

which would also be released from damaged tissues. But it is an interesting speculation that there is some possibility that this fluid accumulation, together with the pain-producing vasodilator substance which occurs in it, could be formed as a result of nervous activity. Nobody has been able to show exactly whether this occurs in the migrainous subject, and there is certainly no suggestion why it should occur on one side and not on the other. All this is speculation but I think that the possibility of inhibiting this type of activation of the pain-producing substance is well worth further study. If one could find some drug which would inhibit the process of activation one would be able to see whether it had any therapeutic effect in a subject with migraine.

As far as I am aware, ergotamine has no effect on the development of these pain-producing substances, but if you have vasoconstriction, that will reduce the amount of protein-rich fluid which will escape from the plasma into the tissues, and vasoconstrictors might act by diminishing the amount of materials available for activation.

Perhaps I should add that I myself never had any relief from ergotamine.

REFERENCES

- Graham, J. R. and Wolff, H. G. (1937). *Ass. res. nerv. Dis. Proc.*, **18**, 638.
 Chapman, L. F., Ramos, A. O., Goodell, H., Silverman, G. and Wolff, H. G. (1960). *A.M.A. Arch. Neurol. (Chic.)*, **3**, 223.

THE PLACE OF ALLERGY IN MIGRAINE

Vera B. Walker, M.Sc., Ph.D., M.R.C.S., L.R.C.P. (*Oxford*)

Before starting my paper I should like to take this opportunity to thank Professor Keele for giving such a lucid explanation of the late Professor Woolf's work. We have all listened with interest to the previous speakers today, and while a few of us are still depressed, many, I think, see some glimmer of hope.

Whether one has special interest in the more conservative work of Macdonald Critchley, the basilar artery involvement investigated by Bickerstaff, those severe migraine attacks ending in a generalized convulsion described by Brain, or the water retention studied by Campbell and Hay, or, especially, in those cases of menstrual migraine written about by Raymond Greene, everyone must realize

that these great research workers have studied the attack and its control, rather than the prevention of the next attack. How can we prevent water retention or vascular spasm? Why is water retained? And why do vessels go into spasm, or alter their permeability?

It has been my privilege to work on prevention rather than cure during the last 20 years. This has led me along strange paths at times, so today I am attempting to summarize my conclusions after studying some 2,100 cases.

I will explain how I came to look for allergy as a cause of some of these migraines. In 1942 I was invited by the late Mr P. H. Adams, then senior surgeon to the Oxford Eye Hospital, to start a clinic for what he termed "his failures" as he felt there was some so-far unexplored pathology to account for so many patients returning again and again with recurrent attacks of conjunctivitis, or keratitis, or iritis, or headaches.

He and his colleagues, by symptomatic treatment with the drugs then available, and a little "masterly inactivity" could get each patient more or less happily through each attack, but they could not prevent the next attack. Mr Adams was wiser than his generation in that he suspected that my previous research work in cell metabolism, especially that concerning proteins, might have some bearing on these recurrent non-infectious conditions. The clinic gradually enlarged, even while becoming more specialized, as my ophthalmological colleagues became more adept at selecting cases for me, and so the present allergy clinic was born.

We still see a continuous stream of inflammatory conditions, but each week at least half the patients referred to this clinic have reported to the hospital with headaches of various types. Of course, they have been sent by their doctors to find out whether their headaches are really due to some disturbance of vision, and are often surprised when told by the surgeon, "Yes, your vision is quite normal but I would like you to attend another clinic for further investigation". You, as general practitioners, will know that in a big hospital unit today it is quite possible to refer those patients, where the suspected cause of headache is anaemia, diabetes, kidney disease, or psychiatric disturbance to the appropriate department, but I have found that, through the years, I am left with the migraines. Most of the more severe cases have been seen by some neurologist before they ever get to our hospital.

Fortunately for me, in 1944 Urbach published his treatise on allergic diseases of the nervous system, with a most wonderful list of references to early work on migraine in Austria, Germany, and the United States of America.

One of the most interesting conclusions of Urbach is:

From the point of view of heredity, there seem to be two types of migraine: one in which the migraine is the principal disease, transmitted from generation to generation according to the Mendelian law, and chiefly through the female as a dominant, but not sex-linked characteristic; and the other, a type in which the migraine appears alternately with other allergic manifestations in allergic individuals and their families. This frequency of allergic symptoms, partly in the patient and partly in his immediate family, is another important indication of the allergic origin of certain cases of migraine.

