COMMUNICATIONS

AMBLYOPIA AND THE RETINA*

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THIS communication is concerned with patients who had the profound type of amblyopia which was resistant to usual routine methods of treatment (facultative amblyopes being excluded); no obvious pathological lesion was present to account for the poor vision. The investigation was directed to analysing the vision present in the defective eye. The results are discussed with reference to the probable site of the defects which could give rise to these particular effects.

Three sites have been favoured by different workers as the main one concerned in the development of amblyopia, the cortex, the geniculate body, and the retina. Vogt (1939), Wald and Burian (1944), and Dyer and Bierman (1952) thought that the cortex was chiefly affected. Clarke (1941) suggested that, since the cells of the lateral geniculate body rely for their vitality on the link between cortical and retinal activity, an atrophy from disuse might occur in these cells. Since suppression of one image is so essential a part of the mechanism found in the binocular vision of these cases, the higher centres must obviously be involved to a greater or less degree. This is demonstrable in the child whose amblyopic eye recovers normal sight by the simple expedient of covering the dominant eye, but in whom the dominant eye in turn becomes amblyopic from disuse if occlusion is continued too long. Facultative amblyopia is another instance.

Harms (1949), judging by the lowered response to light in an amblyopic eye, thought that the reaction of the retina was at fault. Enoch (1957) found abnormal retinal response.

Since normal binocular vision depends first on the retinal reaction to light of each eye separately, secondly on the passage of the information so received through the tracts and geniculate bodies, and thirdly on the final integration in the cortex, all sites are implicated when one becomes defective. Even so, the initial reaction of the retinal cells to light entering the eye must be the first step to be considered. The kind of asymmetrical vision described

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by these patients suggests that this initial stage is defective and that the retinal receptors do not react in the normal way. The evidence produced in the following pages suggests that the rays of light are not accepted directly along the axes of these cells and that the reaction of the retina is abnormal. The effect that such an abnormal initial stage must have on the higher centres is not included in this discussion.

Method

The patients undergoing investigation and treatment were of ages varying from 10 to 50 years. These who were selected for discussion were capable of accurate observation and each had a series of readings which were analysed for consistency and change, some over months, others over years of observation. In previous reports subjects with irregular astigmatism were excluded from discussion because this condition complicated the findings. In this group of patients several with irregular astigmatism were included, since it was felt that sufficient information had been gained to allow for accurate assessment of any distortion of image due only to this extraneous cause.

In this series all subjects had good central fixation. The minimum visual acuity was 6/24; some had developed this degree of acuity by treatment, others had it at the initial examination. Bearing in mind that the area of the fovea centralis composed wholly of slender cones subtends an arc of 20 minutes, targets subtending 20 minutes or less were used in all the significant analyses. Also, since the highest acuity at the fovea is confined to the central area subtending 7 minutes of arc (Polyak, 1941; Jones and Higgins, 1947), targets of this size were used as soon as treatment had made this possible.

As will be seen under the heading Procedure, all the usual routine examinations were made—fundus, refraction, vision uniocular and binocular—together with a detailed history of the condition.

Apparatus

The lighting installation consisted of a battery of eight 5-foot fluorescent “new warm” white 80-watt tubes suspended from the ceiling. This arrangement increased the amount of light on the test charts by 100 foot lamberts. When these top lights were turned off, the normal lighting of the Snellen type was 32 foot lamberts. By this means the usual illumination on the Snellen type chart could be increased from 32 foot lamberts to 132 foot lamberts when the top lights were lit, the surround being at a luminance of 100 foot lamberts. The battery of lights could be put through a flashing mechanism which allowed varying speeds of flashing per second.

The usual roller type of Snellen chart was used, in which three lines of the smaller letters can be shown at the same time through the opening in the metal frame. When required, this opening was covered with matt black paper which then served as a background for single letters which could be slotted into any position needed to correspond with the underlying chart. The advantage of this arrangement was that a series of single letters was shown and the answers recorded, and these were then compared with the answers which were given either when a full line of the

chart was visible, or when the same letters were seen under the same conditions of lighting and position but with additional letters at either side and/or above and below. A scale was marked along the bottom edge to correspond with the centre area of the 6-metre tangent scale, and this gave an approximate position of $\frac{1}{4}$, $\frac{1}{2}$, and $\frac{3}{4}$ degrees of movement as the eye looked along the line from right to left of centre. A slide of the tangent scale was also used in the orthoptoscope so that the exact angle of the direction of fixation could be noted as soon as the affected numbers appeared blurred.

