

These two groups total 41 per cent. Next, 135 had headaches less severe but of the same frequency, and 212 had headaches just as severe but much less frequent. These two intermediate groups total 35 per cent. In 358 patients (24 per cent) there was no change.

Returning to the 418 for whom no allergy was found, these were more difficult to trace because they had to be referred back to their home address. Most of them had no prophylactic treatment at all. After much correspondence with patients or their doctors we obtained reports from 360. Of these eight or 2.5 per cent were now symptom-free, having lost their migraine gradually through the years; 48 or 15 per cent had some improvement, and many of them suggested that less worry was the cause; and 304, or 84 per cent of the untreated cases said that there was no change or that the position was rather worse.

The idea of food as a common cause of migraine is not a new one. The late Dr John Fothergill, writing at the end of the eighteenth century in a treatise entitled "Remarks on that complaint commonly known under the name of the sick headache", stated:

Not a complaint of any particular age, or sex, or constitution or season—it is incident to all. Having had some little experience of this complaint myself my opinion of this disease is that, for the most part, it proceeds from inattention to diet, either in respect of kind or quality or both.

From the figures quoted above, it must be concluded that every migraine sufferer should be given the opportunity to be tested for allergy. If no positive reactions are obtained, no harm has been done, but about half your patients can be helped greatly, and probably the percentages will rise as we gain more experience.

At present, we are only touching the fringe of this subject of allergy, which, in my opinion, is so far-reaching in every branch of medicine, that it should join the "big five" in the teaching of pathology to undergraduates.

## RESEARCH, YESTERDAY AND TOMORROW

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I first became interested in migraine in my practice, about six years ago, when it was forcibly brought to my attention by the severity of the attacks from which some of my patients were suffering,

that migraine was not, as I had supposed, a mild and rather trivial condition, but could be incapacitating and could follow a patient through many of the years of his life. I was deeply impressed by this incapacitating effect of migraine and its effects on family life.

I became interested in the treatment of this condition and I started to use chorionic gonadotrophins. I am surprised that these have not been mentioned, because I found this a successful form of treatment. I singled out six or seven patients who had migraine of typically menstrual character, and I treated them with chorionic gonadotrophins. The results which I shall give you are merely observations, but I have found them valid. I think that if these methods are used in women who have essentially menstrual migraine, and used with perseverance, the results will be successful.

My interest having been aroused, I attempted a survey into the incidence of migraine in a population. I bullied a local factory doctor into letting me have the use of the employees of the factory in order to do a migraine survey among them. This was in 1959. We circularized them in their pay packets, which is the only way we could make sure they would look at the note. We asked them whether they suffered from migraine, which we roughly defined and they were asked to put their replies in boxes at the gate of the factory. We interviewed all those who said that they had migraine. This migraine survey was carried out by myself and Dr Childs in a factory of 4,700 persons, with a ratio of males to females of 4:1 and the incidence of these suffering from or who had suffered from migraine was found to be 5 per cent in the men and 13 per cent in the women, that is a ratio of 2.7 to 1. All the sufferers from this condition were fully interviewed and the average age of onset was found to be 23 years, well beyond the age of puberty.

Next, we discussed the question of heredity and travel sickness, and this is shown in table I; the family history of migraine sufferers

TABLE I  
FAMILY HISTORY OF MIGRAINE AND PERSONAL HISTORY OF TRAVEL SICKNESS IN  
MIGRAINE SUFFERERS AND A CONTROL GROUP OF NON-SUFFERERS

		<i>Men</i>	<i>Women</i>	<i>Total</i>
Family history of migraine	Migraine cases	18 (28.6%)	20 (48.8%)	38 (36.5%)
	Control group	3 (4.8%)	3 (7.5%)	6 (5.8%)
Personal history of travel sickness	Migraine cases	15 (23.8%)	12 (29.3%)	27 (26.0%)
	Control group	5 (7.9%)	3 (7.5%)	8 (7.8%)

is six times greater than that of a controlled group of non-sufferers, and this applies to both sexes. Another factor which greatly interested me and which may give some underlying clue to the casual factors of this condition is the high incidence of travel sickness amongst migraine sufferers, nearly four times as great as the non-migraine patients.

Another point which we investigated was the type of person who suffered from migraine. It is thought that the business man who uses his brains is the person who suffers from migraine; and this rather erroneous supposition has been carried on from one text-book to another. Is this true? We found that there was a very slight increase in the incidence of migraine amongst the managerial and executive classes, though it is certainly not a big one. The executive in his position adding up figures or interviewing people is totally unable to carry on during a migraine attack whilst the person in the basement who has a similar attack but whose job is shovelling coke, is able to carry on, and in fact, as we all know from our migraine patients, that they would much rather, as they say "work their way through an attack" than stop and go home.

These points are illustrated in table II which shows that 70 per cent of the light manual workers and 44 per cent of the executives carry on at work. They feel that it is better carrying on work than lying in a dark room feeling ghastly.

