Evidence of Undiagnosed Undulant Fever

None of the participants showed any evidence of undulant fever at the time of investigation. From our inquiries into their past histories, however, we believe that two of them had undiagnosed attacks in the past.

Case 6.—This man at first denied any history of febrile illness. The symptoms produced by his brucellin test (malaise, headache, limb pains, sweating) recalled to his memory an illness with exactly similar symptoms which he had suffered 10 years previously. It lasted three months, but was not serious enough to cause more than a few days' loss of work. His doctor found no abnormality, and sent him to hospital for pathological tests. It seems that these were of little help, because no satisfactory diagnosis was made and the symptoms disappeared spontaneously.

It was not possible to obtain further clinical details or the results of the pathological tests. Nevertheless, we believe that the patient's description of his illness is fully consistent with a diagnosis in retrospect of the ambulant form of undulant fever.

Case 12.—Between 1936 and 1940 this farmer had experienced several bouts of fever with profuse sweating, each one lasting several days. At the time he was having much trouble with contagious abortion in his milking herd. His doctor was unable to find the cause of the pyrexia, but commented that the clinical picture resembled malaria. The patient had not, however, been abroad. About the year 1950 he had a prolonged pyrexial illness which kept him off work for three months, including convalescence. The pyrexia was swinging and accompanied by profuse sweating, malaise, and limb pains. There was no response to penicillin or sulphonamides, but the fever subsided promptly with chloramphenicol and there was no recurrence.

Discussion

If either a positive brucellin test or brucella agglutinations to a titre of at least 1 in 40 are taken as evidence of past or present latent infection, then the latent infection rate in this series is 14 out of 20, or 70%. The area is one of mixed arable and stock farming, with no preponderance of dairy herds, and there is no reason to think that these results could not be reproduced in other parts of the country with a similar agriculture. Vaccination of cattle with strain 19 has led to a decreased incidence of abortion (Stableforth, 1960). The proportion of positive milk samples has also decreased, but not to the same extent. In the veterinary section of the Oxfordshire brucellosis survey, between 4.4 and 8% of farms were found to be producing infected milk at the time of the test (McDiarmid, 1960). In spite of recent improvements in the abortion rate in cattle, it appears from the present survey that brucella infection is still widespread among farmers. Although the majority of those who contract the infection suffer no ill-health, it is interesting to find that 2 out of 20 (10%) in this series have almost certainly had undiagnosed undulant fever. This supports Dalrymple-Champney's contention that the real incidence of the disease is higher than its reported incidence. It also emphasizes the importance of considering undulant fever whenever a farmer or farm worker presents with a pyrexia of unknown origin or with vague symptoms such as malaise, limb pains, and sweating.

From the results of the agglutination reactions shown here it is evident that a titre of up to 1 in 320 is of no diagnostic value in a farmer, nor is a rise in titre after a positive brucellin test.

Summary

A survey of 20 farmers for latent brucellosis is described. Brucellin skin tests were performed, and serum agglutination tests both before and after the skin test.

Taking a positive brucellin test or the presence of agglutinins to a titre of 1 in 40 as the criterion of latent infection, we found a latent infection rate of 70%. As a result of inquiries into their past medical histories it is concluded that two of the farmers have almost certainly suffered from undiagnosed undulant fever.

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INCIDENCE OF NON-CENTRAL FIXATION IN CHILDREN WITH SQUINT

BY

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Amblyopia, or diminution of vision in one eye, has long been recognized as a major factor to be reckoned with in the treatment of children with squint. A monocular visual deficiency or a recognizable squint is frequent in the child population of pre-school (under 5) and school (5–15) years in the urban areas in this country, and may reach a figure of 5%. Those children who have monocular convergent squint may develop amblyopia in the deviating eye. It is generally accepted that an eye may be regarded as amblyopic when the visual acuity is less than 6/12 or when the affected eye sees two or more lines fewer than its fellow on the Snellen chart, in the absence of pathological change.