For single targets a set of circles was used, printed in Snellen sizes from 6/60 down to 6/5, each size being printed first as a white circle on a black background, and secondly as a black circle on a white background. A similar set of twelve letters was used, four composed of horizontal and vertical lines, four with oblique lines, and four of circular design, and also a third set of Landolt's rings on cards printed as before in Snellen sizes.

Procedure

In all the tests the patient's dominant eye was first padded so that no light could enter and affect (by binocular light balance) the reaction of the amblyopic eye. When correcting lenses were needed, these were put into a trial frame in front of the amblyopic eye to ensure that they were correctly positioned. The trial frame also allowed varying sizes of pin-holes to be used, so that the tests would not be affected by any small amount of irregular astigmatism which might have escaped observation.

At each visit the visual acuity was taken on the Snellen chart in the usual way; it was then taken showing one line only and finally recorded when each letter of the same line was isolated by a large black mask with a hole in it. The difference in the acuity under these three conditions was noted.

The separate letter-cards were kept in packs so that they could be shown easily, and recordings were made showing which letters were faulted and how they were misnamed. The covering black paper was slipped over the Snellen chart and the separate letters were placed in turn in the central position on this background. Thus each letter appeared black on a small white surround on a main black background, or white on a black background. The results were recorded, and as long as any letters were read correctly the next smallest series was put up and the visual acuity was noted until a point was reached at which no letter of that size could be read. In this way, at each visit, an accurate record was made of the letters most easily seen and also of recurring errors. The patients were also required to make drawings of the letters and rows of characters. Care was taken that these drawings represented the apparent forms uninfluenced by knowledge of the shape of the letter.

Thus the uniocular tests could be summarized as follows:

- (a) Visual acuity at each visit was investigated on the usual Snellen chart and then with separate letters.
- (b) Circles were used to chart the direction of optimum form discrimination, and also to localize pattern distortion in the region of abnormal resolution.

(c) The direction of pattern distortion was charted with reference to the direction of deviation of the visual axis of the amblyopic eye. This was related to the mathematical angle of the prism which would be needed theoretically to correct the deviation.

(d) Drawings of apparent forms were made by the patient, both of single characters and rows of letters.

A detailed examination was then made on the circle targets, first with a black circle and then with the white circle on a black background. Beginning with a 6/60 large circle the subject was asked to look around the circle considering the sharpness of the edges, inside and outside, and also the density of the black or white. Any fading or blurring was described in position as on a clock face; this manner of localization allows a rapid approximation of a vertical, horizontal, or oblique position. Smaller circles were used consecutively until a stage was reached when resolution of any part of the circle became difficult. The position of the blur was recorded on a circular chart already marked out in degrees and therefore easily related to the clock annotation. Landolt ring targets were used in confirmation, but were not as easy as the full circles in the initial stages.

A detailed analysis of each letter was then made. Each patient was asked whether all the component lines of the letter were equal in clearness of outline, blackness (or whiteness), and thickness. He was also asked to draw the letters exactly as he saw them to correlate with his verbal descriptions, and these drawings were compared with the records of the resolution of the circles.

The patient's head was free but was so placed that the amblyopic eye lined up centrally to the target. The eye moved freely as different parts of the circle or letter were considered. While the patient fixed the central single letter, a second letter was placed to the side but within the width of the Snellen chart and therefore at an angle of $\frac{1}{2}$ or $\frac{3}{4}$ degree of abduction or adduction to the primary position. The effect was noted of a second subsidiary image on the sharpness of the central letter. Finally, the single letter was moved from one side to the other, and the patient turned his eye to follow the letter and reported any noticeable difference.

During each visit an objective measurement was made of the exact angle of deviation. The subject was asked to fix a small dot subtending 7 minutes of arc (or less) with the amblyopic eye only, the light was then changed to the dominant eye. Any movement of fixation or lag was noted as the lights were flashed from one to the other. A reduced Maddox scale as a slide was used in the orthoptoscope and presented to the dominant eye, while a slide with corresponding lines was shown to the amblyopic eye; the subjective angle was compared with the objective angle. Care was taken to find any vertical or torsional component of the squint, since these deviational elements were needed to work out the exact angle of deviation for comparison with the direction of distortion seen on the targets. If a vertical as well as a horizontal element was present, the direction of the visual axis was estimated by the formula used for assessing the prism which would correct the combined deviation.