TABLE II

104 CASES OF MIGRAINE: NUMBER WHO STOP WORK OR CONTINUE DURING ATTACKS

<i>Employment Group</i>	<i>Work</i>	<i>Men</i>	<i>Women</i>	<i>Total</i>
Managerial, technical, and foremen	Stop	10	1	11
	Continue	13	1	14
Clerical, heavy and light manual work	Stop	10	14	24
	Continue	30	25	55

Next I have investigated what the general practitioner did for his migraine patients. This is important. We do not know what kind of treatment the general practitioner gives, nor what the person who did not consult the doctor took. To find this out 700 members of the research panel of the College of General Practitioners were circularized and 157 replied. This represented an investigation into nearly half a million patients. The doctors were asked what they did for their migraine patients; whether they sent them to hospital for a consultant's opinion, or for what other purpose; what sort of treatment they gave, dividing the drugs into analgesics and the ergot

group.

Figure 6 shows you what the general public takes and figure 7 shows what the general practitioner gives his migraine patients. About a third of all the patients examined were sent to hospital, but the reason they were sent there—I am sorry to spoil the afternoon of any hospital consultant—was not that the doctor expected them to get better treatment or to get better at all. The doctor wanted to exclude an intracranial lesion which he had not the resources to diagnose. In hospital they have x-rays of the skull and electroencephalograms taken. The hospital is glad to be rid of them afterwards because it does not know what to do with them. About a third are sent to an optician or ophthalmologist to have their sight tested to exclude a refractive error as a trigger mechanism of migraine.

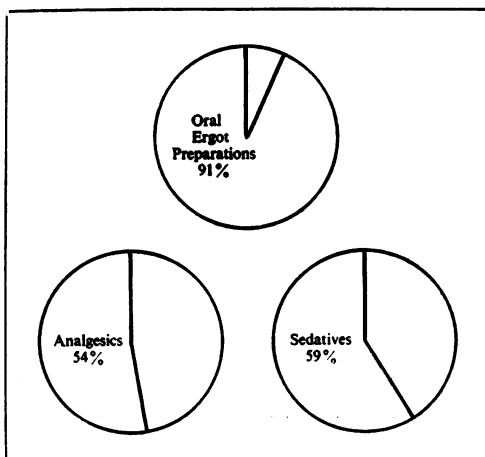


Figure 6  
What the general public takes

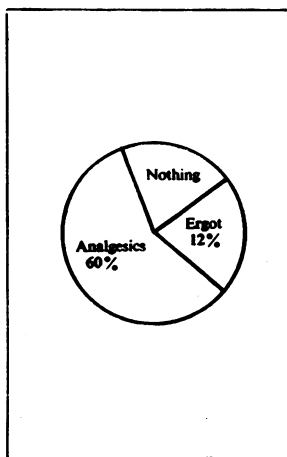


Figure 7  
What the general practitioner gives

For treatment 91 per cent were given ergotamine, 59 per cent sedatives—probably barbiturates—and 54 per cent general analgesics. Very few doctors gave intramuscular ergot. I do not know whether this was due to pressure of time or because oral preparations have improved.

The final statistical survey which I have carried out is that of the incidence of migraine in the intake of the students into Keele University. The number was rather small. There were 227 students taken in last September; six men had migraine, an incidence of 5 per cent, and also six women. These figures grouped together are well

below what one would expect. It is interesting that it proves the point that I have tried to make that the onset of migraine is at an age of 22 or 23. These potential students were aged between 18 and 19.8 years; and so I hope to show that in the course of time that many of the students at the university will have their first migraine attacks whilst they are there. and with the enthusiastic help of the university's medical officer we hope to see whether this is so.

The only other point that was forcibly brought to my notice was that amongst the students who had migraine attacks it appeared that vomiting was directly related to the severity of the attack. I think this is true of migraine and that the severe attacks almost invariably end in vomiting and the less severe do not.

I said that I would talk about research, yesterday and tomorrow. I have told you about yesterday. I have done a good deal of work, which has been very interesting, but probably nothing very new has come out of it. What about the future? There are two surveys in which I am interested which are afoot. I told you that travel sickness appeared to be a big factor. The fact that migraine sufferers have a higher incidence of travel sickness than the general population gives rise to the idea that some of the remedies for travel sickness might be of value in the treatment of migraine, not so much in relieving the actual attacks once they are established but as a method of suppressing them, if used in a way similar to the treatment of epilepsy with phenobarbitone and other anticonvulsants.

