# The natural history of migraine and its management in general practice*

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"DOCTOR! it's Mrs Smith, she says could you call on the way back from surgery—she says she has a terrible migraine, and she can't stand it much longer."

When I started as a trainee I would shudder at so much as the mention of migraine. It immediately conjured up visions of a nervous, highly-strung, demanding patient, expecting a cure which I felt impotent to provide. Initially I must admit I took the easy course and reached for my prescription pad, and became increasingly frustrated with the poor results. However, by the end of my year I have now come to respect migraine, and its sufferers, and I find myself fascinated by the whole subject.

As a disease I am beginning to see it as possibly a manifestation of stress in a constitutionally susceptible group of people. I also believe that if one looks hard enough, one can find some physical manifestation of stress in most people. We already accept that asthma and eczema get worse when stress increases, but what of seborrhoeic dermatitis, pruritus ani, the irritable bowel syndrome, duodenal ulceration, and last, but not least, ulcerative colitis?

I may be over simplifying, but I am trying to emphasise that people with migraine are not really different from anyone else, except that they are genetically prone to react in some circumstances, not always stressful, by developing migraine; whereas another person exposed to the same set of circumstances, but with a different genetic constitution, may develop overt anxiety, or pruritus ani, or perhaps a duodenal ulcer.

It is interesting that all these conditions are in parts of the body with important autonomic nervous control, e.g., sweating in the perianal region and acid secretion from the stomach. It is not therefore difficult to see how cortical impulses acting on the thalamus via the limbic system could affect the delicate control of the autonomic system from the hypothalamus.

## History

Migraine has been known since the start of recorded history. It was being described as hemicrania by Galen as early as A.D. 201.

Because of its variability it has been difficult to define, and most definitions, such as that of Gowers in 1893, really apply to classical migraine which is seen only in ten per cent of sufferers:

"Migraine is an affectation characterised by paroxysmal nervous disturbance, of which headache is the most constant element. The pain is seldom absent and may exist alone, but is commonly accompanied by nausea and vomiting, and it is often preceded by some sensory disturbance, especially by some disorder of the sense of sight. The symptoms are frequently one sided, and from this character of headache the name is derived."

*The 1975 Migraine Trust prize of £100 was open to competition by general-practitioner trainees.

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However, paroxysmal headaches (usually called common migraine) are much commoner, and are characterised only by the unilateral throbbing headache. Also, headache is not the main feature in childhood or in old people.

The family pattern makes migraine an ideal disease to study in general practice. Dalsgaard-Nielsen (1973) found that 75 per cent of sufferers had a family member with the disease. In six per cent both parents were affected, in 50 per cent the mother only, and in 19 per cent the father only.

These figures also illustrate the female predominance. Waters' (1974) studies on a random South Wales sample show that headaches are more common in women than men, and also that the three features of migraine—unilateral distribution, warning, and nausea or vomiting—are all commoner in women.

The incidence of migraine in the population varies in different studies, but is probably about 15 per cent. Some people, however, only have one or two severe attacks in a life time.

So the pattern is a common familial disease affecting women mainly. The age of onset varies a great deal, but 20–30 per cent of people have had their first attack by the age of ten years, and 90 per cent by the age of 40.

As practitioners we, of course, see only a selected group of migraine sufferers. Many people never go to the doctor at all complaining of it.

## Migraine in childhood

However, most cases of childhood migraine are seen, but the diagnosis is often not made. In general, though some children do present with the more classical picture of paroxysmal throbbing, unilateral head pain lasting several hours to days, with a definite prodrome, and contra-lateral neurological manifestations (usually visual) often associated with nausea and vomiting, most present more obscurely.

Childhood migraine is shorter in duration, less severe, but more frequent, is less likely to be unilateral, and may involve no headache at all. It also often appears to lack an aura, but usually has more striking abdominal symptoms. ' Cyclical vomiting ' the classical periodic syndrome of childhood occurs mainly in younger children, but not always. I recently saw a child of seven, who had been seen 49 times by her general practitioner, ten of which had been home visits. This child had had bouts of temperature often up to of 39°C (101°F), vomiting and abdominal pain since the age of one year. Shortly before I first saw her she had spent two days in hospital being observed for possible appendicitis. This child developed vomiting often in her sleep, and in the morning complained of abdominal pain and so was missing much school. It transpired that her aunt and mother both suffer from migraine, and her aunt's migraine had presented exactly the same picture in childhood, progressing to a more classical headache pattern at puberty. The mother described Mandy as a quiet, confident, clever child who had been put up a year at school recently. It was interesting to observe that the attacks of pain and vomiting had increased in frequency to two to three times per week since her promotion to a higher class.

