

moment, but migraine is a good subject from which they may be studied. We are dealing with something more rapid than anything we dealt with at medical school, where one works on x-rays. Some patients show changes of 16 pounds in 12 hours, which is terrific. We are dealing with very rapid changes in body balances and functions, but I am afraid that I cannot answer the questions except by raising more questions.

CHAIRMAN'S SUMMARY

It falls to me to undertake the arduous task of summing up today's discussion. The symposium has greatly helped us because it has presented a diversity of views and approaches to the problem of migraine. It has quite clearly shown that there are many aspects of migraine which merit further research. We have had questions quite clearly set out in such a way that many of them will be capable of being dealt with by the College of General Practitioners.

It is important to formulate the questions in a way which can be answered, because sometimes the form of a question will determine the answer which one gets. It reminds me of the story of two priests who were fond of smoking cigars. They came together one day and their consciences pricked them because they wondered whether they ought to indulge so much in smoking cigars. They decided to write separately to the bishop and to seek his advice. When they met a week later, one was happily smoking a cigar and the other was not smoking and was dejected and miserable. They discussed this and inquired whether they had written to the bishop. They were puzzled by the outcome. The one who was cigar-less and was looking miserable said that he had written to the bishop asking whether it was in order for him to smoke when he said his prayers and the answer had been "no". The other said "I asked the bishop whether it was in order for me to pray when I smoked cigars, and the answer was that it was in order".

Today, we have had many questions clearly set out in a manner which lends itself to investigation. What we have seen today is that migraine is a disease of protean manifestations and that when one considers the predisposing factors, one finds that there are a multiplicity of factors.

In summing up the contributions and discussion one is faced with

problems in the science of aetiology, which is concerned with ascertaining which factors are relevant and casual both in the individual and within the environment in causing particular disorders. These are innumerable, and in practice one has to consider which factors are relevant and casual in a practical sense. In other words, to what extent can they be modified, because the extent to which those factors can be modified will determine our success in treatment and prevention. •

It is possible to classify causal factors into those which are essential—those without which the disease cannot be manifested—and those which are sufficient to make the disease manifest itself clinically when the essential cause is present. Both the essential causes and the sufficient causes are important as dealing with either may help the treatment or the management or the possible prevention of the disorder.

From what we have heard from many speakers there would appear to be a fair degree of agreement that the essential causes or factors in migraine are genetic and constitutional. There are many aspects of this which require further elucidation, but everybody seems to have put forward the idea that the migrainous patient is one who carries a constitutional or genetic predisposition to the disorder which may then be manifested by action of a variety of precipitating causes. It seems to me that the College of General Practitioners could do a great deal to answer some of the fundamental questions relating to migraine which await an answer.

The first is the incidence and prevalence of migraine in the community; the general practitioner is in an ideal position to carry out epidemiological studies of this kind because he has in the community an unselected population. People working in hospitals are already dealing with patients in whom some factor of selection has operated, and samples taken from hospitals are not necessarily representative and random samples of the disorder in general.

With the help of an epidemiologist, a statistician, and a geneticist it should be possible to carry out surveys of migraine to ascertain its prevalence, to ascertain whether it is in fact genetically determined and whether significant relationships occur between migraine and other disorders such as asthma. These are questions which have been brought up during the symposium and they can be elucidated satisfactorily only by a properly designed genetic and epidemiological study.

The question of the differential incidence between sexes in respect of migraine is also controversial. Many people say that it predominates in females to the extent of two or three to one. Others say that the distribution is equal between the sexes. This is another

fundamental question which could be answered by research sponsored by the College of General Practitioners.

In carrying out such an epidemiological and genetical study it would be essential to get proper control groups selected from the general population, matched for age and sex with the group of migraine patients and their families which is being studied. This control group would be of immense value in answering other questions which have been raised—for example, whether there is any significant relationship between the incidence of emotional instability or neurosis and migraine, or whether it occurs merely by coincidence because migraine and neurosis are common complaints in the community and there are bound to be some overlaps between them. Dr Sweetnam favours this view in discussing the possible relationship between epilepsy and migraine.

I now come to the mechanism whereby the various precipitating causes operate in producing an attack of migraine. We have heard from Professor Keele a lucid account of the probable pathogenic mechanisms underlying an attack of migraine. We have heard that physiologically important changes appear to be dilation of the arterioles with increased pulsation, then increased local oedema and a decrease in pain thresholds. These may be regarded as the physiological bases of the attack of migraine.

We must also consider the matter from a biochemical point of view. We have heard about the possible role of polypeptides and the kinins, and the question arises whether these constitute the basic mechanism in biochemical terms. If this is so, we need to know the pathways along which various other mechanisms operate in the setting into action of these pathogenic mechanisms.

Dr Walker explained the allergic reaction in migraine to us. Does the release of histamine by causing dilation and local oedema and possibly effecting the pain threshold facilitate the action of polypeptides? There is also the question of the endocrines, which were mentioned this morning by Dr Greene. He clearly distinguished between the effects of these hormones and the effects of hydration which can accompany attacks of pre-menstrual migraine.

The question is, how relevant and causal is hydration in precipitating an attack of migraine. It would certainly enhance the development of local oedema, which is part of the pathogenic mechanism, but is probably one of many changes which occur.

One thinks again in terms of physiological control and of local tissue functioning, and one turns to the autonomic nervous system. This is important because of its control of the arterioles of the brain. The autonomic system can be affected by many other things. We have heard of the emotional factors and fatigue, and this morning

we heard of the very interesting link between the onset of migraine and certain states of the individual.

In some people migraine occurs not during periods of hard work or strain but during let-up periods following over-activity. We have heard of week-end attacks of migraine among people who were free from migraine during the working week. We also have heard of attacks which occur in the early morning. All these are interesting associations which await elucidation. As a possible hypothesis I suggest that all these correlations of attacks with changes in personal states from sleep to wakefulness and from activity to rest may be correlated with the autonomic nervous system's action. It may be a change in automatic functioning which may be involved, with this may be correlated changes in the functions of the adrenal cortex. There are complicated changes in the neurochemical and neurophysiological process in the organs responsible for reaction to stress both the pituitary and adrenal system being involved.

We have heard that the state of alertness of a patient is linked with the frequency with which he has migraine. This brings us to the functioning of the reticular system which recently has been shown to have an important part in controlling the level of alertness and which is closely linked with the functioning of the autonomic nervous system.

We have heard that in some patients excessive stimulation, such as the exposure to bright sunlight, seems to be a precipitant. But we do not know what is the mechanism. Is this initiated by pituitary hypothalamic mechanism?

There are numerous problems and aspects of migraine which require further research. We have heard today a great deal of information which enables us to have a working hypothesis on the operation of all these multiple factors and the various pathways which may be involved in the precipitation of an attack of migraine, which we all agree to be a disorder of the utmost medical and social importance. I hope that the outcome of this symposium will be to provide sufficient stimulation to you all to consider encouraging investigations which may help towards the elucidation of some of these problems.