A research group, members of the College of General Practitioners who were interested in the treatment of this condition was formed, and the investigation has proceeded as follows. There are 40 doctors scattered throughout the country in family practices who have agreed to give their migraine patients a card on which for three or for more months they can register the number and severity of their attacks. For the next three months they are provided with tablets; half these tablets are stemetil, and half are dummy, so neither the doctor nor the patient knows which one he is receiving. We shall therefore, be able to see, or hope we shall be able to see, at the end of this time whether stemetil is useful as a suppressant of migraine attacks and, furthermore, we shall be able to see what the placebo response is. It is a well-known and very discouraging fact in the treatment of migraine, that any form of treatment or injection appears to help the sufferer for a short period of time.

Lastly, I would like to draw to your attention the investigation in which I have been asked to participate which is being carried out by the Pharmaceutical Research Department of I.C.I. and includes a good deal of biochemical analysis.

In 1960 Wolff and his colleagues from the Cornell Medical Centre published a paper entitled "The Definition of a Biochemical Agent

Implicated in the Mechanism of Vascular Headache of the Migraine Type". A sub-surface fluid was extracted around the arteries of the patient suffering from migraine attacks and the plasma kinin content was estimated by its action on the rat's uterus.

It was thought that this substance might be excreted in the urine of migraine patients and it was with the idea of proving this point that I have been participating in an investigation. I would like to say in passing that this experiment shows the advantage of co-operation between a hospital, a family doctor, and a pharmaceutical firm; and in my part of the world I must say that the relationship between consultants and the family doctors is on the very highest level.

Through the courtesy of the consultant neurologist, Dr Hutchinson, we started this investigation by searching the 3,000 records of patients registered in the Neurology Department at the North Staffordshire Royal Infirmary; of these 128 had been referred to the department suffering from migraine. I interviewed 104 and from these obtained about 30 people who had very definite migraine, and persuaded them to participate in this experiment. Their urine was first tested for abnormalities and then, when they had a migraine attack, they sent me at once a stamped post card and I endeavoured to obtain a specimen of urine from them the following day. The kinin content of the urine was then estimated.

We have not completed these experiments and calculations, but we shall publish them. I think that the next stage is to see whether kinins occur in urine in other forms of headache. We want to see

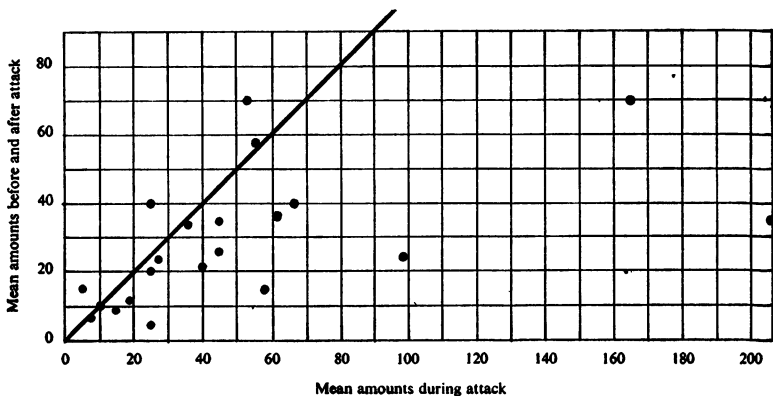


Figure 8

The mean amount of kinin before and after and during an attack

whether they are specific to migraine or specific to headaches in general.

The mean amounts of kinin are shown in figure 8 before, during, and after an attack. If the amounts were equal the results would be scattered equally along the 45 degree line, but in fact, they are scattered all over the place. This shows that there is a significant amount of kinin excreted in the urine of the patient during attacks of migraine.

## DISCUSSION

**Dr O. Morton** (*Romford, Essex*) felt that Dr Hay's material was not typical of that seen in general practice since it might consist of cases resistant to treatment. He disagreed with Dr Hay in that he found migraine sufferers stable and relaxed, rather than tense. He doubted whether migraine was a single entity: so many precipitating factors existed that no single method of treatment would be uniformly effective.

**Dr H. J. Carne** (*London*) felt that Dr Critchley's wide definition of migraine might cause confusion, and preferred to apply the diagnosis to a narrower symptomatology, although agreeing that travel sickness, cyclical vomiting, and infantile eczema might all be associated with what he regarded as migraine in the same individual. A narrower definition might clarify the problem of migraine, and facilitate organized research. Where tension was associated with migraine, it was vital to eliminate the tension.

**Dr B. B. Rose** (*Norwich*) observed that migraine attacks often occurred early in the morning. This was also a feature of gout. Had uric acid levels in migraine sufferers been studied?

**Dr G. W. Clark** (*Glamorgan*) agreed that a narrower definition of migraine would facilitate investigation. He wondered whether veterinary surgeons recognized any condition comparable to migraine in their patients. He regarded migraine as a surviving physiological process from some earlier phase of man's evolutionary progression from the primeval swamp.

**Dr Evelyn MacLagen** (*St. John's Wood, London*) felt that cerebral arteriosclerosis might be associated not so much with migraine as with the use of ergotamine in its treatment, and felt that ergotamine tablets in dosage of one milligram were preferable to those con-