A NEW LOOK AT MIGRAINE

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MIGRAINE is so variable that it is very difficult to define. Its spectrum extends from the vascular type headaches of Horton to atypical facial pain, with the 'classical' picture lying somewhere between. It has recently been defined[1] as:

> A condition characterized by paroxysmal attacks of headache, often unilateral, which are preceded by various types of visual or other sensory and, in rare instances, motor disturbances; and which are followed usually by nausea and vomiting. In some cases, believed to be of similar or identical cause, visual or other cerebral manifestations may occur without headache.

This definition is not much different from that of Gowers in 1893.[2]

Statements about migraine in textbooks are often erroneous and are copied from one edition to another. Thus, in a recent textbook, the following statements on migraine are made:[3]

> The sexes are equally affected.
>
> Subjects of migraine are commonly of an energetic and intelligent type and many have a meticulous standard of thoroughness and precision almost amounting to an obsession.
>
> Women usually have attacks in association with the menstrual periods.

None of these statements appears to be correct and evidently migraine attacks will have to be carefully studied to collect more accurate information. Unfortunately, the phenomena in this condition are often transitory and subjective, and sufferers have therefore found it difficult, unless they were trained and skilled observers, to record what in fact occurred. It therefore seemed worth approaching doctors or their wives who suffered from migraine for co-operation in observing and recording their attacks.

The trial

In 1962 and 1963 all doctors in the United Kingdom who either themselves or whose wives suffered from migraine were asked if they would be willing to take part in a trial. Two hundred and sixty doctors were eventually provided with history sheets, on which the relevant data on their attacks or those of their wives were recorded. They then noted in detail on a special calendar their attacks for the

following three months, and then for a further three months using as treatment a new sublingual preparation of ergotamine, Lingraine (Bayer).

Of these 260 doctors, 160 returned information at the end of the six months. Of these, 73 did not contain enough data to be acceptable, usually because their attacks had become infrequent. This is always the difficulty in following migraine attacks because they inexplicably stop for many months or even years and then, for equally unknown reasons, return again. Most of those who were excluded were having one attack in six months, or less often, which made it impossible for statistical reasons to include them. Several were excluded because, although they had attacks in the first three months on their usual treatment, their attacks disappeared or became very infrequent during the second period of treatment.

Another 16 were omitted for various reasons. Two became pregnant and it was felt to be inadvisable to prescribe ergotamine during pregnancy; one was rediagnosed as having essential hypertension rather than migraine; six were intolerant of the ergotamine, four because of nausea and two because of vascular spasm which was transitory and disappeared once treatment was stopped; seven have an O at the end. Such negative records are valuable in chronic people wrote that they had tried the ergotamine preparation but found it unsuccessful and so returned to their previous treatment. It was interesting that in three of these the previous treatment included parenteral ergotamine; it is well known that once this form of treatment is started any other is likely to be at least second best. One person failed to complete the trial, giving no reason.

Basic information

The basic information about the 71 people left in the trial cannot be regarded as typical of persons suffering from migraine in the population. They comprise a specific group, older than the general run, and with a sex distribution greatly in favour of males—whereas the incidence of migraine is three times greater in females. There were 35 men and 33 women with an average age of 39. Fifty-seven per cent had a family history of migraine, 42 per cent a personal history of travel sickness, and 36 per cent had had some sort of allergy. Among the women only 15 per cent noticed any correlation between migraine and menstruation.

The family background of migraine is well known, and 60 per cent is the figure usually quoted. The high incidence of travel sickness is also known, 42 per cent being much higher than in the general population. The incidence of allergy too is high, although a possible reason for this is its accurate observation by trained persons. In

spite of the large number with a past history of allergy, few quoted it as a precipitating factor in their attacks.

Prodromata

Most of the subjects experienced prodromal symptoms, though not on all occasions. Only 19 per cent had attacks with no prodromata at all, though 69 per cent had some attacks without prodromata. Visual symptoms were far the most frequent: 216 attacks (from a total of 834) were preceded by fortification spectra, and 80 by scotoma; other visual disturbances were hemianopia in 12, photophobia in 12, a rather vague dimness of vision in four, pain and aching in the eye in 16, and watering of the eye (Horton) in two. Other sensory phenomena occurred in 50 attacks: in 21 the hand, arm or leg was affected, in 15 the nose, throat, tongue or side of the face, and in 14 the site was not specified. Other prodromata mentioned were fatigue and general malaise in 21 attacks; vertigo in six; nasal obstruction in two; cold hands in two; and nausea in eight. Motor prodromata were very rare; dysphagia was mentioned in one attack, and aphasia in a further one.