Even in babies vomiting, crying, photophobia, and ptosis appearing with cyclic regularity are signs of early migraine. A clue is that the symptom appears suddenly in a child not usually prone to it; for example, the baby which vomits for no reason one day every week. In some children attacks are associated with nose bleeds.

The older school child more closely resembles the adult patient. Parents may be able to tell when a child is going to get an attack because of excessive restlessness, or an excessive euphoria the day before. During the pre-headache phase the child usually becomes listless, or may complain of abdominal discomfort and visual disturbances

varying from scintillating scotomas, photophobia, spots, and circles to coloured lines. Rarely hemiplegias and aphasias occur. The childhood pain is unilateral in about 70 per cent of cases, but may also be bilateral. It usually begins over one eye and moves occipitally or *vice versa*.

It used to be thought that there was a specific migraine personality and that it was commoner in hard working, clever, ambitious people, who tend to be compliant with authority, but recent evidence discounts this. This concept probably arose because most early work was done on highly selected patients seen at neurological clinics instead of in the community.

However, I still believe that in general practice more intelligent patients are seen, but this may merely be that as a group they are more motivated.

One recent paper from Los Angeles, Menkes (1974) did come to some conclusions, but again only on a highly selected small group of ten children. She found that her ten children showed certain features in common:

(1) They had a family role which deemed them as very good, but incompetent, fragile, or vulnerable.

(2) They tended to have a character structure forbidding the overt expression of aggressive hostile impulses, and thus carried an excessive load of angry feelings which she felt often caused tension and in two cases could obviously be seen to lead to migraine attacks.

The incidence of migraine in schoolchildren (7–15) is about four per cent, but the incidence increases to five per cent at puberty. There is a highly significant increase in incidence as females reach puberty. At younger ages there are more boys, but after puberty girls have it more often.

The adolescent group get paroxysmal headaches (common and classical migraine like the adult group), menstrual headache and basilar migraine.

*Exacerbating features*

Some environmental factors are known to provoke attacks. In the childhood group stress at school must be considered. Some children get their attacks after periods of stress such as in the late afternoon after school. There are some who suggest juvenile migraine is getting more common and equate this with the increasing academic demands on children. Other factors include stroboscopic effects (television films, glare), fatigue, allergens, excess sleep, irregular meals, certain foods, emotional stress and hormonal changes such as menstruation.

The association with allergy is interesting. Most reports agree that up to 35 per cent of sufferers have some allergic history with an increased incidence of angioneurotic oedema, urticaria, and asthma. The incidence of allergic disorders in the general population is only five to ten per cent. There is also a tendency to travel sickness—another manifestation of autonomic instability.

The outcome of childhood migraine is usually good. Minrichs and Keith (1965) found that 33 per cent were completely free of headache nine to 14 years after diagnosis, and 46·6 per cent considerably improved. Only 21 per cent were unchanged. Thus the outlook for 79 per cent is good.

Most adult sufferers experience attacks at intervals throughout life, though prolonged remissions of several years are not rare.

Whitty and Hockaday (1968) followed 92 patients re-assessing them 15–20 years after their first clinic attendance, and found no consistent change in attacks that could be related to the menopause, or to age of onset, or duration of the migraine. However, there is a recognised group of women who first develop migraine at the menopause.

Migraine attacks also vary from one to another, sometimes being classical migraine with an aura, sometimes common migraine (just the throbbing unilateral headache). Sometimes (although rarely) the aura only occurs, without the following headache.

## Basilar migraine

Basilar migraine (or the basilar artery syndrome) has been described. The manifestations are thought to be entirely due to vasomotor changes in the basilar artery resulting in transient ischaemia of the reticular formation of the brain stem. It is usually seen in adolescent females, and is often associated with menstruation.

There is usually a prodrome of visual phenomena, loss or impairment of vision, vertigo, multiple paraesthesiae with drowsiness and sometimes total loss of consciousness. The prodrome is followed by occipital headache and vomiting. Although there is an increased incidence of epilepsy in migraine sufferers these are not thought to be an epileptic phenomenon because the prodrome is too long and there are no convulsions.

