia, like hypermetropia itself, is to some extent latent at first, depending on its amount, but, as age advances, progressively becomes manifest. It is implicit in this hypothesis that the eyes exert unequal accommodation—no evidence is available on that subject, however.

Any explanation must take into account the effect of optical corrections on the sizes of retinal images. Before anything final could be decided on that subject, it would be necessary to know to what extent (spherical) anisometropia is axial or refractive in origin. In their study of "Emmetropia and its Aberrations", Sorsby, Benjamin, Davey, Sheridan, and Tanner (1957) have included some anisometropes, of whom most were anisomyopes; in by far the greater number the origin was axial, and the refracting system of the more myopic eye compensated, usually, by being less powerful. Clinical impression gives some support to an axial cause for anisomyopia; if "myopic degeneration" be taken as a criterion for an ametropia's being mainly axial, then the greater degeneration often seen in the more myopic of two anisometropic eyes suggests that the difference between the two refractions derives from inequality in the axial lengths of the globes.

It is probably an over-simplification of the problem to suggest that accommodating anisohypermetropes will tolerate only that amount of spherical spectacle difference which produces aniseikonia still compatible with binocular vision, but sacrificing some clarity in the image of the more defective eye on that account (or exerting some extra accommodation in the

more ametropic eye to achieve final clarity of the image without altering much further its size). That would be expected to apply only to eyes which are (mainly) refractively, not axially, anisometropic because full spectacle correction of any purely axial anisometropia reduces the aniseikonia (but see below). Now, if anisohypermetropia were partly axial and partly refractive in origin and two eyes could dissociate their accommodation and choose spectacle lenses which would equalize the two optical images, they would adopt the following system: (a) allow full correction of the manifest hypermetropia of the better eye, combined with (b) a positive lens before the worse eye more powerful than its fellow by an amount greater than the axial element of the anisohypermetropia, along with (c) extra accommodation in the worse eye by less than the amount of the refractive element in the inequality.

If, on the other hand, anisohypermetropia were axial, but partly compensated by an increased power of the refracting surfaces in the worse eye, the full anisometropic correction might well be tolerated because it would produce the nearest possible (with spectacles) approximation to iseikonia. Variations in the ability of anisohypermetropes to accept full, partial or no correction of their (spherical) inequality may be explained by these considerations.

Difficulties arise in the interpretation of some observed facts, however. If an axial cause for the anisometropia be accepted in cases of anisomyopia with different degrees of degeneration in the fundi, then poor binocular vision would be expected when contact lenses are used because aniseikonia of the optical images on the retinae would be maximal (the aniseikonia would be even greater with lenses in the anterior chambers); on the other hand, aniseikonia would be minimised by the wearing of spectacles so that better binocular vision would be expected with them. Surprisingly, many observers have recorded that contact lenses will improve the aniseikonia of anisometropia (for example Alajmo, 1953; Littwin, 1957; Comberg, 1950). Their statements are supported by the following typical example:

A female aged 31 had a visual acuity of 6/6 in the right eye with -2 D sph., and 6/9 (some letters) in the left with -9.5 D sph., -1 D cyl., axis 30° ; with these spectacles, left suppression was elicited on the synoptophore, but with contact lenses stereoscopic vision was achieved. It is unlikely that the improved acuity of the left eye with contact lenses (to 6/9 plus some letters of 6/6) accounted for the great improvement in binocular vision.

Having seen the fundi, one is reluctant to attribute the patient's anisomyopia to a purely, or even predominantly, refractive cause which the above observations on binocular vision suggest: one would prefer the tentative conclusion that the macular cones in the worse eye had "spread out" as the

eyeball enlarged, *after* good binocular vision had been established in childhood, and that they had retained their correspondence, cone for cone, with those in the fellow eye. Thus, with contact lenses the brain would receive equal "images" although the optical images at the level of the retinae would be unequal. No comparable cases of anisohypermetropia have been found.

To sum up the problem of optical treatment of anisometropia: children, myopes, and patients who no longer have power of accommodation will tolerate full correction of the anisometropia well, but bilateral hypermetropes who are able still to accommodate (and who have not worn fully corrective glasses previously) usually prefer equal spheres, or spheres less unequal than the amount of the spherical anisometropia; it is suggested that the more hypermetropic eye has learned to exert, constantly, a greater accommodative "tone".

As a postscript to this discussion, a comment is relevant on the standards of corrected acuity which can be achieved in hypermetropia *vis-à-vis* those in myopia. A widely held clinical impression is that moderately hypermetropic eyes may achieve only 6/9 (or 6/6) acuity with correction (the term "amblyopia" being sometimes applied) whereas corrected moderately myopic eyes usually achieve 6/5 or even 6/4. It is suggested that the difference arises because an axially hypermetropic eye corrected with a lens at the spectacle point will receive a retinal image *smaller* than an emmetropic one, though larger than in its previously uncorrected state, whereas an axially myopic eye, if corrected at the spectacle point, will receive a retinal image *larger* than an emmetropic one, though smaller than in its previously uncorrected state. It could be argued that the macular cones are less concentrated in axial myopes than in hypermetropes (no observations seem to have been made on that subject), so that the effect of different image sizes would be neutralized; on the other hand, imperfections in the image from aberrations produced by the refractive media of the eye would be less able to cause "blurring" in the image transmitted to the optic nerve if the cones are more widely spaced as they may be in myopia.

SUMMARY

Anisometropia *per se* does not cause squint. Comparison between forty non-squinting hypermetropic anisometropes and 53 squinting hypermetropic anisometropes showed that the better eyes of the first group were significantly less ametropic than those of the second group. There was no significant difference in the amount of anisometropia, the incidence of astigmatism, or the sex ratio of the two groups. Patients in the first group were, in general, much older than those in the second group and had not usually been refracted under full cycloplegia, so that only an estimate of their refractive state at the age of 7 years, the "base-line" to which all cases were calculated, was

possible. Squint and amblyopia were very rare in anisometropic myopes. The findings in the small group of antimetropes are discussed.

The term "anisometropic amblyopia" is suggested to describe a common and important clinical entity which is independent of strabismus. Its treatment by occlusion at least until the age of 13 years is possible.

The absence of squint in many cases of anisometropia even with dense amblyopia suggests the presence and importance of peripheral fusion. Because of their larger Panum's areas the peripheral retinae will retain their ability to fuse in spite of aniseikonia or unequal clarity of images which, in the central area, would cause "suppression" or "disuse" amblyopia.

Full correction of their anisometropia was well tolerated by children, bilateral myopes, and all patients who no longer retained ability to accommodate; hypermetropes who still retained accommodative power preferred their spectacles to have equal spheres, or spheres differing less than the full amount of the spherical anisometropia, probably because their more ametropic eyes had learned to exert, constantly, an extra accommodative tone. Anisohypermetropia may be decreasingly latent as age advances. A simple "subjective binocular test" can be used to decide the advisability of a full anisometropic correction. For example, each eye separately in a patient aged 39 years achieved 6/6 with right +1 D sph. and left +2 D sph., but the line looked clearer *binocularly* when a -0.75 D sph. was added to the left eye. Hence the glasses prescribed were +1 D sph. in the right eye and +1.25 D sph. in the left.

The problems of the correction of axial, refractive, and mixed anisometropia are mentioned in relation to aniseikonia and possible relative differences in inter-cone distances at the maculae.

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