These prodromata are not consistent, often absent or transitory, and the same person may experience different symptoms on different occasions.

Severity, site and duration

Information was obtained on the severity, site and duration of headaches. It is extremely difficult to assess the severity of so subjective a phenomenon as headache, and so it was categorized into four groups according to the disability caused. The people in the trial did skilled intellectual work, involving writing, reading and other techniques, and it was obvious that migraine would be more severely incapacitating to them than it would to, say, manual labourers. The severity must be judged against this background. The original history sheet required subjects to judge the severity of their own attacks, and the same criteria were used to assess attacks in the next six months:

1. Minor severity with transient or no disability.
2. Moderate severity, where the subject can maintain activity.
3. Severe, but not quite wholly incapacitating.
4. Blinding and totally incapacitating.

On the history sheets the subjects fell into these categories as follows:

1. 14 per cent
2. 25 per cent
3. 44 per cent
4. 17 per cent

In 78 attacks there was no headache at all (10 per cent of the

attacks). This is a rather high figure and difficult to explain. The attacks without headache occurred in nine people, and in seven of them were interspersed with normal attacks with headaches; only two patients had attacks never associated with headache. It may be asked whether these people can be truly said to suffer from migraine.

Did a particular person always have the same severity of attacks, or did it vary, and could any factors account for this? It was found that 22 people experienced headaches of the first three grades, but not the blinding type. Fifteen people had, at times, headaches of all four kinds, 11 of two grades, and only three had headaches of only one category. In two people this was category 4, and in one category 2.

The site of headache was recorded in 528 attacks. In 40 per cent the attacks were either left or right frontal, being roughly equal for either side. In 32 per cent headache was stated to be right or left-sided, more frequently left, and in 16 per cent it was stated to be frontal. In eight attacks it was said to be one-sided, without specifying which side, and in only two was the headache said to be generalized. In six attacks it was stated to be bilateral, in two occipital and in four vertical. In a few it was said that the headache became generalized, having started in one place. From these results a migraine headache seems to be essentially one-sided, with little difference between left or right. It is rarely bilateral and rarely generalized, though a generalized headache may occasionally follow a localized one. The site appears to bear no correlation with severity.

It is difficult to assess the duration of headache, as it often starts insidiously, and it may disappear during sleep. In all cases, however, the average duration was found to be six hours. As might be expected, there was a considerable scatter around this mean, from less than one hour to as long as 72 hours. It also appeared that the more severe attacks were more prolonged, the duration of headache in category 4 being 7.6 hours.

Nausea and vomiting

Sixty-four per cent of the attacks were succeeded by nausea and 12 per cent by vomiting; 32 per cent were associated with neither. Of the most severe attacks 37 per cent were not succeeded by nausea or vomiting; of the severe attacks 78 per cent, and of the mild attacks 70 per cent. Thus it appears that nausea and vomiting are more prevalent in the very severe attacks, whereas in the milder and less severe ones it occurs in only a quarter of persons.

Precipitating factors

The record sheet divided precipitating factors into physical,

emotional or any other actual factor which could be specified. The differentiation between physical and emotional factors was difficult, because many of the sufferers recorded fatigue as a big factor. So in assessing the final results, fatigue, rush, anxiety and tension have all been grouped together. Final results were as follows: in 53 per cent no precipitating factor could be specified; in 18 per cent it was anxiety and tension; in one per cent rush; in 17 per cent fatigue, making a total of 36 per cent, by far the largest group of precipitating factors. Other factors mentioned were travel in about one per cent, alcohol in one per cent, glare in two per cent, cold in one per cent, menstruation in two per cent, and food allergy in 0.5 per cent. It thus appears that even with the most careful observers more than half of migraine attacks appear to have no precipitating factor, and when there is one, anxiety, tension and fatigue are undoubtedly by far the commonest.

Treatment

The treatments previously taken for attacks were analgesics in 42 per cent, ergot preparations in 58 per cent, sedatives in 19 per cent, other treatments in seven per cent and no treatment in six per cent. All kinds of proprietary analgesics were taken, and as might be expected, the largest group were those taking aspirin, then codeine, followed by phenacetin with of course mixtures of these three. Among ergot preparations the brands containing caffeine and other substances were much more commonly taken (70 per cent); ergotamine tartrate by itself was taken by only 22 per cent of those on ergotamine preparations. Of these 12 per cent took the ergotamine by injection.