The initial data collected was:

(1) Routine vision test of each eye. Refraction of each eye, under mydriasis when possible.

(2) Observation of the fixation of the amblyopic eye.

(3) Uniocular tests on the amblyopic eye with the purpose of noting the aberrations described when a simple plane circle is viewed; investigations as to which letters proved easy to name correctly and which were consistently misnamed; the errors in counting the letters in a row on a Snellen chart. These three main tests aimed at assisting the elucidation of one with the other. A record sheet was used to include these details, which were necessary to the statement of the problem.

The objective measurement of deviation was taken by the displacement method, with and without correcting lenses. This was noted together with the subjective results of tests for fusion and stereoscopic vision. Detailed investigation of light balance between the eyes was made with regard to effects of central suppression and/or movement of very small targets; the light balance was not significant in this inquiry except inasmuch as any movement which was not controlled by binocular adjustment had to be considered as a uniocular manifestation.

The data collected objectively gave the line of vision which would be affected by any error of astigmatism in the refraction of the eye, the exact angle by which the visual axis was deviated from the normal line of sight in its daily usage. The subjective data gave details of position, kind, and degree of abnormality apparent in the type of form vision described as seen by an amblyopic eye.

Finally, the influence of refractive error, together with that of the obliquity of the visual axis, on the effectiveness of light incident on the fovea was worked out theoretically. This was then correlated with the clinical findings as reported by the patient.

Results

This new series of cases showed, as before, that, when an amblyopic eye attempted to read the letters in a line on a Snellen chart, the acuity was poorer by one, two, or three sizes of letter than when the letters were presented singly. When the neighbouring letters along the line were masked, each single letter was seen clearly enough to be read correctly. Confusion occurred when the patient tried to read consecutive letters in a row because of interference by multiple part-images from the next letter. On the side of poor resolution, overlapping images produced hybrid characters with an apparent loss or addition of a letter.

When the subject was asked to count the letters in the line he often counted too many or too few. The spacing between the letters was described as irregular. The letter at the optimum end of the line was followed by a reasonable gap, but the second, third, and even fourth letters were reported to be "bunched together". Finally it became evident that the first letter on the clear side of the line was seen almost normally but the succeeding letters were either duplicated, giving the impression of extra ones, or combined together to look like too few. The same directional preference was present in the whole line as was seen in single letters, in that a right amblyopic eye which was esotropic read the first left-hand letter of the line most clearly, and a similar left eye read the last right-hand letter of the line more easily than the

rest—*i.e.* in each case the letter placed to the nasal side of the patient was seen most clearly.

Together with diminishing definition in the form and number of letters, a diminishing brightness of the background, also in the same direction, was reported. The effects varied in degree and position according to the angle of heterotropia and the degree of amblyopia. In a typical case, the direction of optimum resolution coincided with that of the direction of the visual axis in its abnormal position of heterotropia. It pointed towards that part of a single letter most clearly seen, to the side of a row of letters most easily isolated, and to the brightest background.

Simple convergent amblyopes, with or without a vertical deviation, were the most numerous, and their visual reactions agreed one with the other so that a typical record could be expected in such a condition. To widen the range of data, other subjects were obtained in whom the amblyopic eye had altered its direction of deviation from convergence to divergence. This had occurred in some cases post-operatively, in other subjects through continuous over-correction by spectacles worn constantly, and so on. Some subjects were exotropic at close range but esotropic at distance, thus having the amblyopic eye stimulated by light which struck the fovea with a gradient brightness, which altered direction. An example of the effect of such a condition was seen in a group of six patients, each having an amblyopic eye which had changed direction from convergence to divergence (actual or relative). Two of these with a small degree of exotropia had kept to the original configuration typical of esotropia. Two who had developed a constant marked divergence showed the directional distortion typical of an exotropic eye. The two others gave variable signs; for example, on Snellen lines, the area of ghosting appeared to be positioned as in the original esotropic deviation, but on circles and letters a certain amount of flattening and interference was noticed on the opposite side. This was especially noticeable with the man who was exotropic most of the day doing fine close work but who recovered a small degree of esotropia when not at work. On balance he spent more hours with the eye divergent than convergent and this varying position of the visual axis appeared to be affecting the position of clearest resolution. The vision was in the region of 6/12 to 6/9, so that examination of details of design was possible.