Considerable interest has been taken in this subject recently, and it has been shown by Cole (1959) that 7.7% of children up to the age of 10 are amblyopic in one eye, compared with a figure of 5.27% for all age-groups in the adult population. The greater proportion of the amblyopia of childhood is due to squint, and the classical treatment—occlusion of the fixing eye (when performed up to the age of 7)—results in cure or improvement in visual acuity in those patients who persevere in the treatment. There remains, however, a number of patients in whom the amblyopia is intractable; in a recent series at the Manchester Royal Eye Hospital this intractability was found in 17% of patients under 10 with convergent strabismus (Naylor and Wright, 1959). A large proportion of these amblyopes

have fixation in the squinting eye which is not centred on the fovea. The incidence of such non-central fixation in amblyopia has been given by Von Noorden (1960) as 44% and Cüppers (1958) as 35.5%. The incidence of non-central fixation in squint in this country is not known and may well be different from that on the Continent, since the school medical and maternity and child welfare services here have been active over many years in the ascertainment of squint. Reference to the school ophthalmic clinics and to eye hospitals, where correction of refraction and orthoptic supervision is available, is (or should be) a routine matter.

In order to elucidate the incidence of non-central fixation in children in this country, routine examination of the fixation in patients attending for the first time with a squint at an eye hospital (Manchester Royal Eye Hospital) and at a school ophthalmic clinic (Salford Education Department) has been carried out, together with a similar routine examination of patients attending the school clinic who have already had treatment for their squint. The primary purpose of the present paper is to assess the frequency of non-central fixation in the new patients attending the hospital, and to study the factors which influence this frequency.

Method

Young patients with squint who attended the Manchester Royal Eye Hospital for the first time were examined under mydriasis to determine the refractive error and the type of fixation. The latter was determined by using the "visuscope," which is an instrument similar to the ophthalmoscope whereby a small black star is projected on to the retina and the child is asked to look at it, the other eye being covered temporarily. The observer can see the image of the star resting on the fundus; if central fixation is present, the star remains steadily on the foveola, but if non-central fixation is present the star is seen in one of the following five different areas (see Fig. 1):

FIG. 1.—Diagrammatic representation of fundi seen with visuscope. Right eye: central fixation. Left eye: (1) parafoveal, (2) paracentral, (3) eccentric, fixation.

A. Unsteady Central Fixation: In this case the star hovers over the foveola and the perifoveolar area but is not steadily fixated on the foveola.

B. Parafoveal Fixation: The star is fixated steadily but rests slightly to one side of the foveola.

C. Paracentral Fixation: The star is fixated steadily but rests a little further to one side (at the edge of the granular, avascular area which is regarded ophthalmoscopically as the macula).

D. Eccentric Fixation: The star is fixated steadily and usually at a point between the foveola and the disk, but it may even rest on the disk itself or to the nasal side.

E. Wandering Fixation: There is no steady fixation; the star wanders in an irregular fashion over the area between the foveola and the disk but is not located in one spot.

This classification has been discussed more fully by Graham (1961). Since many of the children examined were very young it was difficult to assess parafoveal fixation accurately, and for the purpose of this paper the few cases in which this type of fixation was diagnosed have been included with those of the paracentral type.

The non-squinting eye was examined first as a routine in order to familiarize the child in seeing the star and in recognizing it later with the other eye; to form an estimate of the powers of attention of the child; and, finally, to satisfy the examiner that central fixation was reliably present in the "good" eye. If the fixation in the non-squinting eye was not steady and central, but showed a tendency, through lack of attention, to move from the foveola then the fixation in neither eye was recorded. Inevitably there were some very young children in whom a record was unobtainable because they were crying, or struggling, or showed no tendency to co-operate.

At the same visit the sex, type of squint (unilateral-convergent, alternating-convergent, or divergent), family history of squint, age at onset of squint, interval of time between onset of squint and first examination, and any possible cause (usually an illness is given as a precipitating factor) were all noted.