In the sedative group 24 per cent were taking barbiturates, but the commonest drug used was stemetil which was taken in 65 per cent of attacks, though other tranquillizers seemed to be rarely used. Seven per cent of people were taking various other treatments, including oral diuretics, pethidine, plain caffeine, phenergan, bellergal and diconal. It appears that doctors, with a ready access to all sorts of drugs and some knowledge of their therapeutic applications, were trying one drug after another to determine which was the most suitable. Ergotamine on its own seems now to be superseded by ergotamine combined with caffeine or other substances as the common remedy in migraine attacks—though a person might take ergotamine in an attack and follow this later by an analgesic or sedative to allay the pain and produce sleep.

Psychological study

Besides these investigations of the details of attacks and of treatment, the type of personality in these migraine subjects was assessed

in a psychosomatic study by Dr Whiteley of the department of psychological medicine of Westminster Hospital.[4] Subjects were asked to fill in a Maudsley Personality Inventory, which contains 48 questions, and a questionnaire on body build. Dr Whiteley's report was:

> The survey failed to show a significant difference of migrainous subjects in respect of body-build, extroversion or introversion, neuroticism, or adjustment to home, health, social or emotional affairs. The only significant difference at the five per cent level was that women with migraine were more poorly adjusted to their health. There is, however, a consistent tendency to neuroticism, extroversion, indecision, and poorer adjustment in the migrainous subject.

As regards precipitating factors, 24 people were considered to have a predominantly anxiety factor, and when collated against their personalities the results were the same as those noted above.

Drug trial

Lingraine (a sublingual tablet containing 2 mg. of ergotamine tartrate) was used to see whether this preparation would be more effective than other forms of ergotamine, in that being absorbed from buccal mucosa, it would not produce the nausea and vomiting sometimes associated with oral ergotamine. Subjects were asked to chart the time at which they took their medication and the time at which they noticed any initial abatement of symptoms. This was rather a difficult point to fix, but less so than the time when the attack ended, because a migraine subject (rather like an epileptic) may have a period of general malaise following an attack. The results are given in the following table:

TABLE

RESULTS OF TREATMENT WITH LINGRAINE

		First three months on usual treatment	*Second three months on lingraine*
1	Number of attacks per month ..	5.7	5.4
2	Time before drug began to act ..	4.6 hours	3.9 hours
3	Time before drug began to act (ergotamine preparations only) ..	4.0 hours	3.9 hours

Thus lingraine appears to act more quickly than the other drugs used by the subjects. When compared only with other ergot preparations, however, there seems to be little difference in its speed of action—although it should be noted that this group included parenteral ergotamine, which acts more quickly than any oral preparation. Two subjects said that they felt that lingraine acted more

quickly, and two said they found the drug helpful. Three said that the drug did not help, and three who previously took intramuscular ergotamine tried lingraine but reverted to their previous treatment.

Summary

The definition of migraine quoted at the beginning of this article probably includes about 90 per cent of sufferers. Nevertheless, 19 per cent of subjects had migraine headaches without any prodromata, and ten per cent had attacks without any headache. Thirty-nine per cent of the subjects found that stress factors precipitate attacks, but in over half of the subjects no factor could be pin-pointed at all. As this group of people probably suffered stress as part of their daily life, the coincidence of stress and migraine was likely to occur in any case. It is very difficult to say to what extent stress was a true precipitating factor, and Dr Whiteley's analysis of the so-called migraine personality suggests that this psychological label has little foundation in fact.

With regard to treatment there is no doubt that most subjects found the oral ergotamine preparations useful, especially when combined with an analgesic. Those who were used to parenteral ergotamine found the oral forms hardly any use, and this is perhaps one of the dangers of parenteral treatment in this condition. Lingraine appears to be neither better nor worse than other ergotamine preparations now on the market.

Although if any single factor precipitates migraine it is stress, this has been over-emphasized in the past. The migraine personality does not exist. This clears the air and allows us to proceed to the hypothesis that migraine is not so much a functional condition as a disease caused by some biochemical abnormality, probably associated with release of kinins. Thus many of the unfortunate people inheriting this abnormality are suffering from a true organic disease.

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REFERENCES

1. British Migraine Association (unpublished) 1963.
2. Gower's *Neurology* (1893), vol. 2, p. 836.
3. Price's *Textbook of the Practice of Medicine*, Donald Hunter (1956) 9th Edition, Oxford University Press.
4. Whiteley, J. Stuart. Personal communication.