A small group of patients in whom the amblyopic eye had irregular astigmatism as well as a refractive error was investigated especially to find out whether any extra image due to irregularity of refraction influenced the fringed diplopia due to heterotropia. The subjective findings were much more complicated. True astigmatism might fortify the area of maximum resolution, or according to the angles of both deviation and astigmatism it might minimize the effect. When erratic part-images, due to irregular astigmatism, were added to the problem, analyses of vision were much more

difficult. Small pin-holes were always used during tests and the subjects with irregular astigmatism found them helpful; distracting smudges and blurs in the surround were eliminated, leaving the central aberrations to be analysed with a greater degree of certainty. Since cyclophoria cannot be measured objectively and the subjective measurements are variable, discussion of its effect was deferred at this stage.

The findings in four cases here included (Figs 1 to 4, overleaf) were selected to illustrate the typical picture, first of a simple case of a right esotropia, secondly that of a left esotropia, thirdly the design of a hypertropia, and fourthly that of an exotropia. Records of some patients extend over a period of 10 years and show that alteration in the asymmetry occurs with time subsequent to an alteration of the deviation of an eye brought about by surgery or other measures. More complicated cases with uncorrected astigmatism and an added torsional deviation give more complicated records than the simple ones included here, but the main asymmetry correlating to the main deviation remains.

The illustrations of the appearance of the letters along the lines of Snellen charts have been built up from the patients' own drawings helped by their descriptions. Each letter was drawn singly as it actually appeared to be and then the aberrations analysed when the letter was known. All the subjects found considerable difficulty in drawing the appearance of a whole line.

Discussion

From these results it would seem that biased vision is an integral part of the condition of that profound amblyopia which reacts slowly to treatment.

Previous work on this subject (Pugh, 1951, 1954, 1958) has led to the same conclusions and an explanation has been proposed that the constantly tilted position of the visual axis over many years causes a relative tilting of the foveal receptors with possible changes in the pigmentary layer underlying the receptor cells. Enoch (1957, 1958, 1959), working with laboratory methods, also found the Stiles-Crawford effect in amblyopia and came to the conclusion that this was most likely due to disorientation of the receptors. He made experiments to plot the response of the retina to light entering different parts of the pupil (1958).

In the present series of cases with amblyopia all were heterotropic. Even eyes which appeared to be straight proved to be deviated from the normal position when the two eyes were dissociated. For the purpose of discussion the subjects selected all had central fixation. The typical description of a symmetrical target fixed by the foveal cells was described as being asymmetrally and consistently graded. This effect was constant in direction and the direction was always related to the angle of heterotropia. Apart from the graded effect within the target, extra fragments of the target's image appeared

Subject 1

Female aged 47; right eye amblyopic and esotropic

Refraction: Right eye, +0.75 D sph. (Left eye, +0.5 D sph., +0.5 D cyl., axis 10° = 6/5)
(Padded during uniocular tests)

Visual Acuity Right Eye:

Single letters = 6/9 +.

Snellen chart less good = 6/24–6/18.

The patient was unable to be sure how many letters there were in each line because secondary ghost letters impinged on the real ones, or overlapped from left towards right. This was marked in the central letters following the first clear left-hand letter.

Subject's Description:

6/60	T	"Good."
6/36	XU	"The first X good, a shadowy X or backwards K between X and U."
6/24	DZA	"One letter between D and Z which could be a T and perhaps another letter between Z and A—could be four or five letters in all."
6/18	PNFH	"The first P clear, N could be an R or the R could be just left of the N, followed by E and F or two F's. End letter is H. Five or six letters."

She was doubtful about a smudge following the end left-hand letter. She said words dragged to the right in reading, overlapping from left to right in the same way.

The bottom composite diagram correlates the objective measurement of the visual axis, *i.e.* 8°d esotropic, with the subjective measurement of the clearest definition at 9 o'clock and the area of poor resolution at 3 o'clock. The arrow on the outside scale indicates the esotropic direction of the convergent visual axis in daily usage.