Results

A total of 512 patients were seen during the 12-month period from September, 1959, to August, 1960, at the Manchester Royal Eye Hospital. Of these, 72 had alternating convergent squint and 21 had divergent squint; in all of those in whom the fixation was recorded it was found to be central. Among the remaining 419 patients with unilateral convergent squint there were 76 in whom the fixation was not recorded for the reasons mentioned above, and in a further 39 other data—for example, history, refractive error—were incomplete. A total of 304 patients with unilateral convergent squint therefore remained for further analysis. 68 of these had non-central fixation of the following types: 13 unsteady central, 9 parafoveal, 35 eccentric, and 11 wandering.

The relationship between the incidence, sex, family history, presence of a possible cause, and the eye affected is shown in the Table. None of these factors had a statistically significant effect on the incidence.

Incidence of Non-central Fixation According to Various Factors

Fixation	Sex		Family History		Cause Ascribed		Eye Affected		Total
	M	F	Yes	No	Yes	No	R.E.	L.E.	
Central ..	122	114	112	124	98	138	107	129	236
Non-central	32	36	36	32	26	42	36	32	68
Total ..	154	150	148	156	124	180	143	161	304

The relationship between the age at the time of first examination and the incidence is of no statistical importance (Fig. 2), but a scrutiny of the age at onset of the squint shows that the incidence of non-central fixation is highest in the lower age-groups (Fig. 3). Similarly, the incidence is lowest in those children who attended at an early date after the onset of the squint (Fig. 4). In ascertaining the influence of anisometropia (Fig. 5), the meridian with the greatest refractive error

FIG. 2

FIG. 3

FIG. 4

FIG. 5

FIG. 2.—Incidence of non-central fixation according to age at first examination. FIG. 3.—Incidence of non-central fixation according to age at onset of squint. FIG. 4.—Incidence of non-central fixation according to interval between onset of squint and first examination. FIG. 5.—Incidence of non-central fixation according to amount of anisometropia. In Figs. 2-5 and 9 the shaded areas show numbers with non-central fixation; figures above each column show percentage incidence.

FIG. 6

FIG. 7

FIG. 8

FIG. 10

FIG. 6.—Incidence of non-central fixation according to interval and age at onset of squint. FIG. 7.—Incidence of non-central fixation according to interval and degree of anisometropia. FIG. 8.—Incidence of non-central fixation according to age at onset of squint and degree of anisometropia. FIG. 10.—Incidence of non-central fixation according to interval and refractive error of fixing eye. In Figs. 6-8 and 10 the shaded areas show percentage incidence; figures in each block show total number of patients concerned.

in each eye was used for the purpose of deciding the degree of anisometropia; patients with one dioptre or less of anisometropia were regarded as having low anisometropia and those with more than one dioptre as having high anisometropia. This division has been found to correspond best with the incidence of amblyopia (Stevens, 1960). It will be seen that there is a highly significant tendency for high anisometropia to be associated with non-central fixation.

Further analysis was undertaken to see if the three significant factors of age at onset, interval, and anisometropia were independent. The relationship between the age at onset and the interval is shown in Fig. 6. It will be seen that in each age-at-onset group there is an increase in the incidence of non-central fixation as the interval between onset and examination increases. The relationship between interval and anisometropia is shown in Fig. 7; the influence of interval is again considerable in both groups of anisometropia; generally, the patients with a high anisometropia have a higher incidence than those with low anisometropia. The relationship between age at onset and anisometropia is shown in Fig. 8. The influence of anisometropia is again clear, and there is also a suggestion that the age at onset is a factor of importance. Preliminary analysis of the larger numbers of patients from the school

ophthalmic clinic substantiates the view that these three factors are independent, the interval and degree of anisometropia being of particular importance.

In a series such as this, in which the fixation was assessed at first examination, it is impossible adequately to correlate it with the type of squint present, but an idea of the accommodative effort required by the child can be obtained from the refractive condition of the fixing eye, assessed as the average refractive error of the two principal meridians. Fig. 9 shows that it is

FIG. 9.—Incidence of non-central fixation according to refractive error of fixing eye.

only in the group of low refractive error (which includes two cases with a low myopic correction) that there is an appreciable excess of non-central fixation; this suggests that it is the non-accommodative squints that tend to have non-central fixation when first examined. Analysis of the interval between onset and first examination of these cases (Fig. 10), however, shows that a greater proportion of the patients with low refractive error attended in the later interval groups, and it appears, therefore, that the apparent increase in non-central fixation in these patients may be due to this relatively long interval before attendance. Once again the association of a long interval with increased incidence of non-central fixation is shown in both refractive groups. There was no significant association in this series between the refractive error and either the age at onset or the degree of anisometropia.