## Causes of migraine

There are many theories about the cause of migraine. In general I regard migraine as a disturbance in the autonomic control of the cerebral arteries leading to vasoconstriction and later vasodilatation, the unilateral throbbing pain being the result of the changes which have taken place in the vessel wall, which may be vasodilation, exudation and/or the release of certain amines. Why certain vessels should be affected at different times is not known.

However, a significant aspect of the clinical picture of migraine is the occurrence of provoking factors. Most attacks are provoked by more than one factor, while in other cases no factor is obvious. The factors may be somatic and psychic, and no common theme is characteristic, so I feel they must all be regarded as non-specific irritants.

It is probably a combination of many factors which finally tips the scales and causes a migraine. It is by using this simple model of the scales that I assess and treat migraine sufferers. I imagine the fine balance of the hypothalamic control being disturbed by the progressive build up of various influences; when this is too great the balance is disturbed, and the vascular changes ensue.

The factors which have been shown to upset the balance can be considered in turn.

(1) *Inherited tendency*

First is the inherited tendency to suffer from migraine. This makes the autonomic " balance " more sensitive to provoking influences. In support of this, migraine sufferers tend to get travel sickness and allergic conditions such as eczema and angioneurotic oedema. A strong family history is useful in assessing the atypical, or childhood case. The mode of inheritance has been suggested as autosomal dominant with 69 per cent penetration.

Other factors are:

(2) Personality structure,

(3) Emotional stress,

(4) Endocrinic factors—menstruation—contraceptives,

(5) Allergic triggers,

(6) Hunger,

(7) Alcohol,

(8) Fatigue,

(9) Cerebrovascular disease—hypertension—atherosclerosis—anaemia,

(10) Stroboscopic effects (television, films, glare),

(11) Football migraine and cervical migraine.

I have already discussed a " migraine personality ". In adults Dalsgaard-Nielsen found 31 per cent were psychologically normal, 33 per cent fitted the previously described personality pattern, and 36 per cent had slight psychological symptoms. If we regard personality as just a factor in some people and not as the cause, it becomes useful.

One interesting study was a " Comparison of personality traits in ulcerative colitis and migraine sufferers " (Schucman and Thetford, 1970) using the " personality assessment system ". They showed that in general, migraine sufferers were " externalisers " or people who by their nature gained psychological satisfaction from relationships, and were physically active. However, instead of behaving in this way they consciously tried to be more inward looking and more self sufficient.

In contrast the ulcerative colitis sufferers who by nature are " internalisers " gaining their psychological satisfactions in the privacy of their own experience, consciously tried to be more out-going. So both groups are trying to be something they are not, which leads to tension. Also it is interesting that the migraine group experience their symptoms in the organs of perception, and the motor system which fits in with their natural extravert, outgoing nature, while the ulcerative colitis group experience their symptoms in the bowel.

Emotional stress can be, and often is, an obvious trigger in migraine. This includes the insomnia and fatigue of anxiety neurosis and depression. Migraine is also common in the let-down period after situational anxiety, e.g. after a busy week at the office, after an examination or interview and during the first days of a holiday.

One of the paradoxes of migraine is that lack of sleep, and too much sleep can both act as triggers. Some people have to choose between a Sunday morning lie-in and a migraine.

Endocrine imbalance has a definite trigger effect and migraine becomes commoner in both males and females at puberty.

It is very rare for migraine sufferers to get migraine only with menstruation, and in fact " classical " migraine sufferers only rarely report attacks occurring at menstruation. However, the association of common migraine and menstruation seems to be common, occurring at some time in 10–20 per cent of all women. Attacks are usually premenstrual, but some women experience attacks during and after menstrual flow. Rarely menstrual migraines continue with the same periodicity after the menopause.

In women, 80–90 per cent experience a remission of symptoms during their first pregnancy, and to a lesser extent during subsequent pregnancies. However, remission is less striking in patients suffering from classical migraine.

Menstruation is complicated by the psychological changes of fluid retention and the tendency to develop a premenstrual tension. This in itself may act as the trigger, or may produce a tension headache which can be confused with the unilateral throbbing headache of common migraine.