Deviation: Objective measurement +8°d with or without correcting spectacles, in distant vision.

Directional Preference:

Subjective definition on a circle was reported to be good on the left side from 12 to 6 o'clock with the clearest area between 10 and 8 o'clock. The temporal side of the circle was said to appear much less clearly defined with the most blurred area between 2 and 4 o'clock.

ACUITY
ON SINGLE LETTERS

	6/24	6/18	6/12	6/9	6/6
H	✓	✓	✓	✓	
T	✓	✓	✓	✓	
E	✓	✓	✓	✓	✓
F	✓	✓	✓	✓	✓
X	✓	✓	✓	✓	
N	✓	✓	✓	✓	
Z	✓	✓	✓	✓	
A	✓	✓	✓	✓	✓
O	✓	✓	✓	✓	
U	✓	✓	✓	✓	✓
D	✓	✓	✓	✓	
C	✓	✓	✓	✓	

ACUITY ON SNELLEN CHART

RIGHT EYE ESOTROPIC

FIG. 1.—Right eye esotropic.

Subject 2

Male aged 16; left eye amblyopic, esotropic, and hypotropic

Refraction: (Right eye, emmetropic = 6/5). Left eye, +2 D cyl., axis 90°.
(Padded during uniocular tests)

Visual Acuity Left Eye:

Single letters = 6/9 less ii, 6/6 some.

Snellen chart = 6/18–6/12, *i.e.* less good by two grades.

The right side of the line was seen clearly, but secondary images appeared to the left side of the real letters. More than the actual number of letters in the line were counted.

Subject's Description:

6/60	T	"Right side of T sharper."
6/36	XU	"Right side of U best, a second left side of U between the U and the X; the left part of the X poor."
6/24	DZA	"Right-hand A much blacker all over and clearer; the last letter a smudgy O and a blurred letter between Z and D."
6/18	PNFH	"Right-hand H best letter; N worst and looks nearer to one of the F's—there are two F's; the left side of P is poor. Five letters."
6/12	UZTXD	"The right-hand D (or O) clearest; the next letter X had three or four letters close behind ? T's and the last left-hand letter a misty U."
6/9	NAFDHZ	"Right-hand letter ? Z; the rest of the letters are smudged together."

The bottom composite diagram correlates the objective direction of deviation of the visual axis down and in at 135 degrees with the subjective measurement of the area of clearest definition between 4 and 5 o'clock and the direction of poor resolution between 10 and 11 o'clock. The arrow indicates the average angle of deviation of the left visual axis in daily usage.

Deviation: Objective measurements varied from month to month. The convergence was between 3°d and 8°d and the vertical deviation varied between 3 R/L and 5 R/L. The visual axis was thus directed down and in (nasally) varying between 120 and 153 degrees—average 135 degrees.

Directional Preference:

Subjective definition on a circle was reported to be good on the right side between 2 and 7 o'clock with the clearest areas between 4 and 5 o'clock. Blurring was described on the left side between 7 and 2 o'clock with the foggiest area around 10 to 11 o'clock.

The influence of the astigmatism had to be considered; the angle of clearest definition by refraction would have been horizontal unless the correcting spectacles had been worn constantly as prescribed. The patient had worn spectacles from an early age so that this factor would have had little or no effect.

ACUITY
ON SINGLE LETTERS

	6/24	6/18	6/12	6/9	6/6
H	✓	✓	✓	✓	✓
T	✓	✓	✓	✓	✓
E	✓	✓	✓		
F	✓	✓	✓	✓	✓
X	✓	✓	✓	✓	
N	✓	✓	✓	✓	✓
Z	✓	✓	✓	✓	✓
A	✓	✓	✓	✓	✓
O	✓	✓	✓		
U	✓	✓	✓	✓	
D	✓	✓	✓	✓	
C	✓	✓	✓	✓	

ACUITY ON SNELLEN CHART

5 LETTERS
6 OR 7 LETTERS

LEFT EYE ESOTROPIC & HYPOTROPIC *

FIG. 2.—Left eye esotropic and hypotropic.

Subject 3

Female aged 34; right eye amblyopic and mainly hypertropic

Refraction: Right eye, +0.25 D sph., +0.25 D cyl., axis 50°.