I closed the clinic for a month and read everything I could find on the subject of migraine. From these papers I realized that no longer could we say vaguely to any patient "Your migraine might be due to food allergy so try to avoid chocolate and eggs". We had to do a real test, with a long follow-up period so as to avoid the criticism of "spontaneous remissions".

From 1946-48 a group of energetic biochemically-minded allergists worked hard to improve the techniques of testing, so that for the last 10-15 years, it has been possible to support trial diets and avoidances by reliable intradermal testing with food extracts: and when the tests have been done, the interpretation of the results is a difficult job, for not all food allergies are of the immediate, extra-cellular types, but may be of the delayed type, showing a satisfactory positive or negative result only after 24-48 hours: some allergens are exogenous and some endogenous, and some indeed of the auto-allergic type similar to those being investigated for allergic encephalitis.

In addition to the usual clinical investigations, all patients included in the lists I am about to quote to you have been tested thoroughly for allergy, the chief guiding factor being a detailed history of type of attack, interval between attacks, whether associated with any nasal catarrh or with hay-fever or with asthma or with any indigestion. Where possible we have tried to get a detailed account of dietary habits.

When any inhalant or food gave a marked positive reaction the patient was encouraged to avoid that food or inhalant absolutely for at least three months, preferably longer, before any attempt at desensitization or other treatment was suggested. All were encouraged to avoid drugs, especially ergot derivatives, as far as possible during this trial period.

I would like to digress here to say that the most difficult patients of all are those who report that they have been taking cafegot, migril, or orgraine every 36-48 hours and cannot do without it. These unfortunate people do not realize that their headaches are often post-ergot headaches; they seem to have developed a toxicity to their drugs. The only method of treatment I can suggest is similar

to that for chronic alcoholics — a very gradual withdrawal accompanied by moral support from their physician.

When a patient reports that his migraine occurs in a definite cycle, say every 10, 14, 17 or 20 days, then allergy to one of the commonest of daily foods should be suspected. If wheat is the trouble, then he does not get a migraine after every slice of bread, but only after a definite number of meals in which bread is included. The body can tolerate wheat, milk, eggs, and so on for just so long and no longer, this time interval being sometimes shortened if some physical shock or nervous tension intervenes as a precipitating factor. Occasionally a patient gets his migraine in the spring and summer only and may be found to be sensitive to some tree pollen, for example horse chestnut trees, or scotch firs, or perhaps to grass pollen, his migraine being an alternative manifestation of the family hay fever.

As we are to have time for discussion of other points of special interest, I will present my figures now. The total number of cases studied was 2,100 of which 52 per cent were men. I tend to see more men than women patients as I live in a predominantly male community. Someone tried to explain to me that it is because a man with migraine likes to take his problem to a woman, whereas a woman likes to tell her problem to a man.

The total number of cases studied was 2,100. Some allergy was found in 1,682. Of these, 1,460 was due to food, 98 to inhalants, 25 to drugs, including tobacco, and 99 were endogenous—mainly bacterial.

I do not claim that only this number had some allergy, because if we were a little wiser we might be able to find some offending allergen or toxin in the others. With our present knowledge, we are not in a position to know.

Of the 1,460 due to foods, the most common cause of trouble were wheat, cow's milk and cheese, tomatoes, chocolate, fish, and shell-fish. Sometimes there is a rare cause such as ginger, parsley, guavas and passion fruit—possibly something eaten only occasionally. These are very difficult to find. You must get the patient to keep a list of the attacks and a very detailed account of what he ate 24 hours before that.

It has been a major work to follow up all the information, and I should like to make a public acknowledgement to my two secretaries and to my family who have done all the clerical work and who have collected these results together. Of the 1,682 allergic people, 1,500 have reported back to the clinic or have sent a written account of their history over at least a five-year period. Of these, 251 have had no further headaches, avoiding their allergy or being desensitized to it; 364 had no more than three migraines in a year.

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

M. T. Sweetnam, M.B., B.S., (*Stoke-on-Trent*)

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,