Discussion

The overall incidence of non-central fixation (22.4%) found in this series of young patients with unilateral convergent squint indicates that this defect in fixation constitutes a considerable factor in the management of the amblyopia of squint.

The analysis in this paper has shown that one of the main factors influencing the incidence of non-central fixation is the interval between the onset of the squint and the time of first examination; if this interval is short, there is a low incidence of non-central fixation. This has been confirmed by a similar analysis of the patients attending the school clinic, which will be published elsewhere (Scully, 1961). Moreover, evidence is accumulating to suggest that if occlusion treatment can be instituted early it may result in a re-establishment of central fixation, whereas it is generally agreed that well-established non-central fixation will not respond to such simple measures. Treatment, which can be instituted only at an age of not less than 7 years, is by complex methods involving projection of after-images (Cüppers, 1956), or direct stimulation of the macula (Bangerter, 1953). This treatment may require from 30 to 120 attendances and is expensive both in the time spent by the patient and in the personnel and facilities required. The prevention of non-central fixation is therefore clearly desirable.

The interval between onset and examination on which the incidence of non-central fixation is so clearly dependent is a factor largely under the control of the family doctor. Since this factor appears to be independent of the others it is reasonable to assume that if all patients could be seen with the minimum of delay after the onset of squint the incidence of non-central fixation would be very much smaller. It cannot be emphasized too strongly that as soon as a child is seen to squint it should be referred for examination. This applies to infants, to the toddlers of pre-school age, and to children of school age. There should be no hesitation in referring the child on the grounds of age or of the intermittency of the squint. Early treatment can then result in a saving of much time and energy on the part of both the ophthalmic specialist and the orthoptic department, as well as a considerable economic saving to the patient's family.

Summary

A survey of the incidence of non-central fixation, which is associated with one of the more intractable

forms of amblyopia, in children with squint attending an eye hospital for the first time shows that a short interval between the onset of squint and attendance for examination is associated with a low incidence of non-central fixation. The incidence is also low in those patients with a late age of onset and in those with a low degree of anisometropia. These findings are similar to those in a parallel series attending a school clinic.

It is concluded that referral of children with squint to a hospital eye department or school ophthalmic clinic as soon as the squint is noticed can be expected to minimize the incidence of non-central fixation, and therefore to make a major contribution to the prevention of loss of vision.

We are indebted to the surgeons of the Manchester Royal Eye Hospital for allowing us to investigate these patients under their care, and we gratefully acknowledge the helpful criticisms of Dr. A. Stanworth, Reader in Ophthalmology, University of Manchester, in the preparation of this paper.

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ERYTHEMA MULTIFORME AND NEPHRITIS

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Erythema multiforme is a reaction of the skin and mucous membranes to various agents, among them drugs such as the sulphonamides, codeine, and the hydantoins. It is seen fairly often in dermatological practice in this country, and is characterized by erythema (which may assume the classical "target figure" form), purpura, and sometimes vesicles and bullae. There is usually systemic upset with fever and malaise, and in the severe form (so-called Stevens-Johnson syndrome) the mucous membranes of the mouth, eyes, and genitalia may be affected. Histologically there is a cellular infiltrate, particularly around the dilated vessels, with oedema of the dermis and prickle-cell layer, which may proceed to vesicle formation. Certain infections, especially streptococcal, may precede erythema multiforme, and some investigators maintain that the common recurrent type is a hypersensitivity reaction to streptococci (Welsh, 1948). Most dermatologists do not accept this view, and many think a viral cause more likely. Herpes labialis is a common accompaniment of erythema multiforme,