(Left eye, +0.5 D cyl. = 6/5)

(Padded during uniocular tests)

Visual Acuity Right Eye:

Single letters = 6/6 less *i*.

Snellen chart = 6/12, 6/9 partly.

The central letters in the lines 6/18, 6/12, and 6/9 overlapped.

Subject's Description:

6/60 Z "Lower half of Z blurred and wider."

6/36 DA "Lower half of each letter worse."

6/24 FXH "Bottom of each letter blurred and fainter. ? Shadow letter between X and H."

6/18 PTND "Top of left-hand P clear, T and N close together, N touching top of T, or an extra N between."

6/12 XAZFN "Bottom of letters not clear; Z overlaps on to A; whole line smudgy."

6/9 HTXUDF "First two clearer—rest too muddled to read."

The bottom composite diagram correlates the objective measurement of the hyperphoria with the subjective measurement of the direction of clearest definition at 12 o'clock and the area of poor resolution at 6 o'clock, and indicates that the significant deviation was vertical. The area between 7, 6, and 5 o'clock on the black circle was reported to be smudged and faint, and even up to 3 o'clock it was still not good; this temporal lack of definition suggests that the eye was probably slightly convergent post-operatively and that the effect of esotropia as well as that of the main hypertropia was still present. As will be seen below, the vertical deviation had probably remained at 2°d for 24 years, but the horizontal deviation had been adjusted by surgery to "straight", and remained so for some 20 years until a tendency for divergence developed.

Deviation: Objective measurement in 1937:

Lateral	+12°d	} with glasses	+31°d	} without glasses
Vertical	2°d R/L			

Surgery was performed in March, 1937, but the patient did not return after the operation.

Objective measurement in 1961:

Lateral	0 to -12°d variable	} with or without glasses
Vertical	2°d R/L	

Directional Preference:

Subjective definition on a circle was reported to be clear from 3 through 12 to 9 o'clock. The lower half from 9 around to 3 o'clock was less good, with a very blurred area between 5 and 7 o'clock and the 4 o'clock area less good than the 8 o'clock area.

ACUITY
ON SINGLE LETTERS

	6/24	6/18	6/12	6/9	6/6
H	✓	✓	✓	✓	✓
T	✓	✓	✓	✓	✓
E	✓	✓	✓	✓	✓
F	✓	✓	✓	✓	✓
X	✓	✓	✓	✓	✓
N	✓	✓	✓	✓	
Z	✓	✓	✓	✓	✓
A	✓	✓	✓	✓	✓
O	✓	✓	✓	✓	✓
U	✓	✓	✓	✓	✓
D	✓	✓	✓	✓	✓
C	✓	✓	✓	✓	✓

ACUITY ON SNELLEN CHART

? 3 LETTERS
4 OR 5 LETTERS
5 OR 6 LETTERS

FIG. 3.—Right eye hypertropic.

Subject 4

Male aged 17; right eye amblyopic, exotropic, and hypertropic

Refraction: Right eye, -0.25 D sph. (Left eye, emmetropic = 6/5)
(Padding during uniocular tests)

Visual Acuity Right Eye:

Single letters = 6/9–6/6.

Snellen chart = 6/18–6/12.

The right-hand side of the line was seen more clearly, *i.e.* the side temporal to the patient; this was opposite to the right esotropic eye which saw the nasal side clearest. More than the actual number of letters were counted, extra secondary letters were described as occurring in the centre and left centre of the line. Even the 6/24 line was said to have an extra letter at times, and 6/18 and 6/12 always had doubtful extra letters.

Subject's Description:

6/60	Z	"Top right and bottom right of letter clearest."
6/36	DA	"Right-hand side of A black and clear, bottom and left of each letter poor."
6/24	FXH	"H clearest—sometimes looks like a smudged letter between X and F."
6/18	PTND	"D good, N, 'something', T, P,—five letters or six" (<i>i.e.</i> from right to left).
6/12	XAZFN	"N good, F, another F, Z, or A, another letter, A and X, about 6 or 7 letters."

The bottom composite diagram correlates the objective direction of deviation, *i.e.* up and out at an average angle of 40 degrees, with the subjective measurement of directional preference at 2 o'clock, and the area of poorest resolution from 7 to 8 o'clock. The arrow indicates the angle of deviation of the right visual axis in daily usage.