In general the contraceptive pill tends to aggravate migraine, but not in all people, and not consistently with any particular preparation. So it is sometimes worth trying a different combination.

I have already stressed the common association of allergic disorders and migraine. However, about one third of sufferers describe food allergies, and many of these substances have a high content of tyramine. For this reason it has been suggested that people with food-triggered migraine should not receive mono-amine oxidase inhibitors,

or isoprenaline inhalers for asthma. Foods which have been found to be triggers include wines (red and white), sherry, yoghourt, chocolate, cheese, eggs, and fish.

There may be delay between the ingestion of the food and the migraine, making the cause and effect relationship difficult to prove.

Fasting can also trigger migraine in some people. It may well be the explanation for some of the Sunday morning " lying in " migraines which have been attributed to too much sleep. The exact mechanism is not certain but it may be related to hypoglycaemia. Dalton (1973) describes people who develop fasting migraine only at the time of menstruation, and she explains this by suggesting that they become more sensitive to fasting at this time.

Alcohol in very small quantities can act as a trigger in the susceptible. When this occurs it is with any form of ethyl alcohol, not just specific wines and sherry which affect the other group. Bright lights and sunlight can also be a problem to some people.

Cerebrovascular disease is interesting. Many cases have been reported of migraine starting in middle aged people, and being associated with elevated blood pressure. However, most hypertensive patients do not get any headache, until they are told they are hypertensive. One fact is certain however, and that is that hypertension is commoner in patients with migraine, but curiously the incidence of stroke is not commoner. Leviton *et al.* (1974), however, have shown that migraine sufferers are more likely to die of a heart attack. They showed that people under 70 years of age had a 2·7 risk of a heart attack (average population 1·0), and that this figure was statistically significant.

Finally there are two rare syndromes of footballers' migraine and cervical migraine.

Most headaches after head injury and neck injury are tension headaches, and a psychogenic aetiology. However, rarely a headache with migrainous characteristics and responding to clonidine or ergotamine does occur.

One footballer seen by Espir *et al.* (1972) developed flashes of light and shimmering effects, which lasted 30 minutes, shortly after banging heads with another player. During this time he could not focus properly or see to either side. This was followed by bifrontal and vertical throbbing headache for two to three hours without sickness. He then went on to develop the prodrome and headache about twice a year, sometimes associated with heading the ball.

## Clinical approach

It is rare for migraine to start after the age of 50, and migraine tends to improve with age. The menopause and its often associated depressive illness is sometimes the trigger for a first attack of migraine, but this is unusual. One interesting pattern of migraine which does, however, develop in older people is that they may have the classical migraine aura, often with a feeling of light headedness, dizziness, and unsteadiness, but no headache. Here a careful history can be rewarding and reassuring.

The management of migraine in general practice consists of four phases:

(1) Establishing the diagnosis,
(2) Recognition of precipitating factors, their treatment or removal,
(3) Treatment of acute attacks,
(4) Long-term prophylaxis.

### *Differential diagnosis*

Firstly, cluster headaches are often classified as being a type of migraine. These are severe paroxysmal pains which are felt mainly in the supra-orbital region or behind the eye. They are unilateral and usually last no longer than two hours. During a bout there is usually at least one paroxysm each 24 hours. Bouts recur usually no more than once

a year. They affect males more than females in a ratio of 6:1, and a family history only occurs in 16 per cent.

Secondly, intracranial neoplasms situated in the occipital lobe may give rise to headaches, vomiting, and visual disturbance, and, of course, are commoner in children. Angiomas or arteriovenous malformations either on the surface or in the substance of the brain may also cause diagnostic difficulties, as these patients often develop periodic headaches of a migrainous type beginning in early life. The presence of such a lesion, therefore, must always be kept in mind when the headache is persistently unilateral in the absence of a family history. This is especially true if there is a history of subarachnoid haemorrhage, focal epilepsy, or signs of motor or sensory dysfunction in contralateral limbs. Auscultating the skull is useful in such cases to rule out a bruit. Where there is a measure of doubt they should have neurological investigations performed.

When looked for, migraine is not usually a difficult diagnosis to make even in children. To establish the diagnosis it is of course first necessary to take a good history of the headache, its frequency and characteristics, to establish whether there is an aura, and to take a family history. As tension headaches are common, and are often also seen in migraine sufferers, they must be identified. They are often continuous day and night, and they get worse with middle age, whereas migraine gets better. Also the headache is rarely unilateral or throbbing.