Deviation: Objective measurement varied from 5° d to 6° d divergence with a variable 3° d to 6° d of right hyperphoria. The average angle of deviation was approximately up and out at 40 degrees.

Directional Preference:

Subjective definition on a circle was reported to be good between 11 and 5 o'clock, with the sharpest area between 1 and 2 o'clock. Down and in between 11 and 6 o'clock was seen less clearly, the most blurred area being between 7 and 8 o'clock.

RIGHT EYE HYPERTROPIC & EXOTROPIC

FIG. 4.—Right eye hypertropic and exotropic.

to one side of the main image. These extra fragments were seen in the opposite direction to that of the angle of deviation of the visual axis; if a vertical component was present in the one it was also present in the other. Care was taken to exclude the effects of irregular astigmatism by the use of pinhole occluders, and any refractive errors were carefully corrected. The effect described was almost as if the target were seen through a neutral density wedge, except that distortion of form and extra part-images were added on the dimmer side of the image. Refractive errors had to be considered in the elucidation of the picture but could be discounted as a cause of the main biased effect.

Because in these subjects the amblyopic eye was deviated to a greater or lesser degree from the normal position during the waking hours of life, light from the main luminous field entered obliquely through the cornea, aqueous, and lens. The resulting light at the fovea would thus be a blurred patch, which according to Weber's law, would have greater luminance on one side than on the other. The image being reversed during its passage to the retina, the side of greater luminance would be opposite to the direction of obliquity of the incident rays so that the gradient of the field of luminance would be constant in direction and position as long as the visual axis remained deviated in the same direction. This would mean that an eye constantly squinting nasally would have the rays of light parallel to the normal line of sight of the dominant fixing eye, entering its optical system to the temporal side of cornea and lens. These rays refracted within the eye would be focused in turn into a patch of light graded in intensity at the fovea, with the highest degree of luminance to the nasal side. The structures at the fovea must thus be stimulated for years with light of a regular gradient of intensity.

Stiles and Crawford (1933) and Stiles (1939) showed the effect of the angle of incidence of light rays, and "that pencils reach the retina with approximately equal intensities but that the brightness-producing efficiency of rays incident on the retina varies with their angle of incidence". These authors concluded that the variation of luminous efficiency is probably retinal rather than pre-retinal.

The anatomical structures most likely to be affected by this "gradient" light stimulus would be first the receptor cells themselves, and secondly the cells of the pigment epithelium together with their protoplasmic processes in which the outer segments of the receptors are embedded. Evidence continues to accumulate that pigment epithelium may have more than the passive function of absorbing light, *cf.* the anti-halo backing of a photographic plate, and may have a positive role to play in the visual process. Thus Dowling and Gibbons (1961) showed the close functional relationship between the receptors and their underlying epithelium when they fed rats on a vitamin A deficient diet supplemented by vitamin A acid which the retina could not use, and they demonstrated that the myeloid bodies of the pigment epithelium and the outer segments disintegrated. On feeding back vitamin A, the

myeloid bodies regenerated in a couple of weeks and the outer segments of rods reconstructed themselves. Wald (1956) even suggested that the pigment epithelium may represent the sheath of Schwann of the retina and as such may play a part in generating nerve impulses. The inquiry which is apposite to the problem is whether "gradient" light stimulus over many years, such as occurs in an amblyopic eye, may have an effect on the structure of these cells. The cuboidal cells of this layer are in close contact with the receptor cells, the tips of the outer segments being sometimes in direct contact with the surface epithelial cells. Also the numerous processes from the optical surfaces of the cuboidal cells interdigitate between the photoreceptors. Both the cuboidal cells and the processes contain dense pigment granules and it is thought that in the processes these granules are arranged, as a rule, parallel to the axis. This arrangement of dense pigment surrounding the light receptor cells may have a light insulating function, whereby rays entering the outer segment of one receptor are prevented from infiltrating through to neighbouring receptors.

Rays incident in the normal line of sight are normally focused by the optical system to give an even illumination at the fovea. Any resultant reaction in the epithelial cells would presumably be relative to the number of quanta absorbed by the receptors embedded in its apical surfaces. When the fovea is stimulated by "gradient" light, the pigment epithelium cells receiving stimuli from the dim end must have a diminished reaction relative to the smaller number of quanta of light entering the receptors in that area.