Having established that the headaches are migrainous in nature one should try and spend some time making a good relationship with the patients, reassuring them that there is no more sinister pathology such as a tumour, and explaining to them simply some of the ideas as to causation. They are often reassured to know how common migraine is, and find the family history interesting. It is amazing how frequently people return at the next visit with a list of relatives who also suffer, whom they had never known about! Once having made a relationship, they feel the doctor is sympathetic about their suffering, and one can go on and explore the possibility of there being a precipitating factor, or factors.

By this time one is getting some insight into the patient's personality. With children one should try and see the mother on her own to see how she sees her child as a member of the family group. Does the child fit the migraine personality? Are there any abnormal features about the family, or family relationships? In general practice, we have a great advantage, because we will often know of family circumstances which could have an important bearing.

The treatment of the classical migraine personality can be rewarding and even superficially often quite successful.

Some people become interested and gain much insight into their tensions quite quickly. It is the classical migraine personality who is resistant to change, and lacks insight, who often finally needs long-term drug therapy.

*Stress*

To help investigate the possibility of stress, or to clarify more clearly any association with menstruation etc., the use of frequency charts, as recommended by Dalton (1973), is useful. These calendar charts enable us to establish the day, and the intensity of each attack, which is marked on the chart. The charts may show a preponderance of attacks on one day of the week or weekends. She also uses an attack form on which patients fill in details concerning each migraine immediately it is over. This approach is useful when looking for possible food allergies and stress factors, such as in work. It can also be used to study more carefully the exact nature of the attack, by including questions related to the presence or absence of aura, and perhaps relating this to the presence or

absence of other stress factors. I feel both could be useful tools in general practice for selected patients.

If stress is an obvious trigger, it can help to try and resolve some of the problems, and if necessary prescribe a tranquilliser such as a benzodiazepine. The treatment of depression is again important where this is triggering attacks. Here a tricyclic antidepressant such as imipramine or amitriptyline is useful. The use of relaxation is discussed below under prophylactic measures.

*Menstruation*

Women getting migraine during the four premenstrual days have been shown to have a good response to progesterone by suppository or pessary in doses of 50–400 mg daily. A good response is said to occur in 60 per cent (Dalton, 1973).

The problem with menstrual migraine is to identify the causative factor. It can be stress, and possibly fasting, and many of the headaches are not migraines but tension headaches.

Progesterone therapy as suggested by Dalton (1973) is generally impractical in general practice, as it requires either regular injections, or the use of the rectal or vaginal route.

*Food*

The food sensitive group benefit from avoiding the offending food which can include cheese, chocolates, wine, dairy foods, citrus fruits and even fatty meals or caffeine. Many of these foods contain tyramine, the sensitivity to which improves during pregnancy. Clonidine is most successful in this type of migraine, starting with a dose of 0·025 mg twice daily.

## Treatment of acute attacks

In childhood up to 12 years of age, beneficial relief from ergotamine preparations is rare, because the prodrome is short. Usually if the child is given aspirin or paracetamol immediately, and goes to lie down in a darkened room for about 30 minutes or so, the worst attacks will be aborted.

Over the age of 12 years the ergotamine preparations become more useful. Ergotamine is an alkaloid derived from the fungus ergot, which grows on rye plants. It is an effective vasoconstrictor, and is thought to work by constricting branches of the external carotid artery. This is why it is often ineffective once the pain has started. As a vasoconstrictor it can have a rebound action with dilation and pain. There is also a danger that it can be taken in excess by some patients because of this rebound phenomenon, as more ergotamine relieves the rebound headache. Lucas and Falkowski (1973) describe five such patients who developed this vicious circle. They suggest also that caffeine which is added to 80 per cent of ergotamine preparations to enhance absorption, may also cause a rebound headache. Where stress is very high, tranquillisers are much safer, and may be prescribed along with an analgesic, such as ' Distalgesic '.

Because of the variable absorption of ergotamine from the gut, and the inevitable delay in action, other routes of administration can be tried.

A few intelligent stable patients can be entrusted with ergotamine tartrate to give to themselves subcutaneously (' Femergin '), at the start of prodromal symptoms. Others like the sublingual preparation (' Lingraine ').

The ergotamine tartrate suppositories can be useful for the regular sufferer, such as for Sunday mornings and used the night before.

However, most patients with classical migraine with a good prodrome find the oral preparations such as ' Migril ' satisfactory. However, 90 per cent of sufferers get com-

mon migraine, with no real prodrome, and often get more benefit and no rebound headache from aspirin or ' Distalgesic '. Repeat prescriptions of ergotamine preparations should be carefully supervised. Ergotamine cannot of course be used in pregnancy, and in excess can seriously impair peripheral circulation.

## Prophylaxis of migraine

Finally what about prophylaxis of migraine attacks which can be by the use of drugs, or relaxation techniques?

The two drugs which have been most used are methysergide (' Deseril ') and clonidine hydrochloride (' Dixarit ').

I feel methysergide (' Deseril ') is contradicted in general practice, because of the danger of retroperitoneal fibrosis, and the rare but irreversible peripheral necrosis and gangrene. Migraine, after all, is not a fatal condition, so potentially dangerous drugs have no place in its treatment.

Clonidine on the other hand is a useful drug in selected patients. The dosage is 0·025 mg twice or three times a day. It has no effect on acute attacks, but it has been shown to be effective prophylactically. The only side effects are slight sedation, some weight gain, and dryness of the mouth. It is beneficial in patients with frequent migraine attacks, with no obvious precipitating factors.

Also, where some stressful period is unavoidable, such as examinations, it is worth starting six months beforehand to prevent attacks interfering with revision. The patient will only be motivated to use the drug if he can see the benefit, so I see no value in continuing it if there have been no attacks for more than six months.

I also see some promise for the use of relaxation therapy in groups of sufferers. As well as learning the relaxation techniques they also have the opportunity to air their mutual problems in the group. This is a field for the general-practitioner enthusiast, and as has been shown by Hay and Madders (1971), can be successful even in resistant cases.

### REFERENCES

Benson, H., Klemchuk, H. P. & Graham, J. R. (1974). *Headache*, **14**, 49–52.
Blaw, J. N. (1971). *London Clinic Medical Journal*, **12**, 15–24.
Carroll, J. D. (1971). *British Medical Journal*, **2**, 756–757.
Critchley, E. M. (1975). *Update*, **10**, 756–757.
Dalsgaard-Nielson, T. & Ulrich, J. (1973). *Headache*, **13**, 12–18.
Dalton, K. (1973). *Journal of the Royal College of General Practitioners*, **23**, 97–111.
Diamond, S., Baltes, B. J. & Levine, H. W. (1972). *Headache*, **12**, 37–43.
Espir, M. L. E., Hodge, I. L. D. & Matthews, P. H. N. (1972). *British Medical Journal*, **3**, 352.
Hay, K. M. & Madders, Jane (1971). *Journal of the Royal College of General Practitioners*, **21**, 664–669.
Henryk-Gutt, R. & Rees, W. L. (1973). *Journal of Psychomatic Research*, **17**, 141–153.
Legalos, C. (1973). *Seminars in Psychiatry*, **5**, 524–547.
Leviton, A., Malvea, B. & Graham, J. R. (1974). *Neurology*, **24**, 669–672.
Lucas, R. N. & Falkowski, W. (1973). *British Journal of Psychiatry*, **122**, 199–203.
Menkes, M. (1974). *Pediatrics*, **53**, 560–564.
Mitchell, K. R. (1971). *British Journal of Psychiatry*, **119**, 533–534.
O'Brien, M. D. (1971). *Headache*, **10**, 139–143.
Pearce, J. (1969). *Migraine*. C. C. Thomas.
Sacks, O. W. (1971). *Migraine. The evolution of a common disorder*. London: Faber.
Sargent, J. D., Walters, E. D. & Green, E. E. (1973). *Seminars in Psychiatry*, **5**, 415–428.
Schucman, H. & Thetford, W. N. (1970). *Journal of Abnormal Psychology*, **76**, 443–452.
Shafar, J. Tallett, E. R. & Knowlson, P. A. (1972). *Lancet*, **I**, 403–407.
Trued, S. (1974). *Journal of the American Medical Womens' Association*, **29**, 78–83.
Waters, W. E. (1972). *Headache*, **12**, 55–61.
Waters, W. E. (edit.) (1974). The epidemiology of migraine. Bracknell: Boehringer Ingelheim.