If diminished stimulus over the years caused a partial atrophy in certain cells of the pigment epithelium, and if this resulted in a disarrangement of the pigment granules and processes around the outer segments, then an explanation could be suggested for some of the clinical findings. Bernstein (1961), discussing the functional architecture of the pigment epithelium, suggested an arbitrary division of the functions as supportive, nutritional, and secretory. If the processes on the side of diminished entry of light became relatively atrophied, a slight tilt of the receptor cells might result simply from less support to one side; this design would be a gradient-relative atrophy and would produce a group of receptors all tilting in the same direction. If the arrangement or densities of the pigment granules became altered in the interdigitating processes and/or in the cuboidal cells, light insulation between the receptors might become defective; this would allow stray light to pass laterally from its main receiving cell through to neighbouring receptors, causing erratic stimuli in the direction of the dimmer end of the "gradient" light. This might account for the extra images which are seen to one side of the main image and tilted receptors would explain why they always occur to the one side.

The pigment epithelium having been considered as a possible site of change, the receptors are the other structures to be considered. The light received by the receptor cells is absorbed by the molecules of visual pigments. These

occur exclusively in the outer segments and are orientated in preferred positions for absorbing light incident along the axis of the cell. Since the cilium connecting the outer and inner segments is a short bar-like structure, which Wolken (1961) suggests is phylogenetically similar to the simple eye spot with flagellum, it might possibly be affected by years of a stimulus by light of sloping intensity to cause a tilt of the cell towards the side of higher luminance. When "gradient" light strikes a group of receptors, the number of quanta of light received by the cells on one side of the group should be constantly higher, and it is conceivable, since the normal concentric stimulus is changed to an asymmetrical stimulus, that an alteration may occur in some part of the cells so that the affected cells tilt either in part or as a group.

To return to clinical investigations, subjects analysing the vision of an amblyopic eye describe an image which is biased to one side in both definition and brightness, extra confusion on the poor side being caused by distortion and fragmentary images, or by a bunching together of several images. The area of retina reacting in this lopsided manner can be tracked down over a period of years from a group of cells subtending a target of say, 20 minutes down to an area subtending 5 minutes on the 6/6 Snellen line and so on until the defect finally disappears. The cells involved for the resolution of such small targets must be the receptors of the fovea. When a larger area of retina involving the whole of the rod-free macula fixes a target of some 84 minutes, the same asymmetry of vision is described, but localization is more difficult as in these cases the number of receptors involved must be very much greater.

If this hypothesis is correct, the bias of the normal vision should change direction, if, over the years, the direction of the deviated visual axis changes, and this appears to happen. If for some reason the direction of heterophoria changes over a period of years, a relative change in the subjective descriptions of the asymmetry of vision occurs. When this kind of alteration of position occurs, the subject finds analysis of form design difficult, because, although the target still appears to be asymmetrical, extra areas of inaccurate definition occur and confuse the main direction of good resolution.

The effect being discussed is quite different from that of suppression and also from that of scotomata. The subjects in this series of cases were analysing the vision of targets of a size which could be resolved only by the fovea and the difficulty seemed to be in the presence of too much inaccurate form vision, not in a loss of vision as in cases of scotoma.

Summary

(1) The results of analysing the visual acuity of an amblyopic eye (the other eye being padded to exclude any central effects) has shown that biased vision is an integral part of amblyopia. The images were always described as asymmetrical in definition and brightness, one side being relatively clearly seen, but the other side was poorly resolved, being confused by extensions, extra lines, or fragmentary shadows of the main image.

(2) The direction of clear resolution was directly related to the position of the visual axis in the heterotropia which is always present. This relationship is consistent in esotropia, exotropia, and hypertropia.

(3) The biased vision is a sort of Stiles-Crawford effect and suggests that light rays incident in the direction of the visual axis fail to enter along the axes of the foveal receptors. The hypothesis is that the affected receptors are tilted and that the fragmentary extra images on the side of poor definition are due to defective light insulation between one receptor and its neighbouring cells, probably due to changes in the underlying pigment epithelial cells and their interdigitating processes. Thus, whatever auxiliary changes are present in the higher centres, the retina must be the first structure to be affected by daily stimulus from light with gradient brightness.

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